JOURNAL OF THE
PHILIPPINE MEDICAL ASSOCIATION

2014-2015

VOLUME 93, NUMBER 2

JOURNAL OF THE
PHILIPPINE MEDICAL ASSOCIATION

2014 - 2015 VOLUME 93, NUMBER 2

TABLE OF CONTENTS

Journal of the
PHILIPPINE MEDICAL ASSOCIATION
2014 - 2015 VOLUME 93, NUMBER 1

Journal of the
Philippine Medical Association
2014 - 2015 VOLUME 93, NUMBER 1

Editorial Office:
2nd Floor PMA Building, North Avenue, Quezon City 1105 Philippines
Contact Numbers: +(632) 929-7361; +(632)929-6366; Fax: +(632) 929-6951
Website: www.philippinemedicalassociation.org;
E-mail: info@philippinemedicalassociation

Journal of the
Philippine Medical Association
2014 - 2015 VOLUME 93, NUMBER 1

MESSAGES

Now more than ever, international indexing and online publication ensures that locally produced research studies are globally cited. This year, the Journal of the Philippine Medical Association will start publishing bi-annual issues of quality original articles in compliance with the minimum requirements for indexing with the Western Pacific Region Index Medicus. The Western Pacific Region Index Medicus (WPRIM) is a project of the WHO Western Pacific Regional Office in collaboration with several institutions in its Member States. This is the Region's contribution to the Global Health Library (GHL) initiative which aims to extend to all the benefits of the knowledge that is essential to the fullest attainment of health. WPRIM will be deployed and hosted, along with the index medici of other WHO Regions, at the Global Index Medicus portal under the GHL platform, where searches can be conducted individually or simultaneously through a federated search engine.

MARIA MINERVA P. CALIMAG, M.D.
President

This first issue of the Philippine Medical Association's Journal would not have been possible with out the unconditional support given by the editorial board under the Chairmanship of Dr. Arnel Asino. Keeping in mind that a medical journal is a forum for the exchange of ideas and valuable information, it is with pride that this journal is presented to all members of the PMA.

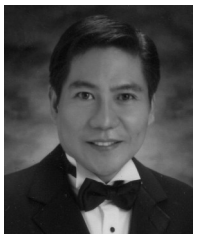
We wish to acknowledge all physicians who have participated by submitting their research papers and case presentations to the PMA. It is to them that we attribute the success of this journal. We fully appreciate their having contributed their work.

A second issue of the PMA Journal will be forthcoming by May, 2015. We encourage all other physicians to have their research papers and case presentations published. The PMA Journal follows the Research Ethics of the Declaration of Helsinski, and we enjoin all participating doctors to do so.

We dedicate this journal to all members of the Philippine Medical Association!
Our sincerest gratitude to all!

MARIANNE L. ORDOÑEZ-DOBLES, M.D.
Secretary General
Chair, Committee on Publications

Journal of the
Philippine Medical Association
2014 - 2015 VOLUME 93, NUMBER 1



Greetings!

The world is a pocket of mystery where things evolve in a very complicated dimension finding solutions to understand unresolved ideas and events. I agree with John F. Kennedy when he said that, "Things do not happen. Things are made to happen." Probably the reason why systematic scientific research are encouraged not to only to harness our curiosity to discover new concepts and modalities, but also to offer new insights, intelligent opinion and strategies. An outcome-based contribution to the human knowledge which may be used as a tool to improve the healthcare system.

Embarking in a research will uncover hidden evidence and encourage investigators to make use of their critical thinking particularly in building theories and conclusion to validate a certain fact in question. It is true that research leads to progress and reduce the rate of errors while improving treatment. According to Thomas Edison, "Our greatest weakness lies in giving up. The most certain way to succeed is always to try just one more time."

I strongly believe that a well-driven researcher always dwell with his work in a formulated thought which reminds me of what Confucius once said that, "The more man meditates upon good thoughts, the better will be his world and the world at large."

God bless us all!

Arnel M. Asino, MD, FPBA
Chair, Sub-Committee on PMA Journal

Journal of the

Philippine Medical Association

Instruction for Authors

General Information

The Journal of the Philippine Medical Association (JPMA) is the official publication of the Philippine Medical Association (PMA).

The JPMA is published twice in a year at the PMA Office, 2nd Floor, PMA Building, North Avenue, Quezon City 1105, Philippines. It publishes original scientific papers pertinent to medicine and allied fields. It also considers for republications of previously published articles, either in their original or modified forms, provided they are accompanied by written permission from the publisher and principal author.

Statements and opinions expressed the articles and communications herein are those of the author(s) and not necessarily those of the Editor(s) or the publisher. The editor(s) and publisher disclaim any responsibility or liability for such materials and do not guarantee, warrant or endorse any product or services advertised in this publication.

No part of the articles and communications published in the JPMA may be reproduced without the written permission of the publisher.

Editorial Policies

The JPMA is a peer-review journal designed to meet the continuing education requirements of PMA members and the medical community. It adheres to the guidelines established by the International Community of Medical Journal Editors (ICMJE); however, for purposes of this issue, the previously circulated JPMA Instructions for Authors, although with some modifications, are still being followed.

Ethical Cosiderations

In the conduct and reporting of research, the JPMA adheres to the ethical considerations set forth by the ICMJE with respect to authorship and and contributorship, editorship, peer review, conflicts of interest, right to privacy and confidentiality of patients, study participants as well as authors and reviewers; and, the protection of human subjects and animals in research.

All financial or personal relationships that could be viewed as presenting a potential conflict of interest must be disclosed by the author(s) and all participants in the review and publication process.

In experiments involving human subjects, authors must indicate in their reports whatever procedures are complaint with the standards of the responsible institutional and national committee on human experimentation as well as with the Helsinki Declaration of 1975, as revised in 2000. In case of doubts as to the procedures, authors mush show proof of approval of their institutional review body or its equivalent.

In experiments involving animals, authors must indicate in their reports compliance with the institutional and national guide for laboratory animal experimentation.

Manuscript Preparation

(This section is primarily based on the previous and existing JPMA Instructions to Contributors but with some modifications based on the ICMJE recommendations. A completely revised version based on the guidelines of the ICMJE will be published in the next issue.

Accomapanied by a cover letter from the principal author, the manuscripts, figures, tables, photographs, and references should be submitted in duplicate (an original and a copy) and typed double-space (including legends and footnotes) on one side of a white bond paper, 8.5 and 11 inches properly numbered consecutively on the upper right-hand corner of each page beginning with the title page. Illustrations must also be in duplicates. An electronic copy of the articles in a CD must be submitted.

The first page should contain the title, subtitle (if any, all authorsí full names and highest earned academic degrees, and hospital or institutional affiliations. It must also include disclaimer, if any.

For the original article, an abstract must be type at the beginning of each paper after the title. It must contain, in structured format, the following: background or context of the study, objectives, methods, results and conclusions of the study, as appropriate. It must not be more than 300 words. No footnotes/references must be in the abstract. For other articles, an unstructured abstract may be preferred. Below the abstractr, identify three to ten keywords or short phrases that will assist in indexers in cross-indexing the article.

Abbreviations and nomenclatures: the use of abbreviations should be minimized and preferably confined to tables only; non-standard abbreviations must be accompanied by legends.

Generic names of drugs are preferred. Trade names may be given only once at the end of the paper or in the acknowledgement and should follow the generic name in parenthesis.

References are to be cited consecutively in the text as superscripts numbers. At the end of each article, references should be listed consecutively in the numerical order as they appeared in the text

Advertisement

Interested advertisers shall be sent advertising rates and requirements upon request.

The editors and publishers do not guarantee, warrant or endorse any product or service advertised in this publication. Neither do they guarantee any claims made by the manufacturer of such product or service.

Submission

Manuscripts, correspondence, and all materials for review and publication should be sent to the Editor-in-Chief of the Journal of Philippine Medical Association at the Editorial Office.

Subscription and advertisements, including change of address should be sent to the PMA Secretariat at 2nd floor PMA Building, North Avenue, Quezon City, 1105 Philippines.

THE MYSTERY OF SALIVARY GLAND TUMORS

Kathleen M. Rodriguez, MD
Author

Celso V. Ureta, MD, FPSOHNS, FPCS
Co-Author

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

ABSTRACT

OBJECTIVE: To present two cases of a rare multiple metachronous behavior of Salivary gland neplasm, its possible etiology and its management.

STUDY DESIGN: Case Report

SETTING: Tertiary Hospital

PARTICIPANT: Two patients

RESULT: This is a case report of two patients with unusual behavior of salivary gland tumors. The first case is a 38-year-old female with an 18 years history of development of mass at the hard palate. Excision of mass was done which revealed a pleomorphic adenoma, however 7 months prior to admission a mass was noted at the right pre-auricular area with bulging mass at buccal area extending to right tonsillar area. Patient underwent wide excision of parotid mass with segmental mandibulectomy, right which subsequently revealed an Adenoid Cystic carcinoma, Parotid. The second case is an eighty nine year old female, with recurrent mass at the right submandibular area, which recurs every 2 years since 2004 to 2013, however on the last admission, there was development of bilateral submandibular mass with multiple neck mass. Patient underwent Excision of Bilateral Submandibular mass with Selective Neck dissection, right. Histopathologic examination revealed a Pleomorphic adenoma, both right and left submandibular glands with a metastasizing behavior at right neck nodes.

CONCLUSION: In conclusion we are presented with two rare events of a multiple and metachronous presentation of salivary gland neoplasms with a benign primary to malignant second primary tumors. The etiology of multiple salivary gland neoplasm still remains unclear and complete excision of mass remains as its primary treatment modality with post radiation treatment to completely extirpate the tumor.

KEYWORDS: Parotid gland, Submandibular gland, Adenoid cystic carcinoma, metastasizing pleomorphic carcinoma, Multiple salivary gland neoplasm, metachronous, synchronous

Definition of terms:

Synchronous –second primary tumors within 2-6 months of diagnosis of first primary tumor [14]

Metachronous – second primary tumors more than 6 months after first primary tumor [14]

CASE REPORT

Salivary gland tumors are group of heterogenous lesions with a wide clinicopathologic feature with distinct behaviors. According to *De Oliveira*, approximately 3-10% of neoplasms in the head and neck are salivary gland tumors. The main aim of this study is to present two cases of salivary gland tumors admitted at this Tertiary institution who presented with a multiple and metachronous behavior of salivary neoplasms, its clinical manifestation, possible etiology and management.

CASE 1

A 38-year-old female from Quezon City came in due to mass at right pre-auricular area.

7 months prior to admission patient noted pre-auricular swelling at right area with no other associated signs and symptoms. However, it was noted to increase in size, which was now perceived approximately 3x3cm in size, with no other associated symptoms. Until 2 weeks prior to admission patient consulted at this institution, there was noted 4x5 cm firm, fixed and non-tender mass at right pre-auricular area with facial paralysis (Figure 1). Trismus was noted with approximately 1.5 cm opening of mouth and noted a bulging buccal mass, which was non-tender protruding up to the right anterior tonsillar fossa (Figure 2). Wedge Biopsy of the buccal mass was done and revealed Adenoid Cystic Carcinoma. Patient was advised to undergo operation. Past Medical History revealed an excision of mass at hard palate, 2005. Histopathologic report was pleomorphic adenoma from minor salivary gland palate. Patient was non-hypertensive, non-diabetic. Family history was unremarkable, patient is a non-smoker and a non-alcoholic beverage drinker.

Patient subsequently underwent Wide Excision of Parotid mass, right; Segmental Mandibulectomy, Elective Tracheostomy tube was subsequently performed (Figure 3). Histopathologic report revealed Adenoid Cystic Carcinoma, Parotid (Figure 4). Patient subsequently underwent post-op irradiation.

CASE 2

An 89 year old female residing at Valenzuela City, admitted for the 5th time due to recurrent mass at right submandibular area.

2 years prior to admission patient noted development of bilateral submandibular masses each measuring approximately 2x2 cm in size, non-tender with no other associated decrease production of saliva or fever. No other masses were noted by the patient, until 2 months prior to admission patient consulted at ENT OPD and on physical examination masses were palpated at left and right submandibular area each measuring approximately 4x4cm, firm, non-tender mass and a 2x2x firm, non-tender, movable at midline anterior neck (Figure 5). Past medical history revealed repeated excision of submandibular mass last 2004, 2006, 2008 and 2010. All of the histopathologic result revealed Pleomorphic Adenoma.

non-alcoholic beverage drinker, who has unremarkable family history.

Patient subsequently underwent Excision of Submandibular mass, bilateral with Selective Neck Dissection, right levels I, II and III (Figure 6). Histopathologic result revealed Pleomorphic Adenoma with metastasizing behavior at right neck nodes and Pleomorphic adenoma at left (Figure 7).

CASE DISCUSSION

Multiple masses in the salivary gland and neck may indicate a possible, inflammatory, non-neoplastic, non-inflammatory disorders and neoplasms.

According to Dale, multiple masses in the neck and parotid area may also indicate inflammatory, non-inflammatory and non-neoplastic disorders of the salivary glands. Among inflammatory salivary gland disorders are sialadenitis, Human Immunodeficiency Infection, Salivary tuberculosis, Sarcoidosis and Sjogrens syndrome. Sialadenitis, which occurs most often at the submandibular gland presents with recurrent swelling of the involved gland while a suspicion of Human Immunodeficiency Infection may be entertained since this may present as a symmetric diffuse enlargement of both parotid glands with or without submandibular glands. Salivary tuberculosis is included since this frequently involves submandibular gland and parotid glands however this is associated with active tuberculosis. A granulomatous disease of unknown case known as Sarcoidosis is said to be an exclusion diagnosis, its swelling may last from months to years with eventual resolution while Sjogrens syndrome presents as unilateral or bilateral swelling of salivary glands however this is associated with xerostomia and keratoconjunctivitis[2].

A non-inflammatory and non-neoplastic salivary gland disorder includes sialolithiasis and Sialodenosis. In Sialolithiasis, eighty percent of salivary calculi occur in the submandibular gland with most of the remainder occurring in the parotid. Sialadenosis is a nonspecific term to describe a non-inflammatory and non-neoplastic enlargement of a salivary gland, usually involves the parotid. The enlargement is generally asymptomatic, and may present bilaterally especially among obese patients[3].

Salivary Gland neoplasm typically presents as a single mass, which is localized to one salivary gland[4]. The most common neoplasm of salivary gland is found at the parotid gland and said to be least in the sublingual gland. Pleomorphic adenoma is said to be the most common benign neoplasm in salivary gland followed by Warthin's tumor, Basal Cell adenoma, Oncocytoma, Canalicular adenoma and myoepithelioma[5]. While the most common malignant neoplasm is mucoepidermoid carcinoma, followed by Adenoid cystic carcinoma, adenocarcinoma, malignant mixed tumor, which includes the carcinoma ex pleomorphic adenoma, acinic cell carcinoma and squamous cell carcinoma[5]. The first case showed nests and columns of cells of rather bland

appearance arranged concentrically around gland-like spaces filled homogenous eosinophilic material, hence signed out as Adenoid Cystic carcinoma right parotid on the other hand second case discloses a well encapsulated tumor with amorphous myxoid stroma with interspersed islands and strands of myoepithelial cells, that resembles ductal cells dispersed in ductal formation, acini and irregular tubules found both on the right and left submandibular glands and same histologic findings were also found at the lymph nodes levels I, II and III, right. The slides were signed out as Pleomorphic Adenoma right and left, and a Metastasizing Pleomorphic Adenoma, right neck nodes.

The etiology of salivary gland tumors is unknown according to Eillis et. al. Risk factors have been identified, including radiation exposure, genetic predisposition, tobacco use, viruses , and exposure to environmental chemicals. In terms of its causative factor, there has been no noted precise etiology. In our case, risk factors have not been identified, since there was no previous radiation exposure, nor any genetic predisposition. Both patients were non-tobacco users.

Could there be an explanation that occurrence of metachronous behavior of salivary glands neoplasms favors female? There was no mention in the study of *Whitt, Kefeli ,Ruiz* nor *Lefo*r that women are more predispose to acquire a metachronous and multiple salivary gland neoplasm. *Eveson* mentioned that females are frequently affected, but there is some gender variation according to the tumour type. Since both cases presented were female, does hormone plays an important role in this presentation? It has been noted that estrogen receptors are reported in a minority of cases of acinic cell carcinoma, mucoepidermoid carcinoma and salivary duct carcinoma, but was not detected in adenoid cystic carcinoma, while reports on pleomorphic adenoma shows estrogen receptors in some studies but absent in other studies, however this finding was not confirmed in recent studies, making this study questionable[7].

A development of multiple salivary gland neoplasm, either at the same or different glands, located either in different glands or more with the same gland are said to be rare event in the development of multiple salivary gland neoplasm[4]. According to *Whitt,* there are combinations of multiple salivary gland tumors have been reported, including multiple benign tumors, as well as both benign and malignant tumors. Multiple malignant salivary gland tumors are more likely to arise synchronously than metachronously. In his literature, there are 20 reported tumors which were identified synchronously, and in 11 of the cases, the second primary malignant tumor was identified metachronously. In correlation with the cases presented, the first case had her first development of mass at the hard palate 18 years ago, which revealed Pleomorphic Adenoma in minor salivary gland, palate, however noted another mass at parotid area only 7 months prior to this admission which revealed Adenoid cystic carcinoma. This is a case of a metachronous and multiple salivary gland neoplasm, initially presented at the hard palate with a

benign biopsy and at a different time in the parotid as malignant tumor. As previously mentioned by Whitt, there are cases such as this that can occur but is said to be as rare event.

The second case shows another metachronous presentation of second primary tumor. A study by *Ruiz et. al* in 2012, presented a case of a benign pleomorphic adenoma also originated at submandibular gland that after 30 years recurred and said to metastasize to ipsilateral neck lymph nodes and parotid gland. It was also cited in his study that Pleomorphic Adenoma rarely undergoes a malignant transformation. Metastasizing pleomorphic adenoma (MPA) is said to be a rare group of tumors, though benign mortality is as high as 22%[8]. However, *Bradley* stated that the metastasizing pleomorphic adenoma is most likely an unrecognized and yet unclassified malignant neoplasm and must be considered a low-grade tumor with a potentially lethal malignant disease, hence we can consider the second case as a transformation of a benign tumor to a malignant multiple metachronous salivary gland neoplasm. The second case presented was somewhat similar with Ruiz's study since the last histopathologic result revealed a pleomorphic adenoma with a metastasizing behavior, such making this case very rare.

According to *Whitt* and *Ruiz* the mean interval between the first primary and the second primary tumor of salivary gland neoplasms was 4.5 to 5 years. In correlation with the cases presented, the second case has a recurrence of tumor every after 2 years while the first case had an interval of 18 years which makes it even rarer.

Kefeli et al., stated that the occurrence of multiple salivary gland tumors with different histological characteristics is extremely rare and makes up less than 0.3% of salivary gland neoplasms. There were 48 cases of salivary gland tumor with two different histologic type as reviewed by *Lefor*, with the most common co-existence of pleomorphic adenoma and warthins tumor. Our cases presented both pleomorphic adenoma as its primary tumor however its second primary was noted of another histologic type, as with the first case, the second primary tumor was adenoid cystic while the second case had evolved to a metastasizing Pleomorphic Adenoma which was believed to be a low grade carcinoma as stated by *Bradley.*

Management of Pleomorphic adenoma and Adenoid cystic carcinoma were both complete excision of mass. The cornerstone of treatment in Adenoid cystic carcinoma is a total conservative or a radical parotidectomy, while radiotherapy has been considered for advanced stages and as adjuvant in the presence of positive microscopic margins [11]. The first case underwent wide excision of parotid mass with segmental madibulectomy, and a post-irradiation to completely extirpate the tumor. On the other hand, the second case underwent multiple excision of right submandibular mass, hence on her 5th admission bilateral excision of submandibular mass with selective neck dissection at right was done. The main treatment of choice for a metastasizing benign pleomorphic adenoma is complete surgical excision[12].

CONCLUSION

In conclusion we are presented with a two rare event of a metachronous and multiple presentation of salivary gland neoplasm with a benign primary to a malignant second primary tumors. The etiology for the occurrence of multiple salivary gland neoplasm still remains unclear and excision of the mass remains as its primary treatment modality.

REFERENCES

1. De Oliveira et. al. Salivary Gland Tumor: A review of 599 Cases in a Brazilian Population. Head and Neck Pathol. 2009 December: 3 (4): 271-275. Published online: 16 September

2. Rice, Dale. Chronic Inflammatory Disorders of the Salivary Glands. Otolaryngologic Clinics of North America Vol. 32, Issue 5, Pages 813-818 .1 October 1999.

3. Rice, Dale. Noninflammatory, Non-Neoplastic Disorders of the Salivary Glands. Otolaryngologic Clinics of North America Vol. 32, Issue 5, Pages 835-842. 1 October 1999.

4. Whitt, J et. al., Multiple Malignant Salivary Gland Neoplasm: Mucoepidermoid Carcinoma of Platae and Adenoid Cystic Carcinoma of Floor of Mouth. Head Neck Pathol. 2008March: 2(1): 41-48. Published online 2007 December 6.

5. Flint,Paul, et al. Cummings Otolaryngology Head and Neck Surgery 5th edition. 2010. P1163-1199.

6. Eillis GL et. al. Salivary gland neoplasms: General considerations. In: Ellis GL, Auclair PL, editors. Surgical pathology of the Salivary glands, 1st ed. Philadelphia, PA: Saunders; 1991. p. 135–164.

7. J.W. Eveson. Tumours of the salivary glands: Introduction. Downloaded: http://www.iarc.fr/en/publications/pdfs-online/patgen/bb9/bb9-chap5.pdf

8. Ruiz et.al. Metastasizing Pleomorphic Adenoma: A Fascinating Enigma. Case Reports in MedicineVolume 2012 (2012), Article ID 148103, 5 pagesdoi:10.1155/2012/148103

9. Bradley PJ. 'Metastasizing pleomorphic salivary adenoma' should now be considered a low-grade malignancy with a lethal potential. Curr Opin Otolaryngol Head Neck Surg. 2005 Apr;13(2):123-6.

10. Kefeli et. al. Two Synchromous and Different Salivary Gland Tumors located in the Parotid Gland and Parapharyngeal region: A case report. DOI 10.5146/tjpath.2009.00970.

11. Marx RE, Stern D. Oral and maxillofacial pathology, A rational for diagnosis and management. :550–3. 2012

12. Marioni G et. al. Benign metastasizing pleomorphic adenoma of the parotid gland: a clinicopathologic puzzle. Head Neck. 2003 Dec;25(12):1071–1076

13. Lefor AT, Ord RA: Multiple synchronous bilateral Warthin's tumors of the parotid glands with pleomorphic adenoma. Case report and review of the literature. Oral Surg Oral Med OralPathol 1993,76:319-324.

14. Mehdi et. al. Synchronous and Metachronous malignant tumors expect the unexpected. J. Pak Med Assoc. 2010 Nov:60 (11): 905-9. African Oncology Institute, Sabratha, Libya

ILLUSTRATIONS

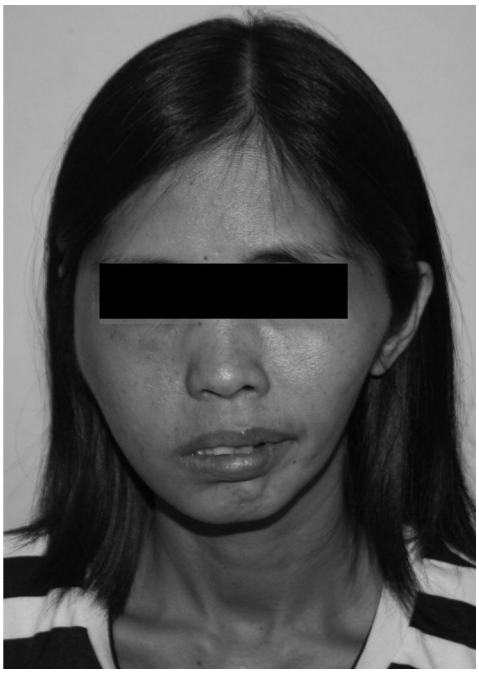


Figure 1. The actual photo of the first case, presenting a mass at the right pre-auricular area which was approximately 4x5 cm firm, fixed and non-tender mass at right pre-auricular area with facial paralysis.

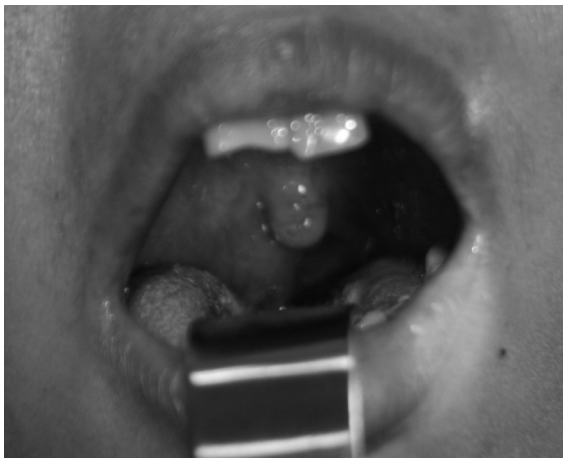
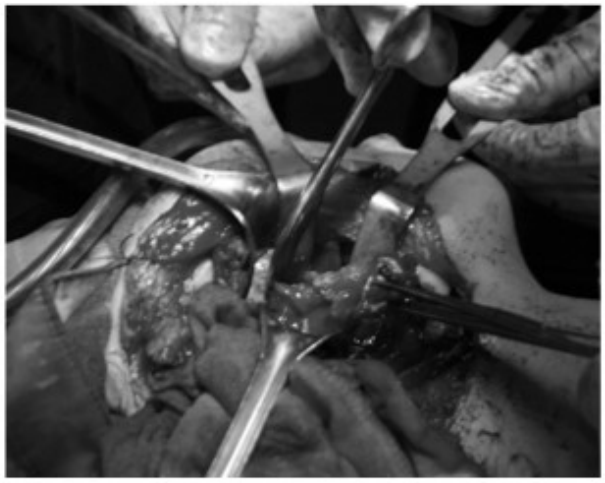


Figure 2. Oral cavity examination of the first case showing bulging buccal mass, which was non-tender protruding up to the right anterior tonsillar fossa.



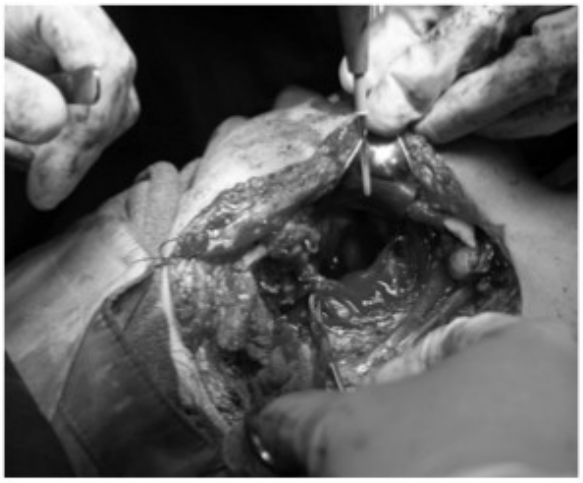


Figure 3. The actual Intra-operative photo of Case 1, showing a Wide Excision of Parotid mass, right; Segmental Mandibulectomy.

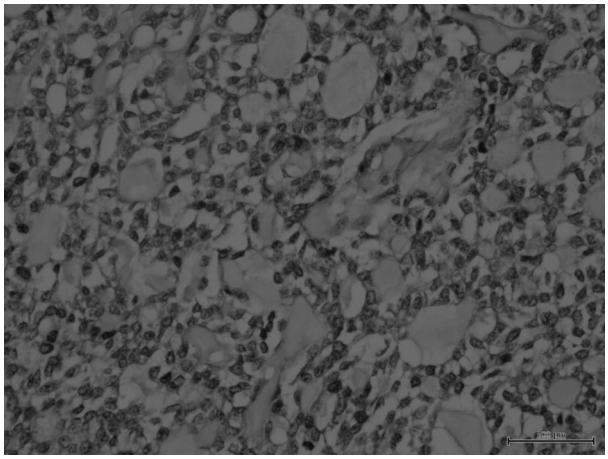


Figure 4. Photomicrograph of the first case, showing nests and columns of cells of rather bland appearance arranged concentrically around gland-like spaces filled with homogenous eosinophilic material, signed out as Adenoid Cystic Carcinoma, right parotid.

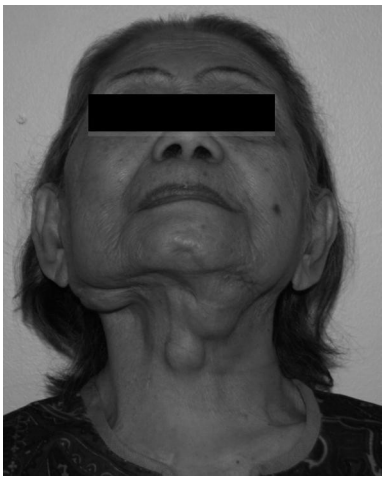


Figure 5. The actual photo of case 2, showing left and right submandibular mass each measuring approximately 4x4cm, firm, non-tender and a 2x2x firm, non-tender, movable mass at midline anterior neck.

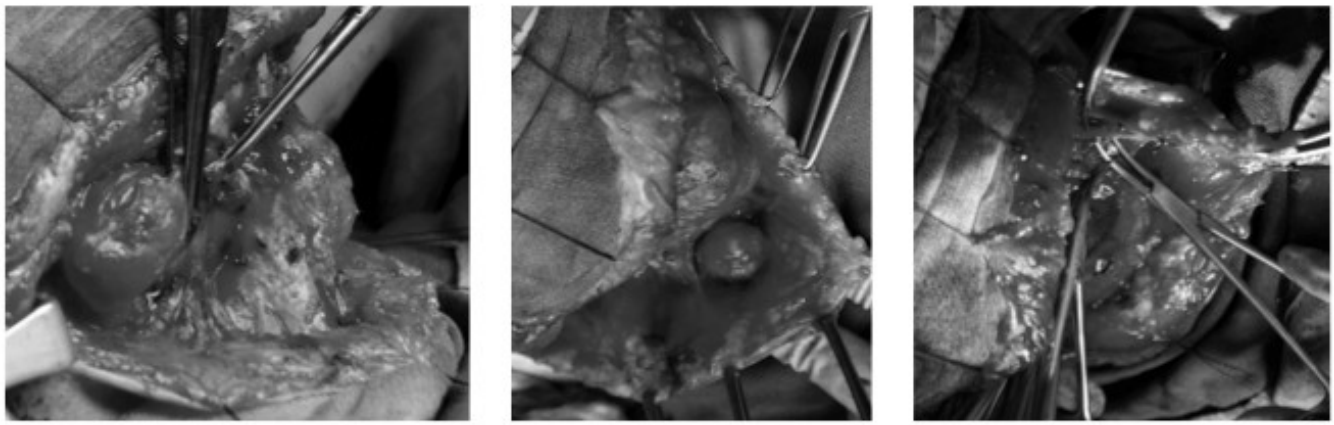


Figure 6. The actual Intra-operative photo of the second case, showing an excision of Submandibular mass, bilateral with Selective Neck Dissection, right levels I, II and III was performed.

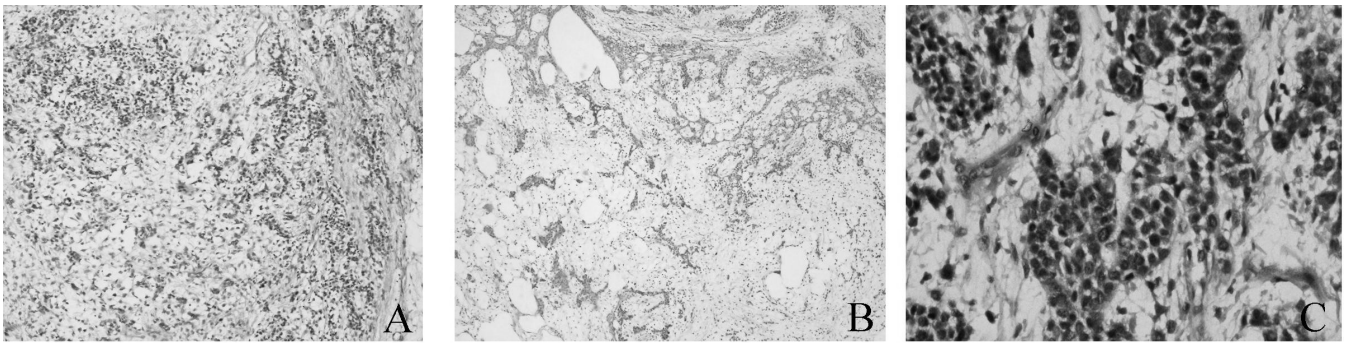


Figure 7. Photomicrograph of the second case.
A, shows circumscribed tumor tissues with biphasic appearance, epithelial component is mostly glandular in appearance with sheets of squamoid cells, right submandibular gland.
B, circumscribed tumor tissues with biphasic appearance, epithelial component are mostly glandular in appearance with sheets of squamoid cells, right left submandibular gland.
C, Photomicrograph of level Ib neck node, the stroma is fibromyxoid to chondroid, showing a metastasizing pleomorphic adenoma.

INFLAMMATORY CONDITION OF THE LARYNX VERSUS A NEOPLASTIC LARYNGEAL MASS: A DIAGNOSTIC DILEMMA

Jeffrey A.. Pangilinan, MD
Principal Investigator

Celso V. Ureta, MD, FPSOHNS, FPCS
Co-Investigator

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

ABSTRACT

OBJECTIVE: This case report aims to present a case of a 56 year old male presenting with a progressive respiratory impairment, its atypical clinical manifestations, diagnostic dilemma and management.

STUDY DESIGN: Case Report

SETTING: Tertiary Hospital

PARTICIPANT: Single patients

RESULT: This case study described the management and unpredicted outcome of a patient presenting with a laryngeal swelling which lead to a diagnostic dilemma between imaging studies and its microbiologic findings.

CONCLUSION: This paper presented a case of a 56 year old immunocompromised patient presenting with an acute upper airway obstruction secondary to a Pseudomonas infection. Repeated direct laryngoscopy with biopsy procedures confirms the presence of the infection despite the CT scan and MRI findings presenting with a soft tissue neoplasm. Prompt tracheostomy tube insertion done was used to secure the airway with adequate antibiotic use prompting gradual resolution of symptoms.

KEYWORDS: laryngeal infections, laryngeal neoplasm, laryngeal swelling, Pseudomonas aeruginosa infections, dyspnea, stridor

"Inflammatory condition of the larynx versus a neoplastic laryngeal mass: A diagnostic dilemma"

Inflammatory conditions of the larynx are infamous "copycats" of neoplastic conditions of the larynx. Patients typically present with a classical picture and symptoms identical to those seen in a neoplastic setting, these include dyspnea, hoarseness, painful swallowing, weight loss, and a history of tobacco and alcohol abuse[1]. This may cause a medical dilemma in the management of a patient and may mislead proper management. Dyspnea is defined as a subjective experience of breathing discomfort[12] that can be caused by narrowing of the airways secondary to an inflammation or by a presence of an obstructing mass which may necessitate the need for an emergency airway management.

OBJECTIVE

This case report aims to present a case of a 56 year old male presenting with a progressive respiratory impairment, its atypical clinical manifestations, diagnostic dilemma and management.

CASE REPORT

A case of a 56 year old, Filipino, male, was admitted with a history of difficulty of breathing. A day prior to admission, patient started experiencing productive cough associated with occasional episodes of difficulty of breathing, hoarseness and throat itchiness. No other associated symptoms were noted like fever, sorethroat or difficulty of swallowing. No medical consult was done nor medications taken.Progression of the difficulty in breathing and hoarseness now associated with stridor prompted his consult at the emergency department where the patient was admitted with an admitting impression of community acquired pneumonia.

Patient was previously diagnosed with Hurthle cell adenoma of the thyroid and underwent total thyroidectomy (2008). He is a known hypertensive and diabetic with a heredo-familial predisposition to maternal hypertension and diabetes; he is a non-smoker and an occasional alcoholic beverage drinker.

On physical examination, his vital signs were BP=130/90mmHg, HR=98bpm, RR=24cpm, T=37.5C. Patient was conscious and coherent. Pink palpebral conjuctivae without naso-aural discharge. There was adynamic precordium with a normal heart rate and regular rhythm. Chest has symmetrical expansion, tachypneic with minimal bibasal rales. The rest of the initial physical exam was unremarkable. He was subsequently referred to an ENT where physical examination and indirect laryngoscopic assessment revealed a hyperemic pharyngeal wall with marked swelling of the aryepiglottic folds and a compromised glottic opening (<3mm). Patient was eventually subjected to an 'E' trache-ostomy tube insertion to secure the airway.

Initial laboratory diagnostics revealed hemoglobin of 141g/dL, hematocrit of 0.42

and a leukocytosis ($14x10^3$) with a neutrophilic predominance (0.70) [Appendix A]; fasting blood glucose revealed hyperglycemia (9.2mmol/L). On chest radiography, the patient was noted with streaky, hazed infiltrates in both infrahilar areas (To consider an interstitial process). A contrast-enhanced CT scan of the neck was done with an impression of an ill-defined soft tissue mass with cystic foci along the posterior transglottic region, larger on the right side, with laryngeal thickening or swelling as well as obstruction (To consider an inflammatory process with abscess formation against a laryngeal neoplasm). No bony or cartilage destruction was seen. He was also noted with enlarged lymphadenopathies on the left upper and lower carotid regions on CT [Appendix B].

An esophagoscopy and direct laryngoscopy with biopsy was done and showed a hyperemic pharyngeal wall with swelling of the aryepiglottic folds, true and false vocal cords; glottic airway was obliterated; no definite laryngeal mass or abscess formation was seen while esophagoscopy showed normal findings [APPENDIX C]. A laryngeal specimen was taken for histopathological evaluation which revealed no evidence of malignancy; similar specimen was sent for gramstain, culture and sensitivity and showed heavy growth of Pseudomonas aeruguinosa [Appendix B]. Patient was started on Imipenem which prompted gradual improvement of symptoms. Blood culture and sensitivity tests showed no growth of micro-organisms.

Due to a CT scan consideration of a soft tissue pathology, an MRI of the neck was done which revealed an ill-defined obstructing, solid mass along the posterior supraglottic and glottic regions, with compression of the hypopharynx (probably neoplastic rather than an inflammatory process); similar nodules or enlarged lymph nodes were noted along the left side of the neck and lower carotid region probably metastatic (thyroid or larynx) [Appendix D].

A repeat esophagoscopy and direct laryngoscopy was done and revealed similar findings of hyperemic pharyngeal wall and an obliterated glottic airway; however, a laryngeal swelling was seen at the anterior commissure of the glottis; still no definite mass or abscess formation was seen; biopsy revealed a necrotizing inflammation of the glottis and subglottis with mild dysplasia(consider pseudotumor) while a separate specimen was obtained from the larynx and hypopharynx which showed chronic inflammation with moderate to severe dysplasia. [Appendix E].

After a week of antibiotic therapy, patient exhibited gradual resolution of symptoms and was discharged; upon follow-up two months post-operatively he was decanulated from his tracheostomy tube which he tolerated well.

DISCUSSION

We are presented with a 56 year old male who was admitted with a history of an acute airway compromise. Causes of an acute

airway compromise. Causes of an acute airway compromise varies, it may be due to an obstructing mass (neoplasm or abscess) or by a narrowing along the airway secondary to an inflammation. The most common etiology of an airway compromise in the elderly is neoplasm rather than inflammatory and such conditions usually exhibit gradual presentation of symptoms. The location of these may be classified as an upper or a lower airway obstruction. Upper airway obstructions include those originating outside the thorax or above the sternal angle (nasopharynx, oropharynx and the larynx); while lower airway obstructions include airway structures below the larynx.[15] Upper airway obstructions may present with an audible stridor, however it is equally important that obstructions from all levels of the airway should be considered. A patient initially presenting with acute symptoms of fever, cough, colds, hoarseness followed by an acute airway compromise may be suspected of an infectious cause.

Initial laboratory diagnostics revealed normal hemoglobin and hematocrit levels while patient was noted with leukocytosis with neutrophilic predominance and this may support the existence of an infection. Moreover, fasting blood glucose revealed hyperglycemia, which contributes to immunosuppression thus placing the risk for developing opportunistic infections. Similarly, on chest radiography, the patient was noted with streaky, hazed infiltrates in both infrahilar areas of the lungs consequently associating the initial impression of a community acquired pneumonia. Laboratory findings at this time likely points to an infection of the lungs as evidenced by the chest radiographs and blood tests. However, the symptom of stridor may not be explained by the chest x-ray.

Initial indirect laryngoscopic findings revealed that the glottic airway was inadequate, thus tracheostomy was done. A person presenting with an acute airway compromise demands prompt medical attention and rapid assessment in order to establish the need to secure the airway. Tracheostomy is an emergency procedure done to relieve airway compromise that may be due to an obstruction. It is performed by creating an anterior opening at the trachea and inserting and anchoring a tracheostomy tube into it. Its principle is to bypass any obstruction occurring in the supralaryngeal and laryngeal areas thus restoring airflow.

Acute airway diseases such as laryngotracheobronchitis and epiglotitis of which both conditions may lead to fatal respiratory compromise. Laryngotracheobronchitis, more commonly referred to as “croup”, refers to the inflammation or irritation of the larynx and trachea and bronchial passageways. The inflammation is usually due to viral invasion especially that of the Parainfluenza type1. However, this could also be caused by other viruses or rarely by a bacterial infection. It is more prevalent in infants and children between 3 months to 3 years old, most common in males, but may occur at any age. It is usually accompanied by a barking cough and lasts for about 5 days but may persist for 10 days if not given medical attention. The main features of

This condition include stridor, hoarseness, brassy cough, fever and dyspnea. If left untreated, the swelling may extend to the epiglottis which could develop to epiglottitis[12,13]. Acute epiglottitis is another form of infection of the larynx (epiglottis), it is usually caused by Haemophilus influenzae type B (HiB) and may present similarly with stridor, dyspnea, hoarseness, chills, drooling, dysphagia and cyanosis. However, these symptoms were not completely consistent in this patient.

CT scan findings showed a laryngeal mass and a compromised airway. However, direct laryngoscopic findings proved otherwise and showed only laryngeal swelling without a definite mass. MRI confirmed that the soft tissue laryngeal mass seen on CT scan was solid indeed.

The dilemma now raises the question if this is a laryngeal neoplastic process? In order to confirm on the diagnosis based on the suspicion of a solid or a soft tissue mass on CT scan and MRI, repeat esophagoscopy and direct laryngoscopy with biopsy was done. Similarly, the endoscopy yielded similar findings of diffused swelling of the laryngeal structures. Histopathologic report of the biopsy showed chronic inflammation and infection rather than neoplastic.

Radiographic presentation of an inflammatory process versus a neoplasm both present with varying degrees of radioopacity depending on the vasularization of the tissues malignant processes may exhibit parastructural invasion characterized by hyperdensity of the affected area on a contrast enhanced CT compared to an infectious process (abscess) which may show lesser radioopacity. Theoretically, MRI has a higher diagnostic value on tissue imaging with excellent soft tissue contrast as compared with CT[9], hence, we usually consider MRI to be of higher specificity in detecting or discri-minating different laryngeal tumors. Neither CT nor MRI findings are histologically specific, and similar appearances can be found with hemorrhage, edema, inflammation or fibrosis. Therefore, examination should be correlated with clinical history[9]. Direct laryngoscopy confirmed laryngeal swelling without definitive mass in this patient.

The laryngeal specimen obtained from the patient revealed heavy growth of Pseudomonas organism. This finding raise question of where or how could this patient might have acquired the organism? Laryngeal infections related to Pseudomonas are unclear as it is unusual. P. *aeruginosa* is a Gram negative, aerobic, coccobacilli and a common human saprophyte, and it rarely causes disease in healthy persons. Most infections by this organism occur in compromised hosts and the most common conditions associated with pseudomonas infection include bacteremic pneumonia, sepsis, burn wound infections, meningitis[8]. However, presence of this organism is uncommon in the larynx and blood cultures obtained from the patient turned-out to be negative. Moreover, the presence of diabetes predisposes the patient in an immunocompromised state which eventually leads to the patient acquiring the pseudomonas infection.

Two studies reviewed identified pseudomonas infection being inoculated in the larynx by transmission through fomites (endoscopes, laryngoscopes and laryngeal mirrors)[6,7]. However, Pseudomonas infection and neo-plasm in the larynx is possible and may co-exist. Is this a case of infection and neoplasm that existed at the same time? Vieira (2008) documented a pseudomonal infection which thrived in a malignancy in a larynx[5]; and that immunosuppression, such as in this diabetic patient could be factor why or how the patient acquired the infection.

Furthermore, the subsequent resolution of the mucosal swelling after a week of antibiotic regimen with Imipenem, a broad-spectrum intravenous beta-lactam antibiotic with an important activity against Pseudomonas[10], downplayed the suspicion of a neoplastic process.Then, is dysplastic changes a sign of a neoplasm presented with pseudomonas infection with this patient? Subsequent follow-up of the patient showed improvement of the swelling in the larynx and was well able to tolerate decannulation of his tracheostomy tube.

A study done by Nakagwa (2007)[3] described the clinical mimicry of laryngeal infections wherein a rare laryngeal carcinoma presented as a pre-laryngeal large abscess, characterized with a markedly swollen false vocal fold. CT scan indicated destruction of the thyroid cartilage. While biopsies from the abscess did not reveal malignancy however, the malignancy was confirmed by laryngo-microsurgery. The abscess was thought to be formed not by direct extension and necrosis of the tumor, but by the leakage of air and mucus through the fistula on the destroyed thyroid cartilage[3]. In this case, repeated direct laryngoscopy with biopsy and esophagoscopy showed inflammatory swelling without evidence of mass or abscess formation.

In another study done by Remacle (1989) he reported a case of laryngeal abscess due to Pseudomonas aeruginosa of the pre-epiglottic space with destruction of the epiglottis and granulomatous reaction of the epiglottic endolaryngeal side. The differential diagnosis of the endoscopic image included neoplasm, granulomatous diseases and laryngeal abscess. Biopsies revealed the diagnosis of laryngeal abscess[2]. Non-neoplastic masses of the larynx caused by infections may be commonly due to tuberculosis, candidiasis or histoplasmosis[4]. The repeated direct laryngoscopy with biopsy confirms the presence of infection or inflammation despite CT scan and MRI findings.

CONCLUSION

In conclusion, this is a case of a 56 year old immunocompromised patient presenting with an acute upper airway obstruction secondary to a Pseudomonas infection. Repeated direct laryngoscopy with biopsy procedures confirms the presence of the infection despite the CT scan and MRI findings presenting with a soft tissue neoplasm. Prompt tracheostomy tube insertion done was used to secure the airway with adequate antibiotic use prompting gradual resolution of symptoms.

RECOMMENDATION

It is therefore recommended that this study increase the awareness of clinicians and that it is possible that pseudomonal infections of the larynx may mimic laryngeal neoplasms which could cause life-threatening upper airway obstruction. Furthermore, diagnostic imaging studies such as CT scan and MRI should be correlated clinically with a well-documented and a complete and thorough physical examination and that a prompt referral to a specialist should be done to provide early intervention to the patients' condition.

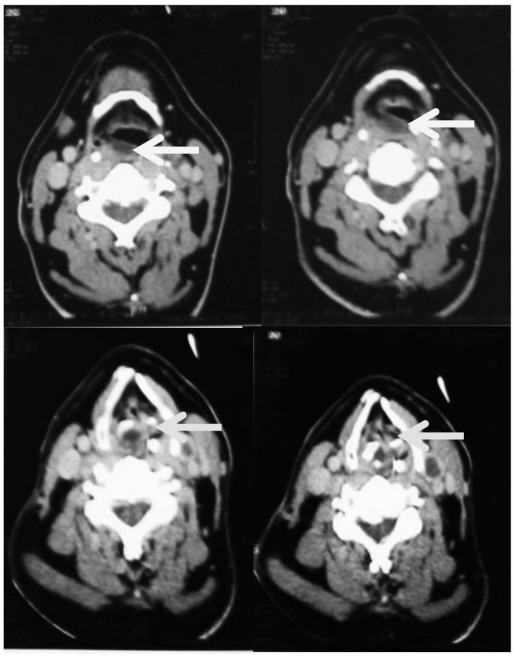
APPENDIX A

Laboratories

	8/12/12	8/15/12	8/21/12	8/23/12	8/23/12	8/26/12	9/2/12	9/9/12	9/9/12
Hemoglobin	141	136	138	131	133	134	127	129	134
Haematocrit	0.42	0.39	0.42	0.39	0.42	0.39	0.38	0.40	0.41
WBC	***14.0***	***14.7***	***10.2***	***9.4***	***12.2***	***9.7***	***7.2***	***6.2***	***9.1***
Neutrophil	0.70	0.73	0.73	0.58	0.61	0.63	0.69	0.56	0.80
Lymphocyte	0.15	0.21	0.20	0.22	0.20	0.19	0.29	0.31	0.13
Monocyte	0.01	0.03	0.07	0.01	0.11	0.11	0.02	0.14	0.04
Eosinophil	0.09	0.03	0.0	0.07	0.06	0.06	0.02	0.0	0.02
Basophil	0.02	0.02	0.0	0.01	0.02	0.0	0.0	0.0	0.02
Platelet	285	351	319	267	298	279	223	289	240
Na (mmol/L)	135.2								
K (mmol/L)	3.78								
Cl (mmol/L)	102.6								
Crea (umol/L)	101.8								
FBS (mmol/L)	**9.2**								
ALT/SGPT (U/L)	40								
AST/SGOT (U/L)	72								
Cholesterol (mmol/L)	3.9								
Triglyceride (mmol/L)	0.37								
HDL (mmol/L)	1.93								
LDL (mmol/L)	1.8								
Uric acid (umol/L)	325.55								

APPENDIX B

CT scan of Neck (with contrast)



1. Ill-defined soft tissue mass (1.5x2.0x3.0cm) with cystic foci along the posterior transglottic region, larger on the right side with laryngeal thickening/swelling as well as obstruction. To consider: A) Acute inflammatory process with abscess formation, B) Neoplasm. Advise correlation with laryngoscopy.

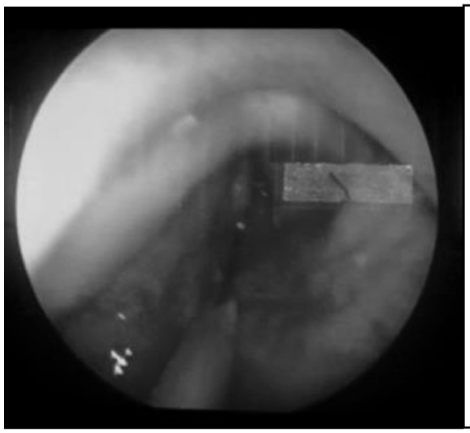
2. Left-sided enlarged lymph nodes (lymphadenitis or neoplastic) on the left upper and lower carotid regions (1.5x1.2cm to 3.0x2.8cm)

3. Tiny cystic foci in the left laryngeal bed with fibrosis (S/p thyroidectomy)

4. S/p NGT and tracheostomy insertion.

APPENDIX C

Esophagoscopy and Direct laryngoscopy with biopsy

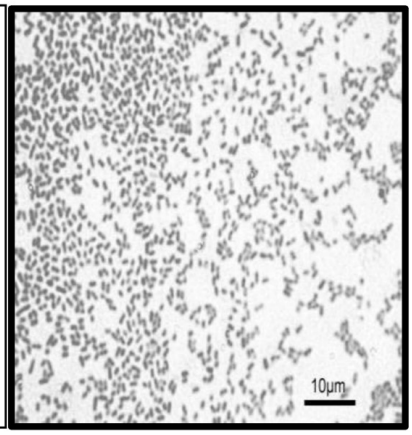


Tracheal cartilage biopsy

No evidence of malignancy

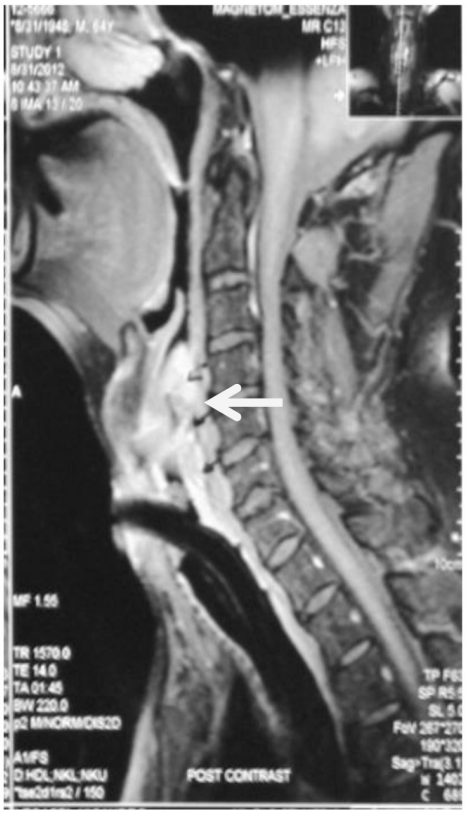
Laryngeal aspirate: GS= Gram (-) bacilli and Gram (-) cocci in pairs

CULTURE: *Pseudomonas aeruginosa* (Heavy growth)



APPENDIX D

Magnetic Resonance Imaging (Neck)



Ill-defined obstructing, inhomogenously enhancing solid mass (2.0x2.5x3.0cm) along the posterior supraglottic and glottic regions, larger on the right side with focal compression of the hypopharynx, probably neoplastic rather than due to an inflammatory process.

1. Secondary non-specific thickening of the infraglottic mucosa

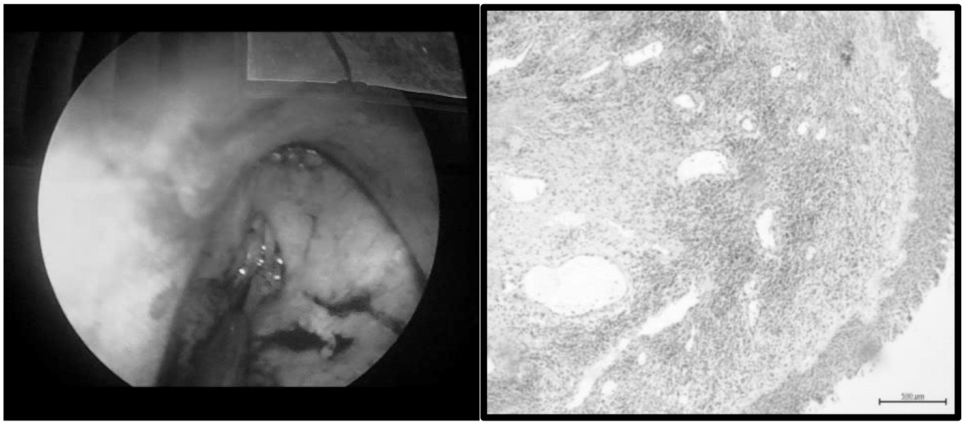
2. Nodules or enlarged lymph nodes, along the upper posterior cervical space and lower carotid region on the left side of the neck probably metastatic (thyroid or larynx) and lower carotid region (2.0x1.5cm to 3x2.5cm)

3. Residual nodular tissue in the left thyroid bed (3x2cm) (recurrent tumor, Hurthle cell or fibrosis) – S/p Thyroidectomy; right thyroid not visualized

4. Severely-narrowed laryngeal opening

APPENDIX E

Esophagoscopy and Direct laryngoscopy with biopsy



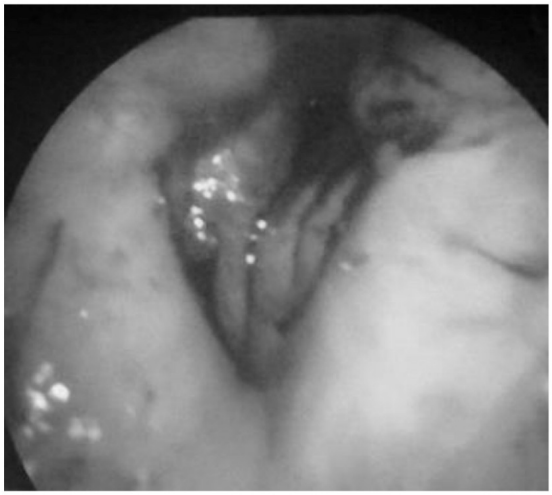
Surgical Pathology Report: Necrotizing inflammation with mild dysplasia

Consider inflammatory pseudotumor, Glottis and Subglottis

Chronic inflammation with moderate to severe dysplasia, larynx and hypopharynx

APPENDIX F

Flexible endoscopy



Swelling of arytenoids with compromised airway

REFERENCES

1. Klein, A.,et.al., ***Malignant Mimickers: Chronic Bacterial and Fungal Infections of the Larynx.*** Voice Foundation Annual Meeting, Farmington, Connecticut, June 2002

2. Remacle M., Van den Eeckhaut J.,et.al., ***Abscess of the larynx resembling a tumor.*** Université Catholique de Louvain, Service O.R.L. et Chirurgie Cervico-Faciale, Cliniques Universitaires de Mont-Godinne, Yvoir, Belgium. 1989

3. Nakagawa H, Shiotani A., et.al., ***Laryngeal carcinoma presenting as a large anterior neck abscess.*** Department of Otolary-ngology, Seibo International Catholic Hospital.Shinjuku-ku, Tokyo, Japan. August 2007

4. Armstrong.W., et.al., ***Cummings Otolaryngology Head and Neck Surgery, 5th Edition.*** Malignant tumors of the larynx. Page 1487. 2010

5. Vieira, F., et.al., Deep Neck Infection. Otolaryngologic Clinics of North America. Volume41, Issue3, June2008, Pages459-483.

6. Muscarella, ***L. Infections Linked To Pseudomonas Aeruginosa***. *Dec 2006 http://www.medicalnewstoday.com/opinions/12889/*

7. Koo,A. ***[Dysphagia] cleaning of laryngeal mirror.*** Aug 2009 http://www.dysphagia.com/maillist/2009-August/msg00085.html

8. Chen, S., et.al, ***Pseudomonas infection.***

9. Wippold, F., ***Cummings Otolaryngology Head and Neck Surgery, 5th Edition.*** Diagnotic Imaging of the larynx. Page 1463 -1481. 2010

10. Clissold, S.P., et.al., ***Imipenem/cilastatin. A review of its antibacterial activity, pharmacokinetic properties and therapeutic efficacy.*** Page 183–241. 1987

11. Ryan KJ, Ray CG (editors) (2004). ***Sherris Medical Microbiology (4th ed.).*** McGraw Hill. ISBN 0-8385-8529-9.

12. American Heart Society (1999***). Dyspnea mechanisms, assessment, and manage-ment: a consensus statement.*** Am Rev Resp Crit Care Med 159: 321–340

13. http://www.entmags.org/Laryngotracheo-bronchitis.asp

14. Cheuk, et.al., ***Cummings Otolaryngology Head and Neck Surgery, 5th Edition.*** Radiation therapy for cancer of the Larynx and hypopharynx. Page 1578. 2010

15. Snell, R. et.al, ***Clinical Anatomy 7th Edition.*** Airway anatomy. Page 746, 752

A CASE OF ACTINOMYCETOMA TREATED WITH CO-TRIMOXAZOLE (TRIMETHOPRIM + SULFAMETHOXAZOLE)

Subekcha Karki, MD[1], Ma. Luisa Abad-Venida, MD[2]

[1]Resident, Department of Dermatology
[2]Consultant, Research and Training Officer

Jose R. Reyes Memorial Medical Centre, Manila, Philippines

ABSTRACT

A 32-year-old man presented with a history of progressive, painful nodular growths with discharge consisting granules over the right thigh, inguinal area and right foot. Histopathological examination of the tissue biopsy was actinomycotic mycetoma. The patient showed improvement with trimethoprim-sulfametoxazole. The novelty of our case is to use Co-trimoxazole as a first line treatment modality for all case diagnosed or suspected as actinomycetoma.

KEYWORDS: actinomycetoma,trimethoprim-sulfamethoxazole, cotrimoxazole

INTRODUCTION

Actinomycetoma is a chronic suppurative and or granulomatous infectious process caused by aerobic filamentous bacteria. Actinomycetomas are caused by members of genera Nocardia, Streptomyces, Nocardiopsis, and Actinomadura.

The term mycetoma, coined by Vandyke Carter in 1860, suggests a fungal growth; however, aerobic filamentous bacteria cause most cases worldwide[1]. We report an advanced stage of actinomycetoma. To the best of our knowledge cure is possible, although a prolonged period is needed. Recurrence is common after an incomplete or irregular course of medical treatment.

There are no existing acceptable treatment protocols or guidelines for mycetoma. The available treatment options are based on personal experience, preference and drug availability.

CASE

A 32-year-old Filipino male who worked as a farmer and a food-vendor, from Tondo, Manila presented with a history of progressive multiple nodules over the right lower limb associated with seropurulent discharge.

Eight years PTC, patient had penetrating injury by a bamboo stick over the right foot, after which he developed a solitary mass measuring approximately 1x1cm gradually increasing in number and size. Surgical consultation was done and underwent tumor excision and split thickness skin graft from the right thigh. I.V. antibiotics was given post-surgically for a week and oral-antibiotics continued for a week later. He was asymptomatic for 8 years after which he sought medical consult, when there was difficulty in breathing, progressive multiple nodules over the right-foot, right-thigh and right-inguinal area associated with seropurulent discharge.He was confined in Internal Medicine and co-managed with Orthopedics with assessment to consider Osteosarcoma R.

Laboratory investigations revealed a decrease in hemoglobin 104g/dL (n.v 135-180g/dL) and hematocrit 0.40-0.54% (n.v 0.25%), leucopenia 21.05 (n.v 5-10 X $10^{9)}$. Urinalysis revealed normal results.

His Chest X-ray PA and Lateral view revealed pleural effusion vs pleural thickening right, PTB R.upper lobe, pleurodiaphragmatic adhesion bilateral. X-ray of the pelvis suggested arthritic hip, probably infectious in origin and R.foot revealed soft tissue masses in the 1st & 2nd intradigital space, beginning osteomyelitis 2ndmetatarsal right.

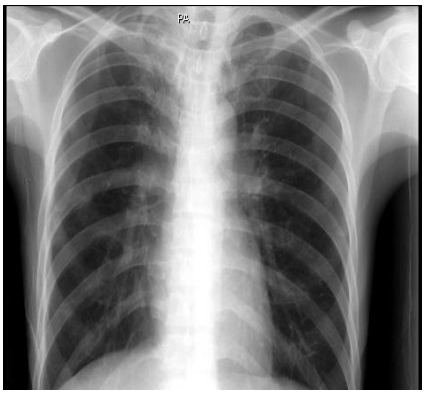


Fig.1 Chest X-ray PA view: Pleural effusion vs pleural thickening right

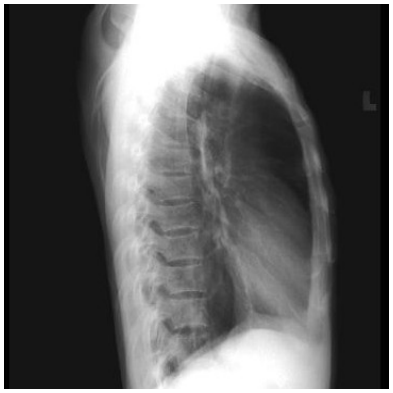


Fig.2 Chest X-ray Lateral view: PTB R.upper lobe, Pleurodiaphragmatic adhesion bilateral

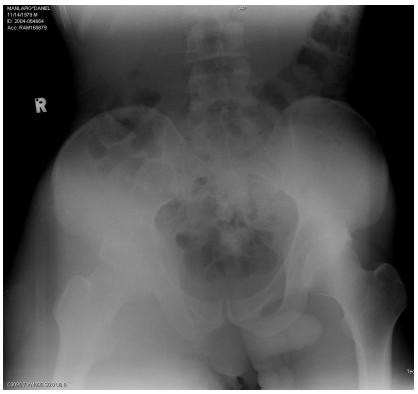


Fig. 3 X-ray Pelvis: Consider arthritic hip, probably infectious in origin

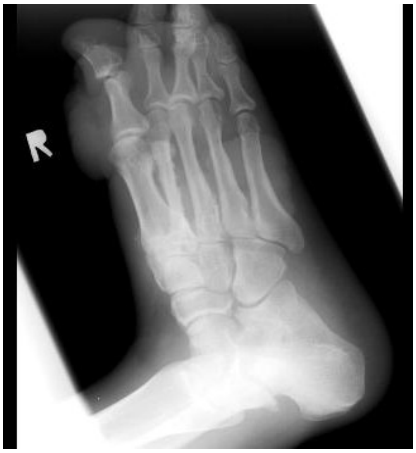


Fig.4 X-ray R.foot : Soft tissue masses in the 1st & 2nd intradigital space, Beginning osteomyelitis 2nd metatarsal right

Patient was also referred to our service for further evaluation and management, hence; this consultation.

The system review revealed pallor and weight loss. Patient was non-hypertensive and non-diabetic, but history of pulmonary tuberculosis four-years back for which he was treated with Anti-Koch's drugs for 1 year. Past history of penetrating injury by a bamboo stick over the right foot. He is smoker with four-pack years, occasionally drinks alcoholic beverages and admits to have only one-sexual partner (wife).Lives with nine-other family members in a crowded environment. No similar illness in his family. He had been working as a farmer in the province until he moved to Manila and became a food-vendor. He admitted to being a habitual barefoot walker.

The patient had Blood pressure of 100/70mm Hg, heart rate 89bpm, respiratory rate of 28/min and temperature of 36.5^{o}C. He had pale palpebral conjunctiva.

On dermatological examination, he was found to have multiple, ill-defined, soft to firm, confluent erythematous nodules productive of seropurulent discharge associated with tenderness and swelling over the anterior right thigh and right foot

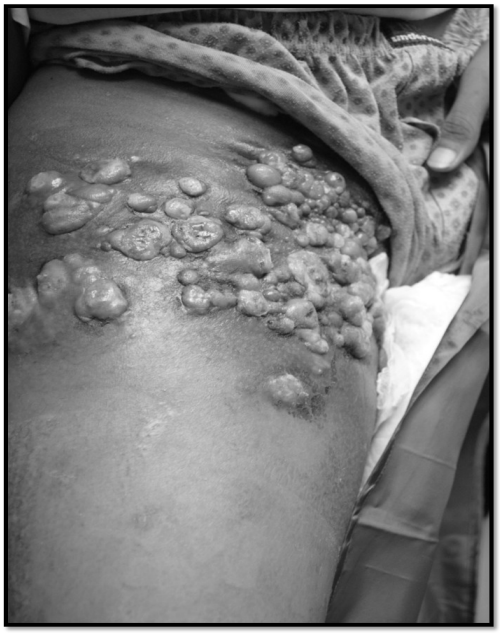


Fig.5 Lesions over the Right-Thigh spreading towards the inguinal area

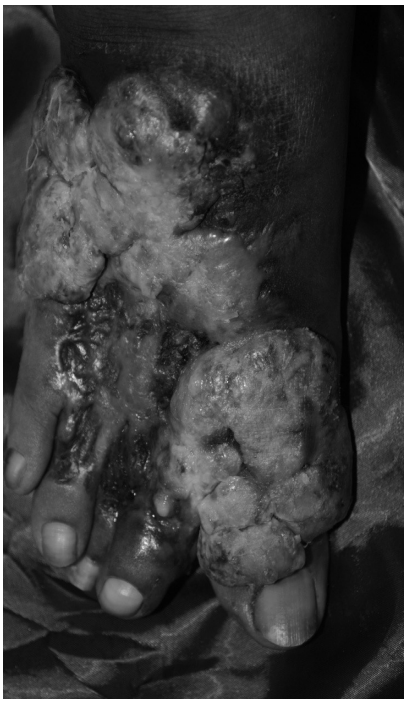


Fig.6 Lesions over the Right-foot

The findings on an incision biopsy on the right-thigh revealed Actinomycetoma. The epidermis showed presence of pseudocarcinomatous hyperplasia, parakeratosis, and presence of sulfur granules. Dermis showed: dilated capillaries along with sulfur granules, neutrophils, lymphocytes and plasma cells. Periodic Acid Schiff Stain of the sulfur-granules was suggested which was Positive. Fungal culture however suggested and done showed no growth after incubation for 4days.

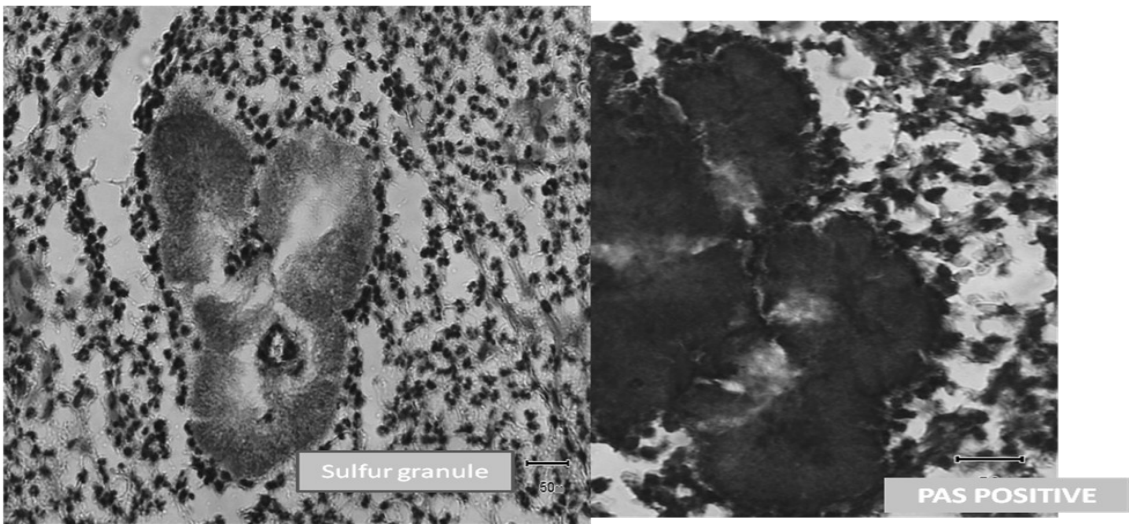


Fig.7 Characteristic sulfur granules which stained positive for Periodic Acid Schiff Stain

DISCUSSION

Actinomycetoma is a non-contagious chronic infection, characterized by the triad of localized lesions, tumefactions, and multiple draining sinuses. Involves the cutaneous, subcutaneous tissues, fascia and bone. The exudates contain grains, which may be yellow, white, red, brown, or black depending on the causative agent.

Mycetoma is classified as Eumycetoma or true-mycetoma caused by fungi and Actinomycetoma caused by aerobic filamentous bacteria. Actinomycetomas are caused by members of genera Nocardia, Streptomyces, Nocardiopsis, and Actinomadura.

The term mycetoma, coined by Vandyke Carter in 1860, suggests a fungal growth; however , aerobic filamentous bacteria cause most cases worldwide.[2] It has a worldwide distribution, with preponderance over the tropics and sub-tropics. The disease has also been reported in areas of temperate climate. It is predominantly a disease of men in rural areas, who work bare foot on land such as cultivators and daily laborers.[3] Poor hygiene, low socioeconomic status and low nutrition are suggested risk factors.[4]

The causative organism is usually found in the soil and enters the host through a breach in the skin or the mucosal membrane by sharp objects . The legs and feet are most commonly affected sites. Organisms gain entry into the skin through traumatic inoculation causing localized infection that is focally aggressive but does not typically disseminate. Early diagnosis and treatment can affect morbidity associated with this condition. Thus, it is important for clinicians to be aware of this disorder's clinical presentation and methods available for confirming the diagnosis.[5, 10]

Clinically, patients experience formation of erythematous papulonodules with drainage of purulent material and sinus tract formation. Ultimately, fibrosis and destruction of underlying soft tissue and bone will ensue. Severe edema and regional lymphadenopathy are common as the disease progresses.

Beyond the clinical appearance, histopathological analysis of affected skin is a critical step. A reaction pattern of granulomatous inflammation, abscess formation and fibrosis is typical.[6, 8] Presence of the sulfur granules, on examination of smears of the discharge or tissue biopsy confirms the diagnosis of mycetoma.

Treatment regimens vary according to the organism causing the infection. The duration of treatment is dictated by the clinical response to medication, but reported cure rates are 60-90 percent with a mean duration of therapy greater than one year. Second-line agents include minocycline, co-amoxiclav, amikacin, cefuroxime, ceftriaxone, quinolones, imipenem, and linezolid. Involvement of underlying bone often requires more aggressive measures, including surgical debridement or even amputation of the affected areas. [7, 9, 11]

Actinomycetoma lesions involving soft tissues are only mildly painful; those affecting

bones or joints are more so. Systemic symptoms are absent or minimal.

"Since there are no existing acceptable treatment protocols or guidelines for mycetoma, and the available treatment options are based on personal experience, preference and drug availability. **The novelty of our case is to use Co-trimoxazole as a first line treatment modality for all case diagnosed or suspected as actinomycetoma**. Because of the associated potential morbidities, empiric treatment based on clinical and histological findings alone should be initiated, even if specific microbiologic confirmation cannot be obtained. Also because studies have stated that; actinomycetomas are more responsive to antibiotics."

Our patient's incision biopsy showed the presence of sulfur grains, positive PAS stain. Fungal culture was negative. These features were consistent with actinomycetoma. Incison and Trochar biopsy as suggested by the department of Orthopedics was done to rule out Osteosarcoma. Results revealed soft tissue mass, epidermal inclusion cyst, infected acute and chronic inflammation and granulation tissue formation; final result ruled out osteosarcoma.

As suggested in Basilio J Anía, MD et al; Staging of actinomycetoma according to bone involvement

Based on the radiological findings and the staging according to bone involvement, our patient is Stage4 i.e. longitudinal spreading along a single ray.[12]

The patient was then started on Co-trimoxazole (SMX-TMP) 800/160mg one tablet three times a day together with supportive therapy consisting of Multivitamin 1 capsule two times a day, Ferrous sulfate 1 capsule twice a day, and Tramadol + Paracetamol 500mg one tablet as needed for pain. Wound care was with Potassium permanganate (kmno4) compress two times a day for ten minutes followed by application of tetracycline ointment.

He was on regular follow up every two weeks. Four months after treatment, marked improvement was seen with decreased discharge, drying up of lesion, ease of pain on ambulation.

Although compliant with medications, new lesions, discharge and painful ambulation observed on his third-month of follow-up. As revealed by the patient there was shift of the medication from a branded to a generic brand due to economic constraints.

However, when Cotrimoxazole was shifted back to the previous brand, good response regarding decrease in the discharge, drying up of lesions with no new lesions was observed.

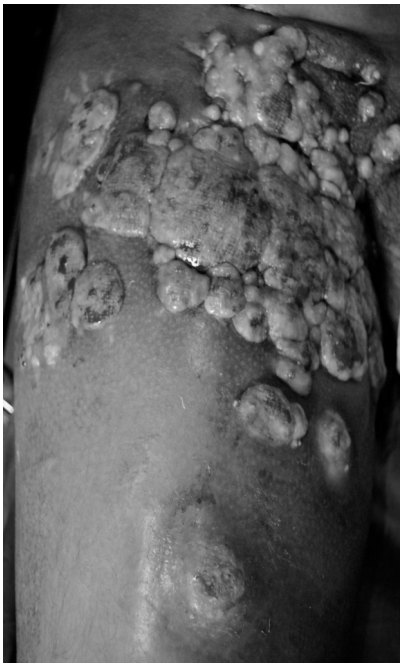


Fig.8 New lesions over the right thigh with discharge

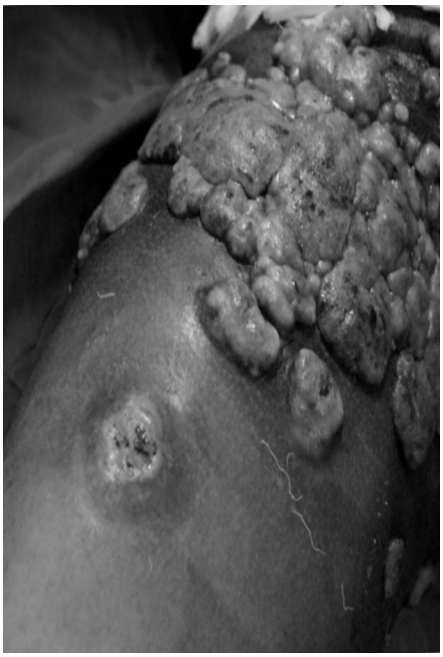


Fig.10 Improvement of lesions over right thigh and inguinal area, 3weeks after restarting Co-trimoxazole to the original brand

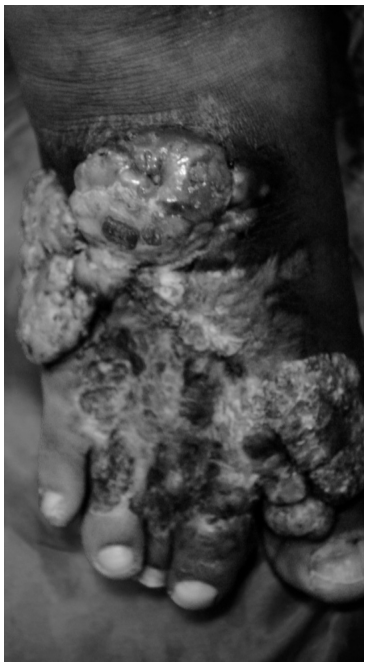


Fig.9 Discharge from the lesions over the right foot

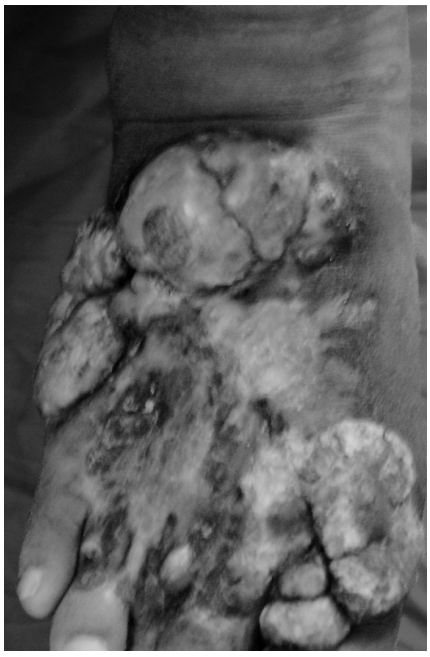


Fig.11 Improvement of lesions over right foot, 3weeks after restarting Co-trimoxazole to the original brand

Unfortunately, two weeks later; patient died while at home. He was still being treated with Cotrimoxazole for past 6 months. According to the death certificate death due to cardiopulmonary arrest 2^0 to hypovolemic shock and underlying chronic anemia.

REFERENCES

1. Tellez I and Franco-Paredes C. A Woman with Chronic, Subcutaneous Swelling og the Right Foot associated with sinus Tracts Dis charging Yellow Granules. PloSNegl Trop Dis. 2010September; 4(9): e 772

2. MEDSCAPE,Author:Basilio J Anía, MD Associate Professor of Infectious Diseases, Universidad de Las Palmas de Gran Canaria; Consultant in Internal Medicine, Hospital Universitario Dr. Negrín, Spain Raphael J Kiel, MD is a member of the following medical societies: American College of Physicians-American Society of Internal Medicine and American Geriatrics Society

3. Turiansky GW et al. Phialophora verrucosa: A new cause of mycetoma. Journal of the American Academy of Dermatology, 1995, 32:311–5.

4. Mcgininis MR, Fader RC. Mycetoma: a contemporary concept. Infectious disease clinics of North America, 1988, 2:939–54.

5. Yaghoobi R, Ranjbari N, Rasaii S. Actinomycetoma. Report of 4 cases of mycetoma from Khoozestan (Ahwaz). Quarterly dermatology journal, 1999, 2(4):43–8.

6. Klokke AH et al. The causal agents of mycetoma in South India. Transactions of the Royal Society of Tropical Medicine and Hygiene, 1968, 62:509–16.

7. Ameen M and Arenas R.developments in management of mycetomas. Clinical and experimental Dermatology, 2008; 34:1-7

8. Desai SG et al. Studies on mycetoma. Clinical, mycological, histologic, radiologic studies on 40 cases of mycetoma with a note on its history and epidemiology in India. Indian journal of surgery, 1970, 32:427–47.

9. Mahgoub ES. Medical management of mycetoma. Bulletin of the World Health Organization, 1976, 54:303–10.

10. Fitzpatrick's Dermatology in General Medicine 7th edition.

11. Ahmed Hassan Fahal. Management of Mycetoma. *Expert Rev. Dermatol. 5(1), (2010)*

12. Basilio J Anía, MD etal. Mycetoma. Emed.com staging of actinomycetomas

ACKNOWLEDGEMENT

This case report would not have been possible without the help of Ma.Flordeliz Casintahan, MD, FPDS, and Dr. Daisy K. Ismael the histopathologists who signed our case as actinomycetoma; my senior A. Venida M.D. JRRMMC, who helped me manage this case regularly. My consultant; Dra. Elizabeth Tianco, MD, FPDS who inspired me to submit this case report and Dr. A.K. Jha NMCTUTH who inspired me to pursue my medical career as a Dermatologist.

EVALUATION OF SUPRACRICOID PARTIAL LANGECTOMY WITH CRICOHYOIDOEPIGLOTTOPEXY IN A TERTIARY HOSPITAL

Kathleen M. Rodriguez, MD
Author

Jeffrey A. Pangilinan, MD
Celso V. Ureta, MD, FPSOHNS, FPCS
Co-Authors

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

OBJECTIVE: To present cases of supracricoid partial laryngectomy with Cricohyoidoepiglottopexy SCPL-CHEP) done in this institution and describe the operative procedure performed in the patients.

To evaluate the post-operative deglutition and speech of patients who underwent supracricoid partial laryngectomy with cricohyoidoepiglottopexy (SCPL-CHEP).

To determine the association factors as age, length of hospital stay, day of decannulation, aspiration, stage of cancer lesion and speech outcome among post-operative deglutition of patients who underwent supracricoid partial laryngectomy with cricohyoidoepiglottopexy (SCPL-CHEP).

DESIGN: Restrospective analytic study

SETTING: Tertiary medical center

SUBJECTS: Seven male patients with a mean age of 66 years (range, 52-87) with T1 and T2 glottic lesions who underwent supracricoid partial laryngectomy with cricohyoidoepiglottopexy (SCPL-CHEP) in a tertiary medical center.

RESULTS: Seven cases of T1 to T2 squamous cell carcinoma of the glottis who underwent supracricoid partial laryngectomy with cricohyoidepiglottopexy (SPL-CHEP) were presented. Post-operatively, all patients were successfully decannulated. The speech and aspiration grading of the seven patients were evaluated and scored. Post-op deglutition was evaluated using the Grading Scale of the Fiberoptic Endoscopic Evaluation of Swallowing, among the seven cases one patient had aspiration and retention and underwent gastrostomy while the remaining six patients were able to return to normal deglutition. In terms of speech, all seven patients were graded with moderate dysphonia using Pinho's classification of auditory-perceptive evaluation. Statistical analysis showed no significant correlation between hospital stay and speech, however an inverse trend was noted between age, stage of cancer lesion, decannulation of tracheostomy and aspiration score.

CONCLUSION: This paper presented seven (7) patients who underwent conservative surgery using SPCL with CHEP. Six out seven patients were assessed with normal post-op deglutition while one patient had marked spillage, retention and aspiration. In terms of speech all seven (7) patients were graded with moderate dysphonia. Due to the limited number of cases no significant correlation was noted between length of hospital stay and speech but the study showed an inverse trend between the age of patients , decannulation of tracheostomy, NGT removal, and aspiration. Supracricoid Partial larygectomy is an organ preserving surgical technique with high local control rate of disease while preserving swallowing and speech.

KEYWORDS: Supracricoid Partial Laryngectomy, Cricohyoidoepiglottopexy, and Organ Preservation, Radiation therapy

INTRODUCTION

According to WHO, cancer or malignant neoplasm is the third most common cause of death in the Philippines[1]. The percentage of laryngeal cancer is one to 2% of malignant tumors worldwide[2] and ranks 12th type of cancer in the Philippines[3]. Its is associated with smoking and alcohol abuse, professional exposure to chemicals and a family history of cancer[2]. It affects men aged between 50 to 60 years although women and individuals of any age may also acquire this type of cancer, and the main surgical procedure recommended is partial, subtotal or total laryngectomy [2,4].

Total laryngectomy is said to be the mainstay of treatment for advanced laryngeal cancer[4]. Theodore Billroth was the first to perform this procedure in 1873 and was perfected through years by increasing expert advocates. The overall 5 year survival of patients after total laryngectomy is around 70%, and reported to be one of the highest rates of survival among cancer cases[5], however despite the good prognosis, removal of the larynx requires tracheostoma. The quality of life assessments were performed in 2002 in patients who have received a near total laryngectomy or total laryngectomy shows that permanent tracheostomy, regardless of voice quality is one of the factors with negative psychosocial impact on patients. Therefore organ preservation has a positive effect on patient's perception of self and adjustment to cancer therapy, though the function is not perfectly maintained[11].

Protocols regarding treatment of laryngeal cancer also include the organ preservation, its principle is to control the disease with preservation of laryngeal function for speech and swallowing. The term "organ preservation" was used to denote the advent of combined chemotherapy and radiation since it does not alter the anatomy of the larynx thereby the physiologic function of the larynx was not altered[8]. Supracricoid partial larngectomy (SCPL) is an organ preserving surgical technique allowing speech and swallowing without tracheostomy[12]. This type of surgery is limited to early stage of glottic cancer[13.] And only few surgeons in our country were practicing this procedure.

This paper aims to present cases series of supracricoid partial laryngectomy with Cricohyoidoepiglottopexy (SCPL-CHEP) done in this institution and describe the operative procedure performed with the patients. To evaluate post-operative deglutition and speech intelligibility of supracricoid partial laryngectomy who underwent cricohyoidoepiglottopexy (SCPL-CHEP). To determine the association factors as age, length of hospital stay, day of decannulation, aspiration and speech outcome among patients who underwent supracricoid partial laryngectomy with cricohyoidoepiglottopexy (SCPL-CHEP).

DEFINITION OF TERMS

- Tracheostoma - This is a permanent opening of the trachea for airway after total larnygectomy[20]

- Fiberoptic Evaluation of Swallowing (FEES) - Passing an endoscope through the nasal cavity, nasopharynx, and pharynx to evaluate swallowing[18]

- Spillage - Food bolus entering the hypopharynx more than 30 seconds before the onset of swallowing as seen in video-endoscopic evaluation [19].

- Aspiration – Passage of food contents into the larynx or respiratory tract below the level of the true vocal folds[21]

- Retention – Retained food bolus entering the hypopharynx as seen in video-endoscopic evaluation[18]

METHODOLOGY

This is a retrospective study from 2001 to 2013. All patients who underwent supracricoid partial laryngectomy with cricohyoidoepiglottopexy (SCPL-CHEP) done in this institution were included in the study. Only patients who were at early stage of Laryngeal cancer are included in the study, either T1 or T2. A total of seven (7) male patients were included in the study, five (5) patients were T1aNoMx while two (2) remaining were T2NoMx glottic or supraglottic, moderately to well-differentiated squamous cell cancer of the larynx with one of the seven patients having a selective lateral neck dissection. (see appendix ,Table 1)

All patients had post-operative evaluation of swallowing through the standard Fiberoptic endoscopic evaluation of swallowing (FEES) technique. A topical anesthesia and decongestant was applied at the nasal cavity, followed by insertion of a flexible endoscope attached to a camera. The base of tongue, throat and larynx can be visualized. The patient was asked to drink liquid, followed by puree, then soft food then lastly with a solid food, as the patient eats and drinks, the examiner will be able to assess swallowing. Objective evaluation of swallowing was assessed with the use of a new modification criteria and protocols of FEES[14] described by Zacharek[15] at al. and Schindler et. al[6]. The parameters include premature spillage of material, retention/pooling of material and/or secretion and the entrance of material and/or secretion into the larynx or trachea and the presence/absence of a reflex cough. The Parameters were scored based on a scale from one (1), which represents poor performance to five (5), which corresponds to excellent performance (See appendix, Table 3).

Speech was assessed based on auditory-perceptive evaluation according to Pinho[2], graded from 0 with normal voice to 3 with severe dysphonia (see appendix, Table 5).

Spearmans statiscal analysis was used to determine the association among other factors such as length of hospital stay, day of tracheostomy decannulation, age, speech, aspiration, day of NGT removal and stage of cancer (see Appendix, Table 7). The mean of each variables mentioned were also computed (see appendix, Table 8)

SURGICAL TECHNIQUE of Supracricoid Partial Laryngectomy with Cricohyoidoepiglottopexy (SCPL-CHEP) by Laccourreye under general anesthesia was done as follows:

I. Exposure

NGT was initially inserted. A U-shaped skin incision between the mastoid process is done to allow neck dissection to be performed (Fig. 1). A superiorly based flap is elevated 1 cm above the hyoid bone to prevent skin retraction at the time of closure.

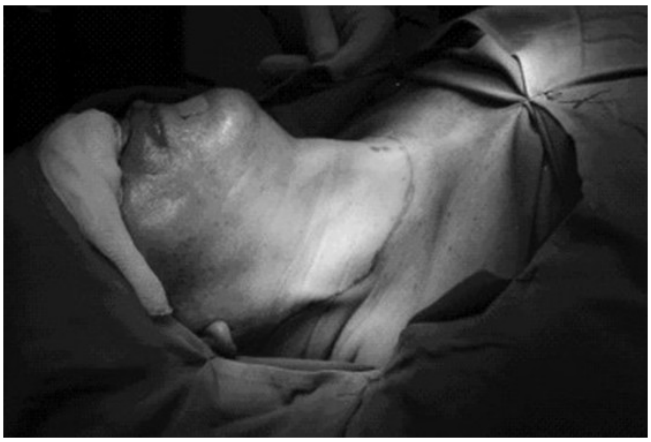


Figure 1

The sternohyoid and thyrohyoid muscles are transected along the superior border of the thyroid cartilage. The sternohyoid muscle are then inferiorly mobilized in order to expose the underlying sternothyroid muscles and transected along the inferior border of the thyroid cartilage (Fig. 2).

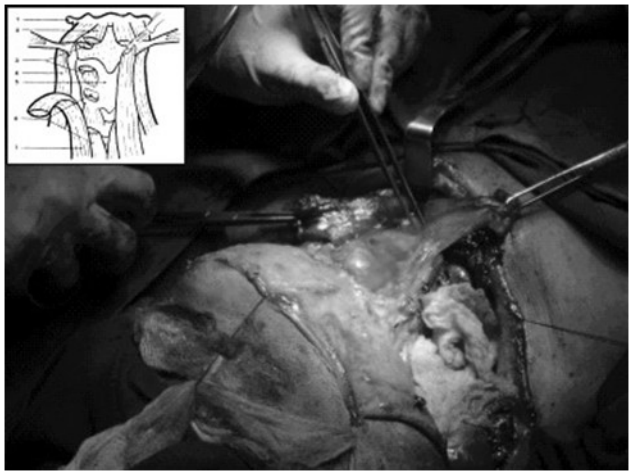


Figure 2

The inferior pharyngeal constrictor muscle and the external thyroid perichondrium are transected along the posterior border of the thyroid cartilage lamina (Fig. 3).

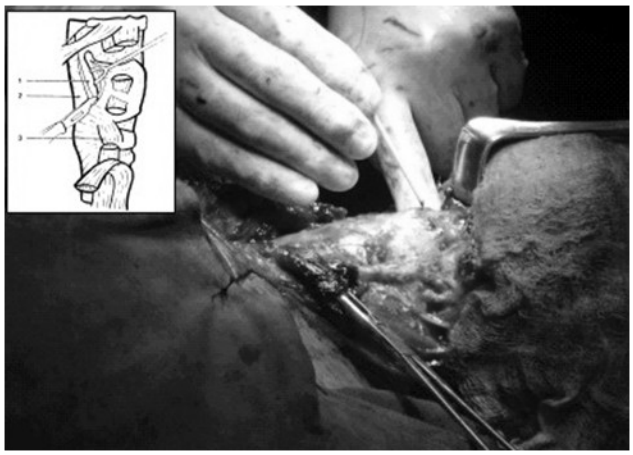


Figure 3

The pyriform sinuses are released by use of freer elevator. The cricothyroid joints are disarticulated. The isthmus of the thyroid gland is transected and ligated. A blunt dissection is performed with a finger along the anterior wall of the cervicomediastinal trachea to the level of the carina to allow upward mobility of the trachea at the time of closure.

II. Resection

Once the exposure is completed, the larynx is entered superiorly through a transverse transepiglottic laryngotomy along the superior border of the thyroid cartilage and inferiorly through a transverse medial cricothyroidotomy along the superior border of the cricoid cartilage (Fig.4).

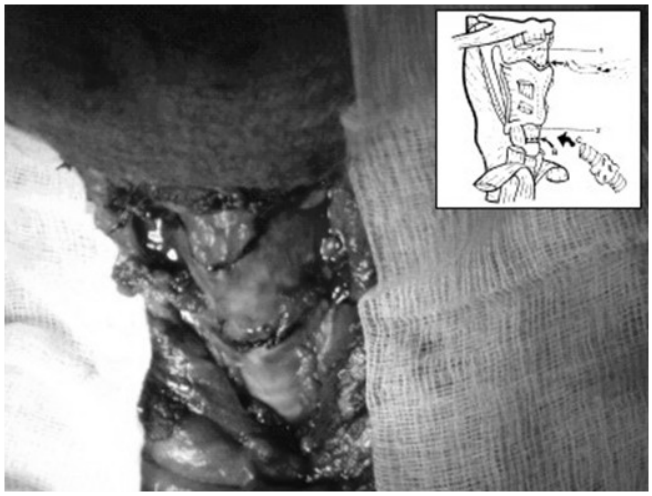


Figure 4

The oroendotracheal tube is removed and a tracheal tube is inserted via the medial cricothyroidotomy. The surgeon moves to the head of the table. The larynx is grasped with an Allis clamp and pulled inferiorly and anteriorly. The precise tumor location can be asserted by direct visualization from above.

The endolaryngeal resection is then performed under direct vision starting on the non-tumor bearing side which on our case is the left side. A vertical prearytenoid incision from the aryepiglottic fold to the superior border of cricoid cartilage is performed with scissors. This first cut is made by placing one blade of the scissors in the laryngeal lumen and the other blade between the elevated thyroid perichondrium and the thyroid cartilage.

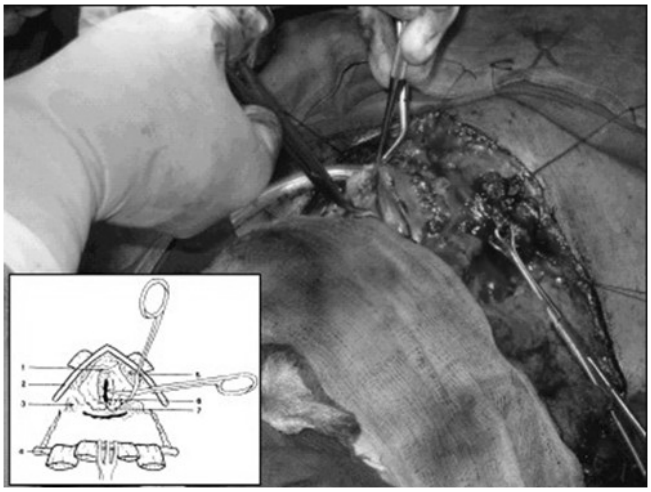


Figure 5

The vertical prearytenoid incision and the medial transverse cricothyroidotomy are then connected on the non-tumor bearing side. The thyroid cartilage is then gripped between the surgeon's hands and broken forward along the midline. The fracture allows complete visualization of the tumor-bearing side. Excision of the tumor is then performed under direct vision with use of the horizontal incision along the superior border of the cricoid cartilage and a vertical prearytenoid incision (Fig.6).

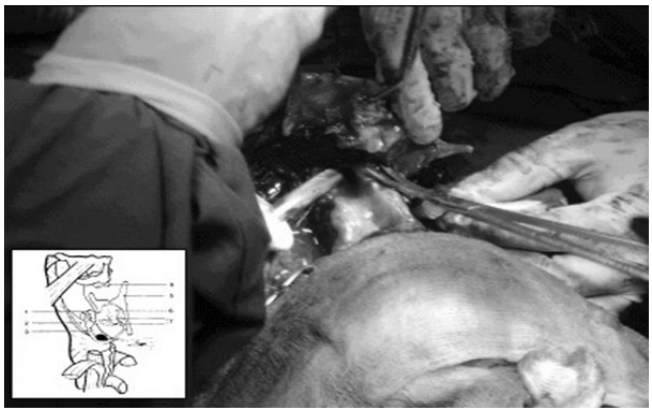


Figure 6

III. Closure/Reconstruction

The mucosa of only the upper part of the arytenoids is sutured to cover the exposed cartilage. Each remaining arytenoid cartilage is then pulled forward to the postero-lateral part of the cricoid cartilage to avoid posterior rotation of the arytenoid cartilage.

Impaction of the hyoid bone to the cricoid cartilage is then performed. Three submucosal 0 vicryl sutures are looped around the cricoid cartilage, passed through the remaining epiglottic cartilage and looped around the hyoid bone (Fig. 7).

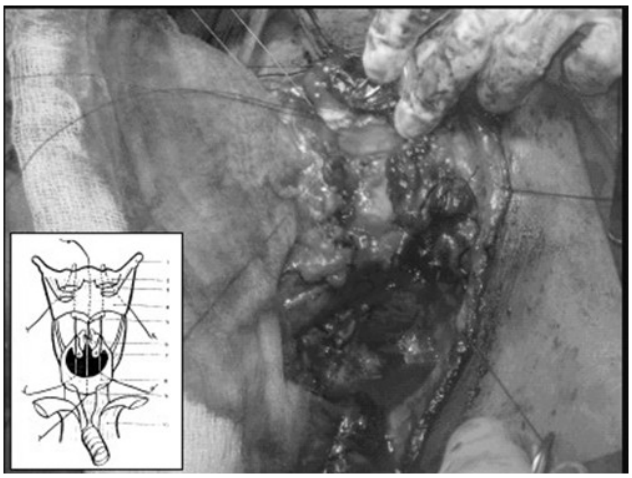


Figure 7

First in the midline, the other two are set bilaterally .5 cm from the midline. The sutures are then pulled together to allow the previously released cervicomediastinal trachea to move upward. At this point, tracheotomy is performed to allow for ventilation while closure is performed. The three sutures are cinched tightly so as not to leave a gap between the cricoid cartilage and the hyoid bone. Two suction drains are placed, then skin closure is performed in two layers.

RESULTS

All seven patients underwent Supracricoid Partial Laryngectomy with Cricohyoidoepiglottopexy in our institution. All patients were men with mean age of 65 (see table 8). Swallowing of all seven patients were assessed with the use of a new modification criteria and protocols of FEES[2] described by Zacharek[15] at al. and Schindler et. al[6]. Table 4 (see appendix) shows the results of Grading scale of the Fiberoptic Endoscopic Evaluation of swallowing (FEES) with six (6) patients having a point value of 5 which corresponds to no spillage of material, no retention or pooling and with no entrance of material into the larynx or trachea, while one (1) patient had a point value of 2 corresponds to marked spillage, marked retention/pooling and with entrance of material into trachea.

All patients in the study presented a moderate dysphonia through Pinho's classification based on auditory-perceptive evaluation (see appendix table 6).

NGT was placed in all patients during the time of operation, this was subsequently removed and all patients were started with oral feeding. The computed average day of removal of NGT was on the 15th post operative day (see appendix, table 8), however one (1) patient accidentally removed his NGT on the 4th post-operative and subsequently underwent gastrostomy tube on his 24th post-operative day.

Spearman statiscal analysis (see appendix, table 7) was used to evaluate the association of hospital stay, day of tracheostomy decannulation, age, speech, aspiration, day of removal of NGT and Stage of cancer. The study failed to show a significant correlation as shown by all correlation coefficients with p values of >0.05. Although an insignificant p value were noted, a trend showing an inverse correlation that as the age decreases the removal of NGT is prolonged, the stage of cancer lesion is advanced and the aspiration score increases. Decanulation of tracheostomy showed also an inverse correlation trend seen in that those whose age is <60 years old, the decannulation time was longer than those whose age is >60 years old (see appendix table 10).

All patients were discharged with average stay in the hospital of 22 days, while the computed average day of decannulation of tracheostomy was 10 days (see appendix, table8).

DISCUSSION

Supracricoid Partial Laryngectomy with Cricohyoidoepiglottopexy (SCPL-CHEP) is a conservative surgical technique for treating selected laryngeal carcinomas classified as T1 -T4[2]. Supracricoid laryngectomy, is a form of subtotal laryngectomy, described by Majer and Rieder in 1959 and thereafter by Labayle and Bismuth in 1972[7]. It was Laccourreye who coined the name “partial horizontal supracricoid laryngectomy” (SCPL), which for him best describes the surgical procedure and resection and “cricohyoidoepiglottopexy” (CHEP), which pertains to the mode of reconstruction[3] that approximates the cricoids to the hyoid bone, for glottic region tumors[7]. The surgery removes the paraglottic and pre glottic space which are the area of extension of laryngeal cancer.

Supracricoid Partial laryngectomy is based on the concept that the main functional anatomical unit of the larynx is the cricoarytenoid unit which includes the arytemoid cartilage, intact cricoarytenoid joint, posterior and lateral cricoarytenoid muscles and recurrent and superior laryngeal nerves[9]. The cricoarytenoid unit and not the vocal folds allows physiologic speech and swallowing and thus the primary advantage of this type of resection is the absence of permanent tracheostoma while maintaining the physiologic speech and swallowing[8,9].

Early laryngeal cancers with T1 and T2 should be treated with the intent to preserve the larynx. In 1990, Laccourreye presented 36 patients who underwent the procedure, all of which recovered physiologic deglutition and phonation, and none of them required a permanent tracheotomy, his paper was presented as a useful alternative to radiotherapy and included that the 3-year actual survival rate was 86.5%[7].

Supracricoid partial laryngectomy is a reasonable alternative to radiotherapy[16], however in the study of Szyfter, radiotherapy had a local control rate of 79% while partial laryngectomy had a better initial control rate of 84%. Several studies show that SCPL results

with low recurrence rate and acceptable 5-year actuarial survival rate even in the elderly, among the T1-T2N0 tumor with invasion of the anterior commissure, 3-year and 5-year survival were 93.3% and 86.5%, respectively, recurrence rate was 1.8%[7].

In the study by Laccourreye, H. et al.[7] which included T1b and T2 lesions who underwent SCPL with CHEP, the following indications were: (1) Bilateral T1 glottic carcinomas with or without anterior commissure involvement; (2) Unilateral T1 glottic carcinomas with ant. commissure involvement; (3) T1 glottic carcinomas with various areas of dysplasia or hyperplasia; and (4) unilateral or bilateral T2 glottic carcinomas w/ or w/out impaired mobility of the true vocal cord[3]. Later studies by Dufour et al.[17,] showed that SCPL provided a significant advance in management of selected laryngeal cancer classified as T3.

Most of the patients admitted in this institution were at advanced stage, in this study, only seven patients were qualified to undergo SCPL due to its stringent indications,. The lesions of patients included in the study were T1 to T2 tumors with both arytenoids mobile, Five patients were T1 while the remaining two were T2. The preservation of both the arytenoids in all patients were done, hence the cricoarytenoid unit was preserved which is said to be the functional unit of larynx, allowing physiologic speech and swallowing in all patients.

One of the seven cases developed marked aspiration, this was due to the accidental removal of the NGT of the patient, thus delaying the wound healing causing marked retention and entrance of material into the trachea, patient subsequently underwent gastrostomy tube insertion on his 24th post-operative day.

Swallowing was evaluated with the use of new FEES protocol, while the remaining six (6) patients do not have retention/pooling with no entrance of material into the trachea. The resumption of normal deglutition was attributed to bilateral preservation of both recurrent laryngeal nerves and superior laryngeal nerves that maintains the sensation and mobility of the remaining laryngeal structures[7]. Aside from nerve preservation, It was also observed that preventive precautions for aspiration also includes suturing and positioning the cricoarytenoid unit as anterosuperiorly as possible, early decannulation and early swallowing rehabilitation[10]. It was mention in the study of Nemr in 2007, that dysphagia may be further reduced by preserving two arytenoids which was observed in all our patients.

Regarding speech outcome, all seven (7) patients in the series satisfactory moderate grade of dysphonia. It was mentioned earlier that it is the cricoarytenoid unit and not the vocal fold that allow physiologic speech[11], though arytenoids do not completely reach a complete closure thereby resulting in air loss during phonation[8], which explains the variable degree of hoarseness present in all the patients, it remains to have a positive effect on the patients.

Laryngeal cancer frequently occurs around 50-60 [2], in this study the mean age is 66 (52-87). An inverse correlation was noted between age and aspiration score. Correlation indicates that as the age decreases there is increasing aspiration score. An increasing score of aspiration signifies normal, which connotes that younger patients had better healing and showing functional swallowing was preserved, however due the limited sample size significant correlation was not established.

In this study the average day for decannulation was 10th post-operative day, it was made possible because the circumferential integrity of the airway was maintained through impacting the hyoid bone to the cricoid cartilage[3]. An inverse correlation was noted with decannulation, wherein as the age decreases there is a longer time for decannulation. Factors such as pain and fear of possible outcome may attribute to the result, however since the cases were limited, again significant correlation was not shown.

Stage of lesion was also noted with inverse correlation with age. As the age decreases an advanced stage of lesion can occur. The correlation can't be explained due to the limited number of cases.

Other factors such as speech and hospital stay did not show significant correlation. All patients were subsequently discharged with no complications, with an average 22 hospital days.

All patients have regular follow-up

CONCLUSION

In conclusion we have presented seven (7) patients who underwent conservative surgery using SPCL with CHEP. Supracricoid Partial larygectomy is an organ preserving surgical technique with high local control rate of disease while preserving swallowing and speech.

Swallowing was evaluated using the new FEES protocol, results showed that six out seven patients were assessed with normal post-op deglutition while one patient had marked spillage, retention and aspiration. In terms of speech all seven (7) patients were graded using the Pinho's Classification based on auditory-perception with moderate dysphonia. Due to the limited number of cases no significant correlation was noted between length of hospital stay and speech but the study showed an inverse trend between the age of patients, decannulation of tracheostomy, NGT removal, and aspiration.

RECOMMENDATION

Due to the limited number of cases, it is therefore recommended to increase the number of sample size in order to obtain a significant correlation between the variables such as age, decannulation of tracheostomy, speech, aspiration, removal of NGT and stage of cancer lesion.

The procedure should be part of armamentarium in laryngeal surgeries and should be considered when discussing treatment plan with the patient with early stage of laryngeal cancer.

REFERENCES

1. WHO. Leading causes of Mortality. Downloaded at http://www.doh.gov.ph/node/198.html

2. Nemr, Nair et. al. Functional study of the voice and swallowing following supracricoid laryngecrtomy. Rev Bras Otorhinolaryngol. 2007; 73(2): 151-5.

3. Cancer and the Cancer Philippine Program. Downloadedat:http://jjco.oxfordjournals.org/content/32/suppl_1/S52.full

4. Cummings, C.W., Haughey, B.: Total Laryngectomy and Laryngopharyngectomy, Otolaryngology, Head and Neck Surgery, 116: 2229-2241

5. Evans, Montgomery and Gullane, Principles and Practice of Head and Neck Oncology, 2005

6. Schindler, Antonio et. al. Long-term voice and swallowing modifications after su pracricoid laryngectomy: objective, subjective, and self-assessment data. American Journal of Otolaryngology-Head and Neck Medicine and Surgery 27 (2006) 378-383.

7. Laccourreye H, Laccourreye O, Weinstein G, Menard M, Brasnu D. Supracricoid Laryngectomy with Cricohyoidoepiglottopexy: A Partial Laryngeal Procedure for Glottic Carcinoma. Ann Otol Rhinol Laryngol 99:1990:pp 421-427.

8. Tufano R. Otolaryngol Clin North Am. 2002 Oct;35(5):1067-80.

9. Yuceturk AV, Tarhan S, Gunhan K, Pabuscu Y. Videofluoroscopic evaluation of the swallowing function after supracricoid laryngectomy. Eur Arch Otorhinolaryngol. 2005 Mar;262(3):198-203 Epub 2004 Apr 30.

10. Pellini, Raul MD et.al. Functional Outcome of Supracricoid Partial Laryngectomy With Crohyoidopexy. Downloaded from: http://archotol.jamanetwork.com

11. Tufano, R. Organ Preservation Surgery for Laryngeal Cancers. Otolaryngol Clin N Am (2008) 741-755.

12. Park, MD et. al. Functional and Oncologic Results of Extended Supracricoid Partial larygectomy. Arch Otolaryngol Head and Neck Surg. Vol 137 (no.11).Nov 2011.

13. Allegra, et. al., Modified Supracricoid laryngectomy: oncologic and functional out comes in the elderly. Clinical Intervention in Aging 2012:7 475-480.

14. Topaglogu, MD et. al. Analysis of Swallow ing Function after Supracricoid Laryngectomy with Cricohyoidoepiglottopexy. Downloaded from http://oto.sagepub.com

15. Zacharek, et. al. Functional outcomes after supracricoid laryngectomy. Laryngoscope 2001: 111.1558-1564

16. Szyfter, W. et. al. Outcome after supracricoid laryngectomies in the material of ENT Department, Poznan University of Medical Sciences. Eur Arch Otorhinolatyngol (2011) 268:879-883

17. Dufour X, Hans S, De Mones E, Brasnu D, Menard M, Laccourreye O. Local Control After Supracricoid Partial Laryngectomy for "Advanced" Endolaryngeal Squamous Cell Carcinima Classified as T3. Arch Otolaryngol Head Neck Surg. 2004 Sep;130(9): 1092.

18. Nacci, A. et. al. Fiberoptic Endscopic Evaluation of Swallowing (FEES): proposal for informed consent. Acta Otorhinolaryngol Ital. 2008 August; 28 (4): 206-211.

19. Ureta, MD, Narajos, MD, Research , Video-endoscopic Evaluation of Swallowing, PSO-HNS Annual Descriptive Research Contest, 2007

20. Koch, W. Total laryngectomy with tra cheoesophageal conduit. Otolarygol Clin N Ann 35 (2002) 1081-1096

21. Marcot, P. Critical Review: Effectiveness of FEES in comparison to VFSS at identifying aspiration. Downloaded from: http://www.uwo.ca/fhs/csd/ebp/reviews/2006-07/Marcotte.pdf

APPENDIX

Table 1. Demographics, history, pre-operative findings and management of the seven patients who underwent supracricoid partial laryngectomy from 2001 to 2013.

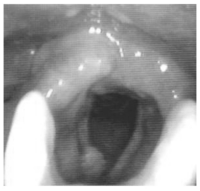
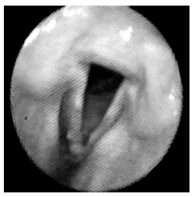
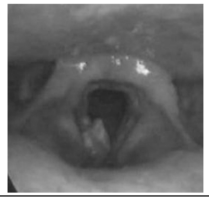
CASE	(1)	(2)	(3)	(4)
SEX	Male	Male	Male	Male
AGE	67	87	58	69
HISTORY	(+) hoarseness x 2 mos (+) 40-pack year smoker & 3-4 bottles of beer four times a week.	(+) hoarseness x 1 year (+) 47 pack year smoker	(+) intermittent hoarseness x 3 mos (+) 5 pack year smoker	(+) intermittent hoarseness x 2 yrs (+) 36 pack year smoker
HISTOPATH	Well-differentiated squamous cell carcinoma	Well-differentiated squamous cell carcinoma	Well-differentiated squamous cell carcinoma	Well-diferentiated squamous cell carcinoma
P.E. (Direct Laryngoscopy Finding)				
OPERATION	Supracricoid laryngectomy w/ CHEP	Supracricoid laryngectomy w/ CHEP	Supracricoid laryngectomy w/ CHEP	Supracricoid laryngectomy w/ CHEP
NECK DISSECTION	Selective lateral neck dissection	None	None	None

Table 1. Demographics, history, pre-operative findings and management of the seven patients who underwent supracricoid partial laryngectomy from 2001 to 2013.

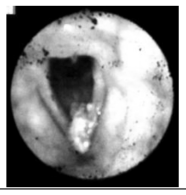
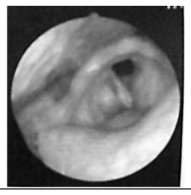
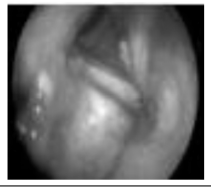
CASE	(5)	(6)	(7)
SEX	Male	Male	Male
AGE	62	52	65
HISTORY	(+) hoarseness x 15 mos (+) 50-pack year smoker & ½ bottles of brandy 2-3 times a week.	(+) hoarseness x 1 year (+) 30 pack year smoker, Occ. alcoholic drinker	(+) hoarseness x 1 year (+) 40-pack year smoker & ½ bottles of brandy 2-3 times a week.
HISTOPATH	Moderately-differentiated squamous cell carcinoma	Well-differentiated squamous cell carcinoma	Moderately-differentiated squamous cell carcinoma
P.E. (Direct Laryngoscopy Finding)			
OPERATION	Supracricoid laryngectomy w/ CHEP	Supracricoid laryngectomy w/ CHEP	Supracricoid laryngectomy w/ CHEP
NECK DISSECTION	None	None	None

Table 2. Post-operative results and findings of the seven patients who underwent supracricoid partial laryngectomy from 2001 to 2013.

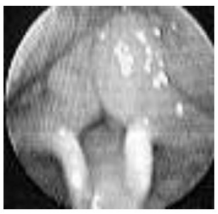
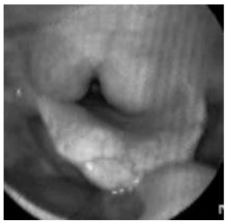
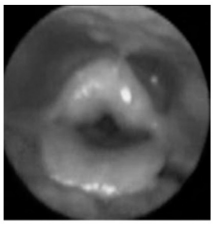
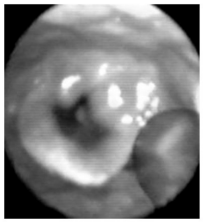
CASE	(1)	(2)	(3)	(4)
TRACHEOSTOMY DECANNULATION	13th postop day	7th postop day	9th postop day	7th postop day
FLUID CHALLENGE	14th day sips of water 17th day general liquid 19th day soft diet	4th day NGT removed 13th day sips of water 24th day gastrostomy tube insertion	14th day cold, clear liquids/ice chips then general liquids 16th day diet as tolerated	12th day clear liquids then general liquids 13th ice chips & hard candies
ASPIRATION	None	None	None	None
POST-OP DL FINDINGS	 (+) good bilateral mobility	 (+) good bilateral mobility	 (+) good bilateral mobility	 (+) good bilateral mobility

Table 2. Post-operative results and findings of the seven patients who underwent supracricoid partial laryngectomy from 2001 to 2013. (Continued)

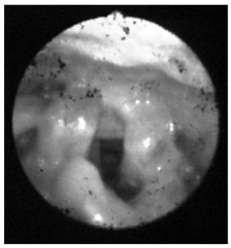
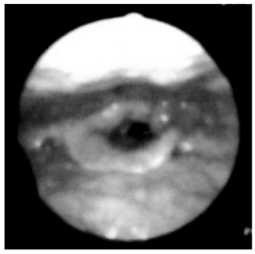
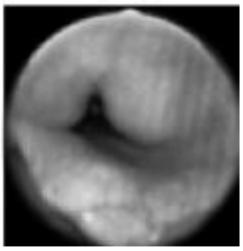
CASE	(5)	(6)	(7)
TRACHEOSTOMY DECANNULATION	6th post-op day	22nd post-op day	7th post-op day
FLUID CHALLENGE	12th day sips of water 15th day general liquid 16th day soft diet	22nd day sips of water 23rd day general liquid 26th day soft diet	13th day clear liquids then general liquids 17th soft diet
ASPIRATION	None	None	None
POST-OP DL FINDINGS	 (+) good bilateral mobility	 (+) good bilateral mobility	 (+) good bilateral mobility

Table 3. Grading Scale of the Fiberoptic Endoscopic Evaluation of Swallowing (FEES)

Point Value	Premature Spillage of Material	Retention/Pooling of Material and/or Secretion	Entrance of Material and/or Secretion into the Larynx or Trachea; Presence/Absence of Reflex Cough
1	Severe	Severe retention/pooling	Entrance of material into trachea; no reflex cough
2	Marked	Marked retention/pooling	Entrance of material into trachea; with reflex cough forming
3	Moderate	Moderate retention/pooling	Entrance of material into larynx, remaining above the trachea; no reflex cough
4	Mild	Mild retention/pooling	Entrance of material into larynx, remaining above the trachea; with reflex cough forming
5	None	No retention or pooling	No entrance of material into larynx or trachea; no reflex cough

Table 4. Results of Seven Patients using The Grading Scale of the Fiberoptic Endoscopic Evaluation of Swallowing

PATIENT	AGE	GRADING SCALE
1	67	5
2	87	2
3	58	5
4	69	5
5	62	5
6	52	5
7	65	5

Table 5. Pinho's Classification on an auditory-perceptive evaluation

0	Normal Voice (absence ofhoarseness, roughness/soprosity,asthenia or tension
1	Mild Dysphonia (hoarse/rough/tense/soprous voice with sonorization)
2	Moderate dysphonia (hoarse/rough/tense/soprous voiv=ce with no sonorization)
4	Severe dysphonia (voice with no sonorization)

Table 6. Results of Seven Patients using Pinho's Classification on an auditory – peceptive evaluation

PATIENT	AGE	GRADE
1	67	2
2	87	2
3	58	2
4	69	2
5	62	2
6	52	2
7	65	2

Table 7. Spearmans Correlation showing Hospital stay, Decannulation of Tracheostomy, Speech/auditory –Perceptive Evaluation,Aspiratio/Penetration, NGT Removal and Staging of Seven Patients who underwent SCPL

Correlations

			HS	DD	AGE	SPEECH	ASPIRATION	NGT	STAGE
Spearman's rho	HS	Correlation Coefficient	1.000	.519	-.179	.	-.408	.414	.158
		Sig. (2-tailed)	.	.233	.702	.	.363	.355	.735
		N	7	7	7	7	7	7	7
	DD	Correlation Coefficient	.519	1.000	-.408	.	.212	.673	.000
		Sig. (2-tailed)	.233	.	.364	.	.648	.097	1.000
		N	7	7	7	7	7	7	7
	AGE	Correlation Coefficient	-.179	-.408	1.000	.	-.612	-.667	-.632
		Sig. (2-tailed)	.702	.364	.	.	.144	.102	.127
		N	7	7	7	7	7	7	7
	SPEECH	Correlation Coefficient	.	.	.	.	.	.	.
		Sig. (2-tailed)	.	.	.	.	.	.	.
		N	7	7	7	7	7	7	7
	ASPIRATION	Correlation Coefficient	-.408	.212	-.612	.	1.000	.618	.258
		Sig. (2-tailed)	.363	.648	.144	.	.	.139	.576
		N	7	7	7	7	7	7	7
	NGT	Correlation Coefficient	.414	.673	-.667	.	.618	1.000	.399
		Sig. (2-tailed)	.355	.097	.102	.	.139	.	.375
		N	7	7	7	7	7	7	7
	STAGE	Correlation Coefficient	.158	.000	-.632	.	.258	.399	1.000
		Sig. (2-tailed)	.735	1.000	.127	.	.576	.375	.
		N	7	7	7	7	7	7	7

Table 8. Average of Hospital stay, Decannulation of Tracheostomy, Speech/auditory –Perceptive Evaluation,Aspiratio/Penetration, NGT Removal and Staging of Seven Patients who underwent SCPL

One-Sample Statistics

	N	Mean	Std. Deviation	Std. Error Mean
HS	7	22.29	5.219	1.973
DD	7	10.14	5.728	2.165
AGE	7	65.71	11.011	4.162
SPEECH	7	2.00	.000[a]	.000
ASPIRATION	7	4.57	1.134	.429
NGT	7	15.86	6.619	2.502

a. t cannot be computed because the standard deviation is 0.

Table 9. Variables including Hospital stay, Decannulation of Tracheostomy, Speech/auditory –Perceptive Evaluation,Aspiratio/Penetration, NGT Removal and Staging of Seven Patients who underwent SCPL

HOSPITAL STAY	DECANNU-LATION OF TRACHEOSTOMY	PATIENTS	SPEECH	ASPIRATION/ PENETRATION	NGT REMOVAL	STAGING OF CANCER LESION
22	13	67/M	2	5	19	T1
27	7	87/M	2	2	4	T1
19	9	58/M	2	5	16	T1
15	7	69/M	2	5	13	T1
18	6	62/M	2	5	16	T2
29	22	52/M	2	5	26	T2
26	7	65/M	2	5	17	T1

Table 10. Comparison of the Hospital Stay, Speech Score, Aspiration Score, Decanulation Score of Patients Aged ≤ 60 y/o and >60 y/o

	< 60 y/o	≥60 y/o	P value
Hospital Stay	24.00 ± 7.07	21.60 ± 5.13	0.63 (NS)
Decanulation	15.50 ± 9.19	8.00 ± 2.83	0.09 (NS)
Swallowing Score	0.00 ± 0.00 (0)	0.80 ± 1.79 (0)	0.52 (NS)*
Speech Score	3.00 ± 0.00	3.00 ± 0.00	1.00 (NS)

Values are mean ± SD (Median)
t-test
*Mann Whitney U test

MIDLINE NECK FISTULA: 4TH BRANCHIAL CLEFT FISTULA VS INFECTED THYROGLOSSAL CYST

Kathleen M. Rodriguez, MD
Author

Celso V. Ureta, MD, FPSOHNS, FPCS
Co-Authors

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

ABSTRACT

OBJECTIVE: To present a case of a 19 year old female with recurrent mucopurulent discharge draining through midline neck fistula

: To present its clinical presentation, diagnostics and management

STUDY DESIGN: Case Report

SETTING: Tertiary Hospital

PARTICIPANT: One patient

RESULT: This is a case study which described an uncommon location of a 4th branchial cleft fistula in a 19 year old female with recurrent episodes of mucopurulent discharge. Complete ENT examinations were done and CT scan of the neck was requested with an initial impression of a 4th branchial cleft fistula versus an infected Thyroglossal duct cyst. The patient underwent neck exploration to trace the fistula tract. Its location was noted leading to a 4th branchial cleft. Excision of the tract was done and the specimen was submitted to the Department of Pathology for histopathologic finding, which revealed branchialcleft fistula. The patient improved after the operation and was eventually discharged.

CONCLUSION: This paper presented a case of a 19 year old female diagnosed with 4th branchial cleft fistula, presenting with an unusual presentation midline neck fistula draining with mucopurulent discharge. With the aid of CT scan, the tract of the fistula was identified. The patient was subjected to neck exploration and excision of the fistula tract.

KEYWORDS: Midline Neck Fistula, 4th Branchial cleft fistula, Thyroglossal duct cyts

CASE REPORT

Congenital anomalies of the neck occur as a consequence of disruptions in the complex development of the branchial apparatus of the fetus. This is classified according to branchial cleft or pouch of origin and its anatomic relationships. Congenital neck anomalies must be considered in the diagnosis of head and neck masses in children and adults. These include thyroglossal duct cysts, branchial cleft anomalies, dermoid cysts, and midline cervical clefts. It may be in the form of a fistula, sinus, or cyst, based on the completion of development of the anomalous structure[1]. Fistula is referred to as an anomaly when both external and internal openings are present[2] or may be defined as communication between two epithelized surfaces[3].

A detailed understanding of the embryology and anatomy of each of these lesions is essential to provide accurate preoperative diagnosis and appropriate surgical therapy, which are essential to prevent recurrence[2].

The objective of this study is to present a case of a midline fistula, which is unusual course of a 4th branchial cleft anomaly, and to report its management.

A 19 year old Filipino female from New Intramuros, Quezon City presented to the ENT outpatient with a history of fistula with an intermittent draining mucoid discharge in the midline of the lower neck since 6 years old which was associated with productive cough. Patient did not complain of any pain or difficulty of swallowing. The patient consulted a General Physician in a private institution where several antibiotics were given with incision and drainage. However, despite completing the course of antibiotics and Incision and Drainage, the midline neck fistula draining with mucopurulent discharge would recur almost every 2 years. No diagnosis was made nor disclosed to patient. The patient suffered from the condition of having intermittent discharge for 13 years.

One month prior to consult, cough was noted. There was no fever and swelling was noted on the left lower anterior neck which was painful and the fistula on the midline of neck was again draining with purulent mucopurulent discharge. Hence, patient decided to seek consult with an ENT specialist.

The past medical, personal and social and family history were unremarkable.

The clinical examination revealed a fistula with swelling and granulation it which was tender upon palpation and with purulent mucopurulent yellowish discharge in the midline of the anterior lower neck (*See Appendix A, Fig 1*). No cervical lymphadenopathy was present. Other physical examinations were unremarkable.

CT scan of neck with contrast was requested *(See Appendix A, Fig. 2)* which revealed an elongated left paramedian tract with central hypodensity that extends from the left infrahyoid region down and deep into the left

strap muscles near midline and ends in a pouch-like structure at the level anterior to the superior pole of left lobe of the thyroid gland. The length measures 2.6 cm with the superior end pouch measuring 1.5 x 0.8 cm, while the tract within the strap muscle has a diameter of 0.3m and the inferior pouch is 0.9 x 0.7 cm. Another round heterogeneous nodule was also seen at the region of the lower pole of the right lobe of the thyroid gland, which measures 1.0 x 1.2 x 1.4 cm. The impression was Thyroglossal duct cyst vs. 4th branchial cleft cyst, and a consideration of right cystic thyroid nodule.

The patient was subjected for Neck Exploration with excision of cyst under general anesthesia. Curvilinear incision was made along the skin crease to include the fistulous tract. Flaps were elevated on both sides for a better view of the surgical field. *(See Appendix A, Fig. 3).* The Fistula tract was noted at left paramedian area at the lower part of left sternocleidomastoid muscle. The tract was followed and on superior dissection the fistula tract was noted going laterally along the mid sternocleidomastoid muscle level. At this point the fistula tract was noted going medially to the left superior of thyroid lobe. The tract was followed and was noted inferior to the superior laryngeal nerve and superior to the recurrent laryngeal nerve. The superior end of the tract was noted at the hyoid bone. The body of the hyoid bone was cut together with the end of the fistula tract. No tract was noted to enter the pyriform sinus.

A nodule was excised approximately 1.1 cm x 0.5 cm which was seen at lower pole the right thyroid gland.

All specimen were sent to the pathology department along with the fistula tract which measures 6 cm x 1.1cm x 0.9 cm *(See Appendix A, Fig 4*). Histopathological examination revealed a tan elongated partly cystic tissue with lining of pseudostratified ciliated columnar type of epithelium with a few lymphoid aggregates in the wall confirms microscopically a branchial cleft cyst *(See Appendix A, Fig. 5).*

The patient improved and was subsequently discharged.

DISCUSSION

Congenital cervical cystic, sinuses and fistulae must always be considered in diagnosing head and neck masses in children and adults[2]. Complete clinical history and physical examination and knowledge in embryology is always warranted for a proper diagnosis[8]. The diagnosis may easily be established based on the presence of lesion. In our case, the patient presented with a midline neck fistula with recurrent mucopurulent discharge, we can consider an infected thyroglossal duct cyst, as well as an infected dermoid cyst and midline cervical cleft which is found primarily in the anterior midline neck[8], however a third or fourth branchial anomaly may also be found terminating in thyroid gland or paratracheal lesion[3].

Thyroglossal duct cysts are the most common midline congenital neck masses,

accounting for as many as 70% of all congenital neck anomalies. No gender predilection has been reported, and the age of affected patients ranges from birth to 70 years; approximately 50% of patients present before the age of 20 years[5].

An infected dermoid cyst is considered since this is another midline congenital anomaly which results from the entrapment of epithelial elements along embryonic lines of fusion. This presents as painless superficial subcutaneous masses at the anterior neck, this can be close to hyoid and moves with swallowing and tongue protrusion. It gradually increases in size. Infection is rare but the cyst can rupture and may present with granulomatous inflammation. This is commonly diagnosed before 3 years of age[2], however was ruled out because there is no obvious submental swelling[5] in the patient, as commonly seen in patients with infected dermoid cyts. Histologic findings may further rule out this diagnosis.

Another congenital neck anomaly is the midline cervical cleft. This is usually present at birth as cutaneous ulceration with overhanging skin or cartilaginous tag found at the anterior lower midline of the neck. Commonly, a sinus tract is noted which extends downward from the skin and may connect to the sternum or mandible or end in a blind pouch[2]. However this was unlikely the diagnosis since this congenital anomaly is present a birth and was commonly associated with other cleft abnormalities of tongue, lower lip or mandible[2].

The clinical features and usual locations of congenital neck anomalies are summarized in the table (*See Appendix B, Table 1*), which aids in ruling out dermoid cyst and midline congenital cyst.

We can consider branchial cleft anomaly, this said to be a common neck mass and is approximately 30% of congenital masses[2]. It was assumed that the congenital masses result from the cervical sinus of His. This type of neck mass usually presents with a non-tender, fluctuant mass that may become inflamed and abscess during a respiratory infection[9], later with a draining fistula as its presenting sign and symptom. The branchial cleft cyst is commonly located in the medial side of the sternocleidomastoid muscle[10]. Branchial cleft cysts gradually enlarge and frequently are not visible until the second or third decade of life [2]. They are equally common in males and females and usually present in childhood or early adulthood [2] however according to *Mandell*[11] there is a slight female preponderance. There are four branchial anomalies reported, and most branchial anomalies is the second branchial arch and occurs in 95%, while the remaining 5% remaining are from the first and third branchial remnants. Fourth branchial anomalies are said to be rare, with 45 cases reported literature [13] or approximately 1-2% of all branchial anomalies[11].

A fourth branchial anomaly has two distinct clinical presentations, in the first, the lesions was said to be present in neonates as lateral neck cysts or abscesses with

obstructive airway symptoms, while, second group, the lesions were present in children, adolescents, and occasionally adults as recurrent lateral cervical abscesses or as recurrent acute suppurative thyroiditis[11]. According to *Cote*[4], fourth branchial cleft sinuses are frequently diagnosed after recurrent episodes of infection in the sinus tract, the sinus might be misdiagnosed for years, and the patient may undergo multiple procedures before the diagnosis is properly made and treated.

Mandell cited in his literature that 97% of fourth branchial pouch anomalies occur on the left side, its tendency has yet to be explained, however it can be due to the asymmetric development of fourth arch vascular structures. On the other hand, Thyroglossal duct cyst as previously mentioned is located at midline near the level of hyoid bone because the tract passes anterior to the hyoid bone [9]. Seventy-five percent of cases of thyroglossal duct cyst is located in midline or slightly off midline (25%) in the anterior neck; however within 2 cm of midline. Paramedian location is most in thyroglossal cysts and occurs on the left for the reasons not well understood [14].

Clinical history and physical examination is the most important factor in evaluating congenital neck anomalies. In correlation with this case, the clinical presentation of the patient may mislead us in the diagnosis, presenting with a midline fistula however very low in the neck with recurrent mucopurulent discharge, associated with upper respiratory infection. Such midline presentation is uncommon in a 3rd or 4th branchial anomaly, the midline location is said to be the clinical presentation of a thyroglossal duct cyst. Confusion to whether the mass is a third or fourth branchial cleft cyst or an infected thyroglossal duct cyst arises.

CT scan of neck was requested, to trace the fistula tract. It was cited in *Koeller*[8] that radiologic images of 4th branchial may appear as cyst fluid which may vary in signal intensity on T1-weighted images depending on the protein concentration and is typically hyperintense relative to muscle on T2-weighted images. A fourth branchial cleft cleft cyst or fistula is seen connected to pyriform sinus[8]. While a thyroglossal duct cyts manifests as either in the midline of the anterior neck at the level of the hyoid or within the strap muscle just off midline[8]. Current tomography is able to demonstrate the fistula in up to 64% of cases. Barium esophagram can also be helpful with a 50% to 80% sensitivity for third and fourth branchial fistulae [3]. In this case CT scan revealed an elongated left paramedian tract with central hypodensity that extends from the left infrahyoid region down and deep into the left strap muscles near midline and ends in a pouch-like structure at the level anterior to the superior pole of left lobe of the thyroid gland, due to its location the impression was 4th branchial cleft cyst vs Thyroglossal duct cyts. The role of computed tomography is still being defined however it has been reported as helpful in making the diagnosis in some instances[11]. The result of the CT scan of the patient guide us in diagnosis, however regarding Branchial anomalies, it was cited in *Mandell*[11] that both third and fourth branchial anomaly is found

terminating in pyriform sinus, thus tracing the tract is necessary.

Intraoperative finding of our case showed that the fistulous tract was noted laterally along the lower part of sternocleidomastoid and continuous upward until it swings back again at the midline toward the hyoid bone. The tract has no connection from the thyroid gland and there was no attachment to pyriform sinus. *Mandell*[11] reported that third and fourth branchial pouch sinuses may be difficult to distinguish, because both types commonly begin at the pyriform sinus and travel a short distance before ending blindly in the paratracheal or thyroid gland regions. The connection or attachment of pyriform sinus was not observed in this case and probably the tract has finally degenerated or fibrosis might have occurred.

Fourth branchial anomalies usually contain thymic tissue as do cysts and sinuses that result from thymic or parathyroid rests, but only branchial anomalies have the connection to the pyriform sinus. The anatomical variation of the fourth arch anomalies depends on the infected side. On the right *(See Appendix A, Fig. 6)*, the lesion loops around the subclavian artery, pass deep to the internal carotid artery, ascending to the level of the hypoglossal nerve,descending along the anterior border of the SCM to enter the pharynx at the pyriform apex or cervical esophagus. While on the left, the tract descends into the mediastinum, looping around the aortic arch, medial to the ligamentum arteriosus, then ascends in a similar course to the right side. Fourth arch lesions present as lateral cysts in the lower third of the neck. However, a complete fourth branchial fistula has never been clinically described, perhaps because of the extremely convoluted course it would have to take[15].

Fourth pouch sinuses that actually leave the neck and descend below the clavicles into the mediastinum are rare, hence, of key importance in distinguishing a third from a fourth arch sinus is the relationship of the anomalous tract to the superior and recurrent laryngeal nerves. This must be determined surgically. *Mandell*[11] cited that if the tract was found to course inferior to the superior laryngeal nerve (a fourth arch derivative) and superior to the recurrent laryngeal nerve (a sixth arch derivative), a fourth pouch origin is suggested, however if the tract is found to pass cranial to the superior laryngeal nerve and inferior constrictor muscle, a third pouch origin is likely. In this case, intraoperative finding shows that the tract is more likely a fourth branchial anomaly as described by *Mandell*[11] because the tract is inferior to the superior laryngeal nerve and superior to the recurrent laryngeal nerve.

A case report by *Ureta and Ponce*[18] cited the Davies model that shows the tract of a 4th branchial cleft tract, which ascends above the thyroid cartilage, and its internal opening is found in the thyrohyoid membrane. It was also mentioned in the case report that embryologic anatomy involved in predicting

the course of the 4th branchial anomaly is complex and a complete 4th branchial fistula may never be surgically demonstrated since exposure of the tract would be too aggressive and unnecessary.

The histologic findings of the four midline neck congenital anomaly were presented in the table *(See Appendix B, Table 2)*. Branchial anomalies are lined with respiratory or squamous epithelium. Fistulae are more likely to be lined with ciliated, columnar epithelium, while thyroglossal duct cysts reveals a stratified squamous epithelium or ciliated pseudostratified columnar epithelium with ectopic tissue, which is present in 3 to 20%. Lymphoid nodules in the wall of the thyroglossal duct cyst are found 15 to 20% of cases as compared with branchial cleft cyst which is present in about 75% to 80%. . It has been reported in the study of Gilmour that accessory thymic tissue may originate from the fourth branchial pouch[17].

The most precise manner is to distinguish the histologic findings of cellular components of the cyst wall and surrounding tissue, however in some cases the preexisting inflammation of infected thyroglossal duct cyst may produce metaplasia of the lining of a thyroglossal duct cyst, which will make histologic differentiation from a branchial cleft cyst difficult[14]. Immunoperoxidase staining for thyroglobulin may be helpful in such cases[16].

In this study, the histologic finding revealed a lining of pseudostratified ciliated columnar type of epithelium with few lymphoid aggregates, pathologic report revealed a Branchial Cleft Fistula.

CONCLUSION

In conclusion, this paper presented a case of a 19 year old female diagnosed with 4th branchial cleft fistula, presenting with an unusual presentation of midline neck fistula draining with mucopurulent discharge. With the aid of CT scan, the tract of the fistula was identified. The patient was subjected to neck exploration and excision of the fistula tract.

RECOMMENDATION

It is important to remember that 4th branchial cleft fistula is a rare branchial anomaly with recurrent episodes of infections and should be considered in diagnosing a congenital midline neck fistula.

ACKNOWLEDGEMENT

My sincerest thank you to our very own Department Head for guiding and assisting me with this paper, to our Assistant Department Head and the rest of the Consultants and residents of Department of ORL-HNS for the critics and support. To the Department of Pathology, who helped me find references regarding pathologic examination. To my family, especially my mom and my boyfriend who never fails to believe in me. And above all, to God for giving me the strength and the courage to finish this paper.

REFERENCES

1. Tewfik, Ted, MD et al. Congenital Malformations, Neck. 2010. http://emedicine.medscape.com/article/837477-overview# aw2aab6b3

2. Acierno, Stephanie MD et. al. Congenital Cervi cal Cyst, Sinuses and Fistulae. Otolaryngology Clinics of North America 40 (2007)161-176.

3. Bajaj, Y, MD. et. al. Branchial anomalies in children. International Journal of Pediatric Otorhinolaryngology 75 (2011)1020-1023.

4. Cote, Donald, MD et. al. Otolaryngol Head Neck Surg January 1996 vol.114 no.1 95-97

5. Cox MF, Scully C, Cox, MF, Scully Maitland N. Viruses in the aetiology of oral carcinoma? Examination of the evidence. Br J Oral MaxilloFacSurg 1991;29:381-7.

6. Tucker, HM and M. L. Skolnick, "Fourth branchial cleft (pharyngeal pouch) remnant," Transactions of the American Academy of Ophthalmology and Otolaryngology, vol. 77, no. 5, pp. 368–371, 1973.

7. Nicollas, R. et. al, "Congenital cysts and fistulas of the neck," International Journal of Pediatric Otorhinolaryngology, vol. 55, no. 2, pp. 117–124, 2000.

8. Koeller, Kelly, CDR, MG, USN. Et. al. Congenital Cystic Masses of the Neck: Ra diologic Pathologic Correlation. Archives of the EFP. 1999

9. Flint, Paul, et al. Cummings Otolaryngology Head and Neck Surgery 5th edition. 2010. p 2814, vol III.

10. Haba R, et al. Intrathyroidal branchial cleft-like cyst in chronic thyroiditis. *Pathol Int.* 2000; 50:897–900.

11. Mandell, David L. MD. Head and Neck Anomalies Related to the Branchial Apparatus. Otolaryngologic Clinics of North America. Volume 33, Issue 6, Pages 1309-1332, 1 December 2000

12. Smith, Jonathan, MD., Neck Cyst. 2011.http://emedicine.medscape.com/article/848730-overview#showall

13. Lin, Yuh-Jhy M.D. et. al. Fourth Branchial Cyst Presenting with Neonatal Respiratory Distress. Annals of Otology, Rhinology and Laryngology (2000) Volume 109-2000

14. Johnston R, Wei JL, et.al. Intra-thyroid thyroglossal duct cyst as a differential diagnosis of thyroid nodule. Int J Pediatr Otorhinolaryngol. 2003;67:1027–1030

15. Koeller, Kelly et. al, Congenital Cystic Masses of the Neck: Radiologic Corelation Archives of the EEP.1999

16. Pilch, Ben MD. Head and Neck Surgical Pathology. 2001. p 8-15.

17. Gilmour JR . The embryology of the parathyroid glands, the thymus, and certain associated rudiments. Journal of Pathology and Bacteriology . 1937;45:507–552

18. Ureta, Celso MD and Ponce, Rita MD. Fourth Branchial Cleft Fistula. Archive, De partment of Otorhinolaryngology, Head & Neck Surgery Veterans memorial Medical Center. 2005 Volume 1, No. 1. Page 51; 3rd place PSO-HNS Research Competition (Midyear Convention , 1999)

ILLUSTRATION

APPENDIX A

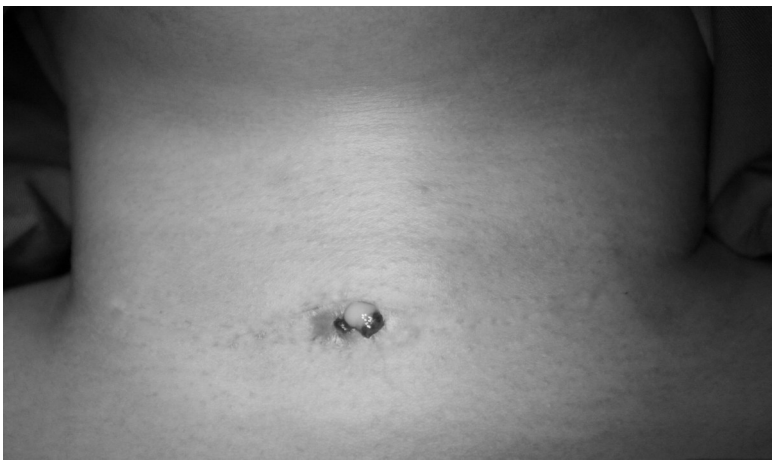
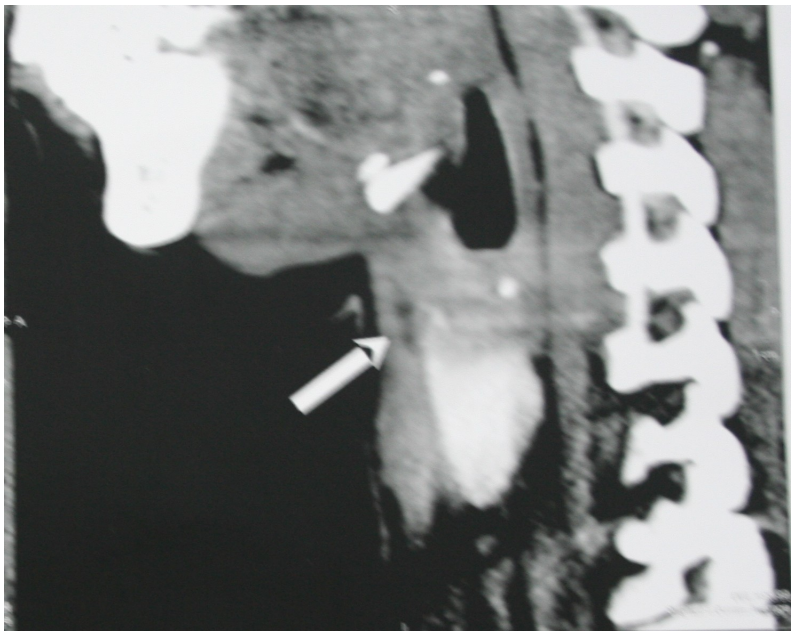


Figure 1. At presentation, granulation tissue are found around the fistula with mucopurulent mucoid discharge at the midline of neck of the patient



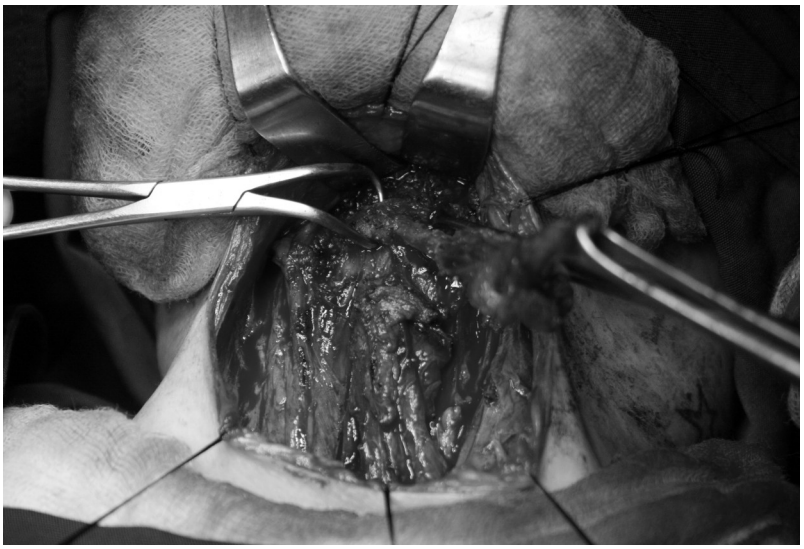


Figure 3. Intraoperative finding shows the fistula tract going from left paramedian of left sternothyroid going medially attached to hyoid bone

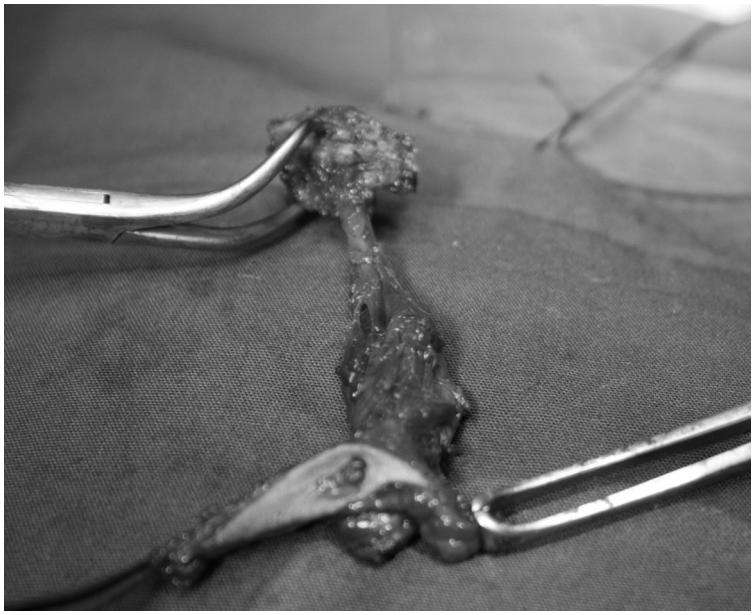


Figure 4. The excised sinus tract of the patient measuring 6 cm x 1.1cm x 0.9 cm

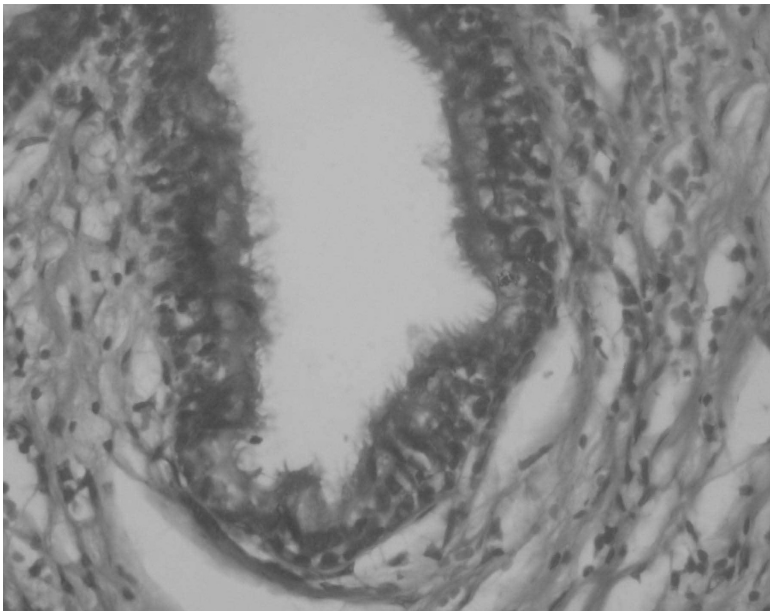


Figure 5. Histopathologic result of the patient revealed branchial cleft cyst showing a lining of pseudostratified ciliated columnar type of epithelium with few lymphoid aggregates.

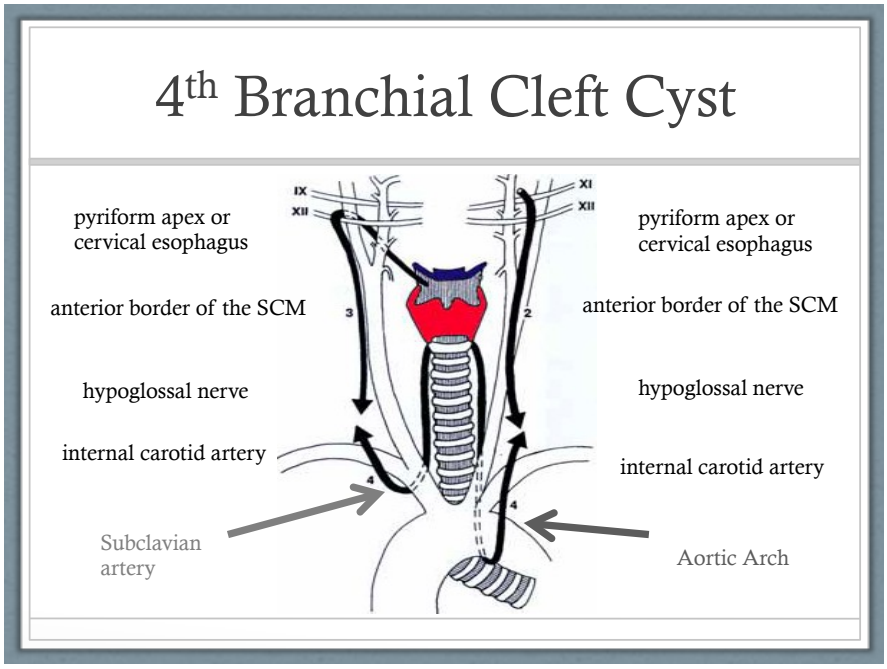


Figure 6. Demonstrating the tract of the right 4th brachial cleft fistula and left 4th branchial cleft fistula

Source: Mandell, David L. MD. Head and Neck Anomalies Related to the Branchial Apparatus .Otolaryngologic Clinics of North America. Volume 33, Issue 6 , Pages 1309-1332, 1 December 2000

APPENDIX A

Table 1. Clinical Features of Congenital Neck Lesions

Lesion	Peak Prevalence (Age)	Sex Predilection	Usual Location
Thyroglossal duct cyst	<10 y	Equal	Hyoid level or below (80%), within 2 cm of midline
Branchial cleft cyst			
First	Middle age	F > M	Parotid, external auditory canal
Second	10–40 y	Equal	Submandibular space, lateral to carotid vessels
Third	10–30 y	...	Left posterior cervical triangle
Fourth	**Any age**	**Female**	**Sinus tract arising from left pyriform sinus; cystic structure located at lower anterior border of SCM**
Dermoid cyst	10–30 y	Equal	Floor of mouth; painless superficial subcutaneous masses at the anterior neck, this can be close to hyoid and move with swallowing; obvious submental swelling
Midline Cervical Cyst	Present at birth		Cutaneous ulceration with overhanging skin or cartilaginous tag found at the anterior lower midline of the neck

Source: *Koeller, Kelly et . al, Congenital Cystic Masses of the Neck: Radiologic Corelation Archives of the EEP.1999; Mandell, David L. MD. Head and Neck Anomalies Related to the Branchial Apparatus .Otolaryngologic Clinics of North America. Volume 33, Issue 6 , Pages 1309-1332, 1 December 2000*

Table 2. Histologic Characteristic of the Four Midline Congenital Anomaly

LESION	HISTOLOGIC FINDING
Branchial Cleft Fistula	**Lined with ciliated, columnar epithelium with lympoid nodules in the wall**
Thyroglossal Duct Cyts	Stratified squamous epithelium or cilitated pseudostratified columnar epithelium with ectopic thyroid tissues; 15-20% lymphoid tissue
Dermoid Cyts	Lined with epithelium with epithelial appendages such as hair, hair follicles or sebaceous glands
Midline Cervical Cyst	Fibrous tissue with interwoven skeletal muscle

Source: *Pilch, Ben MD. Head and Neck Surgical Pathology. 2001. p 8-15. ; Acierno, Stephanie MD et. al. Congenital Cervical Cyst, Sinuses and Fistulae. Otolaryngology Clinics of North America 40(2007)161-176.*

LARGE ERYTHEMATOUS MASS OF THE AURICLE IN A 17-YEAR OLD MALE: AN UNCOMMON PRESENTATION OF ACUTE MYELOGENOUS LEUKEMIA

Eleanor P. Bernas, MD
Author

Natividad Almazan, MD, FPSOHNS, FPCS
Celso V. Ureta, MD, FPSOHNS, FPCS
Co-Authors

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

ABSTRACT

OBJECTIVE: To present an enlarging mass in the right auricle of a 17 year-old male as the initial symptom of Acute Myelogenous Leukemia.

STUDY DESIGN: Case Report

SETTING: Tertiary Hospital

PARTICIPANT: One patient

CASE REPORT: A 17-year old male with on and off fever, ecchymosis on the elbow and knees complained of an enlarging erythematous mass of the right auricle. This was his initial presentation to the attending physician. He was referred to the Otolaryngology (ENT) service were incision and drainage of the right auricle was done and revealed the presence of nonclotting blood. The edematous erythemas of the right auricle progressively enlarged to auricular hematomas. When the laboratory examinations showed pancytopenia with mild splenomegaly, an impression of acute leukemia was made. The diagnosis was confirmed by the findings of myeloid hyperplasia and cytoplasmic myeloperoxidase in his bone marrow. The mass later increased in size to 10 x 7cm, fluctuant, non-tender, fixed and friable occupying the pre auricular and post auricular area. The external ear canal was so edematous that inspection of the tympanic membrane could not be substantiated.

CONCLUSION: Enlarging mass of the auricle is not always due to simple trauma, but may be a cause of other detrimental systemic disease entity like Acute Leukemia in our patient. Incision and drainage of seroma or hematoma of the ear should be done with caution and a good history-taking is a must to avoid complications like bleeding and infection.

KEYWORDS: Acute Myelogenous Leukemia, Auricular hematomas, incision and drainage

INTRODUCTION

Leukaemia is a cancer of cells in the bone marrow (the cells which develop into blood cells). There are many types of cancer which arise from different types of cell. What all cancers have in common is that the cancer cells are abnormal and do not respond to normal control mechanisms. Large numbers of cancer cells build up because they multiply out of control, or because they live much longer than normal cells, or both.

Acute myelogenous leukemia (AML) is a fast-growing cancer of the blood and bone marrow. It is also sometimes called acute myeloid leukemia. In AML, the bone marrow makes many cancerous cells called leukemic blasts and this does not develop properly and cannot fight infections. These leukemic blasts grow quickly and crowd out the bone marrow, preventing it from making the normal red blood cells, white blood cells, and platelets that the body needs.[1]

The signs and symptoms depend on how many normal blood cells you have. It also depends on the number of leukemia cells in your body and where they are[1]. People with leukemia are at significantly increased risk for developing infections, anemia, and bleeding. Other symptoms and signs include easy bruising, weight loss, night sweats, and unexplained fevers. The diagnosis of leukemia is supported by findings of the medical history and examination, and examining blood and bone marrow samples under a microscope.

Auricular hematoma or hematoma auris is a collection of blood between the auricular cartilage and perichondrium. It is more common in males (84%) and the mean age is around 30 years old.[2] It is one of the otological emergencies that occurs secondary to trauma.[2] Although occasionally the spontaneous rupture of a blood vessel may be the cause.[2] Acute auricular hematoma is seen after blunt trauma to the side of the head. A network of vessels provides a rich blood supply to the ear, and the ear cartilage receives its nutrients from the overlying perichondrium. The hematoma occurs almost exclusively on the anterior surface of the auricle where the skin is tightly adherent to the underlying perichondrium, so that sharing forces applied to the ear separate the perichondrium from the cartilage. On the posterior surface, intervening areolar tissue allows the skin to glide over the perichondrium.[3] Auricular hematomas are often encountered in a sports medicine practice, most commonly among wrestlers, but also in boxers, football and rugby players, and judo athletes.[4]

Hematoma is a localized collection of blood, usually clotted, in a tissue or organ. It can occur almost anywhere on the body. Minor injuries occur routinely and the body is usually able to repair the damaged vessel wall by activating the blood clotting cascade and forming fibrin patches. Sometimes the repair fails if the damage is extensive and the large defect allows for continued bleeding. Contusions (bruises) and black eyes are familiar forms of hematoma. Less serious types include hematoma auris (in the tissues of the outer ear, better known as cauliflower ear)[5].

When a blood vessel is damaged blood leaks into the surrounding tissue; this blood tends to coagulate or clot. The greater the amount of bleeding that occurs, the larger the amount of clot formation. Occasionally, diseases may occur that decrease the number of platelets in the bloodstream (thrombocytopenia) or their ability to function. The platelets are the cells in the bloodstream that help initiate blood clot and fibrin formation[5].

Acute myeloid leukemia is an aggressive type of haematological malignancy characterized by abnormal proliferation of white blood cells and their precursors. An extramedullary deposit of leukemic cells in different parts of the body is not unusual. Different forms of leukemia may affect the ear usually middle ear and rarely the inner ear as well[7]. Histologically, the middle ear showed leukemic infiltration and/or hemorrhage much more frequently than did the inner ear or external auditory canal. No sound relationship exists between the anatomical location of hemorrhage in the temporal bone and clinical otological symptomatology[6]. Otologic complications occur almost invariably in those patients with the acute forms, particularly acute lymphocytic leukemia. The changes seen in the temporal bone could be due to leukemic infiltration, haemorrhage or infection[7].

Acute myeloid leukemia (AML) is a cancer of the myeloid line of blood cells, characterized by the rapid growth of abnormal white blood cells that accumulate in the bone marrow and interfere with the production of normal blood cells often vague and nonspecific. The symptoms of AML are caused by replacement of normal bone marrow with leukemic cells, which causes a drop in red blood cells, platelets, and normal white blood cells. These symptoms include fatigue, shortness of breath, easy bruising and bleeding, and increased risk of infection[9].

Enlargement of the spleen may occur in AML, but it is typically mild and asymptomatic. Skin findings in leukemias are very diverse and conventionally divided into specific lesions (leukemia cutis) and nonspecific lesions (leukemids) which may be found in up to 80% of all patients with leukemias[10].

This case is presented to show the consequence of no definitive diagnosis prior to evacuation of hematoma of the auricle and its complications.

CASE REPORT

A case of 17 year old male with on and off fever, ecchymosis on the elbow and knees complained of an enlarging erythematous mass of the right auricle.

History dates back 3 months with erythematous mass of the right auricle. This was associated with ecchymosis at right knee and left elbow, hemoptysis, easy fatigability and night sweats. He consulted at the Davao Regional Medical Center where laboratory work ups revealed pancytopenia. The clinical impression was acute leukemia so 5 units of packed red blood cell was transfused and he was discharged.

The erythematous mass of the right auricle gradually increased in size in a month. He returned back to the hospital for generalized body weakness, fever and abdominal pain and loss of weight. Repeat Complete blood count test was done and showed low hemoglobin, hematocrit and platelet count. Two units of platelet and 3 units of packed RBC were transfused.

Because of the progression of symptoms, he was referred to South Cotabato Medical Center where 6 units packed RBC, 2 units platelet concentrate and 3 units fresh whole blood was transfused. A week before referral and admission to VMMC for Bone marrow aspiration, an incision and drainage was done by the ENT service. There was non-clotting blood removed and so he was given antibiotics. Despite the intervention, the auricle further increased in size.

The past medical, personal and social and family history was unremarkable.

At Veterans Memorial Medical Center, physical examination showed a pale, febrile patient with generalized body weakness and episode of hematemesis. Ear examination showed 2 masses at the auricle 2.5 x 2.5cm and 2 x 2cm non-tender with active bleeding at the right periauricular area. (Appendix I). This later increased in size to (Appendix II) 10 x 7cm, fluctuant, non-tender, fixed, friable mass almost occupying the periauricular area, external auditory canal not visualized and inspection of the tympanic membrane could not be substantiated. CT scan of Temporal Bone was requested which revealed normal finding.

He was seen by the Pediatric Hematologist and Oncologist.

Laboratory investigation revealed microcytic normochromic RBCS, decrease hemoglobin, hematocrit, platelets and increase WBCs, Lymphocytes, positive blasts.

Bone Marrow Aspiration revealed Acute Myelogenous Leukemia. After blood transfusion of 13 units of packed red blood cell and 21 units of platelet concentrate, he was started on cycles of Chemotherapy (Doxorubicin, Cytarabine and Etoposide). Transfusion was given. The patient condition improved and was then discharged.

DISCUSSION

Leukemias are a group of heterogeneous neoplastic disorders of white blood cells. Based on their origin, myeloid or lymphoid, they can be divided into 2 types. Leukemias traditionally have been designated as acute or chronic, based on their untreated course. Acute leukemias usually present with hemorrhage, anemia, infection, or infiltration of organs. All types of leukemia show various degrees of infiltration, depending upon the type of leukemia. The liver and the spleen are common sites of infiltration in myelocytic leukemia. Our patient were mild splenomegaly with pancytopenia, and pale, febrile, weight loss with generalized body weakness, ecchymosis at right knee and left elbow and

edematous erythemas on the right auricle.

Extramedullary leukemic tumors or Granulocytic sarcoma (GS) in AML are uncommon, and may become clinically apparent before or concurrent with clinical evidence of marrow involvement.[10,11,12,13].

The most common otolaryngologic manifestations of GS are oral and pharyngeal lesions[14]. Leukemic infiltration of the ear is uncommon, occurring as acute mastoiditis, conductive or sensorineural hearing loss, vertigo, acute hemorrhagic otitis media, retro-auricular mass or facial nerve paralysis[15,16,17,18]. Paparella et al.[19] reviewed the temporal bones of 25 patients with leukemia and found that 20% of these patients, all being children aged between 11 month-old and 16 years of age, (10% of AML, 50% of ALL) experienced otologic complications directly attributable to their leukemia at admission. When these patients were examined histologically, the middle ear showed leukemic infiltration and/or hemorrhage much more frequently than did the inner ear or external auditory canal. No inner ear involvement and no leukemic infiltration of the mastoid were noted in our patient.

Nonspecific skin findings in leukemias are frequent and very variable. Most of them are the result of impairment function of bone marrow and include purpura, hemorrhage or ecchymoses or they are a manifestation of impaired immunity and include various skin infections. In our case, the patient initially presented with multiple lesions on the right auricle which progressively enlarged to as big as 10 x 7 cm. The incision and drainage was not indicated in this case knowing that the patient was diagnosed as Acute Leukemia. Complications like continuous bleeding and infection could happen.

Skin eruptions are reported to occur in 36% of patients, but most of them have been reported as leukemids, i.e., with no skin infiltration of leukemia cells. Only biopsy could confirm diagnosis. And this was not done in the patient because of the risk of bleeding and infection.

Treatment needs to begin soon after AML is diagnosed, as it progresses very quickly. Chemotherapy is the main form of treatment for AML. It is usually divided into 2 phases: Remission induction (induction) and Consolidation (post-remission therapy).Initially, the aim of treatment is to destroy leukaemic cells and induce a remission.

In our case, patient started on cycles of Chemotherapy (Doxorubicin, Cytarabine and Etoposide). After the first cycle, the patient conditions improved. (Appendix III). Ear examination crusted, non-tender, non-friable mass in right periauricular area, still external auditory canal not visualized. Patient tolerated the chemotherapy treatment and was then discharged. One month after the 1st first cycle, the patient initiated the 2nd cycle of chemotherapy. (Appendix IV). There was noted a decreased size of the mass. Ear examination noted with dry, hyperpigmented, non-tender, wrinkled skin or presence of scarring tissue

on periauricular area. Hyperemic, narrowed ear canal and tympanic membrane not visualized. After one month, the 3rd cycle of chemotherapy has done (Appendix V). A regression of the mass of the right auricle noted with hyper pigmented, wrinkled skin on periauricular area, narrowed external auditory canal with clear fluid, non-foul smell discharge, tympanic membrane not visualized.

In our case, chemotherapy quickly led to resolution of otological manifestations and complete hematologic remission.

The significance of presenting this rare case of skin manifestation in the ear of Acute myelogenous leukemia (AML) is: a.) the awareness of systemic disease like leukemia that could present with skin involvement b.) importance of history taking like bleeding etc. c.) Not all auricle lesions are simply seroma or hematoma d.) Not all auricular lesions are infection that warrants incision and drainage.

It is appropriate for an otorhinolaryngologist to consider complete blood count, peripheral blood smear, and temporal bone imaging and exclude any other systemic disease like leukemia to avoid complications and infection.

CONCLUSION

Enlarging mass of the auricle is not always due to simple trauma, but may be a cause of other detrimental systemic disease entity like Acute Leukemia in our patient. Incision and drainage of seroma or hematoma of the ear should be done with caution and a good history taking is a must to avoid complications like bleeding and infection.

REFERENCES

1. Howlader N, Noone AM, Krapcho M, Garshell J, Neyman N, Altekruse SF, Kosary CL, Yu M, Ruhl J, Tatalovich Z, Cho H, Mariotto A, Lewis DR, Chen HS, Feuer EJ, Cronin KA (eds). SEER Cancer Statistics Review, 1975-2010, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2010/, based on November 2012 SEER data submission, posted to the SEER website, April 2013

2. Al-juboori AN (2013) Treatment of Auricular Hematoma with Compression Using X-ray Films. General Med 1: 101. doi: 10.4172/2327-5146.1000101

3. Loock JW (2008) Haematoma auris. In: Gleeson M, Browning GG, Burton MJ, Clarke R, Hibbert J, et al. (eds.). Scott-Brown´s Otorhinolaryngology, head and Neck Surgery (7thedn) New York, Hodder Arnold 3: 3373-3374.

4. Lane SE, Rhame GL, Wroble RL (1998) A silicone splint for auricular hematoma. Phys Sportsmed 26: 77-78.

5. Dr. Ben Wedro. Hematoma. Nov 19, 2013.www.medicinenet.com › ... › skin center › skin az

6. Michael M. Paparella M.D.et al. Otological manifestations of leukemia. The Laryngoscope Volume 83, Issue 9, pages 1510–1526, September 1973

7. Chapman P. Johnson AN. Mastoid chloroma in acute myeloid leukemia. Journal of Laryngology and Otology 1980-94:1423-1427.

8. http://en.wikipedia.org/wiki/Acute_myeloid_leukemia

9. Büchner SA. Specific and nonspecific skin manifestations in leukemia. Schweiz Rundsch Med Prax 2002; 91(24): 1071–7.

10. Jeong Hee Cho-Vega, MD, PhD, et al. Leukemia Cutis. American Society for Clinical Pathology. Am J Clin Pathol 2008;129:130-142

11. Byrd JC, Edenfield WJ, Shields DJ, et al. Extramedullary myeloid cell tumors in cute nonlymphocytic leukemia: A clinical Review. Journal of Clinical Oncology 1995;13:1800-1816.

12. Billström R, Johansson B, Fioretos T, et al. Poor survival in t(8;21) (q22;22)-associated acute myeloid leukaemia with leukocytosis. Eur J Haematol 1997; 59: 47-52.

13. Hiçsönmez G, Çetin M, Tuncer AM, et al. Children with acute myeloblastic leukemia presenting with extramedullary infiltration: the effects of high-dose steroid treatment. Leuk Res 2004; 28:25-34.

14. Çavdar AO, Babacan E, Gözdaşoğlu S, et al. High risk sub-group of acute myelo-monocytic leukemia with orbitoocular granulocytic sarcoma in Turkish children. Acta Haematol 1989; 81:80-85.

15. Gökcan MK,Batı khan H,Çalgüner M, Tatarağası AI. Unilateral hearing loss as a presenting manifestation of granulocytic sarcoma (chloroma). Otology & Neurotology 2005; 27: 106-109.

16. Todd NW, Bowman CA. Acute myelogenous leukemia presenting as aty-pical mastoiditis with facial paralysis. Int J Ped Otorhinolarynogology 1984; 7:173-177.

17. Almadori G, Ninno MD, Cadoni G, et al. Facial nevre paralysis in acute otomas-toiditis as presenting symptom of FAB M2, T8; 21 leukemic relapse. Case report and review of the literature. Int J Ped Otorhinolarynogology 1996; 36:45-52.

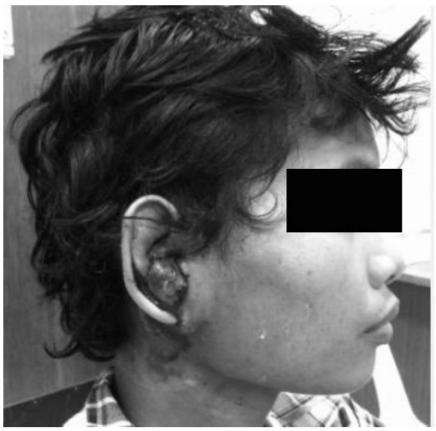
18. Kurtz JE, Andres E, Veillon F, et al. The American Journal of Medicine 2000; 15:509 -510.

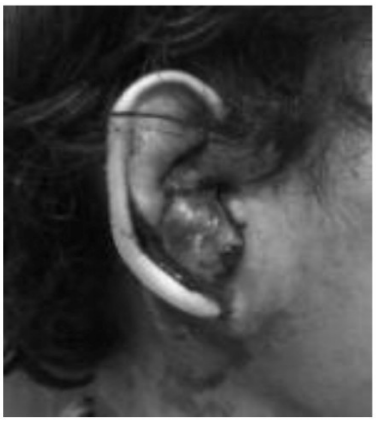
19. Hsu YC, Su CY, Hsu RF, et al. Unilateral sudden hearing loss as a presenting manifestation of chronic myeloid leukemia: Case report. Otolaryngol Head Neck Surg 2004; 130:271-273.

20. Hsu YC, Su CY, Hsu RF, et al. Unilateral sudden hearing loss as a presenting manifestation of chronic myeloid leukemia: Case report. Otolaryngol Head Neck Surg 2004; 130:271-273.

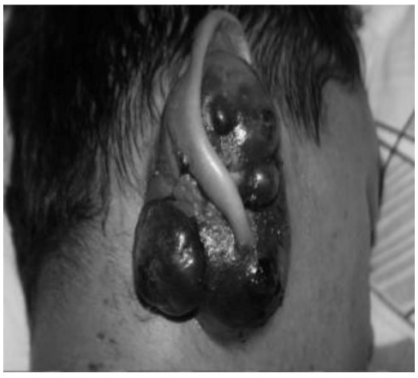
APPENDIX

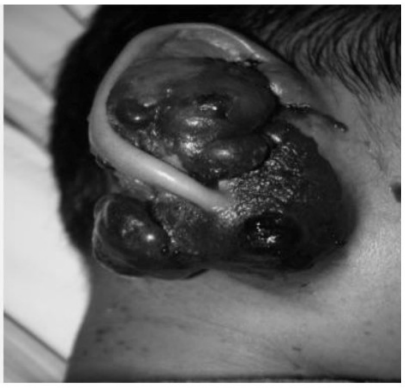
I. 1 week PTA



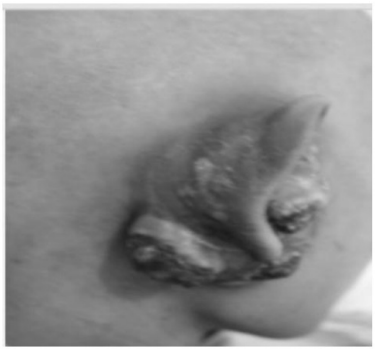


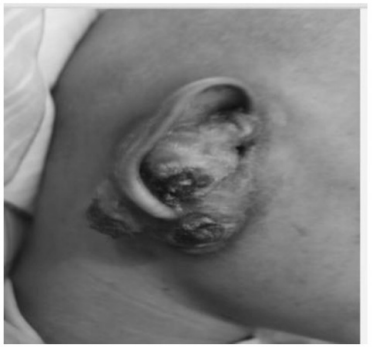
II.



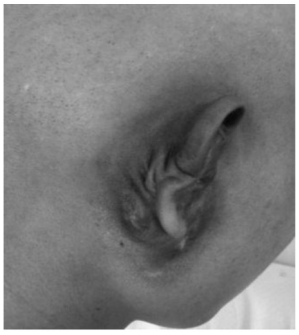


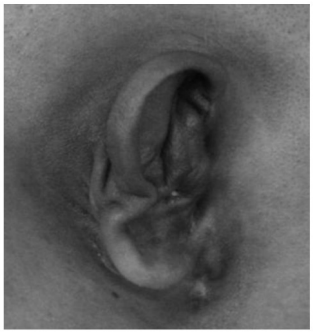
III. After the 1st Cycle of Chemotherapy

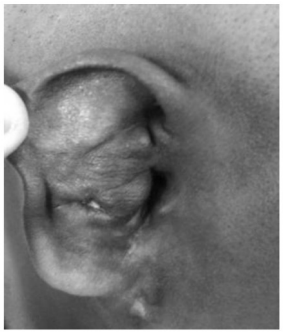




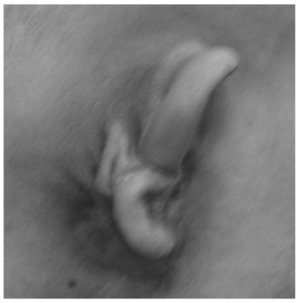
IV. 2nd Cycle of Chemotherapy

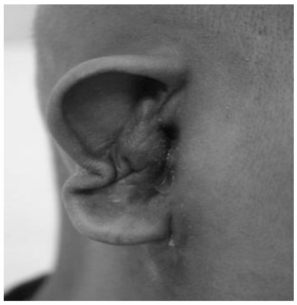






V. 3rd Cycle of Chemotherapy





A RARE CASE OF PARATHYROID CARCINOMA MANIFESTING AS RECURRENT NEPHROLITHIASIS

Ma. Melizza S. Villalon, MD
Correspondence

Celso V. Ureta, MD, FPSOHNS, FPCS

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

ABSTRACT

OBJECTIVES: To present a very rare case of Primary Parathyroid Carcinoma in a 54 year old female

: To discuss the clinical findings and management of Primary Parathyroid Carcinoma

METHODS:

Study Design: Case Report

Setting: Tertiary Hospital

Patient: One

RESULTS: A 54 year old female presented with a 3-year history of recurrent nephrolithiasis despite several shock wave lithotripsy. She had persistent hypercalcemia and parathyroid hormone level was noted to be elevated. Neck ultrasound showed a hypoechoic solid nodule measuring approximately 1.7x1.6cm in the lateral inferoposterior aspect of the left thyroid lobe. Parathyroid scintigraphy revealed a focal uptake on the left lower thyroidal bed. Patient underwent inferior parathyroidectomy, left with subtotal thyroidectomy, left and isthmusectomy Frozen section reported a parathyroid tumor and the final histopathologic results revealed a parathyroid carcinoma.

CONCLUSION: A very rare case of parathyroid carcinoma is presented, manifesting with recurrent nephrolithiasis. Elevated serum calcium and intact parathyroid hormone (iPTH) confirm a primary hyperparathyroid problem. Neck ultrasound and parathyroid scintigraphy help in the localization of a parathyroid tumor. Only final histopathologic result can confirm the diagnosis of parathyroid carcinoma. Complete surgical excision is the treatment of choice and offers a good prognosis.

KEYWORDS: Parathyroid Carcinoma, Primary Hyperparathyroidism

Kidney stone formation or nephrolithiasis is a condition brought about by many factors such as low daily urine volume; saturation of the urine with calcium, oxalate, calcium phosphate, uric acid or cystine, acidic urine; and bacterial infection[1]. The risk of nephrolithiasis is increased by certain medical conditions, including primary hyperparathyroidism, obesity, diabetes, gout, intestinal malabsorption, and anatomical abnormalities[2].

The majority of patients with nephrolithiasis have calcium-containing stones. Therefore, certain conditions that causes increase delivery of calcium to the kidney increases the risk for stone formation. The parathyroid gland is an endocrine organ that secretes parathyroid hormone (PTH) that regulates calcium balance in the body. In hyperparathyroidism, the serum PTH level is inappropriately elevated and the net effect is a rise in the serum calcium concentration leading to kidney stone formation[3].

Primary hyperparathyroidism is the unregulated overproduction of parathyroid hormone (PTH) resulting in abnormal calcium homeostasis secondary to an autonomous hyperfunctioning parathyroid tumor [4]. Less than 1% of urinary stone formers have primary hyperparathyroidism [3]. Hypercalcemia associated with elevated intact parathyroid hormone (iPTH) indicates a primary hyperparathyroidism. Primary hyperparathyroidism, while uncommon, can be benign or malignant.

Benign adenoma is the most common benign tumor of the parathyroid gland. Parathyroid carcinoma is a rare endocrine malignancy and it is also considered as an uncommon cause of PTH-dependent hypercalcemia. A systematic literature review of 22,225 cases of primary hyperparathyroidism reported between 1995 and 2003 revealed that parathyroid carcinoma accounted for only 0.74 percent of the cases [5]. Among all cancers, it has a prevalence of 0.005%, therefore, it is considered as the least common endocrine malignancy. Parathyroid carcinoma typically occurs among those age 40s to mid-50s. It may occur as a primary event or as part of a syndrome e.g. hyperparathyroidism-jaw tumor (HPT-JT) syndrome, multiple endocrine neoplasia types 1 and 2A, and familial hypocalciuric hypercalcemia[6].

There are no published local data on the incidence and prevalence of Primary Parathyroid Carcinoma.

It is the objective of this paper to present a case of a 54 year old female with a very rare case of a primary parathyroid carcinoma and discuss the clinical findings and appropriate management for this case.

CASE REPORT

A 54-year old female consulted due to hypogastric pain radiating to the flank. History started 3 years prior to admission, when patient experienced frequent hypogastric pain radiating to the flank area and burning sensation during urination. She occasionally experienced joint stiffness of both her hands but

with no evident swelling of her joints and occasional easy fatigability. There was no dyspnea, dysphagia, change in voice quality, fever, weight change and bowel habit changes. A consult with her private physician revealed that she had nephrolithiasis and she was advised to undergo shock wave lithotripsy. She would experience the same symptoms and she would undergo the same procedure three more times because of the recurrent nephrolithiasis. She had no other comorbid conditions. She is not taking any calcium supplements. Family history, personal and social history was unremarkable.

One year prior to consult, because of the recurrence of the above symptoms, she was advised urinary stent placement. On medical clearance prior to the procedure, routine serum electrolytes noted hypercalcemia which was persistent on repeated examinations (2.89-3.40mmol/L). Further laboratory tests were requested at that time. Baseline creatinine and BUN was within normal range. Baseline Thyroid function test showed normal results. However, parathyroid hormone (iPTH) was markedly elevated to 33.54 pmol/L.

Neck ultrasound showed an enlarged isthmus measuring 1cm in AP diameter and a hypoechoic solid nodule measuring approximately 1.7x1.6cm in the lateral inferoposterior aspect of the left thyroid lobe wherein a parathyroid etiology is considered. Parathyroid scintigraphy revealed a focal uptake on the left lower thyroidal bed.

Upon physical examination of the patient, multiple hypopigmented patches were distributed all over her body because of Vitiligo. There was no palpable neck mass or lymphadenopathies *(See Appendix A, Fig 1*). The rest of the ENT examination was unremarkable.

Admitting diagnosis was recurrent nephrolithiasis secondary to chronic hypercalcemia secondary to a primary hyperparathyroidism.

The patient underwent exploration of the neck, with possible excision of parathyroid tumor, with frozen section biopsy. Intraoperative findings *(See Appendix A, Fig 2 a-b*) revealed that the left thyroid gland is enlarged, with an approximately 2x2cm firm, dark, irregular nodular mass, located at the inferior pole. There is an approximately 1x1cm smooth, firm nodule at the inferior part of the thyroid isthmus. The right thyroid is grossly normal. Excision of the left thyroid mass was done to include the lower third and middle third of the left thyroid lobe. The whole isthmus including the nodule was excised. The specimen was sent for frozen section and revealed parathyroid tumor, left and benign thyroid nodule, isthmus.

Post-operatively, the serum calcium of the patient was closely monitored every 6 hours. After surgery, it showed a decrease from 3.7 to 2.10mmol/L *(See Appendix B, Fig 1*). Oral calcium supplementation was started. Patient only experienced mild symptoms of numbness of fingers which disappeared after 24 hours. Oral calcium supplementation was started on the first postoperative day and

patient was discharged improved on the fourth postoperative day. Regular follow-up of the patient was unremarkable.

Histopathologic results *(See Appendix A, Fig 3 a-d*) showed cells that are mostly in solid sheets with trabecular pattern and band forming fibrosis in some areas. Some follicles are lined by oncocytic cells and there is note of vascular invasion of the tumor.

Final histopathologic diagnosis reported Parathyroid Carcinoma.

DISCUSSION

Primary hyperparathyroidism is the unregulated overproduction of parathyroid hormone (PTH) resulting in abnormal calcium homeostasis. This is usually secondary to an autonomous hyperfunctioning parathyroid tumor. Secondary hyperparathyroidism on the other hand is the overproduction of parathyroid hormone secondary to a chronic abnormal stimulus for its production. Typically, this is due to chronic renal failure[4].

In primary hyperparathyroidism, the most commonly affected organs are the renal and skeletal systems. The classic, specific symptoms (i.e., bone disease, renal stones, and hypercalcemic crisis) represent obvious manifestations of the disease. Greater than 50% of patients with hyperparathyroidism develop renal symptoms manifested by nephrolithiasis and nephrocalcinosis. Nephrolithiasis is a condition wherein there is formation of stones within the urinary tract, on the other hand, nephrocalcinosis is characterized by the deposition of calcium in the kidney parenchyma and tubules[7]. The patient presented with hypogastric pain radiating to the flank area, burning sensation upon urination and was diagnosed with recurrent nephrolithiasis, for which she underwent repeated lithotripsy procedures. In primary hyperparathyroidism, nonspecific symptoms include malaise, fatigue, depression and other psychiatric symptoms, sleep disturbance, weight loss, abdominal pains, constipation, vague musculoskeletal pains in the extremities, and muscular weakness should be elicited[7]. The patient only complained of occasional joint stiffness and easy fatigability.

On physical examination, this patient did not present any palpable neck mass or lymphadenopathies suggestive of benign parathyroid pathology rather than parathyroid carcinoma because according to *DeVita* et. al., it is extremely unusual for patients with benign parathyroid lesions to have palpable abnormalities in the neck. The same author reported that a malignant pathology will present with palpable neck mass in 22-50% of cases[8].

On patient's routine electrolyte examination, serum calcium was incidentally noted to be elevated and repeated tests showed persistent hypercalcemia. Hypercalcemia may be attributed to medications, familial hypocalciuric hypercalcemia, but most commonly in primary hyperparathyroidism and malignancy [9]. Because of the persistent hypercalcemia, further tests such as parathyroid hormone level determination are needed to confirm the

diagnosis of primary hyperparathyroidism. Indeed, in this patient, intact parathyroid hormone was noted to be elevated which confirmed the diagnosis.

Is the recurrent nephrolithiasis brought about by primary hyperparathyroidism? The physiologic calcium metabolism is primarily regulated by the parathyroid gland. The main effects of parathyroid hormone is to increase the concentration of plasma calcium by increasing the release of calcium and phosphate from bone matrix, increasing calcium reabsorption by the kidney, and increasing renal production of 1,25-dihydroxyvitamin D-3 (calcitriol), which increases intestinal absorption of calcium [4]. The overproduction of parathyroid hormone results in the elevation of serum calcium, and in turn promotes calcium deposition in various organs. Specifically, calcium deposits in the kidneys lead to nephrocalcinosis and nephrolithiasis. The calcium level of this patient was noted to be persistently higher than normal in several occasions. The elevated serum calcium in this patient leads us to suspect a parathyroid pathology which was eventually confirmed by elevated parathyroid hormone level. The presence of elvated calcium and parathyoid hormone is diagnostic of primary hyperparathyoidism. Therefore, in this patient, the recurrent nephrolithiasis was brought about by primary hyperparathyroidism.

The increase in secretion of parathyroid hormone in primary hyperparathyroidism is the result of the autonomous hyperfunctioning of one or more of the parathyroid glands. This may be a benign parathyroid adenoma or parathyroid carcinoma[10].

There are diagnostic tests like neck ultrasound and parathyroid scintigraphy that may help detect parathyroid gland abnormality. Neck ultrasound and nuclear medicine studies such as technetium-99m sestamibi and parathyroid scintigraphy have been useful in localizing hyperfunctional parathyroid masses as well as parathyroid carcinoma. Normal parathyroid glands are rarely visualized by ultrasonography, because of their small size and insufficient acoustic difference compared to adjacent thyroid tissue. However, parathyroid tumors exhibit a relatively hypoechogenic pattern. It is usually well-circumscribed, tend to be solid and homogenously hypoechoic relative to echogenic thyroid tissue [11]. The ultrasound appearance of parathyroid malignancy on the other hand is a hypoechoic soft tissue mass with irregular, poorly defined border with sign of invasion of adjacent structures [5].

The neck ultrasound findings in this patient revealed a hypoechoic solid nodule in the lateral inferoposterior aspect of the left thyroid lobe, suspecting a parathyroid origin. A parathyroid scintigraphy of this patient showed focal uptake on the same area which strongly supports the impression of a parathyroid pathology. In this patient, ultrasound and scintigraphy findings suspected only a parathyroid tumor but cannot assess whether benign or malignant parathyroid tumor.

There are some biochemical parameters that may differentiate benign from

malignant parathyroid tumor. The degree of hypercalcemia and hyperparathyroidism are often more pronounced in parathyroid carcinoma. Calcium levels above 14 mg/dL (N.V. 8.5-9.9mg/dL) are more common in parathyroid carcinoma, as compared to elevations of 1-2mg/dL among other etiologies of primary hyperparathyroidism [8]. In this patient, serum calcium levels range from 2.89 to 3.40mmol/L, consistent with a benign parathyroid tumor rather than a carcinoma.

Up to 14% of patients with parathyroid carcinoma will present with hypercalcemic crisis manifested with depressed level of consciousness, dehydration and extreme hypercalcemia[4]. Our patient did not manifest any of these problems.

According to *De Vita* et.al., the intraoperative findings of a parathyroid carcinoma typically appears to be tan to grayish, hard, lobulated, and fibrous in texture as compared to a parathyroid adenoma which is red or brown, soft, and free of attachment to its surrounding structures. A larger gland size of >3cm has more tendency to be malignant and it has a predilection to occur in the inferior parathyroid gland [8]. In this patient, the only gross findings which may lead to suspect malignancy is the firm, dark, irregular nodular mass that was closely adherent at the inferior thyroid pole. While the mass was initially thought to be a thyroid mass intraoperatively, the pathologist reported it as parathyroid tumor by frozen section. Unexpectedly, the final histopathologic diagnosis was parathyroid carcinoma. According to Shane, if one or all of the malignant intraoperative findings may be absent, examination of frozen sections is of little value in distinguishing benign from malignant disease [12].

The management of primary hyperparathyroidism is excision of the autonomous hyperfunctioning parathyroid gland. If found to be malignant, wide tumor excision should be done. Parathyroid carcinomas are associated with an indolent, slowly progressive course [13]. The most important factor that would affect prognosis is the completeness of tumor resection. In this patient, the parathyroid tumor was completely excised en bloc with adequate margin of safety. According to *Kleinpeter*, et. al., patients who undergo complete en-bloc tumor resection can have survival rates as high as 90% at 5 years and 67% at 10 years[19].

Other treatment options like radiation therapy for parathyroid carcinoma has not been demonstrated to have a significant effect in either the neck or at sites of distant metastases[19].

Histologic diagnosis of parathyroid carcinoma is suggested by the presence of intraoperative features of local invasion and the diagnosis is confirmed by the World Health Organization histopathological criteria for parathyroid carcinoma. These include the presence of vascular invasion, perineural space invasion, capsular penetration with growth into adjacent tissues and/or metastasis [14]. A meta-analysis by Obara et. al. stated that the finding of fibrous bands was the most sensitive histopathological feature, whereas trabecular

growth pattern, capsular invasion and vascular invasion offers the highest specificity[17]. In this patient's microscopic findings of trabecular pattern, fibrous bands and vascular invasion confirmed the diagnosis of parathyroid carcinoma.

Post-operatively, serum calcium level should be monitored regularly with standby IV calcium infusion, when clinical signs of hypocalcemia sets in. This phenomenon of hypocalcemia after surgical removal of the hyperfunctioning parathyroid tumor can be explained by the sudden drop in the serum level of parathyroid hormone and subsequent drop of serum calcium. This phenomenon is called Hungry bone syndrome, wherein calcium is reabsorbed back toward the bone matrix resulting in decrease level of calcium in the blood. This is a temporary event and stabilizes usually after 24 hours[12]. The patient calcium level was regularly monitored postoperatively. It showed decrease from 3.7 to 2.10mmol/L. The patient only manifested temporary mild numbness of her fingers. Oral calcium supplementation was started on the first postoperative day and patient was discharged improved on the fourth postoperative day. Regular follow-up of the patient was unremarkable.

In conclusion, a 54 year old female presented with a very rare case of parathyroid carcinoma, manifesting with recurrent nephrolithiasis. Elevated serum calcium and intact parathyroid hormone (iPTH) confirm a primary hyperparathyroid problem. Neck ultrasound and parathyroid scintigraphy help in the localization of a parathyroid tumor. Only formal histopathologic procedure can definitely confirm the diagnosis of parathyroid carcinoma. Review of literature states that surgery is still the treatment of choice for parathyroid malignancy and offer good prognosis for the patient.

It is recommended that further studies be done to increase awareness among physicians that for patients with recurrent nephrolithiasis, parathyroid pathology should also be considered.

ACKNOWLEDGEMENT

My sincerest gratitude to our Department Head for guiding and assisting me in the construction of this paper. To our Assistant Department Head for his suggestions and support. To the rest of the Consultants and to my co-residents of Department of ORL-HNS, to the residents of the Department of Pathology, and to the fellows of the Department of Nephrology, who helped me fully understand this interesting case. To the patient who provided me with the necessary laboratory test results. To my family and my boyfriend who always stand by me and support my residency training. And above all, to our Almighty God for giving me the strength and the courage to finish this paper.

REFERENCES

1. Hall. Nephrolithiasis: Treatment, Causes, and Prevention. Cleveland Clinic Journal of Medicine. October 2009 vol. 76

2. Fink et.al. Medical Management to Prevent Recurrent Nephrolithiasis in Adults: A Systematic Review for an American College of Physicians Clinical Guideline. Annals of Internal Medicine. 2013;158(7):535-543

3. Craven et. al. Hypercalcemic States Associated with Nephrolithiaisis. Reviews in Urology. 2008 Summer; 10(3): 218–226

4. Kim et.al. Hyperparathyroidism. Medscape. November 2012

5. Daly BD, Coffey SL, Behan M. Ultrasonographic appearances of parathyroid carcinoma. Br J Radiol.1989Nov;62(743):1017-9

6. Parathyroid carcinoma. J Clin Endocrinol Metab, 86 (2001), pp. 485–493

7. Flint et.al. Cummings Otolaryngology Had and Neck Surgery. 5th ed.

8. DeVita, Hellman, and Rosenberg's Cancer: Principles & Practice of Oncology, Chap. 44 Cancer of the Endocrine System. 1684-1687. Vol. 2. 8th ed. 2008

9. Carroll et. al. A Practical Approach to Hyper calcemia. Am Fam Physician 2003 May 1;67 (9):1959-1966.

10. Essig Jr. et.al. Parathyroid Physiology. Emedicine. 2012

11. Mohebati & Shaha. Imaging techniques in parathyroid surgery for primary Hyperpara thyroidism. Am J Otolaryngol. 2012 July; 33(4): 457–468.

12. Shane. Parathyroid Carcinoma. Clinical Review. The Journal of Clinical Endocrinology & Metabolism. Vol. 36. No. 2. 2001.

13. Fang & Lal. Parathyroid Cancer. Endocrine Practice. Vol.17. 2011

14. DeLellis RA (2006) World health organisation classification of tumours. Pathology and genetics of tumours of endocrine organs. AIRC, Lyon

15. Dudney et.al., Parathyroid Carcinoma. Otolaryngol Clin N Am 43 (2010) 441–453

16. Witteveen et.al., Challenges and Pitfalls in the Management of Parathyroid Carcinoma: 17-Year Follow-Up of a Case and Review of the Literature. HORM CANC (2010) 1:205–214

17. Obara et.al. Flow cytometric DNA Analysis of parathyroid tumors with special reference to its diagnostic and prognostic value in parathyroid carcinoma. Cancer. 1990; 65: 1789-93.

18. Berkoben & Quarles. Hungry bone syndrome following parathyroidectomy. Up todate. November 2012

19. Kleinpeter KP, Lovato JF, Clark PB, et al. Is parathyroid carcinoma indeed a lethal disease? Ann Surg Oncol.2005;12:260–266.

ILLUSTRATIONS

APPENDIX A

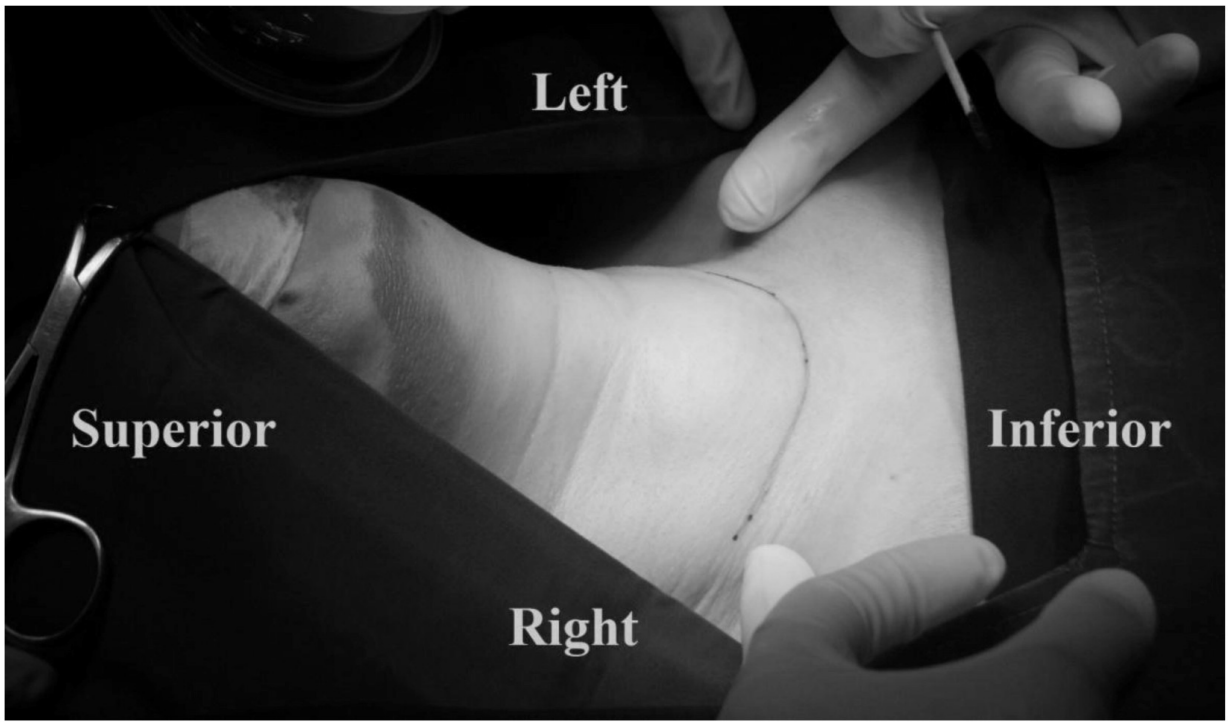
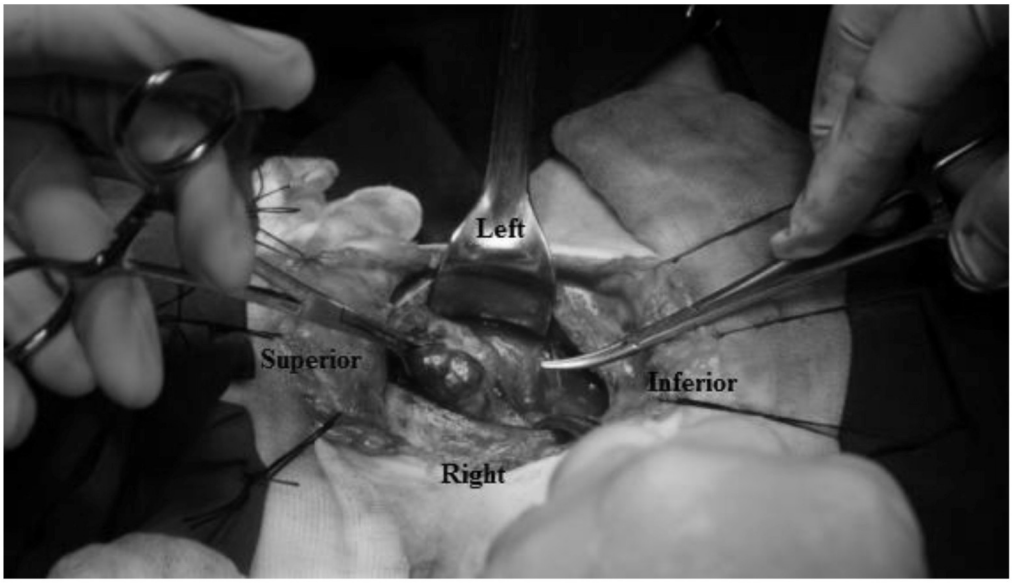
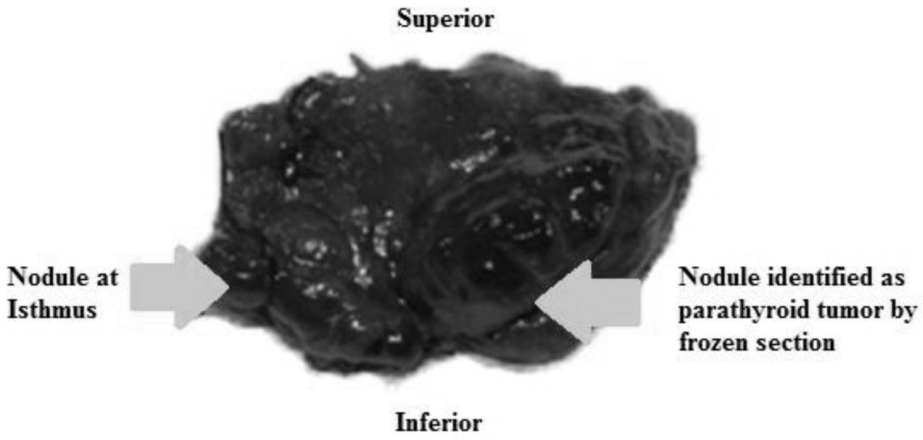


Figure 1. The patient had no palpable neck mass or lymphadenopathies



(a)



(b)

Figure 2. (a) Intraoperative findings (left thyroid lobe is freed and retracted from its bed) showed that the left thyroid gland is enlarged, with an approximately 2x2cm firm, dark, irregular nodular mass, located at the inferior pole. There is an approximately 1x1cm smooth, firm nodule at the inferior part of the thyroid isthmus. The right thyroid is grossly normal. (b) Specimen

APPENDIX A

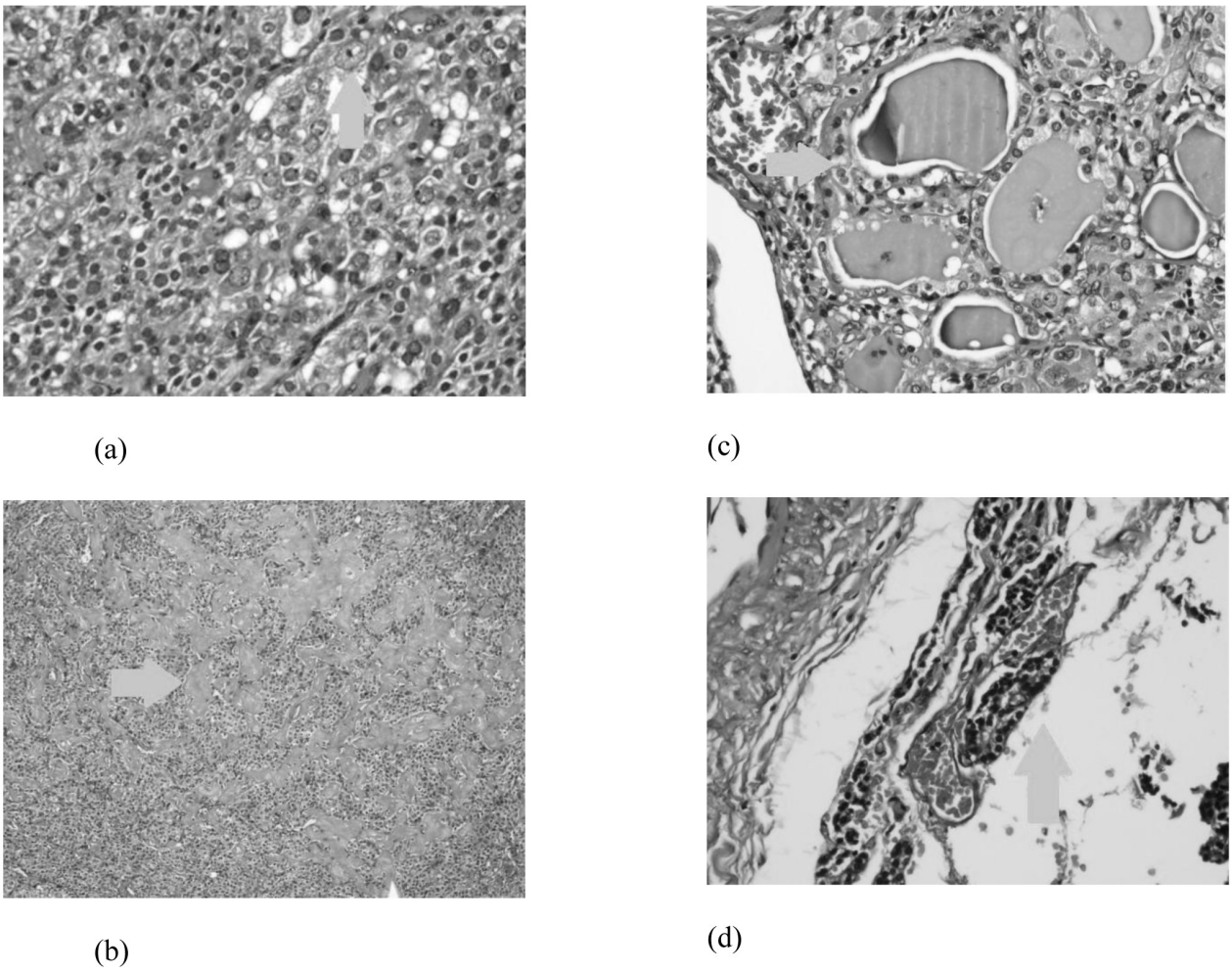
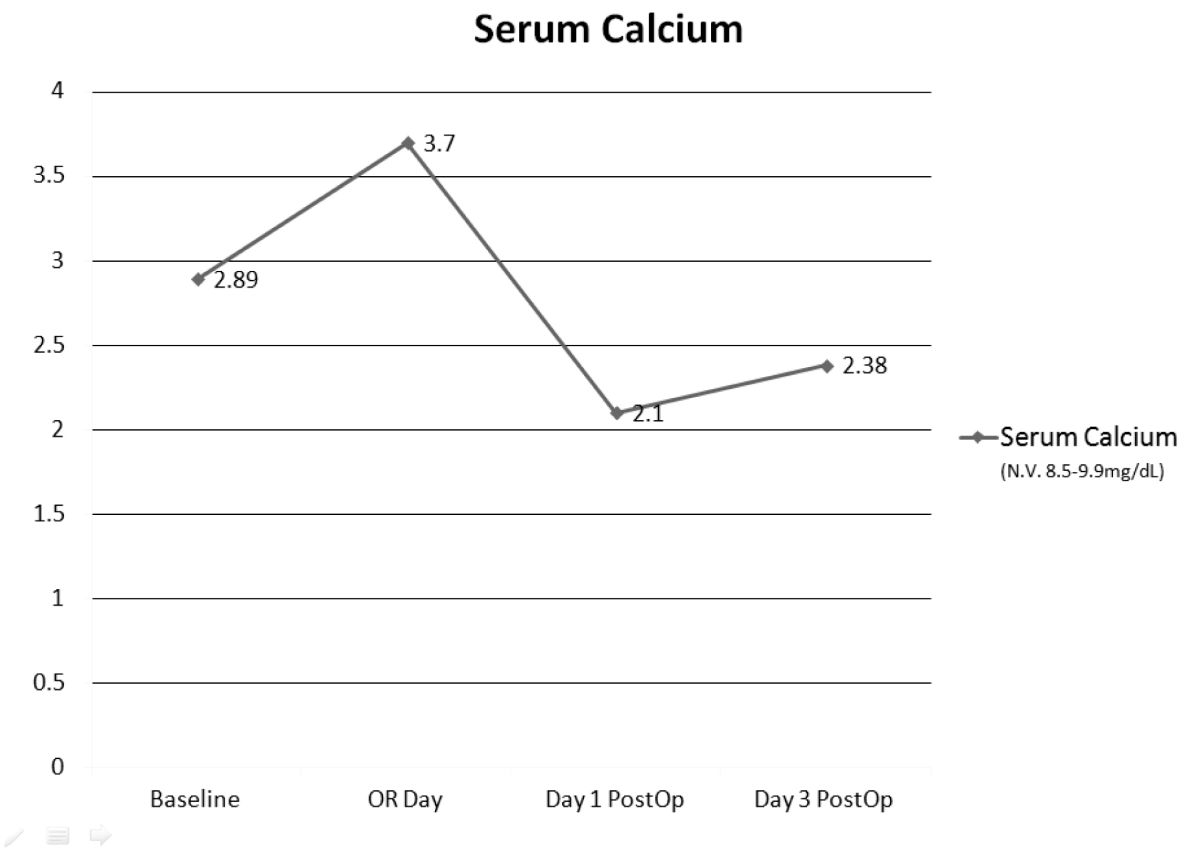


Figure 3. Microscopic appearance of parathyroid carcinoma as seen in the patient. (a) Cells mostly in solid sheets with trabecular pattern (hematoxylin and eosin stain (H&E); magnification 200x). (b) Band forming fibrosis (H&E; 20x), (c) Follicles lined by oncocytic cells (H&E; 200x), (d) Note of vascular invasion of the tumor (H&E; 200x)

APPENDIX B



Graph. 1. After surgery, serum calcium of the patient was monitored every 6 hours

REHABILITATION OF A DIGITAL VIDEOSTROBOSCOPY SYSTEM: A PRACTICAL SOLUTION TO AN INOPERABLE AND UNSERVICEABLE DIGITAL VIDEOSTROBOSCOPY UNIT

Jeffrey A. Pangilinan, MD
Principal Investigator

Celso V. Ureta, MD, FPSOHNS, FPCS
Co-Investigator

Department of Otorhinolaryngology Head and Neck Surgery
Veterans Memorial Medical Center
Institutional Affiliation

ABSTRACT

OBJECTIVES: The objectives of this paper are to present a rehabilitated and functional videolaryngostroboscopy system from an old, unserviceable digital videolaryngostroboscopy unit adapted and fitted with readily available digital hardwares and software; and to present the examination results of patients using the rehabilitated videolaryngostroboscopy system.

METHODS:

Study Design: Surgical Instrumentation

Setting: Tertiary Hospital

Patient: Veteran patients or their dependents presenting with dysphonia

RESULTS: The newly installed videolaryngostroboscopy system was successfully rehabilitated and yielded satisfactory performance in detecting laryngeal observations comparable with the old videolaryngostroboscopy unit. The new system has performed more than fifty videolaryngostroboscopic tests with successful results.

CONCLUSION: This study presents a rehabilitated and functional videolaryngostroboscopy system from an old, unserviceable digital videolaryngostroboscopy unit adapted and fitted with readily-available digital hardwares and software. The results of videolaryngostroboscopic study among patients using the rehabilitated videolaryngostroboscopy unit shows comparable results with the old videolaryngostroboscopy unit.

KEYWORDS: Videostroboscopy, videolaryngostroboscopy, laryngeal stroboscopy, videostroboscopy rehabilitation, Kay-Elemetrics stroboscopy rehabilitation

The field of medical surgical instrumentation has been continuously evolving into an ever faster phase than it has already been in the past years. However, the present highly sophisticated medical equipments come with their towering prices; their optimum operating lifetime lasts for only a few years and the cost of maintenance and repairs castigate health institutions with a huge financial burden.[1,2,3]

Videolaryngostroboscopy utilizes a highly sophisticated, fully-integrated medical workstation machine that provides laryngologists with a magnified view of a patient's larynx, so they can identify and assess pathologic laryngeal findings, send images and critical feedback to surgeons. It combines videorecording with a technique called stroboscopy to evaluate the function of the vocal cords, or larynx, in people with voice disorders. During speech, the vocal folds in the larynx vibrate too rapidly that it is almost impossible to examine with the use of the common light source. Stroboscopy overcomes this challenge by using a strobe light to illuminate the larynx. The strobe emits light pulses at a rate slightly slower than the vibration frequency of the vocal folds, causing the vocal folds to appear to move in slow motion. An examiner, using a rigid or flexible endoscope may observe the mucosal movement and function of the larynx.[4]

Our department established its Voice and Swallowing Center in 2005 and was privileged to be provided with a state-of-the-art videolaryngostroboscopy unit. However due to its continuous wear-and-tear the unit bugged-downed and was considered unserviceable by Its makers' service crew due to hardware and software malfunctions after seven years of service. Parts and software replacement was attempted but ended futile.

With the department's Voice and Swallowing unit's desire to provide continuous services to its main clientele, another attempt was done to save the strobe system by modifying and altering some of its parts and save its functional pieces without purchasing another costly digital videolaryngostroboscopy unit.

OBJECTIVES OF THE STUDY:

The objectives of this paper are:

1. To present a method of rehabilitating an old, unserviceable digital videolaryngostroboscopy system from an old, unserviceable digital videolaryngostroboscopy unit, adapted and fitted by using readily-available digital hardwares and software.

2. To present the examination results of patients using the rehabilitated videolaryngostroboscopy system.

METHODOLOGY AND RESULTS

Study Design: Surgical Instrumentation

Setting: Tertiary care hospital

Participants: Veteran patients or their dependents presenting dysphonia

METHODS

I. Identification and conservation of the Kay-Elemetrics digital videolaryngostroboscopy system's func-tional components.

The remaining functional components or parts of the old videolaryngostroboscopy unit were identified which were used for the rehabilitation of the new videolaryngostroboscopy system. (Table 1)

II. Identification and replacement of the non-serviceable components of the Kay-Elemetrics videolaryngostroboscopy system.

A. Identification of the non-serviceable components of the videolaryngostroboscopy system

The technical assessment of the videolaryngostroboscopy unit identified the following components as non-functional and unserviceable: the central processing unit's computer module and internal hard drives used for video-recording, for operating system, for database and system backup and the computer-controlled 3-chip video camera. (Table 1)

B. Acquisition of new digital hardware systems as replacement for the non-serviceable components of the videolaryngostroboscopy system. (Table 2)

After careful planning for the rehabilitation of the videolaryngostroboscopy unit, the department acquired new alternative and available computer hardware systems namely: a new central processing unit with a one terabit internal memory and an allotted 2GB video card (Fig.2); a high-definition network multimedia recording station (Fig.3); an audio-video capturing device (Fig.4); and a digital video camera (Fig.5).

III. Step-by-step procedure for the rehabilitation of the unserviceable Kay-Elemetrics digital videolaryngostroboscopy system (Appendix E)

A. Detachment of the digital videolaryngostroboscopy's unserviceable central processing unit

The unserviceable digital videostroboscopy central processing unit which housed the malfunctioned computer module and the three internal memory hard disk drives were detached from their cabling systems (monitor, printer, digital storage units, light source, etc.)

B. Installation of the new computer system

The newly-acquired central processing unit (CPU) installed with a genuine Microsoft Windows operating system was fitted within the system steel cart's compartment. The system's old LCD monitor was connected via a VGA cable while the keyboard, mouse and cabling systems were connected to the new CPU.

C. Installation of a new Network Multimedia Recording Station (Fig.3)

A one terabit (1TB) digital internal memory storage device was mounted and installed inside the network multimedia station. This served as the system's backup video recording device. This recording station can be accessed by the system's computer via a universal serial bus (USB) connection.

D. Installation of a new Audio-video Grabber (Fig.4)

The audio-video capturing device was installed together with its corresponding software program.

E. Installation of a digital video color camera unit (Fig.5)

The video-camera's video output was connected to an RCA video three-way splitter. One of the RCA splitter's female sockets served as a video input from the camera, and the other two served as video outputs to the network multimedia recording station and audio-video capturing device, which delivers both video and audio inputs to the computer system via a universal serial bus (USB) connection.

F. Re-installation of the previous digital videostroboscopy unit's functional parts (Table 1)

a. Powered speaker
b. Rigid 70 degree (Berciwald) endoscope
c. Electroglottograph
d. Laryngeal and lapel mic
e. Printer
f. Light source (halogen and strobe light)
g. Foot control pedals
h. Uninterruptible power supply and power isolation unit

IV. Actual patient examination and video recording using a newly refurbished videolaryngostroboscopy system

Testing of the software and system was done by performing actual videolaryngostroboscopic examination. The newly installed system yielded satisfactory performance in detecting laryngeal observations comparable with the old Kay-Elemetrics videolaryngostroboscopy unit, these include: vocal fold edges, amplitude, mucosal waves, vibratory behavior, glottic closure, ventricular folds, arytenoids, periodicity, salivary/mucous retention, mass/lesions, hyperfunction, vascularizations and voice frequency.

We have successfully used this newly rehabilitated videolaryngostroboscopy system in more than fifty test subjects performed by a trained laryngologist to with successful results (Table 3).

DISCUSSION

Videostroboscopy is a procedure that utilizes a highly sophisticated machine that provides a magnified view of a patient's larynx and aid laryngologists in the clinical evaluation of laryngeal diseases. It combines video-

recording with a technique called stroboscopy to evaluate the function of the vocal cords in patients with voice disorders.[4]

In 2013, the videolaryngostroboscopy unit's system of the Voice and Swallowing Unit of our institution crashed and became inoperable. It was immediately referred to its manufacturer's service staff (Kay-Pentax), and after a thorough evaluation the assessment was due to a computer module and operating system's boot failure. The videolaryngostroboscopy unit is considered unserviceable by its manufacturer.

Technically, the system's central processing unit uses three hard drive internal disk memories: a 120 gigabit (GB) internal hard drive memory for operating system and other software installations, a 73GB SCSI internal hard drive for video-recording and a 120GB internal hard drive for database and systems backup. All the three hard drives are controlled by a fourth specially-engineered KDS internal drive compiling and archiving computer module.[5] This fourth hard drive is the one which malfunctioned; without this, all data files from all other three disks are invaluable, because this carries the Kay-Elemetrics' exclusively-engineered software program for video-audio capture, processing, and playback. This rendered the videolaryngostroboscopy system inoperable and previous patients' examination records and results inaccessible.

After the manufacturer considered the unit unserviceable, the department experimented on making the unit functional by applying available and alternative computer hardwares. The department has identified the components and parts that are functional and those that are not functional (Table 1). Finally, new computer hardwares that are needed are purchased and fitted to the old and functional components of the VLS system. The audio-video feed from the endoscope and lapel mic attached to the new camera system is connected to the USB audio-video grabber, which in turn delivers the photo and video recordings to the CPU (via the audio-video grabber software) and the network multimedia recording station (for backup). The attempt is successful and the new refurbished VLS started to operate again.

The department's videolaryngostroboscopy unit was donated at a cost of three million pesos (Php3,000,000) in 2005. At present this state of-the-art equipment costs up to six million pesos (Php6,000,000) (Appendix C). The cost of the equipment is prohibitive especially for an institution largely dependent for its major budget from government funds.

With the difficulty in acquiring new equipment, the department has no choice but to try and experiment on making the unserviceable unit functional again in order to prevent disruption of its services to its clientele. The department spent only twenty-one thousand pesos (Php21,000) to make the unserviceable unit operate again. The amount is for the purchase of the new computer hardware, camera system and other minor materials. The cost of installation including

the cost of labor is free as it is done by the authors themselves.

The newly rehabilitated VLS system (excluding the network multimedia recording tation's 1TB exclusive internal memory drive) is capable of storing thirty-two thousand endoscopic examinations and tests at approximately 30MB of data storage space per patient, this is equivalent to three thousand hours of video recording capacity, as compared to the previous system's seven hours capacity[6]. The network multimedia recording station's 1TB exclusive internal memory drive is presently used as a backup memory drive. Moreover, the software can perform both audio-video recording and still-photo capturing simultaneously.

The new system has satisfactorily performed more than fifty digital videolaryngostroboscopic examinations (Table 3). The results of the endoscopic examinations using the new system with its improvised digital video camera yielded comparable results (Fig.8,9). It is still able to observe similar parameters observe with a regular videolaryngostroboscopy unit like vocal fold edges, amplitude, mucosal waves, vibratory behavior, glottic closure, ventricular folds, arytenoids, periodicity, salivary or mucous retention, mass or lesions, hyperfunctions, vascularizations and voice frequency. At present, the department is able to maintain the services of the Voice and Swallowing unit for all patients.

In conclusion this study presents a rehabilitated and functional videolaryngostroboscopy system from an old, unserviceable digital videolaryngostroboscopy unit adapted and fitted with readily-available digital hardwares and software. The results of videolaryngostroboscopic study among patients using the rehabilitated videolaryngostroboscopy unit shows comparable results with the old videolaryngostroboscopy unit.

ACKNLOWLEDGEMENTS

I would like to sincerely extend my deepest gratitude to my mentors for helping me in the conceptualization and design of this surgical instrumentation research paper, they have extended their endless support in the analysis and realization of this project for which I would be deeply indebted. I would also like to thank Ms.KMR for her extended help to this research work, and to my family for their unwavering support. Thank you very much to all of you.

REFERENCES

1. World Health Organization (WHO). Medical Equipment Maintainance Program Overview: WHO Medical Device Technical Series. 2011

2. Mutia D,et.al. Maintenace Management of Medical Equipment in Hospitals. Industrial Engineering Letters. ISSN 2224-6096. Vol 2, No.3. 2012

3. Skinner JS. The Costly Paradox of Health care Technology. MIT Technology Review. Sept 2013.

4. Margolis S. Video Stroboscopy. 2012 Jan 25. Available from: http://www.healthcommunities.com/ear-nose-throat-tests/videostroboscopy.shtml

5. Kay-Pentax. Digital Video Stroboscopy System, Model 9295. 1996-2011. Available from: http://www.kayelemetrics.com/index.php?option=com_product&Itemid=3&controller=product&task=learn_more&cid[]=33

6. Bohman A. Digital Stroboscopy Training Outline. Kay-Elemetrics. 2004.

APPENDIX A – FIGURES

FIG.1 – Kay-Elemetrics Videolaryngostroboscopy Unit (old/ original)

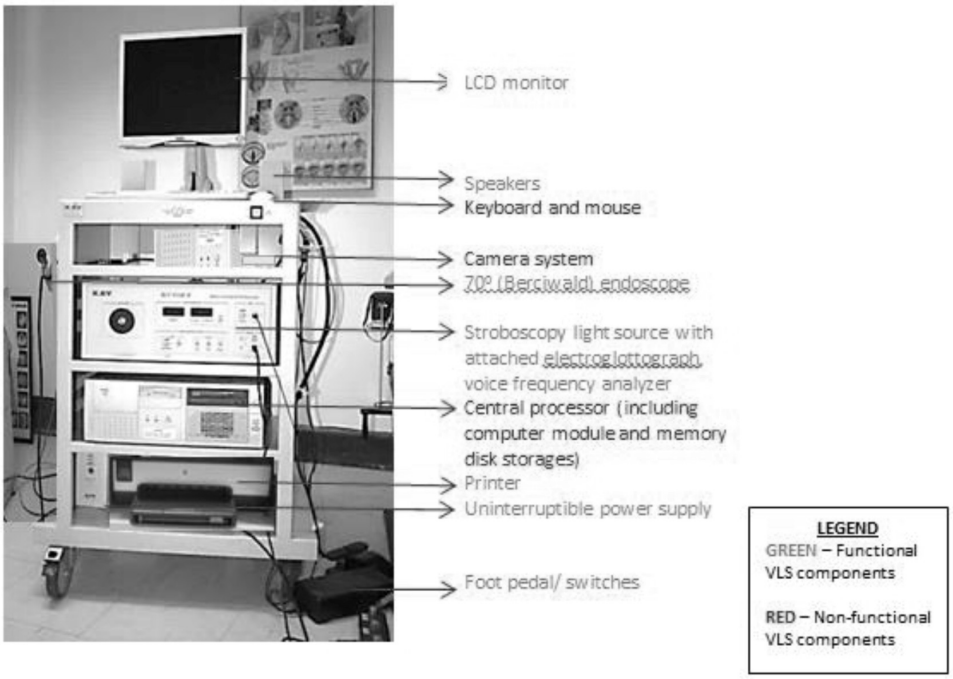


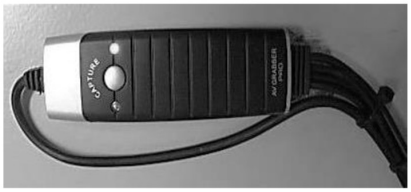
FIG.2 – Compact Central Processing Unit (new)

Intel i3-4130, 3.4Ghz 3Mb LGA1150 processor with 1TB HD SATA (Seagate) digital internal storage device (7200RPM; 64MB) in Microsoft Windows 7 operating system

FIG.3 – Recording Station (new)

AVD1089 Verbatim Network Multimedia Recording Station with High-definition1080p video playback

FIG.4 – Installation of the Audio-video Grabber (new)



USB Audio-video Grabber with AV capturing system software

FIG.5 – Installation of the Camera System (new)

Watec (WAT-202D) 3-chip color video camera

FIG.6 – The Newly rehabilitated Videolaryngostroboscopy System

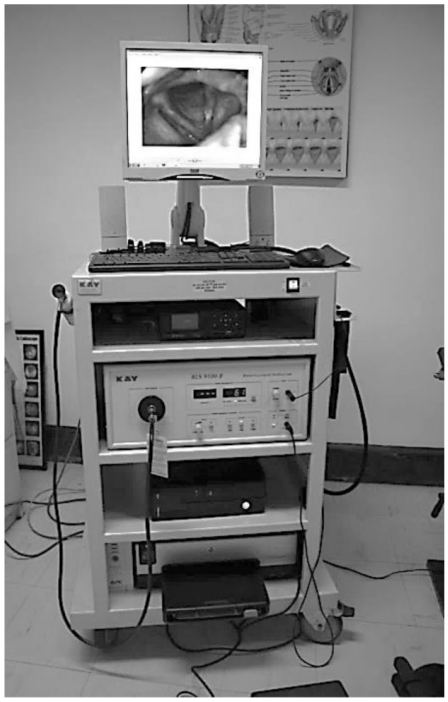
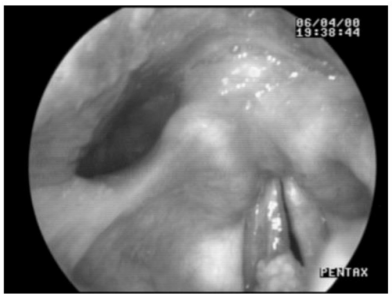
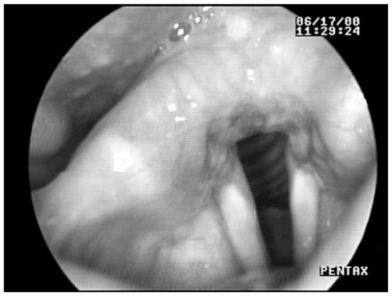


FIG.7 – Actual patient examination and video recording (with informed consent for documentation)

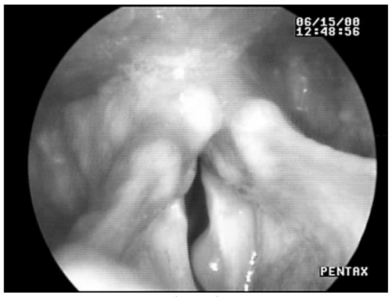
FIG.8
(STILL PHOTOS OF PATIENTS RETRIEVED ON HARD COPY FILES)



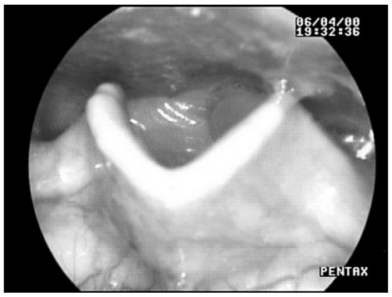
GA / 57 / M
June 4, 2000



EL / 65 / F
June 17, 2000

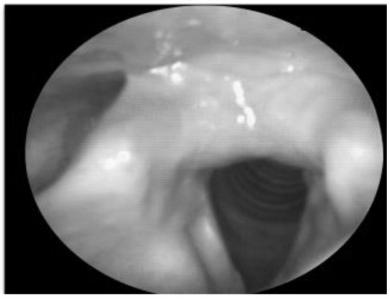


AR / 45 / F
June 15, 2000

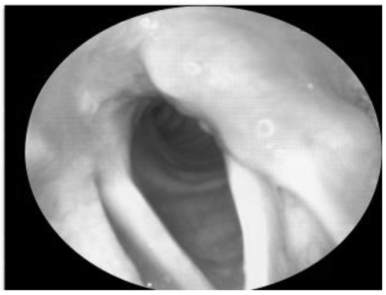


LM / 58 / M
June 4, 2000

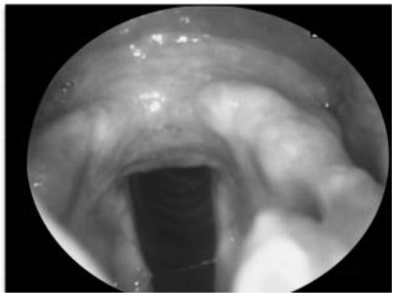
FIG.9
(REHABILITATED SYSTEM'S STILL PHOTOS – Actual Patients)



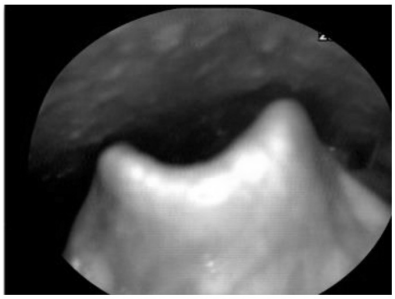
EO / 69 / M
October 23, 2013



CA / 61 / M
November 6, 2013



MT / 56 / F
June 25, 2014



RB / 81 / F
February 5, 2014

APPENDIX B – TABLES

TABLE 1 – KAY-ELEMETRICS SYSTEM COMPONENTS OVERVIEW (old unit specifications)**:**

Model: ***Kay-Elemetrics Digital Stroboscopy System*** (2005) Features: capture still photos, video with audio recording, add headshot, montage, create AVI and generate/ print report.	**Functional Unit**	**Non-Functional Unit**
Flat screen LCD monitor with adjustable arm	X	
Powered speakers with magnet, keyboard and mouse	X	
Electroglottograph (EGG)	X	
Computer-controlled 3-chip Toshiba camera		X
Lens and focus ring, rigid 70 degree (Berciwald) endoscope	X	
Laryngeal and lapel mic	X	
Computer module with Pentium 4 processor in Windows 2000 Professional operating system		X
Hard drives (3): o 73GB SCSI for video-recording (equivalent to 7hrs video recording) (1) o 120GB for operating system and other software (1) o 120GB for database and system backup		X
DVD+RW optical drive for video archiving and copying exams	X	
3½ floppy disc drive for transporting/ transferring reports	X	
Kay-Elemetrics software program for video-audio capture, processing, and playback	X	
Printer	X	
Uninterrupted power supply (UPS) for power backup	X	
14 gauge steel cart with 5" caster wheels	X	
Medical grade power isolation unit	X	
Foot control pedals	X	

TABLE 2 – NEW CENTRAL PROCESSING UNIT SPECIFICATIONS AND AQCUISITION COSTS

Hardware Specifications	**Unite Price**
• AVD1089 Verbatim Network Multimedia Recording Station with High-definition1080p video playback	Php 1,300.00
• Seagate SATA 1TB, 7200RPM, 64MB internal memory drive	2,300.00
• USB Audio-video Grabber with AV capturing system software	500.00
• C+ (PowerLogic) Compact 550-watt computer (CPU) case	1,200.00
Central processing unit (CPU)	16,350.00
• Intel i3-4130, 3.4Ghz 3Mb LGA1150 processor	
• Samsung SH-224DB 24x DVD-W SATA Internal disc writer	
• Hard disk (Seagate) 1TB SATA 6GB/s, 7200RPM, 64MB	
• A-shape A4Tech USB mouse+keyboard	
• Asus H81M-E H61, DDR1150	
• Kingston 4GB 1333MHz DDR3	
• PAlit GT630 2Gb SDDR3 64bit video card	
• 1TB HD SATA (Seagate) digital internal storage device (7200RPM; 64MB)	
• AVR 500 watts with 110 volt socket	
TOTAL	**Php 21,650.00**

TABLE 3 – PATIENT'S VIDEOLARYNGOSTROBOSCOPIC EXAMINATIONS PERFORMED BY THE NEWLY REHABILITATED VIDEOLARYNGOSTROBOSCOPIC SYSTEM

Date	Patient	Age/Sex	Diagnosis	Test Success	Test Fail
18-Sep-13	R.A.	74/M	Laryngopharyngeal reflux disease	X	
23-Oct-13	P.M.	59/M	True vocal cord polyp, right	X	
23-Oct-13	E.O.	69/M	Normal findings	X	
23-Oct-13	R.P.	52/M	Laryngopharyngeal reflux disease	X	
25-Oct-13	M.O.	62/F	Fungal infection, tongue base	X	
06-Nov-13	M.A.	56/M	Anterior commissure polyp	X	
06-Nov-13	C.A.	61/M	Laryngopharyngeal reflux disease	X	
06-Nov-13	S.B.	70/M	Laryngopharyngeal reflux disease	X	
08-Nov-13	D.B.	54/M	Normal findings	X	
08-Nov-13	R.D.	80/F	Normal findings	X	
15-Nov-13	A.C.	74/M	Presbylaryngeus	X	
04-Dec-13	Z.A.	37/F	Incomplete glottic closure etio?	X	
06-Dec-13	M.A.	61/F	Normal findings	X	
11-Dec-13	E.S.	70/M	Normal findings	X	
13-Dec-13	E.R.	64/F	Laryngopharyngeal reflux disease	X	
13-Dec-13	J.L.	68/M	True vocal cord polyp, left	X	
08-Jan-14	F.A.	77/M	True vocal cord mass rt t/c malignant	X	
08-Jan-14	B.B.	82/M	True vocal cord mass ant. commissure	X	
08-Jan-14	H.I.	69/M	True vocal cord mass lt t/c malignant	X	
22-Jan-14	A.C.	50/M	Laryngopharyngeal reflux disease		X
22-Jan-14	N.S.	62/M	Laryngopharyngeal reflux disease	X	
27-Jan-14	M.P.	51/F	Laryngopharyngeal reflux disease	X	
29-Jan-14	H.H.	63/M	True vocal cord cyst left	X	
05-Feb-14	R.O.	52/M	True vocal cord paralysis, left	X	
05-Feb-14	R.B.	81/F	Normal findings		X
12-Feb-14	P.V.	64/F	Laryngopharyngeal reflux disease	X	
21-Feb-13	H.S.	61/F	Laryngopharyngeal reflux disease	X	
21-Feb-13	R.D.	76/M	True vocal cord polyp, right	X	
05-Mar-14	A.R.	54/F	True vocal cord Nodule, lt; LPR	X	
12-Mar-14	B.A.	76/M	Normal findings	X	
26-Mar-14	M.A.	57/M	Squamous papilloma	X	
02-Apr-14	L.C.	91/F	Presbylaryngeus	X	
02-Apr-14	R.G.	65/M	True vocal cord polyp, right	X	
23-Apr-14	S.B.	85/F	Presbylaryngeus	X	
23-Apr-14	J.V.	55/F	True vocal cord Cyst, anterior commissure	X	
23-Apr-14	O.L.	67/M	True vocal cord cyst left	X	
14-May-14	D.D.	60/M	Presbylaryngeus	X	
14-May-14	A.B.	38/F	True vocal cord nodules, bilateral	X	
19-May-14	R.R.	51/F	Dysphonia 2 trauma	X	
21-May-14	J.S.	77/F	Spasmodic dysphonia	X	
28-May-14	Y.J.	49/F	Subglottic polyp, ant.rt; Pseudosulcus vocalis	X	
02-Jun-14	R.C.	62/F	Normal findings	X	
17-Jun-14	J.R.	60/F	Normal findings	X	
17-Jun-14	R.T.	85/F	Normal findings	X	
24-Jun-14	F.G.	75/F	True vocal cord nodule post.third, bilateral	X	
25-Jun-14	M.T.	56/F	True vocal cord nodule, bilateral	X	
02-Jul-14	M.G.	69/M	True vocal cord mass, lt. prob malignant	X	
16-Jul-14	C.N.	60/M	Normal findings	X	
25-Jul-14	L.S.	71/F	True vocal cord nodule, left	X	
25-Jul-14	J.A.	68/M	Normal findings	X	
20-Aug-14	O.P.	63/M	Normal findings	X	
10-Sep-14	E.O.	86/F	Presbylaryngeus	X	
n=52				(n=50) 96%	(n=2) 4%

APPENDIX C

(MTC OPTO Proposal)

MTC OPTO - MEDIC, INC.
3rd Floor, OHI Bldg., 179 Yakal Street, San Antonio Village, Makati City, Philippines
(63-2) 887-0658 ☎ (63-2) 382-4564 0917-8448058
E-Mail: sales@mtceyecare.com

September 17, 2013

In response to your query, MTC Opto-Medic is very pleased to provide you with the following:

1 set KayPentax Digital Video Stroboscope Model 9295E consisting of the following:		**P 6,500,000.00**
Rhinolaryngeal Stroboscope	9400	The light source for endoscopy and stroboscopy includes: • Halogen (constant) and xenon (flash) light sources • Laryngeal and Audio Microphones • Pitch triggering by laryngeal microphone or EGG input • Digital display of pitch, phase & amplitude measurements • Four modes of operation (slow, fast, locked, and manual) • Interface to computer for pitch, amplitude & phase information • Foot switch & pedal for remote control of instrument function • Isolation transformer (maintains line leakage to current) levels less than 50 microamps)
Rigid Endoscope	9106	Rigid telescopic laryngeal endoscope (70° forward angle with Integrated fiber optic cable) with a 10 mm diameter. Excellent Endoscope for stroboscopic and high-speed images.
Camera, 3-CCD	9212	Camera with 3 1/2- inch CCD sensor, S-Video, variable AGC, 470-line Resolution, computer-controllable, and C-mount. NTSC format
22-37 mm Zoom Lens Coupler	9118	Adjustable focal length (22-37 mm) lens with eyepiece adapter. Suitable for all scopes.
Digital Video Capture Module	9200C	Digital video computer system with all hardware and software for recording examinations and interfacing to camera, light source, and printer. System Features: • Computer (current model Pentium 4 at 3.4+GHz) • 2 GBytes of system RAM • A total of 1400 GBytes (1.4 TeraBytes) of hard disk storage • Four removable hard drives (each with 200 GBytes) • 2 Internal hard drives (each 300 GBytes) • External DVD+-R/RW with CD-R/RW writing capability • SM, SD, MMC, MS, CF and microdrive card interface ports • Windows XP Professional • Professional-level video capture with RGB 24 (4:4:4 sampling) • Hardware and software for computer control of camera • SQL database software for patient and examination database management •Electroglottograph input (EGG, Model 6103, purchased separately)

MTC OPTO - MEDIC, INC.
3rd Floor, OHI Bldg., 179 Yakal Street, San Antonio Village, Makati City, Philippines
(63-2) 887-0658 ☎ (63-2) 382-4564 0917-8448058
E-Mail: sales@mtceyecare.com

Digital Video Stroboscopy Model 9295E…….. **Page 2**

		• Comprehensive educational video on use of stroboscopy for assessing Dysphonia (3 DVDs and 1 eBook). • Video Viewer for Kay Digital Video to share exams • Vocal Parts and Vocal Pathology Parts I and II • Database of Stroboscopic Recordings of Laryngeal Pathologies • Digital Strobe Voice Analysis Program NOTE: Computer specifications updated without notice.
Printer, Color	9264C	Color ink-jet printer (digital) which uses 8½" x 11" paper and 4" x 6" high-gloss photography paper. Suitable for reports and image printing. Two paper trays.
Cart	9272E	Portable custom-designed cart (14-gauge steel) for KAY systems. Includes shelves and racks for all components with 5" diameter casters. NOTE: Available to KAY stroboscopy and high-speed video customers only. (220V)

PRICE : FOB Manila.
TERMS : C.O.D
DELIVERY : Within 60-90 days upon receipt of P.O.
WARRANTY : One year on parts and services.

Thank you for the opportunity to submit our best offer for your requirements. We look forward to meet with you personally for a thorough discussion of our proposal.

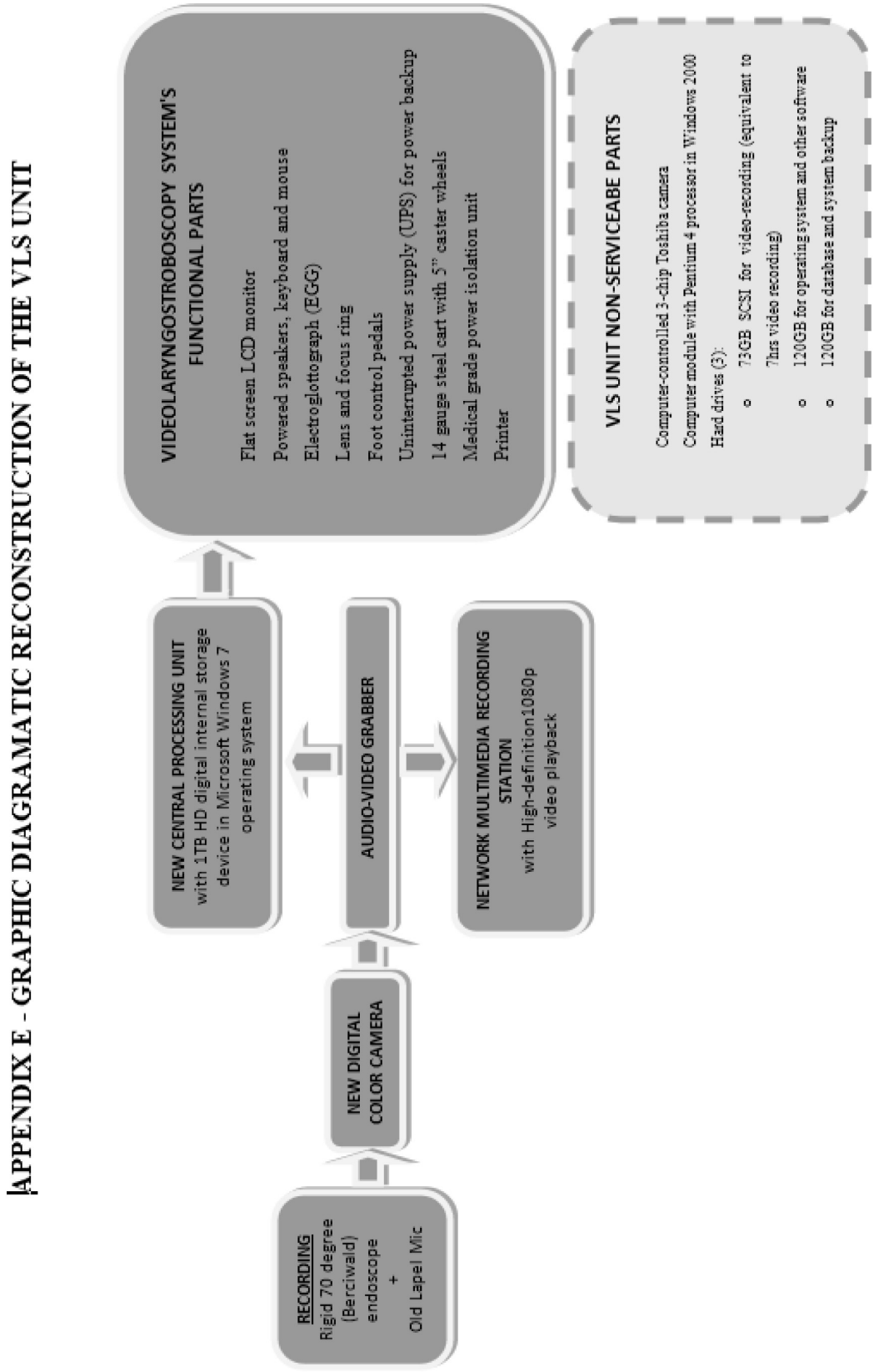
Very truly yours,

MTC OPTO-MEDIC, INC.

APPENDIX D – TERMINOLOGY

VLS	Videolaryngostroboscopy
CPU	Central processing unit
VGA	Video graphics array
USB	Universal serial bus
RCA	Phono or cinch (audio-video) connector (Radio Corporation of America)
KDS	Klee Data System
SCSI	Small Computer System Interface
TB	Terabit
GB	Gigabit
MB	Megabit
LPR	Laryngopharyngeal reflux disease
TVC	True vocal cord

APPENDIX E - GRAPHIC DIAGRAMATIC RECONSTRUCTION OF THE VLS UNIT



RANDOMIZED DOUBLE BLIND PLACEBO-CONTROLLED CLINICAL ON THE EFFICACY AND SAFETY OF *MORINGA OLEIFERA (MALUNGGAY)* 1% CREAM IN THE TREATMENT OF TINEA CORPORIS: A PILOT STUDY

Charo Fionna F. De Guzman-Castro, MD
Author

Catherine B. Rebosa, MD, Maria Jesusa C. Calderon, MD

Elizabeth P. Prieto, MD, FPDS
Adviser

Department of Dermatology
East Avenue Medical Center
Institutional Affiliation

BACKGROUND: All parts of the Moringa tree are edible and have long been consumed by humans. Moringa preparations have been cited in the scientific literature as having antibiotic, antitrypanosomal, hypotensive, antispasmodic, antiulcer, anti-inflammatory, hypocholesterolemic, and hypoglycemic activities as well as having considerable efficacy in water purification.

Tinea corporis is one of the top 10 new cases seen in the Department of Dermatology, outpatient department of East Avenue Medical Center. Tinea corporis refers to dermatophyte infections of the trunk, legs, arms, and/or neck, excluding feet, hands and groin. It is commonly caused by Trichophyton rubrum, T. mentagrophytes and Microsporum canis. There has been no reported or published clinical trial on the efficacy of either antimicrobial or anti-fungal properties of Moringa oleifera. This prompted the investigator to pursue this study.

OBJECTIVE: To determine the efficacy and safety of *Moringa oleifera* (Malunggay) in the treatment of tinea corporis infection among patients at East Avenue Medical Center Department of Dermatology.

METHODOLOGY: A total of 40 patients were randomly assigned to 2 groups, Group A (placebo group) had 20 patients and Group B (Moringa) had 20 patients. Thirty-four patients completed the study period, 16 for placebo group and 18 for Moringa group. Clinical parameters (erythema, pruritus and scaling) were followed-up in terms of improvement. Mycologic cure in terms of KOH smear was also noted at the end of the study. Adverse reactions were noted as well.

RESULTS: There was no significant clinical improvement in terms of erythema, pruritus and scaling observed at the end of the study. Mycological cure rates showed 37.5% for the placebo group and 72.2% in the Moringa group. Among groups, mycologic cure rates using KOH smear showed no significant difference. Minimal pruritus at week one was observed which spontaneously improved at the end of the treatment.

CONCLUSION: Moringa oleifera cream at 1% is not effective in the treatment of tinea corporis

INTRODUCTION

Moringa oleifera, or the horseradish tree, is a pan-tropical species that is known by such regional names as benzolive, drumstick tree, kelor, marango, mlonge, mulangay, nebeday, saijhan, and sajna. It is the most widely cultivated species of a monogeneric family, the Moringaceae, that is native to the sub-Himalayan tracts of India, Pakistan, Bangladesh and Afghanistan. This rapidly-growing tree was utilized by the ancient Romans, Greeks and Egyptians; it is now widely cultivated and has become naturalized in many locations in the tropics. It is a perennial softwood tree with timber of low quality, but which for centuries has been advocated for traditional medicinal and industrial uses. It is already an important crop in India, Ethiopia, the Philippines and the Sudan, and is being grown in West, East and South Africa, tropical Asia, Latin America, the Caribbean, Florida and the Pacific Islands. All parts of the Moringa tree are edible and have long been consumed by humans. The many uses for Moringa include alley cropping (biomass production), animal forage (leaves and treated seed-cake), biogas (from leaves), domestic cleaning agent (crushed leaves), blue dye (wood), fencing (living trees), fertilizer (seed-cake), foliar nutrient (juice expressed from the leaves), green manure (from leaves), gum (from tree trunk), honey-and sugarcane juice-clarifier (powdered seeds), honey (flower nectar), medicine (all plant parts), ornamental plantings, biopesticide (soil incorporation of leaves to prevent seedling damping off), pulp (wood), rope (bark), tannin for tanning hides (bark and gum), water purification (powdered seeds). Moringa seed oil (yield 30-40% by weight), also known as Ben oil, is a sweet non-sticking, non-drying oil that resists rancidity. It has been used in salads, for fine machine lubrication, and in the manufacture of perfume and hair products. This tree has in recent times been advocated as an outstanding indigenous source of highly digestible protein, Ca, Fe, Vitamin C, and carotenoids suitable for utilization in many of the so-called “developing” regions of the world where undernourishment is a major concern.

The benefits for the treatment or prevention of disease or infection that may accrue from either dietary or topical administration of Moringa preparations (extracts, decoctions, poultices, creams, oils, emollients, salves, powders, porridges) are not quite so well known. A plethora of traditional medicine references attest to its curative power, and scientific validation of these popular uses is developing to support at least some of the claims. Moringa preparations have been cited in the scientific literature as having antibiotic, antitrypanosomal, hypotensive, antispasmodic, antiulcer, anti-inflammatory, hypocholesterolemic, and hypoglycemic activities as well as having considerable efficacy in water purification.

An in-vitro study by Chuang PH, MD, et al, in 2007, against antifungal activity of crude extracts and essential oil of Moringa oleifera, showed that ethanol extracts have antifungal activities against dermatophytes such as trichophyton rubrum, T. mentagrophytes, Epidermophyton floccosum, and Microsporum canis.

Another study by Dahot, M.U., MD, et al, in 1998, showed that aqueous extract of M. oleifera leaves posses significant antimicrobial activity against gram positive and negative fungal species.

Tinea corporis is one of the top 10 new cases seen in the Department of Dermatology, out-patient department of East Avenue Medical Center. Tinea corporis refers to dermatophyte infections of the trunk, legs, arms, and/or neck, excluding feet, hands and groin. This may occur at any age, and is more common in warm climates. It is commonly caused by Trichophyton rubrum, T. mentagrophytes and Microsporum canis. As for its transmission, autoinoculation from other parts of the body such as from tinea pedis and tinea capitis may occur. Warmth and humidity favor the growth of the organisms. Contact with infected animals, contaminated soil and fomites can also be sources of infection. This infection is usually asymptomatic but can also be slightly pruritic. Skin lesions usually appear as small, scaling, sharply marginated plaques, with or without pustules or vesicles, usually at margins. Peripheral enlargement and central clearing produces annular configuration with concentric rings or arcuate lesions; fusion of lesions produces gyrate patterns. Single and occasionally multiple lesions may occur. Several treatment options are available in the market. Topical anti-fungal drugs such as ketoconazole, miconazole and clotrimazole and newer generation drugs such as terbinafine and butenafine are being used to treat localized forms of the disease. In choosing the best anti-fungal agent, efficacy, safety and and economics should always be considered by every physician.

There has been no reported or published clinical trial on the efficacy of either antimicrobial or anti-fungal properties of Moringa oleifera. This prompted the investigator to pursue this study.

PROBLEM

To determine the efficacy and safety of *Moringa oleifera* (Malunggay) in the treatment of tinea corporis infection among patients at East Avenue Medical Center Department of Dermatology.

SPECIFIC OBJECTIVES

1. To determine the efficacy of Malunggay cream in the treatment of tinea corporis in comparison with placebo using the following parameters:

    a. Clinical Cure
        i. Erythema
        ii. Pruritus
        iii. Scaling

    b. Microscopic
        i. KOH smear positive
        ii. KOH smear negative

2. To determie the adverse reactions to malunggay cream.

MATERIALS & METHODS

INCLUSION CRITERIA:

- All patients 12 years old to 50 years old seen at the Department of Dermatology, Out-Patient Department, East Avenue Medical Center, between November 2008 and June 2009.

- In good physical health, with no history of systemic diseases.

- No prior treatment.

- Lesions should be erythematous, well-defined, dry, scaly and pruritic plaques with active borders.

- Positive for Potassium hydroxide (KOH) smears.

METHODOLOGY

DESIGN: A double-blind, randomized placebo-controlled clinical trial within patients and between groups in the Department of Dermatology, OPD at East Avenue Medical Center.

PATIENTS/RESPONDENTS: Patients 12 to 50 years old with clinically and microscopically positive tinea corporis.

In the estimation of the sample size, the researcher used an alpha level of 0.05 and statistical power level of 70%, and arrived with a required minimum sample size of 32 and a minimum sample size per group of 16.

STUDY PROCEDURE: Informed written consent from patients and parent/guardian in patients 12-17 years old was obtained. Patients were randomly assigned to 2 groups as they came. Each patient is asked to choose a number between 1-150 from a brown envelop, facilitated by a research assistant. Those who picked an even number will be assigned to group A, while those who picked an odd number will be assigned to group B. Each group was assigned to apply the creams 2 times a day after bath over the lesions with at least one centimeter extension to the normal skin surrounding the lesion. Neither the physician nor patients knew the treatment assignment of each group. Patients were asked to follow-up after 1 week for any adverse effects, and will be re-assessed after 4 weeks of treatment. Clinical assessment parameters are as follows: 1. Erythema; 2. Pruritus; 3. Scaling. Severity grading is as follows: 0- none, 1- mild, 2-moderate and 3- severe.

KOH smear on initial visit and after 4 weeks of treatment will be obtained. Adverse reactions will be noted as well. Photographs of patients on initial visit and after 4 weeks will be gathered as well.

Compounding of Malunggay Cream

Malunggay leaf extract was mixed into cream to make a 1% mixture by a licensed pharmacist and placed into 10g white plastic containers. Placebo (vehicle) will be packaged just the same. Creams will be labeled neither A and B. The color and smell of both creams were indistinguishable.

All patients signed a written consent (parent or guardian for patients 12-17 years old), and filled up a personal data sheet. On initial visit, KOH smear of their lesion was obtained and clinical assessment of their lesions was done by the research assistant. Clinical parameters being presence of erythema, pruritus and scaling and with severity grading from 0-3, none to severe respectively.

Patients were randomly assigned to the experimental group (Malunggay cream) and to the placebo group (vehicle). All creams were placed in similar white containers previously marked. They were instructed to apply the creams 2 times a day after bath over the lesions with at least one centimeter extension to the normal skin surrounding the lesion. Standard verbal instructions were given regarding proper application. Patients were asked to follow-up weekly for 4 weeks. Photographs were taken at baseline and on subsequent follow-ups using a Canon Powershot 5.0 mega pixel digital camera.

At the end of the study period, patients under the vehicle group will be treated accordingly by an antifungal cream, provided by the researcher. Those under the experimental group, who did not improve or was not treated, will be given the same standard antifungal treatment as well. This information is included in the written consent provided at the start of the study period.

Evaluation

Patients were followed-up for assessment and for any adverse reactions for 4 consecutive weeks. The research assistant evaluates improvement using the clinical parameters. At the end of the study period (4th week) a repeat KOH smear was done and evaluated by another research assistant.

Statistical Analysis

The data were compared using the Friedman's Two-way ANOVA and Wilcoxon Rank Signed Test for the clinical parameters and Mc Nemar's Test and chi-square for the KOH smear results.

DATA AND RESULTS

Demographic Profile:

Table 1: Gender Distribution by Group

GENDER	GROUP A (Placebo)	GROUP B (Moringa)
Male	10 (62.5%)	11 (61.11%)
Female	6 (37.5%)	7 (38.88%)
Total	16	18

A total of 40 patients were included in this study. Among this original number, 34 patients completed the treatment period, and 6 patients were dropped from the study (lost to follow-up). In the placebo group (Group A), 16 patients completed the study, 62.5% of whom were males while 37.5% of the total were females. In the Moringa group (Group B), 18 patients finished the treatment period. Among the participants, 61.11% were males while the remaining 38.88% were females.

Table 2. Age Distribution of Patients By Group

AGE DISTRIBUTION	GROUP A (Placebo)	GROUP B (Moringa)
12-20	3 (18.75%)	2 (11.11%)
21-30	4 (25%)	3 (16.67%)
31-40	4 (25%)	7 (38.89%)
41-50	5 (31.25%)	6 (33.33%)
Total	16	18

In this table, it shows that in the placebo group, majority of the patients (31.25%) belong to the 41-50 age group, while 18.75% came from the 12-20 age group. In the Moringa group, majority of the patients (38.89%) belong to the 31-40 age group, while only 11.11% came from the 12-20 age group.

Response to treatment:

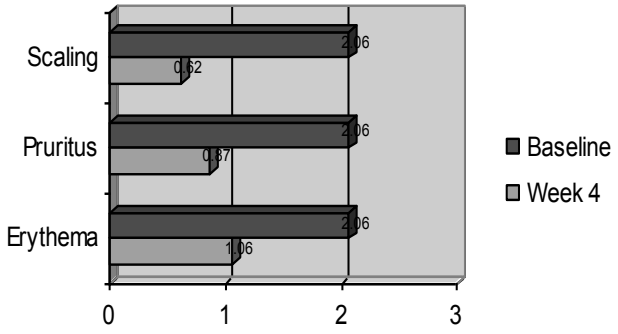


Figure 1. Mean Scores of Improvement of Clinical Parameters (Placebo Group)

This figure shows that among the 3 parameters, all mean scores decreased from baseline to week 4. Scaling showed to have decreased markedly, while erythema decreased the least among the clinical parameters.

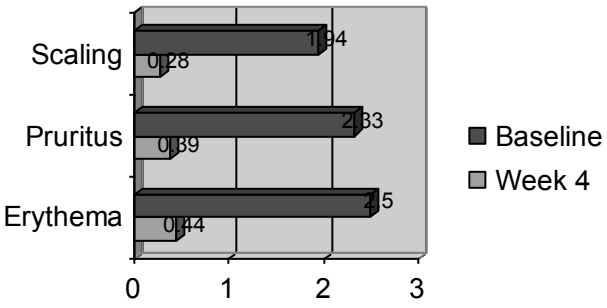


Figure 2. Mean Scores of Improvement of Clinical Parameters (Moringa Group)

This figure shows that in the Moringa group, all 3 parameters improved markedly from baseline to the end of treatment. Scaling improved the most, while erythema showed least improvement compared to pruritus and scaling.

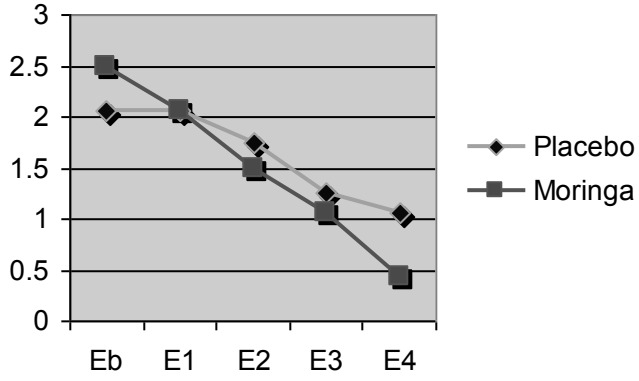


Figure 3. Comparison of Mean Score in Erythema Between Groups

This figure shows that between groups, mean score of improvement was comparable at week 1. During week 2 until end of treatment, improvement in erythema was observed more in the moringa group.

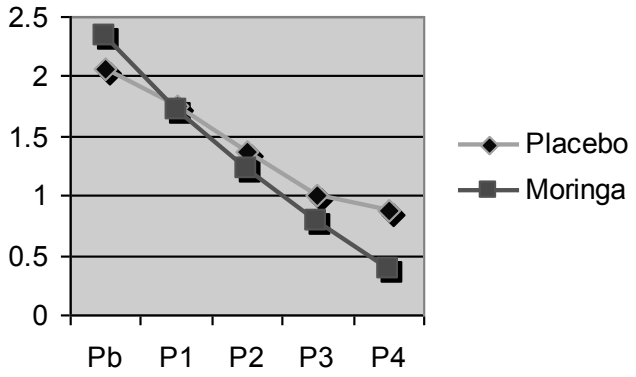


Figure 4. Comparison of Mean Score in Pruritus Between Groups

Both groups showed improvement in terms of pruritus from baseline to week 4. Between the groups, patients under Moringa group showed more improvement from baseline until end of study period.

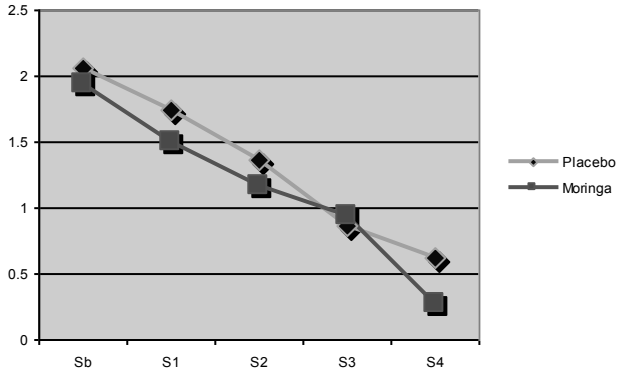


Figure 5. Comparison of Mean Score in Scaling Between Groups

Both groups showed improvement in terms of scaling, from baseline to week 4. Marked improvement was observed in Moringa group from week 3 of study period until end of study.

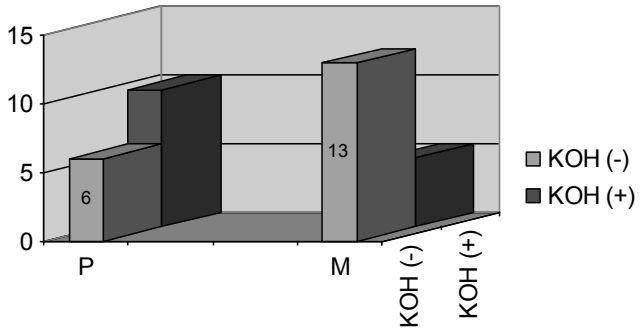


Figure 6. KOH Smear Results at Week 4 Between Groups

This figure shows that at the end of the study period, more patients in the Moringa group showed negative KOH smears at the end of the study.

Analytical Statistics

Table 3: Results of Friedman's Two-way ANOVA on Clinical Parameters (Placebo Group)

Friedman Statistic	p value	Decision
154.5625	26.30	Not statistically significant

Table 4: Results of Friedman's Two-way ANOVA on Clinical Parameters (Moringa Group)

Friedman Statistic	p value	Decision
86.9444	28.869	Not statistically significant

Table 3 & 4 show that among groups, improvement in the clinical parameters (erythema, pruritus & scaling) are not statistically significant.

Table 5: Results of Wilcoxon Rank Signed Test on clinical parameters between Baseline scores & Week 4 scores (Placebo Group)

PARAMETERS	t value	Decision
Erythema	9.405	No significant difference
Pruritus	36.600	No significant difference
Scaling	8.73	No significant difference

Critical t value: 2.131

Table 6: Results of Wilcoxon Rank Signed Test on clinical parameters between Baseline scores & Week 4 scores (Moringa Group)

PARAMETERS	t value	Decision
Erythema	9.380	No significant difference
Pruritus	9.977	No significant difference
Scaling	9.775	No significant difference

Critical t value: 2.11

Table 5 & 6 show that at the end of the study, improvement in clinical parameters between baseline & week 4 among groups, are not statistically significant.

Table 7: KOH results at Week 4 (End of Treatment Period)

	KOH (+)	KOH (-)	TOTAL
Placebo Group	10	6	16
Moringa Group	5	13	18
Total	15	19	34

McNemars Test

$X^2 = (B-C)^2 / B + C$

$= (6-5)^2 / 6 + 5$

$= 1/11$

$X=0.090909$

Critical Value = 3.841

$0.090909 < 3.841$

Therefore: accept null hypothesis, meaning the "drug" has NO impact on the KOH results.

Table 8. Results of chi-square test on the KOH smears

Parameter	Value	df	p value
KOH smear	4.14	1	0.04

KOH smear was used at the start of the study as part of the inclusion criteria. All patients with positive smears were included. At the end of the study the placebo group showed a cure rate of 37.5% while the Moringa group had a cure rate of 72.2% (Figure 6). Results showed that there was a significant difference between the cure rates of placebo group and Moringa group using the chi-square test.

Adverse Reactions

Throughout the study period, only 3 patients from the moringa group complained of increase in pruritus during the first week of treatment, which eventually improved as the study progressed.

DISCUSSION

In the early years, M. oleifera has been planted in large areas in Asia especially in Taiwan and main land China. Most people in these countries have been using the seeds of Moringa as an herbal treatment for athlete's foot and tinea, and discovered that they were effective treatments.[1] An in vitro study, identified 41 compounds in the Moringa crude extracts. In general, heneicosane (17.41%), E-phytol (7.66%) and 1-[2,3,6-trimethyl-phenyl] -2 butanone (3.44%) were the major components of the essential oil of Moringa leaf. Interestingly, there had been no single compound identified to have antifungal activity acting alone. Both benzaldehyde and indole likely might possess antifungal activities, they are also materials nontoxic to human.[1]

A study of the morphological change of the cell, to study the cell lysis mechanism was done. In this study, crude extracts was used to study the shape change of Trichophyton rubrum cells using Transmission electron microscopy (TEM). Fungal cells were treated with crude extracts of Moringa oleifera for 24 hours. Results show that the cytoplasmic membrane of the fungal cell was ruptured and the intracellular components were seriously damaged after treatment. This might indicate that extract compounds interact with the lipid bilayers in membranes leading to subsequent separation of the two membranes, water traverses then cell swells leading to death. [1]

Another study showed that aqueous extract of M. oleifera leaves possess significant antimicrobial activity against positive and negative fungal species. [2]

There were also studies done to evaluate the therapeutic properties of the seeds and leaves of M. oleifera as herbal medicines. Ethanol extracts showed anti-fungal activities in vitro against dermatophytes such as Trichophyton rubrum, Trichophyton mentagrophytes, Epidermophyton floccosum, and Microsporum canis. [4] Recent studies showed that a total of 44 compounds from the recently reported 41 compounds, were isolated from the extracts, which can be utilized in the future in the development of anti-skin disease treatment.[4] Crude extracts showed different MICs (Minimum inhibition concentration) in different fungi, 1.6 mg/ml for Trichophyton rubrum, 0.8 mg/ml Trichophyton mentagrophytes, 0.4 mg/ml Microsporum canis, 0.2mg/ml for Epidermophyton floccossum.[1]

A study which purports to evaluate the safety of the aqueous extract of the leaves of M. oleifera in rats concluded that the plant is relatively safe both for nutritional and medicinal uses. [3]

Tinea corporis refers to dermatophyte infections of the trunk, legs, arms and neck. Most commonly caused by Trichophyton rubrum, M. canis and T. tonsurans. Infection may be through autoinoculation from other parts of the body like from tinea pedis and tinea capitis. Contact with animals or contaminated soil may also be sources of infection. Definite diagnosis may be through KOH smear and culture. Topical antifungal preparations

may be effective in the treatment of dermatophytoses of the skin. Preparations are applied 2 times a day to the involved area optimally for 4 weeks including at least 1 week after lesions have cleared. The topical medications are comparable and are differentiated only by cost, base, vehicle and antifungal activity. Among the treatment options are the imidazoles, allylamines and naphthionates.[4]

CONCLUSION

This study showed that Moringa oleifera could be an effective treatment of tinea corporis. Although it showed improvement in the mean scores of the clinical parameters namely erythema, pruritus and scaling from baseline until end of study period, statistics showed that there was no significant difference among groups. Mycologic cure in terms of KOH smear, showed superior results in the Moringa group compared to placebo group, although appeared to be not statistically significant.

RECOMMENDATIONS

1. Studies using extracts of seeds and roots of Moringa oleifera may also be used in the future to know their antifungal activity in vivo.

2. Different concentrations of the extracts may be used and compared as well, to know the most effective concentrations that may give the highest cure rates.

3. Follow-up of patients after the 4-week treatment period should also be done to assess recurrence rates.

4. A larger study population using a randomized clinical trial is also recommended.

5. A randomized clinical trial comparing Moringa oleifera with a standard treatment is also recommended.

REFERENCES

1. Chen, H. & Chuang, P. Moringa crude extracts and their derived fractions with antifungal activities. Bioresour Technol 2007; 98:232-6.

2. Dahot, M. Antimicrobial Activity of small protein of Moringa oleifera leaves. Journal of Islamic Academy of Sciences 11:1, 27-32, 1998.

3. Adedapo, A. et al. Safety of the Aqueous Extract of the Leaves of Moringa oleifera in rats. Journal of Medicinal Plants Research Vol. 3(8) 586-591, 2009.

4. Wolff, K., et al. Dermatology in General Medicine, 2007.

5. Jabeen, R., et al. Microscopic Evaluation of the Antimicrobial Activity of Seed Extracts of Moringa oleifera. Pak J. Bot., 40(4): 1349-1358, 2008.

6. Fahey, J. Moringa oleifera: A review of the Medical Evidence for Its Nutritional, Therapeutic, and Prophylactic Properties. Trees for Life Journal, 1:5, 2005.

APPENDICES

Clinical Parameters:

Clinical Severity Score

0 – None

1 – Mild

2 – Moderate

3 – Severe

A. Comparison of Baseline and Treatment by Group (At baseline to Week 4)

ERYTHEMA: GROUP A

Patient	*Age*	*Gender*	*Eb*	*E1*	*E2*	*E3*	*E4*
P.L.	19	Male	2	2	2	2	2
T.M.	26	Male	1	2	1	1	1
E.D.	38	Male	1	1	1	0	0
R.R.	49	Male	2	2	2	1	1
C.G.	34	Female	3	3	2	2	2
D.G.	42	Female	2	2	2	1	1
J.R.	24	Male	2	2	2	1	1
D.J.	33	Female	3	3	2	2	2
K.S.	44	Female	2	2	2	1	1
D.F.	18	Male	2	2	2	1	1
E.T.	20	Female	3	3	3	2	2
J.D.	29	Male	1	1	1	0	0
C.S.	21	Male	1	1	1	1	0
R.G.	39	Female	3	2	2	2	1
A.B.	47	Male	2	2	1	1	1
D.R.	42	Male	3	3	2	2	1

ERYTHEMA: GROUP B

Patient	*Age*	*Gender*	*Eb*	*E1*	*E2*	*E3*	*E4*
D.M.	20	Male	3	2	2	1	0
A.B	29	Male	2	2	2	1	1
B.N.	31	Male	3	3	2	1	0
T.Y.	36	Female	2	2	1	1	1
G.T.	44	Female	2	2	1	1	0
R.H.	33	Male	3	2	2	2	1
J.F.	48	Male	2	2	1	1	0
P.R.	50	Female	3	2	2	1	1
P.T.	34	Male	2	2	1	1	0
R.S.	39	Female	3	2	2	2	1
P.C.	33	Female	2	2	1	1	0
M.E.	47	Female	3	2	2	1	1
C.B.	42	Male	2	2	1	1	0
R.T.	49	Male	3	3	2	1	1
A.M.	24	Female	3	2	2	1	1
G.M.	38	Male	2	2	1	1	0
T.P.	29	Male	3	2	1	1	0
N.R.	22	Male	2	1	1	0	0

PRURITUS: GROUP A

Patient	*Age*	*Gender*	*Pb*	*P1*	*P2*	*P3*	*P4*
P.L.	19	Male	2	1	1	1	1
T.M.	26	Male	1	1	1	0	0
E.D.	38	Male	1	1	1	0	0
R.R.	49	Male	2	2	1	1	1
C.G.	34	Female	3	2	2	1	1
D.G.	42	Female	2	2	1	1	1
J.R.	24	Male	2	2	1	1	1
D.J.	33	Female	3	2	2	1	1
K.S.	44	Female	2	2	1	1	1
D.F.	18	Male	2	1	1	1	1
E.T.	20	Female	3	3	3	2	2
J.D.	29	Male	1	1	1	0	0
C.S.	21	Male	1	1	1	1	0
R.G.	39	Female	3	2	2	2	1
A.B.	47	Male	2	2	1	1	1
D.R.	42	Male	3	3	2	2	2

PRURITUS: GROUP B

Patient	*Age*	*Gender*	*Pb*	*P1*	*P2*	*P3*	*P4*
D.M.	20	Male	2	2	1	1	0
A.B	29	Male	2	1	1	0	0
B.N.	31	Male	3	2	2	1	0
T.Y.	36	Female	2	2	1	1	0
G.T.	44	Female	2	1	1	1	0
R.H.	33	Male	3	2	1	1	1
J.F.	48	Male	2	1	1	1	0
P.R.	50	Female	2	2	1	1	1
P.T.	34	Male	2	1	1	1	0
R.S.	39	Female	3	2	1	1	1
P.C.	33	Female	2	1	1	1	0
M.E.	47	Female	2	2	1	1	1
C.B.	42	Male	2	2	2	1	1
R.T.	49	Male	3	3	2	1	1
A.M.	24	Female	3	2	2	1	1
G.M.	38	Male	2	2	1	0	0
T.P.	29	Male	3	2	1	0	0
N.R.	22	Male	2	1	1	0	0

SCALING: GROUP A

Patient	*Age*	*Gender*	*Sb*	*S1*	*S2*	*S3*	*S4*
P.L.	19	Male	2	1	1	1	1
T.M.	26	Male	1	1	1	0	0
E.D.	38	Male	1	1	1	0	0
R.R.	49	Male	2	2	1	1	1
C.G.	34	Female	3	2	2	1	1
D.G.	42	Female	2	2	1	1	1
J.R.	24	Male	2	2	1	1	1
D.J.	33	Female	3	2	2	1	1
K.S.	44	Female	2	2	1	1	1
D.F.	18	Male	2	1	1	1	1
E.T.	20	Female	3	3	3	2	2
J.D.	29	Male	1	1	1	0	0
C.S.	21	Male	1	1	1	1	0
R.G.	39	Female	3	2	2	1	0
A.B.	47	Male	2	2	1	1	0
D.R.	42	Male	3	3	2	1	0

SCALING: GROUP B

Patient	*Age*	*Gender*	*Sb*	*S1*	*S2*	*S3*	*S4*
D.M.	20	Male	1	1	1	1	0
A.B	29	Male	2	1	1	1	1
B.N.	31	Male	2	1	1	1	0
T.Y.	36	Female	2	2	1	1	0
G.T.	44	Female	1	1	1	1	0
R.H.	33	Male	2	2	1	1	0
J.F.	48	Male	2	1	1	1	0
P.R.	50	Female	2	1	1	1	0
P.T.	34	Male	1	1	1	1	0
R.S.	39	Female	2	2	1	1	0
P.C.	33	Male	2	1	1	1	0
M.E.	47	Female	2	1	1	1	0
C.B.	42	Male	2	2	2	1	1
R.T.	49	Male	3	3	2	1	1
A.M.	24	Female	3	2	2	1	1
G.M.	38	Male	2	2	1	1	0
T.P.	29	Male	2	2	1	0	1
N.R.	22	Male	2	1	1	1	0

B. Comparison of Baseline and Treatment Values by Group

Group A (n=16)

Clinical Parameters		None	Mild	Moderate	Severe
Erythema	Baseline	0	4	7	5
	Week 4	3	9	4	0
Pruritus	Baseline	0	4	7	5
	Week 4	4	10	2	0
Scaling	Baseline	0	4	7	5
	Week 4	7	8	1	0

Group B (n=18)

Clinical Parameters		None	Mild	Moderate	Severe
Erythema	Baseline	0	0	9	7
	Week 4	10	8	0	0
Pruritus	Baseline	0	0	12	6
	Week 4	11	7	0	0
Scaling	Baseline	0	3	13	2
	Week 4	13	5	0	0

C. KOH smear Baseline and Week 4

Group A

Patient	*Age*	*Gender*	*Baseline KOH*	*KOH at Week 4*
P.L.	19	Male	(+)	(+)
T.M.	26	Male	(+)	(-)
E.D.	38	Male	(+)	(-)
R.R.	49	Male	(+)	(+)
C.G.	34	Female	(+)	(+)
D.G.	42	Female	(+)	(+)
J.R.	24	Male	(+)	(+)
D.J.	33	Female	(+)	(+)
K.S.	44	Female	(+)	(+)
D.F.	18	Male	(+)	(-)
E.T.	20	Female	(+)	(+)
J.D.	29	Male	(+)	(-)
C.S.	21	Male	(+)	(-)
R.G.	39	Female	(+)	(+)
A.B.	47	Male	(+)	(-)
D.R.	42	Male	(+)	(+)

Group B

Patient	*Age*	*Gender*	*Baseline KOH*	*KOH at Week 4*
D.M.	20	Male	(+)	(-)
A.B	29	Male	(+)	(+)
B.N.	31	Male	(+)	(-)
T.Y.	36	Female	(+)	(-)
G.T.	44	Female	(+)	(-)
R.H.	33	Male	(+)	(-)
J.F.	48	Male	(+)	(-)
P.R.	50	Female	(+)	(-)
P.T.	34	Male	(+)	(+)
R.S.	39	Female	(+)	(-)
P.C.	33	Female	(+)	(-)
M.E.	47	Female	(+)	(+)
C.B.	42	Male	(+)	(-)
R.T.	49	Male	(+)	(+)
A.M.	24	Female	(+)	(+)
G.M.	38	Male	(+)	(-)
T.P.	29	Male	(+)	(-)
N.R.	22	Male	(+)	(-)

WRITTEN INFORMED CONSENT

Pahintulot ng Pasyente

Name *(Pangalan):*
Age *(Edad):*
Gender *(Kasarian):*
Occupation *(Trabaho):*

I have been informed of the nature of the study, and the potential benefits and hazards of the intervention/ treatment.
Naipagbigay alam sa akin ang uri ng pag-aaral na ito, pati na ang mga kabutihan at mga panganib na maaaring idulot ng interbensyon/gamutan.

I hereby voluntarily give my consent to undergo this clinical investigation under the supervision of Dr. Charo F. De Guzman and her co-researchers.
Kusang loob kong ibinibigay ang aking pahintulot na sumailalim sa pananaliksik na ito sa pamamahala ni Dr. Charo F. De Guzman at ng kaniyang mga kasamang mananaliksik.

I have been informed that I may withdraw from this clinical investigation anytime without prejudice against me.
Ipinagbigay alam sa akin na maaari kong bawiin ang aking partisipasyon sa pag-aaral na ito anumang oras na naisin ko, na hindi mamasamain ng mga doctor na namamahala sa pananaliksik na ito.

I have been given the chance to ask questions about the use of the intervention and understand and accept the answers provided.
Ako ay binigyan ng pagkakataon ng makapagtanong tungkol sa interbensyon na gagawin at aking naintindihan at tinanggap ang tugon ukol dito.

I was informed that at the end of the study period (4 weeks), if my condition worsened or persisted, I will be treated accordingly.
Ipinagbigay alam sa akin na sa pagtatapos ng pag-aaral na ito (4 na linggo), kung ang aking kundisyon ay grumabe o nanatili, ako ay bibigyan ng karampatang gamutan.

Signature of Patient/*Lagda ng Pasyente:* _____
Date: _____

I being the physician, confirm that I have fully explained to the patient the nature, purpose and risks of the interventions being used in this study.

Ako, bilang manggagamot, ay nagpapatotoo na ganap na naipaliwanag sa pasyente and uri, layunin at maaaring maging epekto na dulot ng interbensyong ginamit sa pag-aaral na ito.

Charo Fionna F. De Guzman-Castro, M.D.
Date: _____

Clinical Assessment

0 – None 1 – Mild 2 – Moderate 3 – Severe

Patient's Name: _____ Group: _____ Week Number: _____
A. Erythema _____
B. Pruritus _____
C. Scaling _____

KOH ( )

Adverse effects: _____

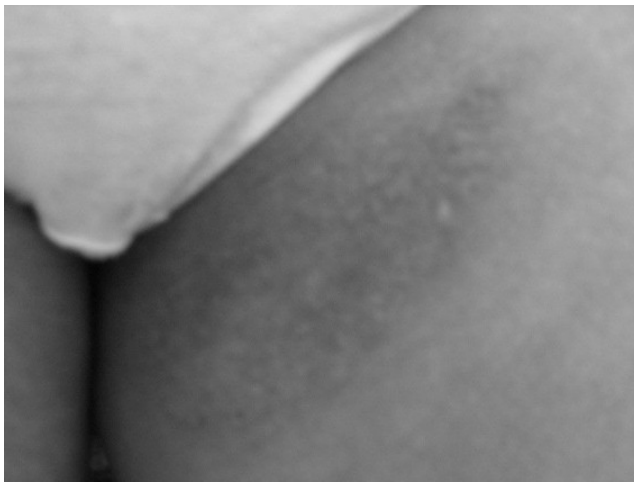
Improvement Score

0 – None (Wala) 1 – Mild (Bahagya) 2 – Moderate (Katamtaman) 3 – Severe (Sobra)

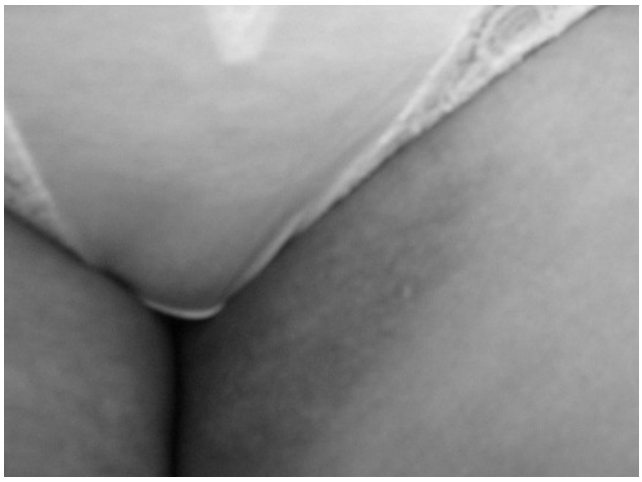
Patient's Name: _____ Group: _____ Week Number: _____

D. Erythema (Pamumula) _____
E. Pruritus (Pangangati) _____
F. Scaling (Kaliskis) _____

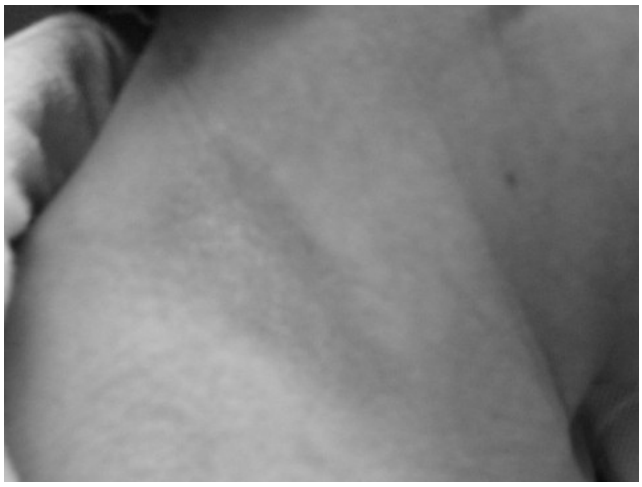
GROUP A: PLACEBO



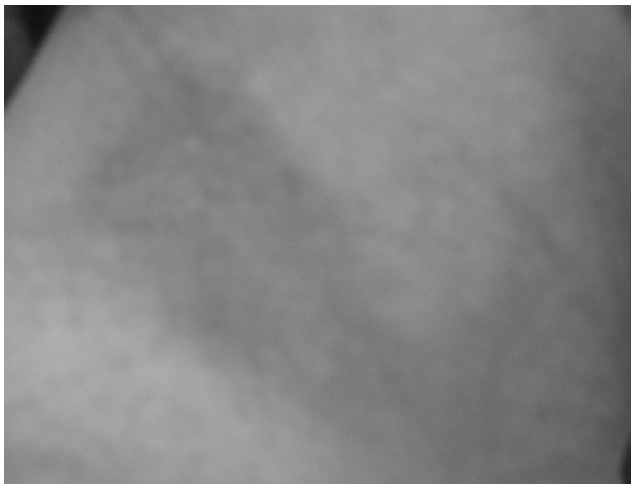
C.G. Baseline



C.G. Week 4

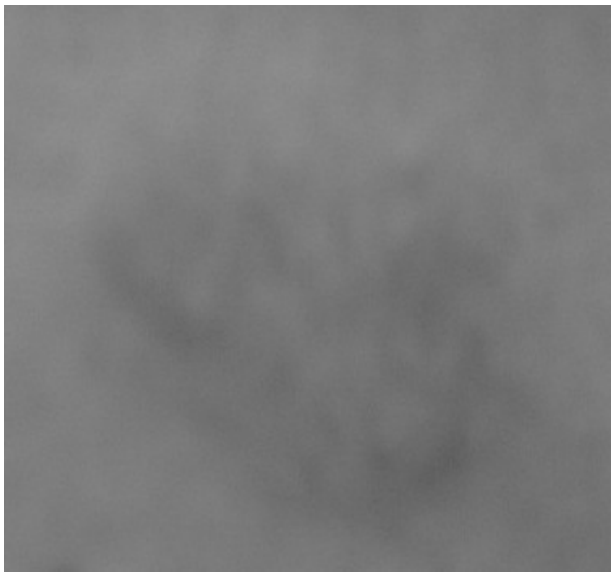


P.L. Baseline

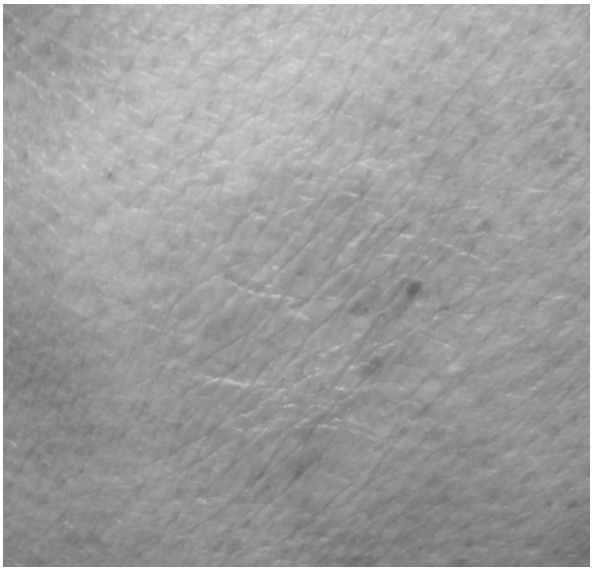


P.L. Week 4

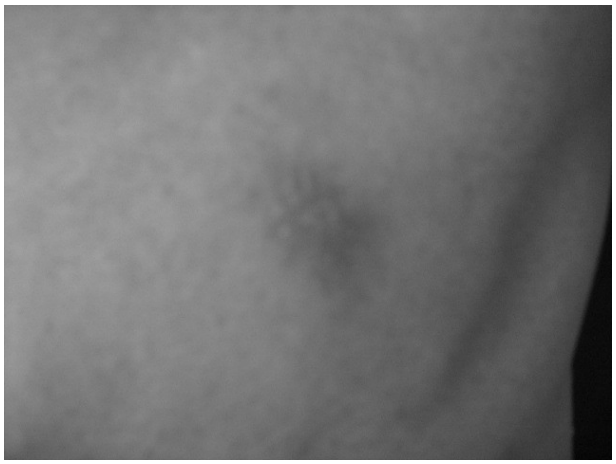
GROUP B: MORINGA



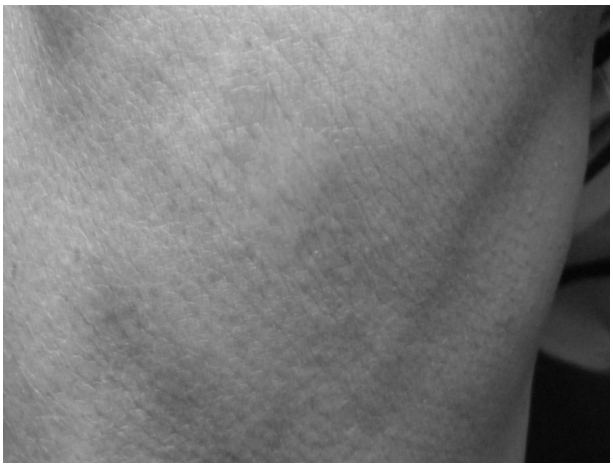
D.M. Baseline



D.M. Week 4



T.Y. Baseline



T.Y. Week 4