THE MYSTERY OF SALIVARY GLAND TUMORS

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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.

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ILLUSTRATIONS

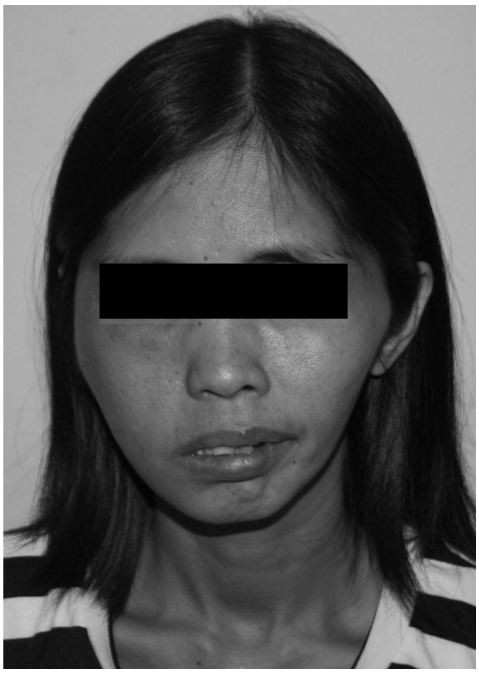


Figure 1. The actual photo of the first case, presenting a mass at the right pre-auricular area which was approximately 4x5 cm firm, fixed and non-tender mass at right pre-auricular area with facial paralysis.

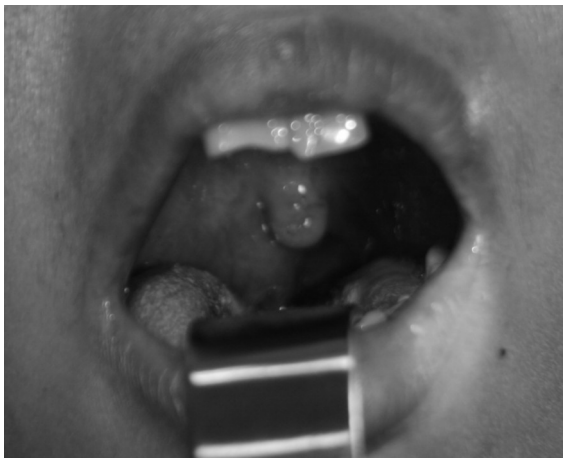
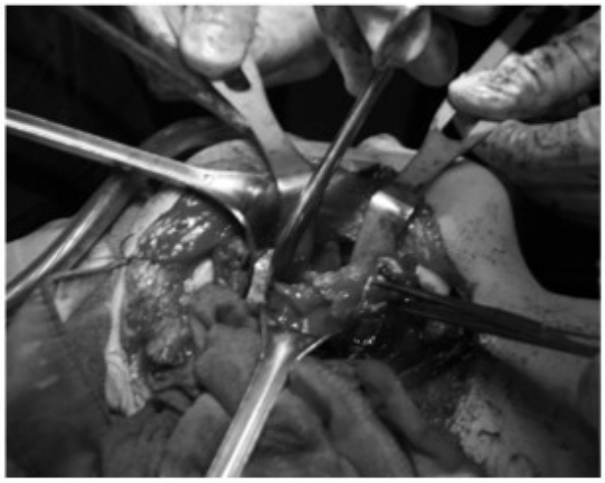


Figure 2. Oral cavity examination of the first case showing bulging buccal mass, which was non-tender protruding up to the right anterior tonsillar fossa.



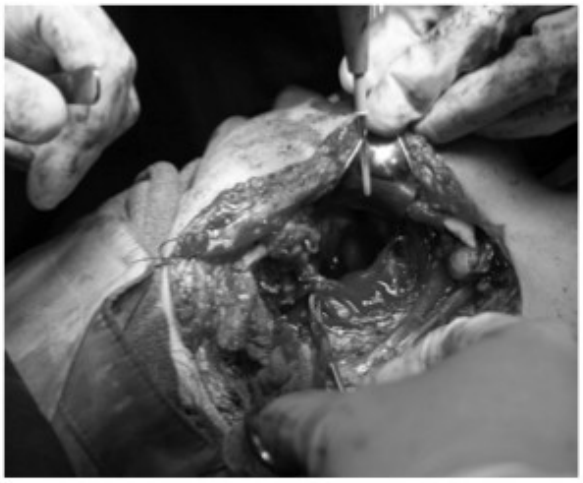


Figure 3. The actual Intra-operative photo of Case 1, showing a Wide Excision of Parotid mass, right; Segmental Mandibulectomy.

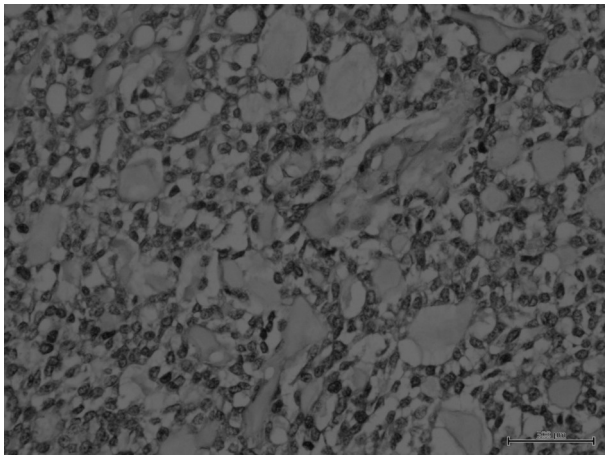


Figure 4. Photomicrograph of the first case, showing nests and columns of cells of rather bland appearance arranged concentrically around gland-like spaces filled with homogenous eosinophilic material, signed out as Adenoid Cystic Carcinoma, right parotid.

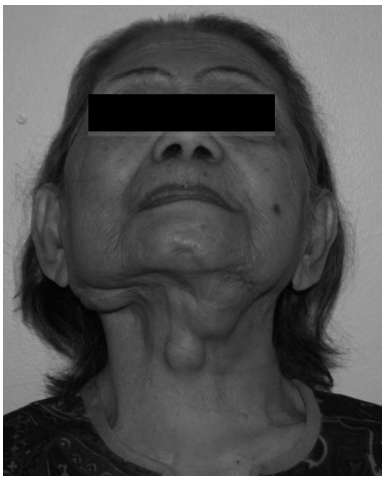


Figure 5. The actual photo of case 2, showing left and right submandibular mass each measuring approximately 4x4cm, firm, non-tender and a 2x2x firm, non-tender, movable mass at midline anterior neck.

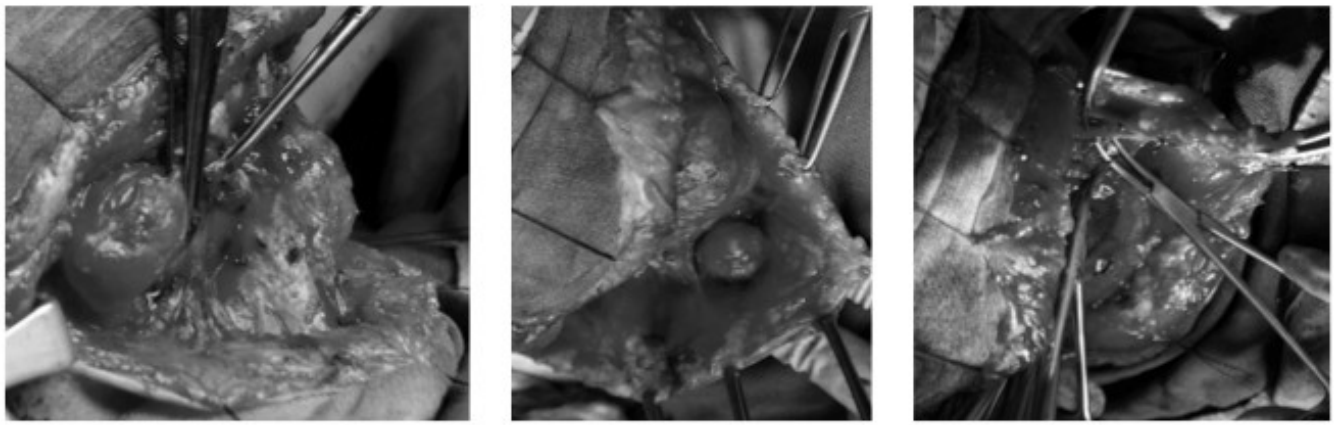


Figure 6. The actual Intra-operative photo of the second case, showing an excision of Submandibular mass, bilateral with Selective Neck Dissection, right levels I, II and III was performed.

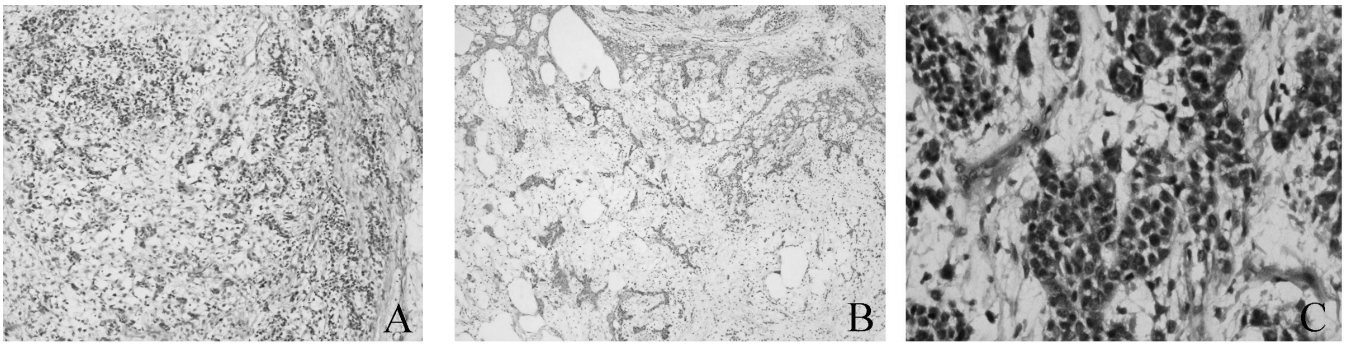


Figure 7. Photomicrograph of the second case.
A, shows circumscribed tumor tissues with biphasic appearance, epithelial component is mostly glandular in appearance with sheets of squamoid cells, right submandibular gland.
B, circumscribed tumor tissues with biphasic appearance, epithelial component are 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.