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Warm greetings from the Philippine Medical Association!

Physicians from healthcare institutions, specialty organizations, medical schools and universities, diligently prepared and completed their papers par excellence. Thus, these research papers are well deserving to be published at this issue of the Journal of the Philippine Medical Association.

PMA strongly supports and promotes the Continuing Professional Development Law or Republic Act 10912 to enhance the practice of the medical profession. In this digital age with rapid advances in technology, our physicians and specialists must have the knowledge and expertise in their respective fields of specialization.

Research has always been an important tool in updating physicians on the current trends and directions in various fields of practice using evidence based medicine. It is one of the components of continuous learning set by Continuing Professional Development which aims to uphold the competencies of clinical practice.

Physicians are strongly encouraged to engage in research and keep abreast with innovations in coming up with valuable research papers. It is our hope that this journal will be a source of valuable pearls of knowledge that will result in high quality healthcare for all Filipinos.

JOSE P. SANTIAGO, JR., MD
President, Philippine Medical Association

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Instruction for Authors

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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.

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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.

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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.

Accompanied 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

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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.

Prevalence, Epidemiology and Clinical Characteristics of Melasma in Philippine Dermatology Patients: A Multicenter, Cross-Sectional Study*

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ABSTRACT

BACKGROUND: Melasma is an acquired hyperpigmentary disorder occurring in the sun-exposed areas of the face and neck. There is little information on its prevalence, epidemiology and clinical characteristics in the Philippines.

OBJECTIVE: To determine the prevalence, epidemiology and clinical characteristics of melasma in Philippine dermatology patients

METHODS: This was a multicenter, cross-sectional study conducted from July to December 2013. The investigators determined the prevalence of melasma in 12,068 dermatology patients from 6 government hospitals and private centers in Metro Manila, Philippines. The melasma patients, aged 18 years and above were examined and given self-administered questionnaires to determine the epidemiological and clinical characteristics of their melasma.

RESULTS: Of the 12,068 dermatology patients who were seen at the selected hospitals and private centers, 153 (1.26%) were clinically diagnosed with melasma. Majority of the melasma patients were Filipinos (73.20%), aged 41 -50 years old (37.91%), with an average age of 42.40 $\pm$ 9.68 years, and Fitzpatrick skin types III and IV (29.41% and 57.52%, respectively). Melasma was more prevalent in females (81.70%), wherein majority had a prior history of pregnancy (76.8% of the females). Oral contraceptive use was also reported in 37.6% of the female patients and 63.83% of those who have used OCP, have used it for only 1 year or less. Majority had no thyroid disease (75.16%) and daily sun exposure was limited to 1 hr or less for most patients (43.14%). Their melasma was mostly malar in distribution (60.13%), epidermal (61.44%), and mild (51.63%) to moderate (27.45%) in severity. The average mMASI score was 4.63 $\pm$ 3.32.

CONCLUSION: Prevalence of melasma was low among the Philippine dermatology patients sampled. Majority of the melasma patients were Filipinos, aged 41-50 years old, with Fitzpatrick skin type IV, limited sun exposure and no thyroid disease. They were mostly females, with a prior history of pregnancy. Their melasma was mostly malar, epidermal, and mild in severity. These descriptive data can serve as baseline information for further studies on melasma in the Philippines.

KEY WORDS: *melasma, Asian skin, chloasma, Philippines, Filipinos*

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INTRODUCTION

Melasma is an acquired hyperpigmentary skin disorder characterized by irregular light to dark brown macules occurring in sun-exposed areas of the skin, mostly on the face and neck.

The three clinical patterns of melasma are centrofacial, malar, and mandibular. The centrofacial pattern is the most common and consists of lesions on the forehead, cheeks, nose, upper lip, or chin. The malar pattern describes lesions located primarily on the cheeks and nose. The mandibular pattern consists of lesions on the ramus of the mandible.

Its histologic subtypes are: epidermal, dermal, and mixed. Wood's lamp evaluation is helpful in identifying these subtypes.

Pigmentation disorders like melasma often comprise a considerable percentage of the cases seeking dermatologic consult. Because it often occurs in the face, such pigmentary dermatoses have a significant impact on the patient's quality of life, prompting a demand for dermatological care. A study conducted in South East Asia reported that melasma accounted for 0.25 to 4% of patients seen in dermatology institutes--- 4% of dermatologic cases reported in Malaysia and 0.98% of cases reported in Indonesia. Despite being a common dermatologic complaint, the incidence of melasma in the population is not precisely known.

Melasma is more common in females (90%) than in males (10%). It affects mainly women of childbearing age (during menacme) (7), with peak incidence in patients aged 30 to 44 years based on the 1995 study conducted in South East Asia. It also occurs more frequently in more pigmented phenotypes (Fitzpatrick skin types IV-VI) such as Hispanic, Asian and African-American skin.

There are many factors that contribute to the pathogenesis of melasma. The most important of these are genetic predisposition, ultraviolet (UV) radiation and hormonal dysfunction.

Genetic predisposition is the most important risk factor for melasma while sun exposure is the most important triggering factor. UV radiation directly induces the increase in melanogenic activity, resulting in epidermal pigmentation. In intertropical regions where the level of UV radiation is higher, the population incidence of melasma is increased.

Hormonal changes involving sexual hormones (estrogen and progestin) such as in pregnancy, Combined Oral Contraceptive (COC) use and hormone replacement therapy, also trigger the appearance of melasma (1). This is attributed to elevations in the level of estrogen and progesterone which can lead to increased pigmentation. In a 2010 prospective study involving 197 patients in Tunisia, sun exposure was reported as the main aggravating or triggering factor by 84% of melasma patients, followed by COC use by 38% and pregnancy by 50%.

Melasma has also been associated with endocrinopathies and autoimmune thyroid diseases.

This study aimed to determine the prevalence, epidemiology and clinical characteristics of melasma in Philippine dermatology patients. With the increasing number of melasma cases seen in our clinical practice, we saw the need to investigate and gather more information on the prevalence and nature of this condition (epidemiological and clinical characteristics) in Philippine dermatology patients. This data will help us gain valuable insights into how we can more effectively manage melasma cases in our country.

MATERIALS AND METHODOLOGY

Trial Design

This was a multicenter, cross-sectional study on the prevalence, epidemiological and clinical characteristics of melasma among dermatology patients from 6 selected government hospitals and private clinics in Metro Manila, Philippines. This study was approved by the Institutional Review Board prior to commencement.

Participants

A total of 12,068 dermatology patients seen at the dermatology sections of 6 selected government hospitals and private clinics in Metro Manila, namely: the Research Institute for Tropical

Medicine (RITM), East Avenue Medical Center, Ospital ng Maynila, Asian Hospital Dermatology Department, Skin Care Solutions, and Casa Medica Health Clinic (in SM Southmall), were screened for prevalence of melasma and assessed for eligibility to participate in the succeeding parts of the study. Patients aged 18 years and above who were newly-diagnosed with melasma (regardless of sex and concomitant diseases) were recruited. Informed consent was obtained from the eligible patients prior to inclusion in the study. This study was conducted for a period of 6 months, from July to December 2013.

Interventions

The study had 3 parts. In Part I, the number of patients diagnosed with melasma and the total number of dermatology patients seen at the selected hospitals and clinics within the 6-month period were noted. From these data, the prevalence of melasma was calculated.

In Part II, the patients answered a questionnaire on demographic information and medical history, which was provided by the investigators during routine dermatologic consultation. The questionnaire was specially developed for this study. It was initially tested among 10 people aged 18 years and above for reliability.

Part III was a clinical assessment to determine the clinical profile of the melasma patients. The assessment and interview were conducted by the investigators, who were also dermatologists, during routine dermatologic consultation. Prior to commencement of the study, the investigators were trained in filling out the Case Report Form (CRF) and given a Fitzpatrick skin color chart to define the skin type of the patient.

Completed questionnaires and CRFs were collected once a week. The total number of patients seen each week per clinic/institution was documented.

Outcomes

The following study parameters were assessed by the investigators: a) prevalence of melasma, b) demographic information and medical history and, c) clinical profile of melasma patients.

Demographic information and medical history of patients included age, gender, race, presence of thyroid disease, history of pregnancy and oral contraceptive (OCP) use, duration of OCP use, and daily duration of sun exposure.

The clinical profile of patients consisted of the Fitzpatrick skin type, melasma classification, type of melasma (by Wood's Lamp examination) and melasma severity using the modified Melasma Area and Severity Index (mMASI). Permission was obtained from the University of Texas Southwestern Medical Center (Dallas, Texas, USA) to use this MASI Training Program ("Material") created by Dr. Amit Pandya.

The mMASI by Pandya *et al.* is a modification of the MASI, eliminating homogeneity as criterion because it had the lowest interrater agreement. It is computed by rating darkness and area of involvement of 4 areas of the face. The rating/score for each of the 4 areas are inserted into an equation, resulting in the final mMASI score. Based on a retrospective study of 79 patients, mean mMASI scores of 3.8, 6.5 and 8.9 corresponded to mild, moderate and severe melasma, respectively.

All data were entered in a database, subjected to range and validation checks and statistical analysis.

Sample Size

The prevalence of melasma among dermatology patients at RITM was 2.2%, 2.4% and 2.2% in 2010, 2011 and 2012, respectively. Using this data to estimate a prevalence rate of 3%, the minimum sample size required for this study was 4,477 patients. This was calculated using a confidence interval of 95% and a 1% desired width of the confidence interval. The total number of patients interviewed and examined in this study was 12,068.

Statistical Methods

Frequency and percentages were used to summarize qualitative variables such as classification of Fitzpatrick skin types, melasma classification and types of melasma. Means and standard deviations were computed for quantitative variables such as age and mMASI score. Missing values were not replaced nor estimated. Microsoft Excel 2016 was used for data processing and analysis.

RESULTS

Participants Flow

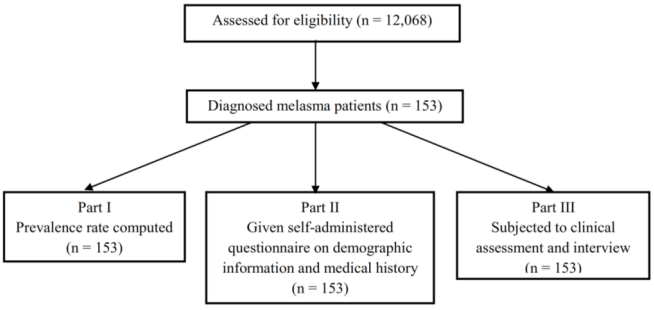

Figure 1. *Flowchart showing the screening and assessment of patients in the study*

Numbers Analyzed

Out of 12,068 dermatology patients seen at the dermatology departments of the selected hospitals and clinics, only 153 were clinically diagnosed with melasma (all newly-diagnosed) and were at least 18 years of age, making them eligible to participate in the current study. All 153 melasma patients were included in the computation for the prevalence rate, given the self-administered questionnaire and clinically assessed by the investigators. However, since participation in the survey is completely voluntary, patients are free to skip an item that they prefer not to answer or is not applicable to them. Hence, the missing data--- the total number of responses per item does not always add up to 153. Questions pertaining to pregnancy and OCP use were only answered by female participants (n=125) and the question regarding the duration of OCP use was only answered by those who have used OCP (n=47). Melasma classification based on distribution on the other hand, was not mutually exclusive. Some patients had one, two or all three types of melasma based on distribution (malar, forehead and centrofacial).

Outcomes and Estimation

Prevalence of Melasma

Out of 12,068 dermatology patients seen at the 6 selected government hospitals and private clinics, 153 (1.26%) were diagnosed with melasma.

Demographic Information and Medical History

Melasma patients were mostly 41 to 50 years old (58/153, 37.91%) and the average age was 42.40 ± 9.68 years. They were predominantly female (81.70%), and of Filipino descent (73.20%) (Table 1). The female to male ratio was 4.6:1.

Table 1. Demographic characteristics of melasma patients from selected hospitals and clinics in Metro Manila, Philippines (n = 153)

	Frequency (%); Mean ± SD
Age	42.40 ± 9.68
20 – 30	28 (18.30)
31 – 40	37 (24.18)
41 – 50	58 (37.91)
> 50	28 (18.30)
Missing data	2 (1.31)
Sex	
Male	27 (17.65)
Female	125 (81.70)
Missing data	1 (0.65)
Race	
Filipino	112 (73.20)
Chinese-Indonesian	1 (0.65)
Filipino-Chinese	1 (0.65)
Filipino-Spanish	1 (0.65)
Missing data	38 (24.84)

From the 125 females diagnosed with melasma, majority (96/125, 76.8%) had a prior history of pregnancy but only 47/125 (37.6%) have used oral contraceptives. Most of them (70/153, 56%) have not used OCP. OCP use lasted only one year or less for 30/47 (63.83%) of the patients who have used it.

Thyroid disease was present in only 25/153 (16.33%) of patients, which means majority (75.16%) had no thyroid problems. Although there are 13 missing data on thyroid condition, the number of patients without thyroid disease still comprised the majority. In terms of sun exposure, majority (66/153, 43.14%) reported a daily sun exposure of 30 minutes or less.

Table 2. Medical history of melasma patients from selected hospitals and clinics in Metro Manila, Philippines

	Frequency (%); Mean ± SD
Pregnancy (n=125)	
Yes	96 (76.8)
No	28 (22.4)
Missing data	1 (0.8)
Oral Contraceptive Use (n=125)	
Yes	47 (37.60)
No	70 (56.00)
Missing data	8 (6.40)
Duration of Oral Contraceptive Use in months (n=47)	
≤ 12	30 (63.83)
> 12	14 (29.79)
Missing data	3 (6.38)
Thyroid Disease (n=153)	
Yes	25 (16.34)
No	115 (75.16)
Missing data	13 (8.50)
Daily Duration of Sun Exposure in minutes (n=153)	
≤ 30	66 (43.14)
31 - 60	51 (33.33)
> 60	25 (16.34)
Missing data	11 (7.19)

Table 3. Clinical profile of melasma patients (n = 153)

Profile of Melasma	Frequency (%); Mean ± SD
Fitzpatrick Skin Type	
Type I	0
Type II	12 (7.84)
Type III	45 (29.41)
Type IV	88 (57.52)
Type V	5 (3.27)
Type VI	0
Missing data	3 (1.96)
Melasma Classification	
Malar	92 (60.13)
Forehead	35 (22.88)
Centrofacial	47 (30.72)
Type of Melasma (Wood's Lamp)	
Epidermal	94 (61.44)
Dermal	13 (8.50)
Mixed	38 (24.84)
Missing data	8 (5.23)
Melasma Severity	
Clear	3 (1.96)
Mild	79 (51.63)
Moderate	42 (27.45)
Severe	23 (15.03)
Missing data	6 (3.92)
mMASI Score	4.63 ± 3.32
< 3	55 (35.95)
3 - 6	57 (37.25)
> 6	38 (24.84)
Missing data	3 (1.96)

Clinical Profile of Melasma Patients

Based on Fitzpatrick skin type classification, the most common skin type was Type IV (88/153, 57.52%) followed by Type III (45/153, 29.41%) (Table 3). Melasma was more commonly epidermal by Wood's lamp examination (94/153, 61.44%) and malar based on distribution (92/153, 60.13%). In terms of severity, most patients presented with mild melasma (51.63%) followed by moderate severity (27.45%). The average mMASI score was 4.63 ± 3.32.

DISCUSSION

Results of this 6-month study showed a melasma prevalence of 1.26% (153 out of 12,068 patients) among dermatology patients from the 6 selected government hospitals and private centers in Metro Manila. Based on a 2014 melasma update, prevalence of melasma varies from 1.5% to 33.3%, depending on the population being studied. Given this range of prevalence rates, we could say that the melasma prevalence calculated in this study is low. However, it is not unusual. A study conducted in South East Asia reported a melasma prevalence of 0.25 to 4% among patients seen in dermatology institutes.

Melasma is more prevalent in females than in males. Although the generally accepted ratio of female to male predominance is 9:1, other studies have shown varying ratios such as 39:1 in Brazil and 21:1 in Singapore. In this study, the ratio is 4.6:1. This is very close to the 4:1 ratio reported in an Indian study of 312 patients. However, since this data is limited to dermatology patients, this ratio may also reflect the greater tendency of women to be more psychologically distressed by cosmetic disfigurement than men and to seek dermatologic consult.

In particular, it is women of childbearing age (during menacme) who are mostly affected by melasma. Hence, female sex hormones have been suggested to play a role in the development of melasma. In this study, most of the melasma patients were females (125/153, 81.70%) and most were aged 41 to 50 years old (58/153, 37.91%), with the average age of 42.4 $\pm$ 9.68 years. Similarly, in a 2006 multicenter study on Asian patients from Korea, Philippines, Singapore, Hong Kong and Taiwan, majority of the patients were also females (248/260, 95.4%) and the average age was 45 years. However, since the age reported in our survey is the age when melasma was first diagnosed and not necessarily the age of onset of the disease, it cannot be concluded whether the patients developed the disease early or late in menacme. On one hand, the high average age of melasma patients in the study could simply mean that older people tend to seek more dermatologic consult. On the other hand, the diagnosis of melasma at a relatively late age could mean late onset of the disease, which is commonly seen in Asian countries such as India, with an average age of melasma development of 30 years old; Singapore, 34 years old and South East Asia, 30-44 years old. This delay in development of melasma has been attributed to melanin, which seems to play a photoprotective role. In this study, majority of the melasma patients were Filipinos (73.2% or 112/153) and majority had a more pigmented phototype, Fitzpatrick skin type IV (57.5% or 88/153).

Some of the factors implicated in the development of melasma like thyroid disease, sun exposure, pregnancy and oral contraceptive pill (OCP) use were investigated in this study.

Endocrinological conditions like thyroid disease have previously been associated with melasma. However, some studies have also shown that prevalence of thyroid diseases in melasma patients is not higher than the general population. In this study, 75.16% (115/153) of the melasma patients reported no thyroid disease or any thyroid problem. Establishing an etiological correlation between thyroid disease and melasma still needs further investigation.

Another factor associated with melasma is exposure to UV radiation without protection. This is said to be the most important environmental triggering factor in melasma. However, it was noted in this study that 43.14% (66/153) of the patients had a self-reported daily duration of sun exposure of only 30 min or less. The minimal daily sun exposure of majority of the patients suggest that sun exposure may not be the triggering factor of melasma in these patients. However, since this data was self-reported, it may be subject to recall error and bias. In future studies, more objective measures of sun exposure such as polysulphone badges worn on a day to day basis may be employed to derive more reliable information.

Pregnancy and OCP use have also been associated with melasma development. There is increased prevalence of melasma with pregnancy and OCP use possibly due to hormonal influences, as previously suggested. High levels of the female hormones estrogen, progesterone and melanocortin are said to be possible triggering factors of melasma during pregnancy. In a study involving 2000 pregnant women in India, 50.8% had melasma. In our study, 96 out of 125 (76.8%) women had been pregnant. OCP use was common, with 37.60% (47/125) of the female patients admitting to having used OCP but majority (70/125, 56%) haven't used OCP and the rest have not confirmed either. More than half (30/47, 63.83%) of those who used OCP have used it for a duration of only 12 months or less. These data suggest that pregnancy but not OCP use may be the main triggering factor for melasma in this particular group of patients. However, this needs further investigation.

In terms of skin type, most patients had Fitzpatrick type IV (88/153, 57.52%) followed by type III (45/153, 29.41%). These findings parallel one Brazilian study that shows that majority of melasma occurred in these two skin types. In a multicenter study on Asian patients, most patients also had skin phototype IV (168/260, 64.6%) or III (71/260, 27.3%). The prevalence of melasma in more pigmented phototypes (Fitzpatrick scale III, IV and V) is known to be high. Tamega *et al.* suggested that the low incidence of melasma in extreme phototypes may be due to some stability or homogeneity in their ultraviolet (UV) reaction regarding their pigmentation system. It has also been argued that individuals with skin type I cannot produce additional pigmentation while those with skin type VI already produce it at maximum efficiency.

In our study, the type of melasma was mostly epidermal (94/153, 61.44%) and the most common classification was malar (92/153, 60.13%). Another study conducted in the same institute (RITM) in 2009 also reported malar melasma to be the most common among their patients (49/56, 87.5%). A 2006 study of Asian patients also reported the most common type of melasma to be epidermal (152/260, 58.5%) and the most affected location, malar. Another study involving 85 women in southern Brazil also found the most common pattern of melasma to be malar (46.4%). In contrast, a 2013 study on facial melasma in Brazilian women and a study in Tunisia involving 188 female patients both showed predominance of centrofacial melasma rather than malar. The predominant type of melasma observed apparently varies depending on the population being studied.

Furthermore, most patients presented with mild (51.63%) followed by moderate melasma (27.45%). The average mMASI score was 4.63 ± 3.32. This approximates the mean mMASI score of 3.8, which has also been classified as mild in a retrospective study involving 79 patients. This is unlike majority of published studies where the means of MASI scores are about 10 to 13, which are classified as moderate melasma.

The main limitation of this study is the possibility of recall error and bias. There are also missing data due to inability of some patients to answer certain questions in the survey. Also, this study was a sample of patients seen and newly-diagnosed with melasma in only 6 dermatology clinics in Metro Manila and therefore cannot be representative of people in Metro Manila or the entire Philippine population. As Ogbechie-Godec and Elbuluk (2014) said, prevalence and incidence rates calculated from dermatology clinics may be an underestimate of the number of affected individuals in the population as some patients with milder disease may no longer seek consultation or clinical assessment.

CONCLUSION

Prevalence of melasma was low among the Philippine dermatology patients sampled. Majority of the melasma patients were Filipinos, aged 41-50 years old, with Fitzpatrick skin type IV, limited sun exposure and no thyroid disease. They were mostly females, with a prior history of pregnancy. Their melasma was mostly malar, epidermal, and mild in severity. These descriptive data can serve as baseline information for further studies on melasma in the Philippines. These can also provide us, physicians with a better understanding of the nature of the disease among Philippine patients for improved management of individual melasma cases.

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Behavior and Practices of Family Physicians in the Referral of Dermatological Diseases: A Cross Sectional Study*

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ABSTRACT

INTRODUCTION: Referrals are the link between primary and specialty care. While the referring provider can be any type of physician, the focus in the literature has been on primary care physicians (PCPs). In their area of expertise, specialists are able to provide evidence-based care, and several studies have shown that specialists' co-management of care with PCPs results in better health care outcomes for patients with chronic diseases.

METHODOLOGY: The research design used was cross-sectional. A validated self-made questionnaire was disseminated to the family physicians (FPs) who are active members of the Philippine Academy of Family Physicians (PAFP) from the National Capital Region (NCR).

RESULT: Majority of FPs refer to dermatologists and more than half are affiliated with a hospital. Twenty percent had dermatology training which was not specified, and 44.2% took continuing medical education/seminars in dermatology. The top 3 most common dermatological diseases among the top ten existing dermatological diseases from January to December 2014 seen at the 11 accredited training institutions of the Philippine Dermatological Society (PDS) ranked by FPs as seen in their private practice were contact dermatitis, atopic dermatitis and acne vulgaris.

The primary reason for referral of FPs to a dermatologist was for "treatment" and "difficult cases." Average referral frequency within a month was two times while within a year it was more than five times. The criteria for choosing a particular dermatologist were good medical skill, geographic consideration and good FP-dermatologist communication. For the manner of referral, majority referred through letter, followed by phone calls and text messages. There were 53.8% FPs who were satisfied with the quality of communication with the dermatologists. Few FPs encountered difficulties in referring patients such as unavailability of the dermatologist, patient's financial constraints, patient's refusal, and the patient not being referred back to the primary physician by the dermatologist. According to 68.6% of FPs, their patients followed-up after referral to a specialist.

CONCLUSION: The existing referral system among FPs and dermatologists, based on the study parameters, is generally properly implemented at the NCR. However, further studies should be done to determine the current state of referral system in the rural areas, where further health care management is needed, due to the unavailability of specialists like dermatologists.

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INTRODUCTION

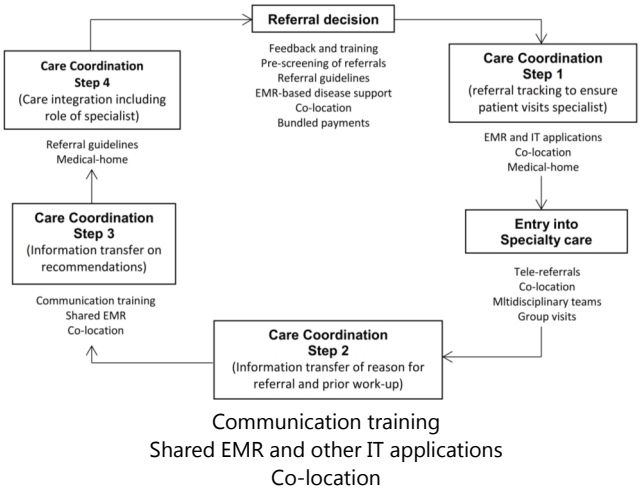
The health care system presents a major challenge in every country. The factors behind this global trend are increasing health costs and diminished returns on healthcare investment for ageing populations. There is growing insight in primary health care in Europe and North America,[1] but data are scarce for many countries, especially in Asia.

The operational framework of health sector reforms in the Philippines was adopted in 2005 and was called FOURmula One for Health (F1). The objective was to undertake critical reforms with speed, precision and effective coordination directed at improving the efficiency, effectiveness and equity of the Philippine health system in a manner that was felt by the Filipinos, especially the poor.[2]

Based on the Philippine Medical Association Handbook on protocol of 2010, the role of the receiving physicians is that they are bound to acknowledge the referral, state the findings and the plan/ management for the patient.[3]

While the referring provider can be any type of physician, the focus has been on PCPs.[4] Family Physicians constitute the largest group of PCPs. Their role as gate-keepers increases the efficacy of the system.[5] When a patient's condition requires treatment outside of their usual practice, a specialist is typically consulted and works with both the patient and the PCP. In their area of expertise, specialists are more likely to provide evidence-based care, and several studies have shown that specialists' co-management of care thru referrals from PCPs results in better health outcomes for patients.[6]

The conceptual framework for the referral process from primary to specialty care divides the process into three components: referral decision making, care coordination, and access to a specialist (Figure 1).



Notes: EMR= electronic medical record; IT= information technology

Source: Mehrotra A, Forrest CB, Lin CY. Dropping the Baton: Specialty Referrals in the United States. The Milbank Quarterly. 2011; 89(1): 39–68.

Figure 1. Idealized steps in specialty-referral process and potential mechanisms for improvement at each step.

In the Philippines, studies on the current status of referral to dermatologists is lacking. The burden of dermatological diseases is often unrecognized, but since the integumentary system is the largest organ system of the body, then skin problems are generally found to be amongst the most common presentations of diseases in primary care settings in tropical areas.[7]

This study aims to determine the behavior and practices of FPs in the referral of their most commonly encountered dermatological diseases in primary care setting to dermatologists. Specifically, this study also determines their knowledge in dermatological cases, reasons for referral, criteria in choosing a dermatologist, manner of referral, difficulties encountered in referral and patient follow-up.

METHODOLOGY

The research design used was cross-sectional. Study subjects were randomly selected FPs, active members of the Philippine Academy of Family Physicians (PAFP), from the National Capital Region (NCR). The participants were assigned a number by the Head Secretariat of PAFP and all odd numbered were included in the study. The sample population was computed using Slovins formula based on the population of active PAFP members within the six

NCR chapters (Manila, Quezon City, Makati-Pateros (MATAPAT), Caloocan-Malabon-Navotas (CAMANAVA), Las Pinas-Pasay-Paranaque (LAMPARA) and Pasig-Mandaluyong-Marikina-San Juan (PAMAMARISAN).

A self-made questionnaire was validated by initially sending out 20 questionnaires to randomly selected FPs then results were tallied and found reliable as evidenced by Cronbach's alpha of 0.721. The 500 validated questionnaires were given to the Head Secretariat of the PAFP, and were distributed via email and personally to the active members.

STATISTICAL ANALYSIS

Data were encoded and tallied in the SPSS version 10 for windows. Descriptive statistics were generated for all variables. For nominal data, frequencies and percentages were computed. For numerical data, mean ± SD were generated.

RESULTS AND DISCUSSION

At the end of the data collection, 156 questionnaires were returned out of the 500 that were initially distributed.

Table 1. Demographic Characteristics of Family Physicians

	Frequency (n=156)	Percentage
Age (in Years)		
≤30	9	5.8
31 – 40	44	28.2
41 – 50	32	20.5
51 – 60	50	32.1
61 – 70	4	2.6
71 – 80	6	3.8
>80	1	0.6
Mean ± SD = 47.16 ± 11.77		
Sex		
Male	106	67.9
Female	48	30.8
Years in Practice		
≤1	2	1.3
1 – 10	47	30.1
11 – 20	36	23.1
21 – 30	45	28.8
>30	10	6.4
Mean ± SD = 3.1 ± 0.99		
Affiliation		
Private Company	1	0.6
Diagnostic/Medical Center	28	17.9
Government Health Facility	1	0.6
Hospital	88	56.4
Rural Health Center	2	1.2
None	27	17.3

A total of 156 FPs was included in the study. Table 1 shows the distribution of respondents according to demographic characteristics. The age ranged from 27 to 81 years with a mean age of 47.16 years. Out of the 146 FPs, 30.8% were females. Their years of practice ranged from less than a year to 55 years with an average of 3.1 years. More than 50% were affiliated with a hospital.

A substantial amount of the referral variation is attributable to the physician's characteristics, including type of training (e.g., any specialist training), years of experience, diagnosis. [12]

Table 2. ***Distribution of Family Physicians who took up training in Dermatology***

	Frequency (n=156)	Percentage
Took up training in Dermatology		
Yes	31	19.9
No	123	78.8
Took up Dermatology CME/Seminars		
Yes	69	44.2
No	84	53.8

Table 2 shows out of the 156 FPs, 31 (19.9%) took up training in dermatology, however, it was not specified what kind of training was obtained, while 69 (44.2%) took up dermatology continuing medical education (CME)/ seminars.

According to the Philippine Dermatological Society (PDS) Health Information System, out of the 83,586 patients seen from all 11 PDS accredited institutions, the top ten dermatological diseases based on existing cases from January 1 to December 31, 2014 were the following, in descending order: acne vulgaris, scabies infestation, allergic contact dermatitis, atopic dermatitis, verruca vulgaris, seborrheic dermatitis, lichen simplex chronicus, verruca plana, large plaque psoriasis and tinea corporis.

Table 3: Ranking of the Most Commonly seen Dermatological Diseases by Family

Dermatological Diseases	Ranking										Median Rank
	1	2	3	4	5	6	7	8	9	10	
Scabies (n=141)	15 (9.6%)	26 (16.7%)	17 (10.9%)	25 (16%)	17 (10.9%)	13 (8.3%)	8 (5.1%)	6 (3.8%)	7 (4.5%)	2.7 (4.5%)	**4**
Contact dermatitis (n=149)	53 (34%)	35 (22.4%)	32 (20.5%)	12 (7.7%)	10 (6.4%)	1 (0.6%)	1 (0.6%)	3 (1.9%)	1 (0.6%)	1 (0.6%)	**2**
Acne vulgaris (n=136)	34 (21.8%)	17 (10.9%)	26 (16.7%)	19 (12.2%)	15 (9.6%)	13 (8.9%)	5 (3.2%)	4 (2.6%)	2 (1.3%)	1 (0.6%)	**3**
Atopic dermatitis (n=141)	33 (21.2%)	35 (22.4%)	28 (17.9%)	22 (14.1%)	13 (8.3%)	7 (4.5%)	1 (0.6%)	0	0	2 (1.3%)	**3**
Verucca vulgaris (n=114)	4 (2.6%)	4 (2.6%)	9 (5.8%)	10 (6.4%)	14 (9%)	16 (10.3%)	21 (13.5%)	21 (13.5%)	10 (6.4%)	5 (3.2%)	**6.5**
Lichen simplex chronicus (n=115)	0	2 (1.3%)	3 1.9%	4 2.6%	8 (5.1%)	22 (7.7%)	20 (14.7%)	25 (12.8%)	18 (16%)	5 (11.5%)	**8**
Dermatophytosis/ tinea (n=127)	8 (5.1%)	13 (8.3%)	16 (10.3%)	18 (11.5%)	23 (14.7%)	16 (10.3%)	16 (10.3%)	8 (5.1%)	7 (4.5%)	2 1.3	**5**
Molluscum contagiosum (n=116)	1 (0.6%)	3 (1.9%)	1.2 (1.3%)	1.5 (3.2%)	1.4 (2.6%)	9 (5.8%)	10 (6.4%)	15 (9.6%)	25 (16%)	42 (26.9%)	**9**
Seborrheic dermatitis (n=138)	7 (4.5%)	14 (9%)	15 (9.6%)	28 (17.9%)	23 (14.7%)	22 (14.1%)	13 (8.3%)	7 (4.5%)	6 (3.8%)	3 (1.9%)	**5**
Dyshidrotic eczema (n=109)	3 (1.9%)	1 (0.6%)	1 (0.6%)	3 (1.9%)	5 (3.2%)	8 (5.2%)	3 (3.3%)	26 (16.7%)	24 (5.4%)	25 (16%)	**8**

Table 3 shows the ranking of the most commonly seen dermatological diseases of FPs. Ranking highest was contact dermatitis, followed by atopic dermatitis, acne vulgaris, scabies, dermatophytosis, seborrheic dermatitis and verruca vulgaris. Lowest ranking was given to molluscum contagiosum.

Table 4. ***Referral of Skin problems to a Dermatologist by Family Physicians***

	Frequency (n=156)	Percentage
Refer to dermatological for skin problems		
Yes	142	91
No	14	9

Table 4 shows 91% of the FPs refer to a dermatologist for skin problem. This shows that majority of FPs refer to a dermatologist.

The decision to refer varies widely. Often it is associated with the PCPs decision and factors related to the patient, such as the nature of the presenting problem, the patient's expectations, and the burden of morbidity.[13-16]

Table 5. ***Distribution of Family Physicians' Reasons for Referral and the Most Prevalent Dermatological Diseases for referral to a Dermatologist***

	Frequency (n=156)	Percentage
Reasons for Referral		
Special test	54	34.6
Difficult case	87	55.8
Establish a diagnosis	52	33.3
Second opinion	68	43.6
Treatment	88	56.4
Reassurance of patient	34	25
Reassurance of physician	20	12.8
Others		
Difficult patients	1	0.6
Lesions involving sensitive areas	1	0.6
Dermatological cases for Referral		
Contact dermatitis	24	15.3
Lichen simplex chronicus	21	13.2
Acne vulgaris	24	15.3
Atopic dermatitis	27	17
Dermatophytosis	14	8.6
Difficult cases	23	14.1
Drug reaction	1	1.2
Melanoma	1	0.6
Psoriasis	35	22.1
Skin cancer	2	1.3
Skin diseases not responding to treatment	8	4.8
Verruca plana	1	0.6
Verruca vulgaris	35	22.3
Chronic skin lesions	5	3
Erythema multiforme	1	0.6
Leprosy	5	3.1
Milia	1	0.6
Neurofibroma	1	0.6
Scabies	6	3.8
Seborrheic dermatitis	12	8.2
Folliculitis	1	0.6
Steven-Johnson Syndrome	7	4.4
Xanthelasma	1	0.6
Bullous disease	1	0.6
Drug reaction with eosinophilia and systemic symptoms	1	0.6
Benign nevus	1	0.6
Systemic lupus erythematosus	3	1.9
Vitiligo	2	1.2
Alopecia areata	1	0.6
Basal cell carcinoma	1	0.6
Epidermal cyst	1	0.6
Staphylococcal scalded skin syndrome	1	0.6

Table 5 shows the reasons for referral are "treatment" followed by "difficult case", "second opinion", "special test" and to "establish a diagnosis". The three most prevalent cases for referral to a dermatologist are psoriasis and verruca vulgaris, atopic dermatitis, acne vulgaris and contact dermatitis.

Table 6. ***Distribution of Family Physicians Referral Frequency to a Dermatologist***

	Frequency (n=156)	Percentage
Referral Frequency (Within a Month)		
1x	26	16.7
2x	30	19.2
3x	22	14.1
4x	11	7.1
5x	9	5.8
>5x	5	3.2
Referral Frequency (Within a Year)		
1x	5	3.2
2x	6	3.8
3x	13	8.3
4x	5	3.2
5x	9	12.2
>5x	23	14.7

Table 6 shows the average referral frequency made by FPs. Based on this data, FPs usually refer dermatological cases twice a month and more than five times in a year. Hence, patients with a dermatological disease are frequently seen in their practice.

A successful referral requires that the patient has adequate access to a specialist. The specialist's characteristics, such as his or her perceived medical skill, prior interactions, availability, and whether the specialist is known to return the patient to the referring physician and the community in which the referring physician practices, also influence which specialist is chosen by the PCP. [17,18]

Table 7. ***Criteria for choosing a particular Dermatologist by Family Physicians***

Criteria	Frequency (n=156)	Percentage
Good Medical Skill	107	68.6
Had a previous referral with the Dermatologist	44	28.2
Related to that dermatologist	6	3.8
Geographic consideration (location)	60	38.5
Patient's request/preference	33	21.2
Good FP-dermatologist communication	52	33.3
HMO-accredited dermatologist	1	0.6
Recommended by other FPs	1	0.6

Table 7 shows that the criteria for choosing a particular dermatologist by the FP are the following: good medical skill (68.6%), geographic consideration (38.5%) and good FP-dermatologist communication (33.3%).

Table 8. ***Rating of the Quality of Communication between the Family Physician and Dermatologist***

	Frequency (n=156)	Percentage
Rating		
Very satisfied	22	14.1
Satisfied	84	53.8
Neutral	37	23.7
Dissatisfied	1	0.6
Very dissatisfied	1	0.6

Table 8 shows the quality of communication between the FP and dermatologist. Twenty-two respondents (14.1%) were very satisfied; 84 (53.8%) were satisfied; and 37 (23.7%) were neutral. One of the FPs was dissatisfied and one was very dissatisfied. This was attributed to the patient's poor compliance because of financial constraints.

Quality of communication between PCPs and specialists is important for the evaluation of the referral system. One study found an eleven-fold increase in the odds of adequate communication between PCPs and specialists sharing an electronic medical record.[19] In other countries, an integrated medical record is used by all medical practitioners. Leading to ease of access and continuity in the management of the patient.

Table 9. ***Manner of Referral between the Family Physician and Dermatologist***

	Frequency (n=156)	Percentage
Manner of Referral		
Text Message	10	6.4
Email (with picture)	2	1.3
Phone call	23	14.7
Referral letter	134	85.8

Table 9 shows the manner of referral between FP and dermatologist. Majority of the respondents 134 (85.8%) referred through referral letters while seven (14.7%) referred thru phone calls and ten (6.4%) referred thru text messages.

Referral tracking is an important task for the referring physician to ensure that the referral was completed.[4] This is an integral part for the care integration, as well as information transfer. Information technology can ease the transfer of data. [20,21]

Deficiencies in the referral process have many adverse consequences, including reduced continuity of care, delayed diagnosis or treatment, duplication of testing, poly-pharmacy, and increased risk of malpractice suits. [20-23]

Table 10. ***Distribution of Family Physicians who encountered Difficulties in Referring***

	Frequency (n=156)	Percentage
Encountered Difficulties		
Yes	7	4.5
No	146	93.6

Table 10 shows FPs who had encountered difficulties in referring patients. Out of the 153 who referred to dermatologists for skin problems, only seven (4.5%) encountered difficulties. The reasons were unavailability of the dermatologist, financial constraint of the patient, patient's refusal, and the patient not being referred back to the PCP.

Table 11. ***Patient's follow-up to Family Physicians***

	Frequency (n=156)	Percentage
Patients Come back after referral?		
Yes	107	68.6
No	37	23.7

Table 11 shows patient's follow-up to FPs. One hundred seven FPs (68.6%) gave a positive response. Patient's follow-up with the primary physician is essential in the care integration. This shows a good referral system between the FP and dermatologist.

CONCLUSION

Dermatological diseases are very common and most patients present in primary care settings. Majority of the FPs refer to dermatologists. Continuing medical education and refresher training courses are important for dermatological disease awareness of FPs.

The most prevalent skin problems referred were psoriasis and verruca vulgaris, atopic dermatitis, acne vulgaris and contact dermatitis. The primary reasons for referral of FPs to a dermatologist were for treatment and difficult cases. The criteria that are highly considered for choosing a particular dermatologist by FPs are good medical skill, geographic consideration and good FP-dermatologist communication. Majority of the FPs referred through letter, followed by phone calls and text messages.

The existing referral system among FPs and dermatologists, based on the parameters included, is generally properly implemented in the NCR.

RECOMMENDATIONS

Despite the importance of specialty referral process, data are lacking on the current status of referral to dermatologists in the country, especially in the rural areas, where further health care management is needed by our fellow countrymen. To secure access to high-quality health care for all, every health system will have to provide strong primary health care as its basis. Hence, proper recording, referral tracking and reporting of cases, especially from the primary care setting, is needed for ease of access and to be able to assess the real status of the dermatological diseases and its management.

Further studies are suggested to determine other deficiencies that can lead to duplicated care, overuse of facilities, and wasting of precious resources that threatened the sustainability of the health system and to identify opportunities for improvement in the referral**.**

In order to make effective plans for the provision of dermatological services, especially on a national level, the researchers suggest that physicians should follow the model of specialty referral.[4] Electronic data recording also helps in ease of access

by both the PCP and Specialist. Other countries were able to integrate their medical data in different specialties, hence, further studies should be done to include medical data integration, changing trends in referral, the reasons for requesting a specialist opinion, and whether the referral is influenced by their knowledge on dermatological diseases and its management.

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Safety and Efficacy of Topical Essential Oil as Steroid-Sparing Agent in the Treatment of Atopic Dermatitis in a Community Outreach Care Program of New Era University Second Year Medical Students, Randomized Double Blind Placebo Controlled Trial*

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ABSTRACT

Background: The high rates of atopic dermatitis among children, treatment failures and treatment costs have created the search for new therapies to control flares of atopic dermatitis.

Objectives: We compared the efficacy and safety of topical essential oil (German Chamomile) versus topical steroids (hydrocortisone 1%) in controlling flares of atopic dermatitis.

Method: We randomly selected 60 children diagnosed of AD or children that qualified to the criteria of AD. They we're randomly grouped into three. Twenty for Essential Oil (EO) group, twenty for Steroid group (SG) and Twenty for placebo (distilled water) group. They were advised to apply medicine kept in uniform brown plastic bottles 3x a day for 4 weeks. Data were recorded weekly using the EASI (Eczema Score Index) scoring. Other topical medications such as emollients and moisturizers were continued.

Results: At week 4 control of flaring was achieved; 42% for EO group and 55% for steroid group. The differences in treatment effects were not statistically significant.

Conclusion: Essential oil was comparable in cure rate to mild topical steroid. Essential oil can be safe and affordable. However further study in a wider scale is recommended.

KeyWords: Atopic Dermatitis, Barrier Function, Eczema, Essential Oils, Roman Chamomile, Jojoba oil, Chamazulene

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INTRODUCTION

Childhood atopic dermatitis is an increasing common condition in young children. The worldwide incidence according to Annals of Nutrition and Metabolism in 2015 is about 20% of children and studies showed that steady increased is most likely to happen for low-income developing countries. Atopic Dermatitis is an interplay of dysfunctional epidermal barrier in genetically predisposed individuals and harmful environmental antigens. Recent studies showed that the focus of treatment of Atopic Dermatitis has shifted from treating symptoms of inflammation to Skin barrier repair. In fact, skin barrier alterations and reduction of innate immune mechanism are now considered the hallmarks of AD. Therefore, barrier repair therapies with steroid-free substances is an important alternative in managing AD.

Essential oils (German Chamomile) and pure carrier oils (jojoba oil) are great option for treating AD. Jojoba oil mimics the oil moisture of the human skin and according to the International Journal of Molecular Science of 2014, this oil effectively increases the absorption of topical drug because of its high content of wax ester. On the other hand, chamazulene is an active agents extracted from German/Roman chamomile flower which according to Pub Med has a good natural anti-inflammatory property. In the study of Safayhi et all published in the Article in Plants Medica (Nov. 1994), they demonstrated in vivo experiments that chamazulene inhibits the Leukotriene B4 in intra cells which blocked the chemical peroxidation of arachidonic acids thus preventing inflammation. The experiments also showed the reduction of TNF alpha in mice and the presence of high concentration of AgNPs/CE5x in chamazulene which has an anti-bacterial activity by inhibiting the H2O2 generated free radicals from fibroblast.

AD poses a significant burden to parents and patients. The chronicity of symptoms (pruritus, sleep deprivation, on and off flares), the financial costs and the deterioration of the quality of life have heightened the interests of researchers, scientists and physicians in the identification of newer and cost effective treatment alternatives.

Methodology:

A double-blind, randomized, interventional parallel assignment and placebo-controlled clinical trial was conducted over a ten (10) months period beginning August 2017 to June 2018 in three multi-center OPD clinics of three (3) collaborative PDS dermatologists (most are done in NEGH).

Sixty three (63) patients, ages 2-17 were recruited and referred by volunteer second year medical students of New Era University from their Community Outreach (Brgy. San Jose, Rodriguez Rizal). They were subsequently invited to seek OPD consults to dermatology consultants involved in this research.

The inclusion and exclusion criteria were as follows.

1. Male or female paediatric patients ages 2-17 years old with history of Atopic dermatitis and stable disease for at least one (1) month according to parents/caregivers.
2. No clinically significant and relevant abnormalities in medical history or upon physical examination.
3. Patients with mild to moderate atopic dermatitis with Physician Global Assessment of 2 or 3.
4. Patients affected between 5% to 40% Body Surface Area (BSA).
5. Volunteer should understand and be willing to fully comply with all study procedures and restrictions.
6. Demonstrates understanding of the study and willingness to participate as evidenced by voluntary written parent's informed consent.
7. Female of childbearing potential, using an effective contraceptive method for at least one month before the beginning of the study, and willing to use throughout the study.

<u>Exclusion Criteria</u>

1. Volunteers having recent history (within 1 year) of alcohol or other substance abuse as determined by medical history.

2. Participation in another clinical study or received of an investigational drug within 30 days of the screening visit.
3. Previous participation in similar study with similar products.
4. Volunteer has any visible skin disease at the site of application that, in the opinion of the investigator, will interfere with the skin assessments.
5. Volunteer has current or relevant previous history of serious, severe or unstable physical or psychiatric illness or medical disorders, such as hepatic or renal disease.
6. Volunteer or patient has a history of hypersensitivity of tropical oils.
7. Volunteer receiving systemic steroids in the last 3 months.
8. Any skin disorder at the site that the investigator's judgement can affect the reading of test results.
9. Pregnant or any plan of having pregnancy during the study.
10. Any concomitant medications that in the investigator's judgment can confused or alter test results.

Intervention:

The 63 subjects were requested to undergo a primary irritancy test, on which the investigators put one drop of the solution in the right arm and sealed with tegaderm plaster and were requested to have a 24-hour patch test. They were requested to return on the following day for the investigators to record the results. Subjects who did no show primary irritancy were deemed eligible for the study.

The subjects were randomly distributed to the study groups EO (Essential Oil Group), SG(Steroid group) and PG (Placebo group) using randomized code generated from CLINSTAT software.

They were instructed to apply the given solution three times a day over eczematous lesions for four weeks. They were instructed to report immediately if any irritation were noted. They were also told to come for follow up weekly for four weeks.

Outcome Measures:

The primary outcome measures are the lowering of EASI (Eczema Assessment Severity Index) to 50% at week 4 and at least a 2- point improvement in the PGA (Physician Global assessment at week 4. The PGA is a standard 5-point overall severity assessment using the following scoring 0-clear,1-almost clear,2-mild flare, 3-moderate flare,4-severe flare.

Standard Analysis:

All statistical was conducted using SPSS software. Demographic variables and other baseline characteristics were summarized by descriptive statistics. The Chi-Square test without continuity connections was used to analyse discrete variables, and analysis of variables was used for continuous variables to assess comparability among the three treatment groups. Further, the Fisher's exact test was used to test the difference. All statistical tests were two-tailed with a significance level alpha = 0.05.

Results:

A total of 63 patients were recruited for the clinical trial but only 55 completed the treatment protocol and were included in the analysis. The patients were randomized to receive placebo (0.9NaCl) solution, Hydrocortisone 1% lotion and Essential Oil (German Chamomile EO diluted with Jojoba oil at 2% concentration).

Table 1 Demographics

Gender	EO	SG	PG	P value
Male Female	9 9	9 11	10 7	.857
Mean Age	7.4	6.6	8.2	.675

Legend: EO9Essential Oil group); SG (steroid group); PG (placebo group)

Table 1 showed that the demographics data have no significant differences among the treatment groups with regards to gender and age.

Table 2 Physician Global Assessment Score

Duration of Treatment	EO (mean PGA score)	SG (mean PGA score)	PG (mean PGA score)
Day 1	2.9	2.45	2.40
Week 1	2.5	2.10	2.35
Week 2	2.0	1.45	2.25
Week 3	1.1	1.10	2.10
Week 4	1.0	0.65	2.0

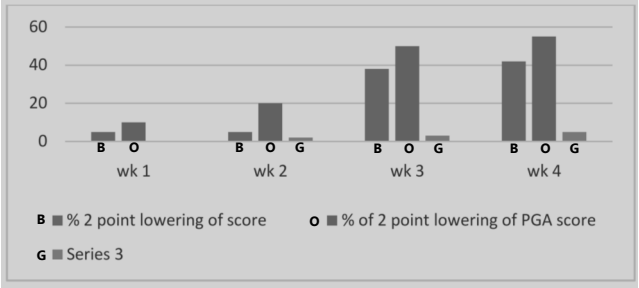
X^2 = 16.816, Ho – PGA Score is independent with duration of treatment; Rejected

Graph A

Legend: Series 1 EO, Series 2 SG, Series 3 PG

The patients were evaluated on the severity of skin redness, welting up, rash, oozing skin and symptoms of itchiness. Table 2 showed the significant improvement of lesions in the SG (steroid group) as early of 2 weeks of treatment duration, while significant improvement was noted on the 3rd and 4th week in the EO group.

Graph B Percentage of 2-point Lowering of PGA Score



Legend Blue – EO, Orange –SG, Grey -PG

Graph B showed that at week 4 around 40-48% of patients achieved the 2-point lowering of their PGA scores in the EO group while around 55-62% achieved the 2-point lowering in the steroid group. No significant changes were seen in the placebo group.

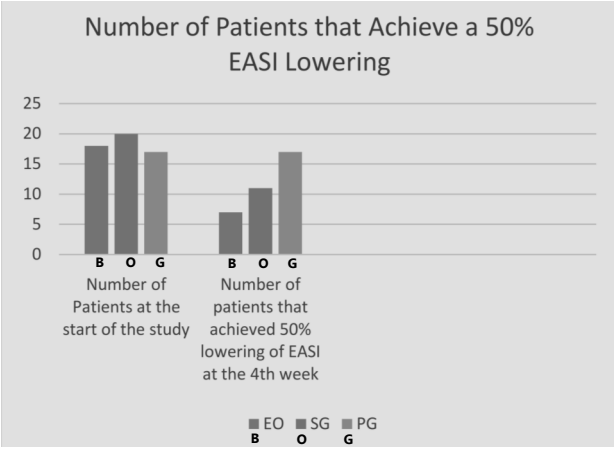
Table 3. Lowering of EASI (mean score)

Duration of treatment	EO EASI mean score	SG EASI mean score	PG EASI mean score
Day 1	38.2	23.4	28
Week 1	32.6	22.4	29
Week 2	24.2	19.2	29
Week 3	20.4	14.0	27.6
Week 4	19.2	11.0	26.35

X^2 = 10.0, Ho –EASI is independent with the duration of treatment, Rejected

Table 3 showed that there was a significant lowering of EASI score to about 50% on both EO and SG. Although, the lowering of EASI score in the SG is higher than in the EO group yet no significant differences between the two were noted. The Placebo control group showed no significant lowering of EASI score.

Graph 3. Number of Patients that achieved 50% lowering of EASI Score



Graph 3 showed that 8 out of the 17 (42%) panellists showed 50% lowering of EASI score in the EO group and 11 out 20 (55%) showed 50% lowering of EASI score in the SG.

Conclusion:

This study demonstrated that German-Chamomile essential oil diluted to Jojoba oil in a 2% concentration, used as topical anti eczema solution have no skin contact sensitization potential. The results of the 10 months' clinical study demonstrated the significant efficacy in lowering Atopic dermatitis lesions severity and showed significant lowering of EASI score to about 50% in almost half of the sample size. Both EO and SG showed no significant difference. The utility of German Chamomile Essential oil diluted with Jojoba oil is very promising as it is well tolerated, easy to make, safe and can be compared to mild potent topical steroids.

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A Pilot Study Comparing the Clinical Efficacy of Freshly Reconstituted and Botulinum Toxin A Reconstituted 1, 2 And 3 Months before Application in the Treatment of Axillary Hyperhidrosis*

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ABSTRACT

Background: Most manufacturers of commercially available botulinum toxin A (BTX-A) recommend that the vials should be used within 24 hours after reconstitution to ensure efficacy, which in some instances would mean wastage of remaining reconstituted solution. Several studies have evaluated the efficacy of stored reconstituted BTX-A and have concluded that the use of BTX-A reconstituted and refrigerated for up to 6 weeks prior to administration does not significantly alter its efficacy in the treatment of facial rhytides.

Objectives: Our study aimed to compare the clinical efficacy and safety of freshly reconstituted BTX-A and BTX-A reconstituted 1, 2 or 3 months prior to administration in the treatment of axillary hyperhidrosis.

Methodology: Patients with primary axillary hyperhidrosis were enrolled in this pilot study. Freshly reconstituted BTX-A and BTX-A reconstituted 1, 2 and 3 months prior were administered in 4 pre-determined areas in the same patient. The degree of hyperhidrosis was assessed subjectively using Hyperhidrosis Disease Severity Scale (HDSS) and objectively using Minor's iodine starch test followed by Sweating Intensity Visual Scale (SIVS) at 0, 2, 6 and 12 weeks after administration.

Results: Five patients were enrolled in the study. Kruskall-Wallis test showed that HDSS at baseline was significantly different from follow-up periods with noted improvement from baseline to 2 weeks follow-up. Using Kruskall-Wallis test, SIVS was found to be not significantly different among these 4 treatment areas. In addition, significantly improved SIVS scores were noted as early as 2 weeks after administration in all 4 areas of treatments. There were no noted adverse effects in all patients at baseline and at all follow-up visits.

Conclusion: The clinical efficacy and safety of BTX-A reconstituted 1, 2 and 3 months prior to administration is comparable to that of freshly reconstituted BTX-A in the treatment of axillary hyperhidrosis.

Keywords: stored botulinum toxin A, reconstituted botulinum toxin A, axillary hyperhidrosis

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INTRODUCTION

Botulinum toxin A (BTX-A) is commonly used in dermatology for facial rejuvenation and in the treatment of axillary and palmoplantar hyperhidrosis. The use of freshly reconstituted BTX-A in the treatment of axillary hyperhidrosis has been established by several studies and is associated with reduced disease severity and improvement of quality of life.[1-7]

One of the drawbacks with the use of BTX-A is its cost. Adding to this is the fact that manufacturers recommend that once reconstituted, the vial should be consumed within 24 hours and any remaining solution be discarded.[8-10] Because of this, a common practice among dermatologists is to pool patients before reconstituting a vial of BTX-A, otherwise, even if the entire vial is not consumed in 1 treatment session, one patient will have to pay for the cost of an entire vial.

Because the recommendation that reconstituted vials should be discarded after 24 hours would mean wasting an expensive product in most instances, there is great interest in the methods of storing reconstituted BTX-A. Several studies have investigated the efficacy of reconstituted BTX-A stored at 4˚C for up to 6 weeks and have concluded that it is equal to that of freshly reconstituted BTX-A, at least in the treatment of facial rhytides.[2,11-13]

In our literature search, there is no published study investigating the clinical efficacy and safety of reconstituted BTX-A stored at 4˚C for more than 6 weeks before use in the treatment of axillary hyperhidrosis. This study aims to compare the clinical efficacy and safety of freshly reconstituted BTX-A and BTX-A reconstituted 1, 2 and 3 months before application in the treatment of axillary hyperhidrosis, which in the future, may contribute in lowering treatment costs with BTX-A.

METHODOLOGY

Study design and study population

A non-blinded, non-randomized, controlled pilot study was conducted at the Jose R. Reyes Memorial Medical Center Department of Dermatology from April 2016 to December 2016 to compare the clinical efficacy of BTX-A reconstituted at 0, 1, 2 and 3 months before application in the treatment of axillary hyperhidrosis. This study was conducted with the approval of the Institutional Review Board and in compliance with Good Clinical Practice guidelines. This study was partially funded by a research grant from Philippine Academy of Dermatologic Surgery Foundation Inc. (PADSFI).

Patients aged 18 to 40 years old, male and female, who were diagnosed with primary axillary hyperhidrosis (see Appendix A) and with moderate to severe hyperhidrosis, defined as having a score of 3 or 4 using the Hyperhidrosis Disease Severity Score (HDSS) (see Table 1), were included in the study.

Patients with concurrent treatment for hyperhidrosis, including aluminum chloride 40%, iontophoresis, anticholinergic drugs and BTX-A within the last 12 months; infection or dermatosis over the axillae; pregnancy or lactation; and negative Minor's iodine starch test were excluded. Patients with regular use of commercially available anti-perspirant were instructed to discontinue its use 3 days before the administration of BTX-A and throughout the duration of the study.

Materials

One 100-unit vial of BTX-A was reconstituted by the co-investigator (AET) by adding 2.5 mL of bacteriostatic 0.9% sodium chloride with resulting dose unit of 4 units/0.1 mL. In addition to freshly reconstituted BTX-A that is reconstituted on the day of administration, vials of BTX-A were reconstituted and refrigerated at 4˚C for 1, 2 and 3 months before the scheduled date of BTX-A administration. These vials were labeled 0, 1, 2 and 3 corresponding to the months the reconstituted vials were stored.

Study intervention and assessment

After screening of eligible participants, the primary investigator (CMP) explained the study to the participants and obtained informed consent. Detailed history was taken and the patients were asked to answer the HDSS (see Table 1). Patients were then instructed to discontinue use of any commercially available anti-perspirant prior to the procedure and were scheduled to follow-up on a specified date.

Minor's iodine test was performed by CMP to determine the location of hyperactive sweat glands before administration of BTX-A and to document improvement in hyperhidrosis on follow-up visits. Minor's iodine test was performed by painting the axillae with 10% iodine solution and applying cornstarch powder after. Subjects were then exposed to room temperature of 30-35˚C and observed after 30 minutes. Sweating was indicated by the onset of a dark-blue color.[5]

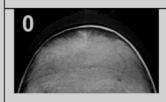
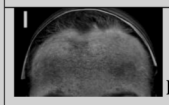
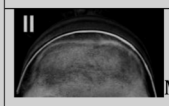
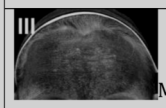
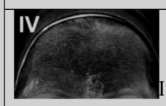
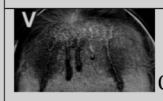
Administration of BTX-A was performed by CMP under the supervision of AET. Two areas per axilla, at least 2 cm x 2 cm, with the highest intensity of sweating as determined using Minor's iodine test, were marked and assigned to receive either freshly reconstituted BTX-A (labelled 0), or BTX-A reconstituted 1 month, 2 months or 3 months before application (labelled 1, 2 or 3, respectively). Photos of the labelled treatment areas subjected to Minor's iodine test were taken at baseline and at all follow-up periods. Injection points, 1 cm. apart, were marked using a fine-tipped marking pen in each treatment area. The treatment areas were then wiped using gauze with sterile water to remove the iodine and cornstarch. Two units (0.05 mL) of BTX-A were administered intradermally in each injection point using tuberculin syringe with gauge 30 needle. No anesthesia was used.

Patients were asked to follow-up 2 weeks, 6 weeks and 12 weeks after administration of BTX-A to assess the reduction of hyperhidrosis. The degree of hyperhidrosis of all the treatment areas were evaluated by 3 independent investigators (senior residents) using SIVS (see Table 2) at baseline and on follow-up visits through photos. Patients were also asked to answer the HDSS on all follow-up visits. Adverse effects, which included pain after injections, bruising and infection, were also noted.

Table 1. Hyperhidrosis Disease Severity Scale (HDSS)[5]

Condition	Score
My axillary sweating is never noticeable and never interferes with my daily activities	1
My axillary sweating is tolerable but sometimes interferes with my daily activities	2
My axillary sweating is barely tolerable and frequently interferes with my daily activities	3
My axillary sweating is intolerable and always interferes with my daily activities	4

Table 2. Sweating Intensity Visual Scale (SIVS)[14]

	Grade
 Minimal or no sweating	0
 Initial, discrete sweating	I
 Mild sweating	II
 Moderate sweating	III
 Intense sweating	IV
 Over-sweating	V

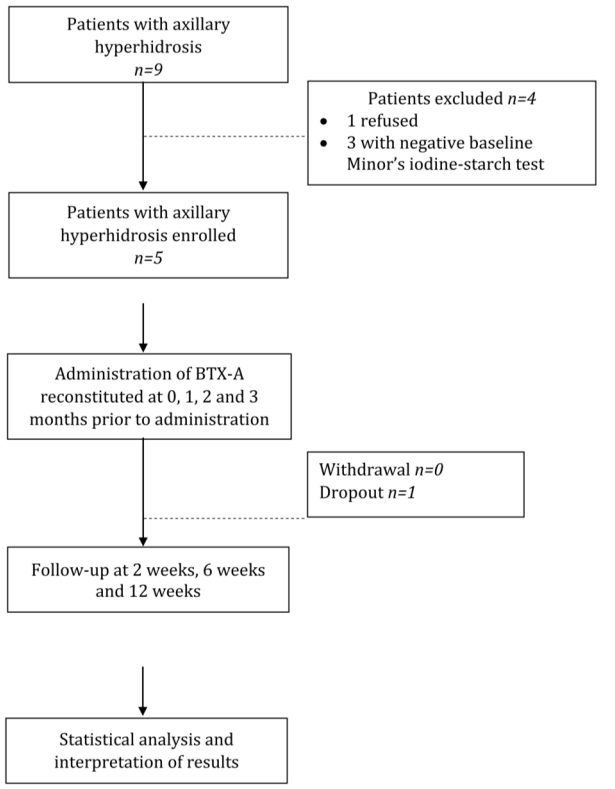
Statistical analysis

Descriptive analysis of the data was performed by determining the percentage or mean with standard deviation to describe the demographic profile of all the subjects, which include age, gender and duration of hyperhidrosis. Means of SIVS scores with standard deviation were also calculated during each follow-up visit.

For inferential statistics, Kruskall-Wallis test at 5% level of significance was performed to determine if there is significant difference in the mean SIVS scores for areas treated with BTX-A reconstituted 0, 1, 2 and 3 months prior to administration. This test was also used to determine if there is significant improvement in the mean HDSS scores during follow-up visits.

Proportion of those who experienced adverse effects was measured to determine the percentage of subjects who experienced the adverse effects.

Figure 1. Schematic diagram of the methodology

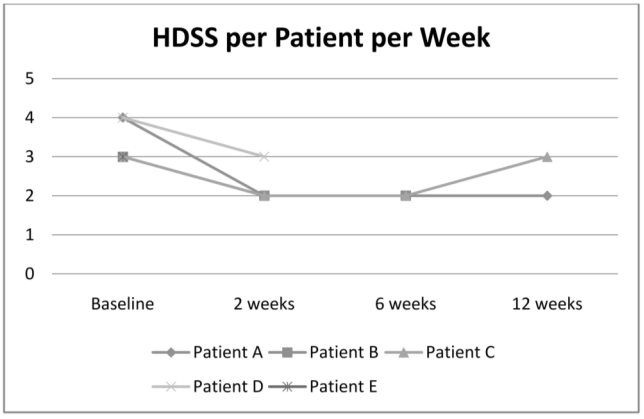


RESULTS

A total of 5 patients, all female, diagnosed with primary axillary hyperhidrosis at Jose R. Reyes Memorial Medical Center Department of Dermatology, were included in the study. The ages ranged from 20 to 29 years old, with mean age of 22.6 years old (SD of 3.78). Duration of hyperhidrosis of these patients ranged from 2 to 10 years, with mean duration of 6.8 years (SD of 3.96).

The severity of hyperhidrosis of these patients was measured using the HDSS where 1 is least severe and 4 is most severe. Patients A and E both have HDSS of 4 at baseline while patients B, C and D have HDSS of 3 at baseline. However, patient E was lost to follow up at 2 weeks and all succeeding follow-ups. HDSS of patient A decreased by 2 scales from baseline, while HDSS of the other 3 patients decreased by 1. HDSS of patient C returned to baseline at 12 weeks follow-up. (see Figure 2).

Figure 2. HDSS of patients at baseline and at 2, 6 and 12 weeks follow-up



To determine if mean HDSS significantly improved from baseline, Kruskall-Wallis test at 5% level of significance was used. Mean HDSS was 3.4 at baseline, 2.2 after 2 weeks, 2 after 6 weeks, and 2.5 after 12 weeks. Results of the test showed that HDSS at baseline was significantly different from follow-up periods (p-value=0.031) with noted improvement from baseline to 2 weeks follow-up (see Table 3).

Table 3. Kruskall-Wallis test - mean HDSS at baseline and after 2, 6 and 12 weeks of administration of BTX-A

Variable	#	Follow-Up				P-Value
		Baseline	2 weeks	6 weeks	12 weeks	
HDSS	5	3.4 ± 0.55	2.2 ± 0.50	2.0 ± 0.00	2.5 ± 0.71	**0.031***

ns – not significant * - significant at 5%

Three non-blinded independent investigators assessed the sweating intensity after Minor's iodine starch test at baseline and during follow-up visits using the SIVS, which ranged from 0 (minimal sweating) to 5 (over-sweating). The average SIVS scores were calculated and recorded.

At baseline, the areas that received freshly reconstituted BTX-A have mean SIVS of 2.7; while mean SIVS were 3.3, 2.8, and 3.3 for those areas that received BTX-A reconstituted 1 month, 2 months, and 3 months prior to administration, respectively. Mean SIVS scores were 0, 0.25, 0.25 and 0.12 at 2 weeks; and 0.33, 0, 0.83 and 0 at 6 weeks; and 0, 0, 0.50 and 0 at 12 weeks for BTX-A reconstituted 0, 1, 2 and 3 months prior to administration, respectively.

Using Kruskall-Wallis test at 5% level of significance, SIVS was found to be not significantly different among these 4 treatment areas at baseline (p-value=0.792), at 2 weeks follow-up (p-value= 0.758), at 6 weeks follow-up (p-value=0.224) and at 12 weeks follow-up (p-value=0.392). This means that the efficacy of BTX-A reconstituted 1, 2 and 3 months prior to administration is comparable to freshly reconstituted BTX-A. In addition, significantly improved SIVS scores were noted as early as 2 weeks after in all 4 treatment groups (see Table 4).

Table 4. Kruskall-Wallis test - mean SIVS for BTX-A reconstituted at 0, 1, 2 and 3 months prior to administration at baseline and at 2, 6 and 12 weeks follow-up

Follow-Up	#	Mean ± SD, SIVS				P-Value
		BTX-A (0)[a]	BTX-A (1)[b]	BTX-A (2)[c]	BTX-A (3)[d]	
Baseline	5	2.70 ± 1.30	3.30 ± 0.45	2.80 ± 1.40	3.30 ± 0.45	**0.792[ns]**
2 weeks	4	0.00 ± 0.00	0.25 ± 0.50	0.25 ± 0.50	0.12 ± 0.25	**0.758[ns]**
6 weeks	3	0.33 ± 0.58	0.00 ± 0.00	0.83 ± 1.04	0.00 ± 0.00	**0.224[ns]**
12 weeks	1	0.00 ± 0.00	0.00 ± 0.00	0.50 ± 0.71	0.00 ± 0.00	**0.392[ns]**
P-Value		**0.012***	**0.010***	**0.036***	**0.013***	

a - Freshly reconstituted BTX-A

b - Reconstituted BTX-A stored for 1 month

c - Reconstituted BTX-A stored for 2 months

d - Reconstituted BTX-A stored for 3 months

ns – not significant * - significant at 5%

In all patients, there were no noted pain after injections, bruising and infection at baseline and at all follow-up visits.

DISCUSSION

Most manufacturers of BTX-A recommend using the toxin within 24 hours of reconstitution to ensure maximum efficacy and that any remaining solution should be discarded.[8-10] Because 1 100-unit vial is not always consumed in most circumstances (e.g., rhytides in the upper part of the face require approximately 70 units), the storage of reconstituted BTX-A has been a subject of great interest, with several studies evaluating the clinical efficacy of stored BTX-A.[2,11-13]

In our knowledge, this is the first study investigating the efficacy of BTX-A reconstituted and stored at 4˚C for more than 6 weeks. In addition, this is the first study investigating the efficacy of stored reconstituted BTX-A in the treatment of axillary of hyperhidrosis, as previous studies were conducted in patients with facial rhytides. In the authors' opinion, treatment of hyperhidrosis provides a more superior assessment of the efficacy of BTX-A, compared to rhytides, since Minor's iodine starch test and SIVS, with its 5-point visual scale, can be used in hyperhidrosis to objectively assess the decrease in sweating. The authors opted to treat only axillary hyperhidrosis and not palmoplantar hyperhidrosis for this pilot study because the latter is associated with more pain on injection and higher incidence of side effects, including weakness.

The results of our study showed that BTX-A reconstituted and stored at 4˚C for 1 month, 2 months and 3 months have comparable efficacy to freshly reconstituted BTX-A in the treatment of axillary hyperhidrosis at 2 weeks, 6 weeks and at 12 weeks after administration. In addition, there were no noted side effects in all patients at baseline and at all follow-up visits.

Because this pilot study showed that reconstituted BTX-A can be stored for at most 3 months before administration, the authors recommend that a randomized controlled trial be conducted to compare the clinical efficacy and safety of freshly reconstituted BTX-A and BTX-A reconstituted 3 months prior to administration to strengthen our findings.

In conclusion, the clinical efficacy and safety of BTX-A reconstituted 1, 2 and 3 months prior to administration is comparable to that of freshly reconstituted BTX-A in the treatment of axillary hyperhidrosis.

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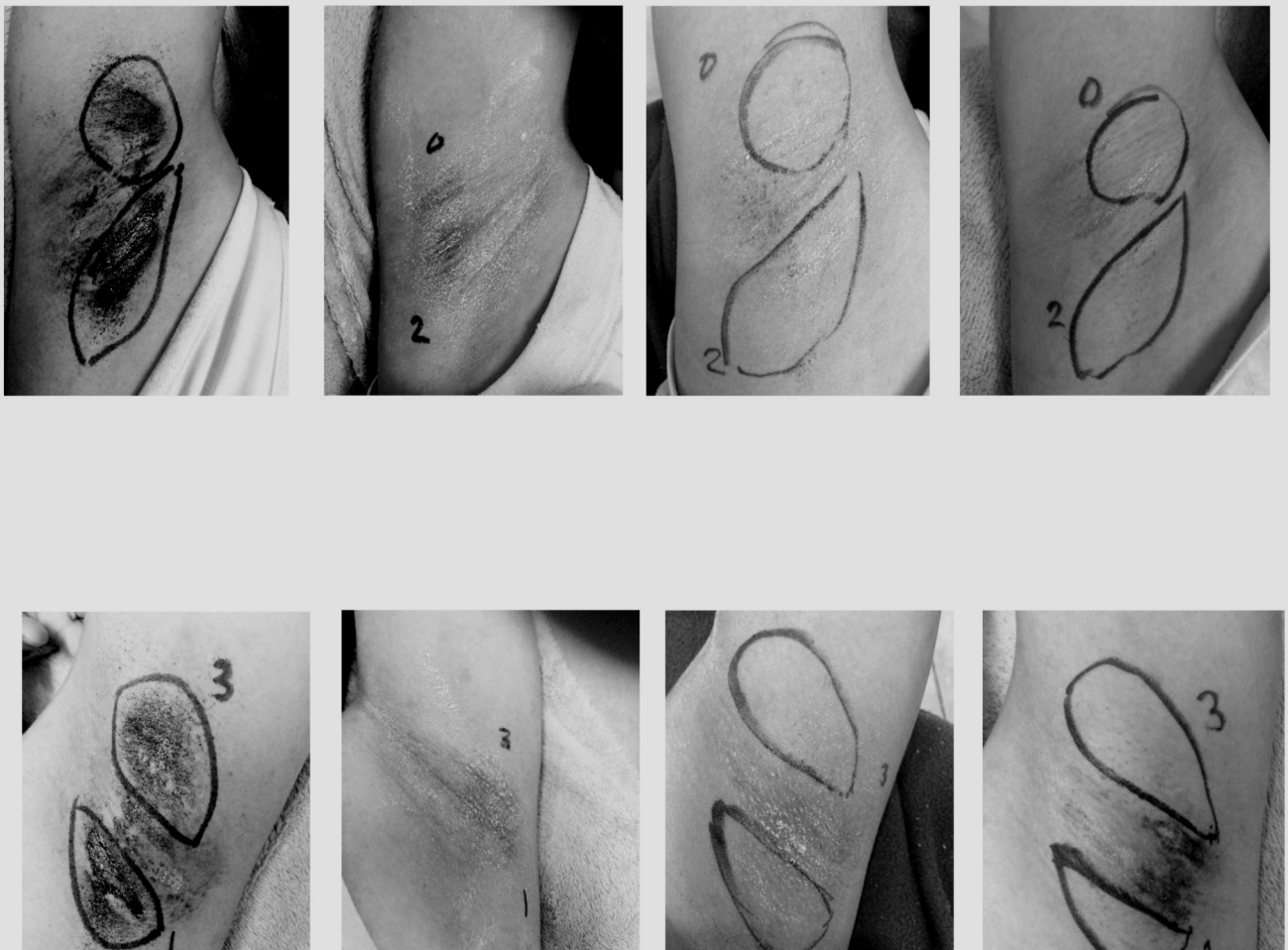
APPENDICES

Appendix 1. Minor's iodine test of patient A at baseline and at 2 weeks, 6 weeks and 12 weeks follow-up. Treatment areas were labelled 0 for area receiving freshly reconstituted BTX-A, 1 for reconstituted BTX-A stored for 1 month, 2 for reconstituted BTX-A stored for 2 months and 3 for reconstituted BTX-A stored for 3 months



Syringocystadenoma Papilliferum Arising Within A Nevus Sebaceous: A Case Report*

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ABSTRACT

Syringocystadenoma papilliferum is a rare benign adnexal skin tumor of apocrine or eccrine differentiation. It usually appears at puberty wherein a third of cases arise within a nevus sebaceous. We report a 14 year-old male with an erythematous fleshy plaque on the scalp of 3 years duration that developed from a pre-existing hairless plaque since birth. Histopathology confirmed the above diagnosis.

Keywords: Syringocystadenoma papilliferum, nevus sebaceous, adnexal tumor

INTRODUCTION

Syringocystadenoma papilliferum is a rare benign tumor derived from apocrine or eccrine glands. First described by Werther in 1913 as an unusual tumor, it was termed as naevus syringadenomatosus papilliferus. It commonly appears at puberty wherein one-third of cases arise from a nevus sebaceous. Syringocystadenoma papilliferum usually presents as a solitary brown to red papillomatous or verrucous, moist plaque on the head and neck that often becomes indurated and crusted due to stromal fibrosis and accumulation of dried blood or exudates from associated apocrine gland secretions. [1,2,3]

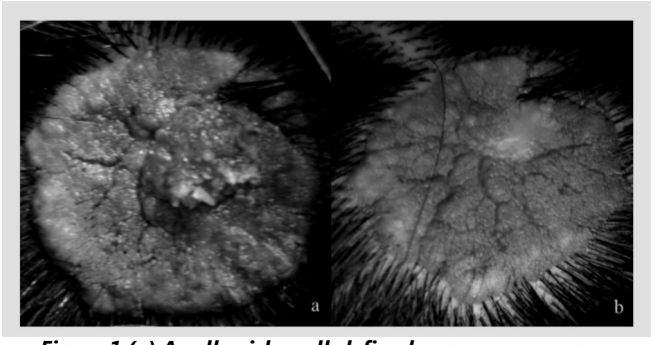

Figure 1 (a) A yellowish, well-defined, waxy, verrucous plaque with an erythematous fleshy plaque on the center, (b) Patient 7 months post excision and Electrocautery of syringocystadenoma papilliferum

CASE HISTORY

An otherwise healthy 14 year-old male presented at our clinic with a slowly growing plaque on his scalp of three years duration. The lesion was noted to develop from a pre-existing hairless plaque since birth. Except for the presence of blood tinged discharge and occasional pruritus, there were no associated signs and symptoms. Clinical examination revealed a solitary, erythematous, well defined, round fleshy plaque measuring 1x1.5cm on top of a yellowish, well-defined, round, waxy, verrucous, hairless plaque measuring 4x4 cm on the scalp. (Figure 1a)

A 3mm punch biopsy was performed on both lesions. Histopathologically, the yellowish, waxy, verrucous plaque revealed hyperkeratosis, orthokeratosis and papillomatosis. Follicular infundibula were widely dilated and plugged by keratin. Enlarged and mature sebaceous glands in the superficial dermis and mature apocrine glands in the deeper dermis were present. (Figure 2a and 2b)

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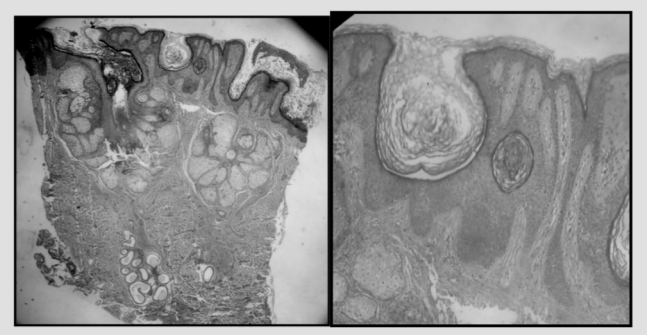

Figure 2 (a) Photomicrograph of a specimen taken from yellowish waxy, verrucous plaque on the scalp showing nevus sebaceous characterized by hyperkeratosis and papillomatosis; follicular infundibulum dilated and plugged by keratin, enlarged and mature sebaceous glands in the superficial dermis and mature apocrine glands in the deep dermis. (b) On higher magnification, Nevus sebaceous exhibiting hyperkeratosis and papillomatosis, dilated follicular infundibulum plugged with keratin

The second lesion consisting of the erythematous, fleshy plaque revealed papillomatosis in the epidermis. Several cystic invaginations extend downward from the epidermis and numerous papillary projections extend into the lumina of the invaginations. (Figure 3 a,b,c) Papillary projections were lined by two rows of cells: an inner layer of high columnar cells with oval nuclei and faintly eosinophilic cytoplasm showing hints of decapitation secretion and an outer layer of small cuboidal cells with round nuclei and scanty cytoplasm. (Figure 4) Also present were dense cellular infiltrates composed nearly entirely of plasma cells in the stroma, papillary projections with dilated and congested blood vessels, apocrine and tubular glands in the deep dermis. (Figure 5) Final clinicopathologic diagnosis was Nevus Sebaceous with Syringocystadenoma papilliferum.

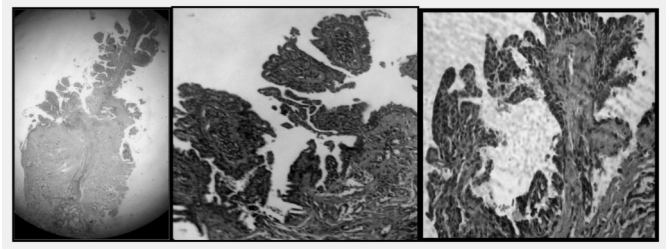

Figure 3 (a) Photomicrograph of a specimen taken from an erythematous fleshy plaque on the scalp shows SCAP characterized by cystic invaginations extending downward from the epidermis, numerous papillary projections, papillomatosis and mature apocrine glands in the lower dermis (b) On higher magnification are numerous papillary projections extending into the lumina of the invaginations (c) papillary folds projecting into the cystic spaces

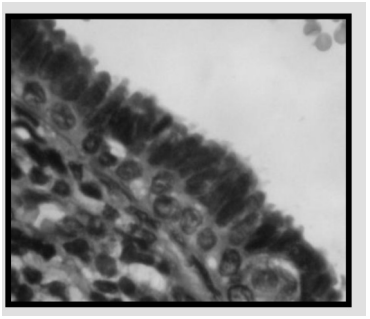

Figure 4 papillary projections lined by glandular epithelium consisting of 2 rows of cells: columnar cells with oval nuclei showing hints of decapitation secretion and cuboidal cells with round nuclei

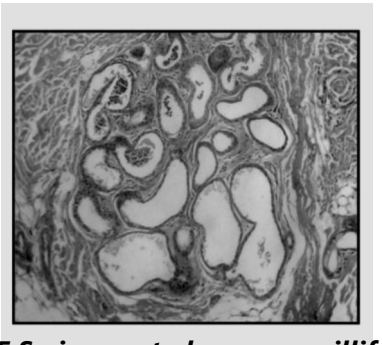

Figure 5 Syringocystadenoma papilliferum showing numerous apocrine glands in the deep dermis

Patient was referred to Pediatrics for general check-up and Ophthalmology for baseline eye exam. Physical examinations and routine laboratory work-ups revealed normal findings. Electrocautery with curettage of syringocystadenoma papilliferum was performed leaving a healed scar with no r ecurrence seven months post treatment. (Figure 1b) Patient was informed about possible occurrence of benign and malignant tumors that may complicate nevus sebaceous and was advised follow-up for any untoward clinical changes (bleeding or development of new lesions).

DISCUSSION

Nevus sebaceous is a benign lesion with epidermal, follicular, sebaceous and apocrine elements. Originally described by Jadassohn in 1895 as a hamartoma composed predominantly of sebaceous glands, it presents at birth as a solitary, yellowish, hairless patch mainly on the head and neck that becomes raised and papillomatous at puberty due to the effect of androgen on the glands.[4,5,] Mehregan and Pinkus described 3 clinico-pathologic

stages: 1) the early or infantile stage clinically appears as a smooth, yellowish-orange patch and is characterized by papillomatous epithelial hyperplasia and underdeveloped hairs, 2) the second, adolescent stage presents as thicker and verrucous lesions characterized by massive development of sebaceous glands, epidermal verrucous hyperplasia, and the maturation of apocrine glands, 3) the third or adult stage is characterized by the development of tumors of epidermal and adnexal origin such as syringocystadenoma papilliferum (5%), trichoblastoma (4.69%), trichillemomma (2%) and sebaceoma (2%). Other benign lesions reported include viral warts (2.4%), nevocellular nevus (0.83%), keratoacanthoma (0.67%), and seborrheic keratosis (0.50%).[4,6] The lifetime risk of malignant transformation of nevus sebaceous vary from 5 and 22% [7] Basal cell carcinoma, once thought to be the most common malignant tumor developed rarely (0.8%).[6] Thus, removal of nevus sebaceous for cancer prophylaxis in children is no longer recommended.[6] In the absence of signs for malignant transformation, the decision to undergo surgery would be based on safety, tolerability of anesthesia and the extent of excision required should there be increase growth of the lesion. Nevus sebaceous causes cosmetic deformity and alopecia.

Syringocystadenoma papilliferum is a hamartoma arising from pluripotent cells derived from apocrine or eccrine glands. Fifty percent are present at birth or infancy and commonly arises during puberty. [2,3] Seventy-five percent occurs on the head and neck although lesions on the trunk, axilla, genitalia and extremities have been reported.[8,9,10, 11] Three clinical types have been described: 1) the plaque type presenting as hairless area in the scalp that becomes nodular, verrucous or crusted during puberty and usually associated with nevus sebaceous, 2) the linear type consisting of groups of multiple, pink to red firm papules or nodules 1-10mm on the neck or face 3) the solitary nodular form appearing as domed, umbilicated or pedunculated lesions measuring up to 1cm on the trunk, shoulder, axilla and genital area. The two latter forms occur less often.[3] Diagnosis is by clinical suspicion and confirmed by histopathology, which shows epidermal papillomatosis, several cystic invaginations extending downward from epidermis and numerous papillary projections extending into the lumen of cystic invaginations. Invaginations and papillary projections are lined by two rows of cells: an outer layer of small cuboidal cells with basophilic nuclei and an inner layer of columnar cells exhibiting decapitation secretion. Apocrine glands are prominent in the dermis and inflammatory plasma cells are present in the stroma within the papillary projections.[3]

Syringocystadenoma papilliferum with nevus sebaceous has increased risk for malignant potential. The most common of which is basal cell carcinoma occurring in 10% of cases and is due to loss of allele at 9q22. Other tumors reported to develop include squamous cell carcinoma, verrucous carcinoma and ductal carcinoma. Long-standing syringocystadenoma papilliferum could evolve into a syringocystadenocarcinoma papilliferum. Complete surgical excision of syringocystadenoma papilliferum is recommended to eliminate risk of malignant degeneration. [1,3,12] Other treatment modalities include carbon dioxide lasers, Moh's micrographic surgery and electrocautery with curettage.

CONCLUSION

Syringocystadenoma papilliferum is a rare benign tumor wherein one-third of cases arise within a nevus sebaceous. There is a risk for malignant degeneration of syringocystadenoma papilliferum and complete surgical excision is the treatment of choice whenever possible. Close observation is recommended for nevus sebaceous. Surgical intervention may be required should there be signs of malignant degeneration.

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Gorlin Syndrome in a 48-year-old Filipino Woman: A Case Report*

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ABSTRACT

INTRODUCTION: Gorlin syndrome is a rare autosomal dominant disorder characterized by a wide range of developmental abnormalities and a predisposition to neoplasms. The estimated prevalence is 1/57,000[1] to 1/256,000[2]. Main clinical manifestations include multiple basal cell carcinomas, odontogenic keratocysts, skeletal abnormalities, ovarian fibromas and other disorders.

CASE: A 48 year old woman presented with multiple brown-black to skin-colored pearly macules, papules and nodules over the scalp, face, neck, trunk, upper and lower extremities. Histological examination at 2 sites revealed basal cell carcinoma. This was accompanied by findings of odontogenic keratocysts, palmar pits, posterior falx calcification, exotropia and multiple myoma uteri. Electrodessication with curettage of superficial basal cell carcinomas (< 1 cm.) was combined with wide excision of nodular basal cell carcinomas on the left temporal area (followed by rotational scalp flap reconstruction), right lateral breast, left inframammary area, right and left anterior thigh.

CONCLUSION: Gorlin syndrome is a hereditary condition affecting various organ systems. Management requires a multidisciplinary approach and regular medical surveillance is required.

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INTRODUCTION

Gorlin syndrome, also known as Gorlin-Goltz syndrome, nevoid basal cell carcinoma syndrome (NBCCS) and basal cell nevus syndrome (BCNS), is a rare autosomal dominant condition with complete penetrance and variable expressibility. This syndrome is characterized by multiple basal cell carcinomas (BCCs), odontogenic keratocysts, palmar or plantar pits, ectopic calcification including calcification of the falx cerebri, skeletal abnormalities and neoplasms.

This disorder was found to arise from mutations in the tumor suppressor PTCH1 gene. Although commonly inherited, it may also arise de novo. The estimated prevalence is estimated at 1/57,000[1] to 1/256,000[2]. Although it may affect any ethnic group, most documented cases are Caucasians.[2,3] In the Philippines there have only been two cases reported. [4,5]

Diagnosis is based on the spectrum of clinical findings. The objective of the present study is to report a case of a 48-year-old Filipino woman with clinical findings consistent with Gorlin Syndrome.

CASE REPORT

A 48-year-old Filipino woman from Laguna presented with multiple brown to black and skin-colored pearly macules, papules, plaques and nodules on the scalp, face, neck, trunk and extremities that were noted to increase in number in size in the past 12 years. This was accompanied by intermittent pruritus and bleeding upon manipulation.

Review of systems revealed prolonged and excessive menstrual bleeding with intermittent tooth pain. There was no weight loss, anorexia, jaw swelling, bleeding gums or seizures. Patient has a history of prolonged sun exposure for 7 years working as a door-to-door saleslady. No similar lesions were noted in other family members.

Physical examination revealed exotropia (FIGURE 1). No teeth abnormalities, jaw masses and skeletal deformities were noted. Examination of the skin revealed brown to black and skin-colored pearly macules, papules, plaques and nodules measuring 0.2 x 0.2 cm to 1.5cm x 1.5cm on the scalp, face, neck, trunk, back, upper and lower extremities (FIGURES 2-5). Numerous tiny pits were noted on both palms (FIGURE 6). No plantar pits were observed.

On dermoscopy of lesions, arborizing telangiectasias and blue-grey ovoid nests were noted.

A 3-mm skin punch biopsy was done at two (2) sites: a macule on the sternal area (FIGURE 7-A, 7-B), and a nodule on the left temporal region (FIGURE 8-A, 8-B). Histopathology of both specimens showed islands of basaloid cells containing dense melanin pigments, some showing hyperchromatic nuclei. The specimens were signed out as superficial BCC and nodular BCC, respectively.

Transvaginal ultrasound revealed multiple uterine myomas (FIGURE 9). Digital panorex x-ray done revealed the presence of odontogenic keratocysts (FIGURE 10). Cranial MRI revealed posterior falx calcification (FIGURE 11). Investigative findings were consistent with our clinical diagnosis of Gorlin syndrome.

The patient was admitted for removal of all skin lesions. Patient underwent electrodessication and curettage of superficial basal cell carcinomas measuring less than 1 cm on the scalp, face, chest, trunk and extremities with wide excision of multiple basal cell carcinomas on the right lateral breast, left infra-mammary area, right and left anterior thigh and left temporal area followed by rotational scalp flap reconstruction.

On follow-up after 1 week, lesions were noted to be healing well. At 3 and 6 months, no new lesions or recurrence of lesions were noted.

DISCUSSION

Gorlin syndrome is a rare autosomal dominant condition with complete penetrance and variable expressibility. Although commonly inherited, 35-50% of cases represent de novo mutations.[6] In 1960, Gorlin and Goltz defined a condition comprising a triad of multiple basal cell nevi, keratocysts of the jaw and bifid ribs characterizing the this syndrome.[7] The estimated prevalence is estimated at 1/57,000[1] to 1/256,000[2]. There is no sexual and racial predilection.[8,9]

The mutation in Gorlin syndrome involves the PTCH gene located on chromosome 9q22.3[1] that acts as a tumor suppressor in the hedgehog signaling pathway which regulates the production of growth promoting transcription factors.[10]

This syndrome is characterized by multiple basal cell carcinomas, odontogenic keratocysts, palmar or plantar pits, ectopic calcification including calcification of the falx cerebri, skeletal abnormalities and neoplasms such as uterine fibromas. Anomalies in Gorlin syndrome are summarized in Table 1.[3] Diagnostic criteria are summarized in Table 2.[8,9]

Table 1. Anomalies in nevoid basal cell carcinoma syndrome[3]

Skeletal anomalies	palatine ridges
Bifid ribs	Odontogenic keratocysts
Splayed/fused ribs	Malocclusion(s) (maxillary hypoplasia
Cervical ribs	and
Absent/rudimentary ribs	mandibular hyperplasia, cleft palate)
Scoliosis	Dental ectopic position
Hemivertebrae	Impacted teeth and/or agenesis
Flame-shaped lucencies hand/feet	
Polydactyly	*Skin anomalies*
Syndactyly	Basal Cell Carcinoma
Shortened 4th metacarpal	Palmar and/or plantar pits
Craniofacial anomalies	*Sexual anomalies*
Frontal bossing	Uterine and ovarian fibromas
Brachycephaly	Calcified ovarian cysts
Macrocephaly	Supernumerary nipple
'Coarse face'	Hypogonadism and cryptorchidism
Calcification of falces	
Tentorium cerebellum calcification	
Bridged sella turcica	*Ophthalmic anomalies*
	Congenital amaurosis
Neurological anomalies	Exotropia
Agenesis/disgenesis of corpus callosum	Hypertelorism
Congenital hydrocephalus	Ptosis
Mental retardation	Internal strabismus
Medulloblastoma	Glaucoma
Meningioma	Coloboma
Schizoid personality	Blindness
Oropharyngeal anomalies	*Cardiac anomalies*
Cleft lip and/or palate	Cardiac fibroma
High-arched palate or prominent	

Table 2. The diagnostic criteria of nevoid basal cell carcinoma syndrome[8,9]

The diagnosis of NBCCS requires the presence of two major, or one major and two minor criteria:

Major criteria:

1. Multiple (>2) basal cell carcinomas (BCC) or one BCC < age of 20 years
2. Histologically-proven odontogenic keratocysts of the jaw
3. Three or more palmar or plantar pits
4. Bilamellar calcification of the falx cerebri
5. Bifid, fused or markedly splayed ribs
6. First degree relative with NBCCS
7. PTC gene mutation

Minor criteria:

1. Proven macrocephaly, after adjustment for height
2. One of several orofacial congenital malformations: cleft lip or palate, frontal bossing, 'coarse face', moderate or severe hypertelorism
3. Other skeletal abnormalities: Sprengel deformity, marked pectus deformity, marked syndactyly of the digits
4. Radiological abnormalities: Bridging of the sella turcica, vertebral anomalies such as hemivertebrae, fusion or elongation of the vertebral bodies, modelling defects of the hands and feet, or flame shaped lucencies or the hands or feet
5. Ovarian fibroma
6. Medulloblastoma

The presence of multiple basal cell carcinomas, odontogenic keratocysts, palmar pits and calcification of falx cerebri in association with exotropia and uterine myomas described in the case presented earlier fulfilled the diagnostic criteria of Gorlin syndrome.

The most frequent skin manifestation of Gorlin syndrome are multiple basal cell carcinomas (BCCs). BCCs are seen more frequently in Caucasians compared to African Americans which probably reflect the protective action of melanin from UV light.[9] It has been demonstrated that UV radiation increased BCC development in mice with PTCH gene mutation.[10] This finding is especially important as early avoidance and sun protection can prevent the appearance of basal cell carcinomas in patients with this syndrome. Lesions usually appear between puberty and 35 years of age, ranging in number from one to thousands and principally affecting the epithelium of the chest and cervicofacial regions.[11] Most are located superficially in the epidermis for years before they begin invading the dermis. Signs of local invasion and

evidence of aggressiveness include increase in size and the development of ulceration, bleeding, and crusting.[3] Aside from chest and cervicofacial areas, patient also had multiple lesions involving the lower back and both upper and lower extremities.

Histopathology of nevoid BCC cannot be differentiated from sporadic BCC and about 30% of patients would present with two or more types of BCC patterns (superficial, morphea-like, solid, cystic, adenoid fibroepithelial).[12] In our patient, histopathology done at two sites revealed findings consistent with basal cell carcinoma. Intraoperative tissue sections revealed scalp nodule to be a mixed nodular and adenoid cystic type while lesions on the body were of the superficial type.

Odontogenic keratocysts (OKCs), which form from cells of the dental lamina, occur in 75% or the cases.[3] OKCs have a very aggressive nature. In patients with Gorlin syndrome, there is continued development of new and recurring cysts until the age of 30 after which it tends to decrease.[13] Most are asymptomatic but can manifest as jaw swelling, toothache or impacted teeth when enlarged. Most common sites are the mandible in the molar-ramus region (44%) followed by the incisor-canine (15%) and molar tuberosity (13%) regions.[13] Our patient presented with intermittent tooth pain. Digital panorex of the jaw revealed presence of odontogenic keratocysts. Patient was advised surgery, however, patient decided to defer the procedure to a later date due to financial constraints.

Palmar and plantar pits appear in 87% of patients with Gorlin syndrome.[9] They are asymptomatic, increase in number with age and are more commonly found on the palms (77%) than the soles (50%).[14] This may explain why our patient had palmar pits in the absence of plantar lesions.

Falx calcification is the most frequent radiologic sign of Gorlin syndrome, appearing in 37-80%[3]. Although usually asymptomatic, this may be of value in confirming the diagnosis.

Ovarian cysts and fibromas are found in 25-50% of affected women and are usually bilateral.[13] Pathologies in the ovary and uterus other than ovarian fibromas have also been documented in patients with Gorlin syndrome.[9] The ultrasonographic findings of multiple uterine myomas/ fibroids in our patient may also be attributed to the defect in tumor suppressor activity in patients with this syndrome. No ovarian abnormality was noted in our patient.

Patients affected with Gorlin syndrome must be evaluated and managed by a multidisciplinary team. Children and siblings must be clinically evaluated for evidence of the syndrome. The approach to adult patients with suspected or known Gorlin syndrome are as follows: Baseline cranial MRI and digital panorex of the jaw, dermatological examination every 4 months and prenatal counseling.[9] Management depends on the specific abnormalities present. Our patient was advised total abdominal hysterectomy and bilateral salpingo-oophorectomy to address symptomatic uterine fibroids and surgical removal of odontogenic keratocysts but patient decided to defer both procedures due to financial constraints.

There are no existing guidelines for the treatment of BCCs in patients with Gorlin syndrome. Frequent examination, counseling about avoidance of sun exposure and removal of small tumors are of particular importance. The type, location, size and aggressiveness of the lesions need to be assessed. The treatment recommendations must ideally have high cure rates, maximum preservation of surrounding tissue, acceptable cosmetic result and short healing time with minimal side effects.

Standard surgical excision with wide margins is a highly effective and common treatment option for BCCs. The 5–year cure rate is more than 99%.[15] Curettage with or without electrodessication is also widely used in the management of low –risk, non-aggressive, superficial BCCs- the type commonly seen in patients with Gorlin syndrome.[16] Cure rates of 95% or higher are possible for well-defined primary lesions.[17]

Non-invasive treatment methods include 5-FU, imiquimod and photodynamic therapy. 5-Fluorouracil 5% cream may be used for small, superficial BCCs in low-risk areas. It interferes with DNA synthesis by inhibiting thymidylate synthetase and inhibits cell proliferation. Cure rates of 91% were achieved after 3-4 weeks of treatment. Imiquimod 5%

cream, an immune response modifier, has been approved for the treatment of non-facial superficial BCC. Histologic clearance rates of 82% were achieved after 5 day application per week for 6 weeks.[19] Photodynamic therapy involves application of a tumor-localizing photosensitizing agent and light to cause selective destruction of malignant tissue. Local control rates of 56.3% at 12 months have been achieved.[20]

Patient underwent electrodessication and curettage of multiple superficial basal cell carcinomas measuring less than 1 cm on the scalp, face, chest, trunk and extremities with wide excision of multiple basal cell carcinomas on the right lateral breast, left infra-mammary area, right and left anterior thigh and left temporal area followed by rotational scalp flap reconstruction. Choice of treatment was based on the superior cure rates and cost-effectiveness compared to the other modalities.

Prognosis depends on the malignant progression of the patient's lesions. Lifetime monitoring is warranted to identify appearance of new and recurrent lesions. However, life expectancy as found to be no different from that of the general population.[2]

SUMMARY

We present a case of a 48-year-old woman with multiple skin-colored and pigmented macules, papules and nodules over the scalp, face, neck, trunk, upper and lower extremities that were histologically confirmed to be basal cell carcinomas. Additional findings were odontogenic keratocysts on digital panorex xray, palmar pits, exotropia, posterior falx calcification on cranial MRI and multiple uterine myomas on ultrasound. The spectrum of findings is consistent with Gorlin syndrome. Electrodessication with curretage of superficial basal cell carcinomas were combined with wide excision of nodules and plaques. In patients with Gorlin syndrome, a multidisciplinary approach involving experts from different specialties is important to appropriately evaluate and manage the different manifestations of the disease. As lesions can be recurrent, regular follow-up and medical surveillance is required. As each child has a 50% chance of inheriting this condition, genetic counseling is also mandatory.[5]

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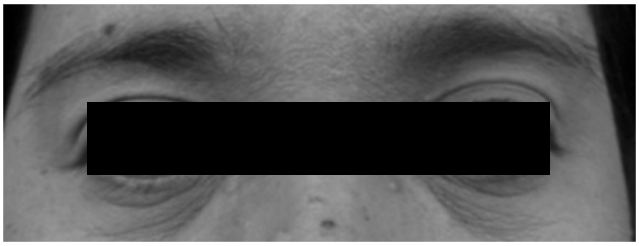

FIGURE 1. Exotropia

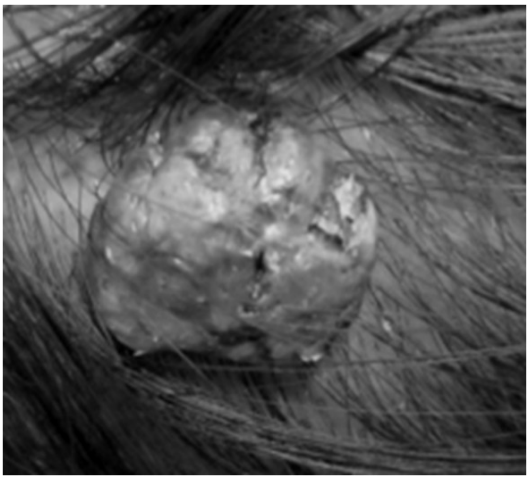

FIGURE 2. Nodule on left temproparietal scalp

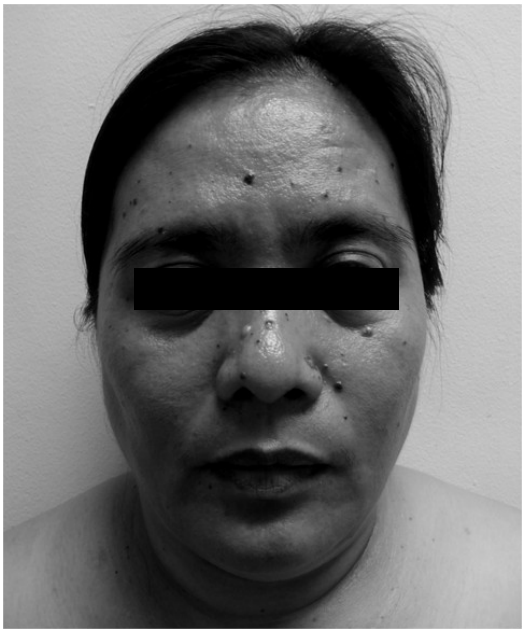

FIGURE 3. Face

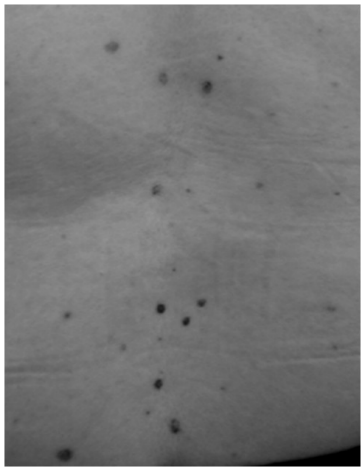

FIGURE 4. Lower Back

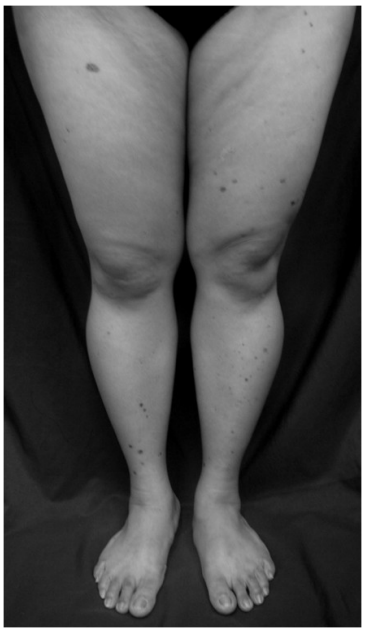

FIGURE 5. Lower extremities

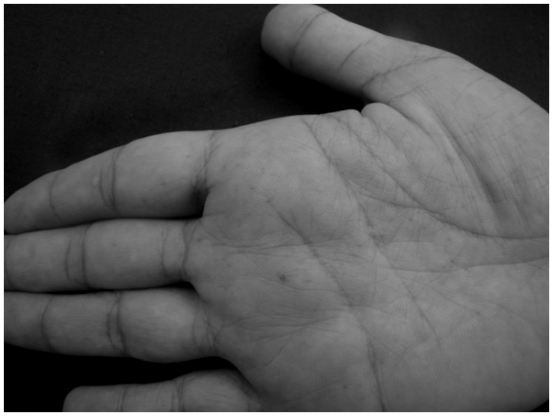

FIGURE 6. Palmar pits

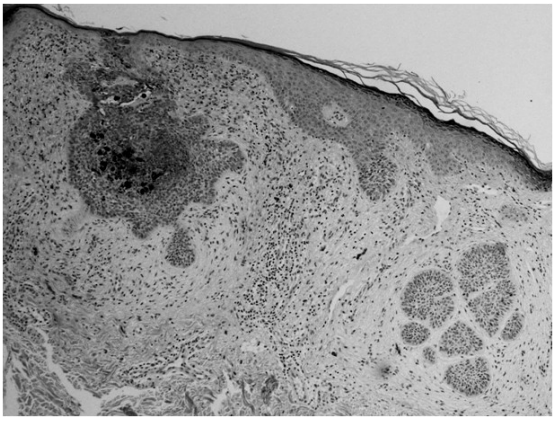

FIGURE 7-A

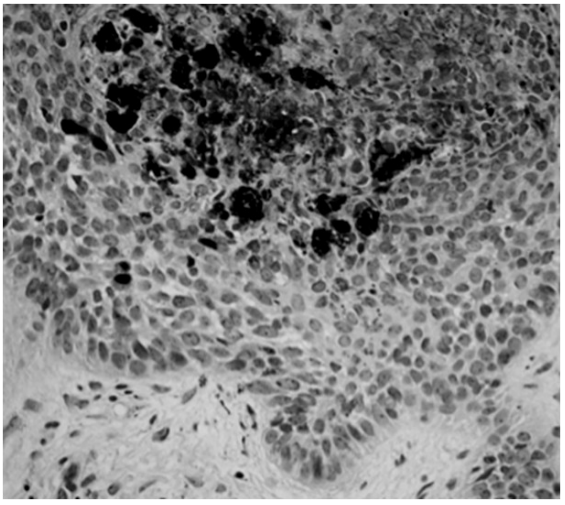

FIGURE 7-B

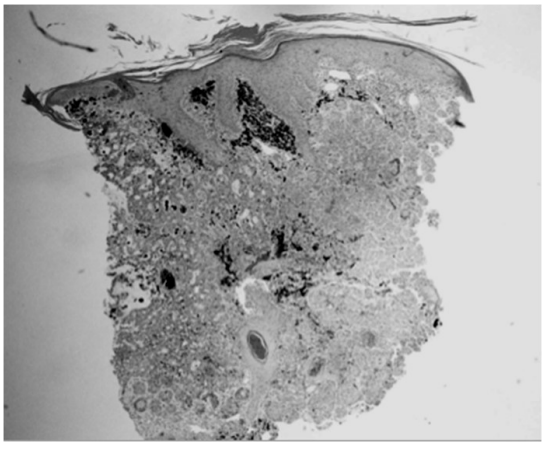

FIGURE 8-A

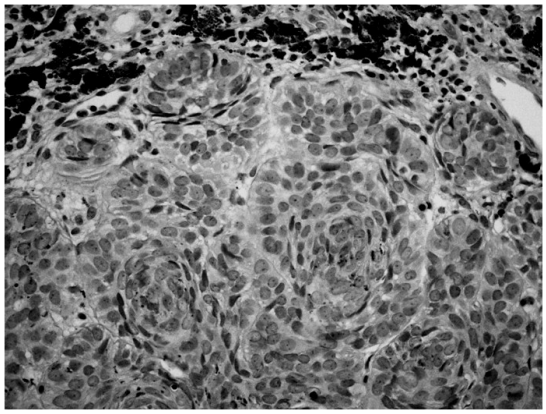

FIGURE 8-B

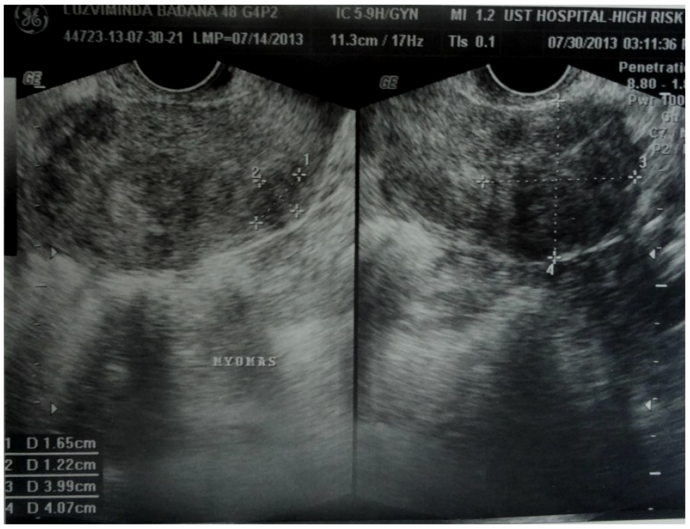

FIGURE 9. Uterine myomas

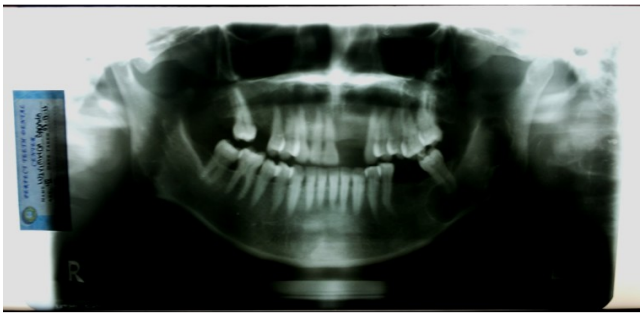

FIGURE 10. Odontogenic Keratocyst, body of the mandible Left

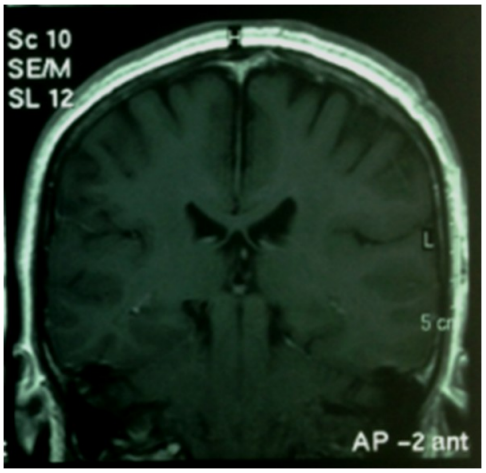

FIGURE 11. Posterior falx calcification

Diffuse Cutaneous Mastocytosis in a Filipino Newborn: A Case Report*

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Maria Jasmin J. Jamora, MD, FPDS[1]

ABSTRACT

INTRODUCTION: Cutaneous mastocytosis is the accumulation of mast cells in the skin. Diffuse cutaneous mastocytosis is a rare variant accounting for only 1.74% of al mastocytosis cases reported. Ninety percent of cases are seen in children presenting with multiple erythematous to yellow-tan papules and plaques with leathery texture. The pathogenesis is in the structure and activity of kit receptor expressed on mast cells, melanocytes and other cells.

CASE SUMMARY: This is a female neonate born to an 18 year old mother, G1P1 via vaginal delivery at 37 weeks age of gestation. Patient presented with a generalized involvement of multiple, well defined, indurated, leathery, brown papules and confluent plaques. Darier sign was positive. Histopathological examination revealed diffuse involvement of the dermis with mast cells. Giemsa stain was positive. Patient was diagnosed both clinically and histopathologically with diffuse cutaneous mastocytosis without systemic involvement. She was treated with H1 antihistamines and topical glucocorticoids.

CONCLUSION: Diffuse cutaneous mastocytosis can be diagnosed both clinically and histopathologically. Treatment is mostly symptomatic. It is always prudent to inform co-managing physicians, the patient, and their families of potential mast cell degranulating stimuli and to watch out for signs and symptoms for systemic involvement.

**From the Skin and Cancer Foundation Inc.*
[1]Consultant, Skin and Cancer Foundation Inc.

INTRODUCTION

Mastocytosis is a sporadic disease characterized by pathologically increased number of mast cells predominantly in the skin, bone marrow, liver, spleen, lymph nodes and gastrointestinal tract. There are seven variants of mastocytosis according to the World Health Organization (WHO) classification: cutaneous mastocytosis, indolent systemic mastocytosis, systemic mastocytosis with associated clonal hematological non-mast cell-lineage disease, mast cell leukemia, extracutaneousmastocytosis, mast cell sarcoma and aggressive systemic mastocytosis.[1]

In our country, based on the data from Philippine Pediatric Society, mastocytosis in general presents in 6 out of 2,598,210 patients aged 0-18 year old seen from May 2006 to present.[2]

Cutaneous mastocytosis (CM) represents over 90% of all mastocytosis cases and is the most common presentation with a predilection for the pediatric age group. CM is made up of three major variants: urticariapigmentosa (UP), mastocytoma and diffuse cutaneousmastocytosis (DCM). Approximately 58-90% of patients have the UP subtype, and 10-40% have mastocytoma. Diffuse cutaneous mastocytosis is the rarest variant accounting for only 1.74%.[3]

In Europe, 71 children with cutaneous mastocytosis were analyzed. 53 (75%) cases present with urticariapigmentosa, 12 (17%) with mastocytoma and 6 (8%) with diffuse cutaneous mastocytosis.[4] A study was done in Israel wherein they conducted a retrospective chart review of all pediatric cases diagnosed with cutaneous mastocytosis over the last 20 years. Of the 180 patients identified, 117 (65%) were diagnosed with urticarial pigmentosa, 62 (34.4%) with mastocytoma and only 1 (0.6%) with diffuse cutaneous mastocytosis.[5]

CASE REPORT

A female neonate with an APGAR score of 8,9 was born with leathery skin and brown nodules all over the body. The patient was born to non-consanguineous parents via vaginal delivery at 37 weeks AOG to an 18 year old, G1P1 (1001) mother. Mother had six prenatal check-ups at a local health center and was prescribed with multivitamins and ferrous sulfate. No systemic illness was noted during the course of pregnancy. Syphilis and HBsAg were both non reactive. No complications were encountered during delivery. No family history of any congenital anomalies or dermatologic disease was elicited on both the maternal and paternal side of the patient.

Physical examination revealed generalized involvement, with lesions consisting of multiple, well defined, indurated, leathery, brown papules and confluent plaques (Figure 1). No vesicles and bullae seen at that time. Darier sign was positive. A clinical diagnosis of diffuse cutaneous mastocytosis was made by the Dermatology service. The mother was advised regarding the condition. The patient's caregivers were instructed to keep the patient in a cool, comfortable environment, and to limit intense rubbing or manipulation of the patient's skin. Caution on giving mast cell degranulating agents such as anticholinergic preparations, aspirin and other NSAIDS, narcotics, polymyxin B sulfate, systemic anesthetics and certain food were also discussed with the people directly involved in the patient's care.

Skin punch biopsy (3mm) was done with consent and sent for H&E and Giemsa stains. Liver enzymes and clotting indices were increased, prompting referral to Pediatric Gastroenterology, Hematology and Oncology respectively, to evaluate for possibility of systemic involvement and rule out systemic mastocytosis. Additional hepatobiliary tree ultrasound, x-ray of skull, chest and pelvis and peripheral blood smear were requested.

New vesicles, bullae and crusted lesion were noted starting on the 8th DOL (Figure 2). Normal saline solution compresses on crusted areas was advised. Mometasone furoate cream was also applied to new bullous lesions.

Histopathological examination revealed diffuse infiltration of mast cells on the entire dermis. Giemsa stain was positive for mast cells. H1 antihistamine, Hydroxyzine was prescribed at 1.2-2 mg/kg TID to mitigate excess histamine release.

At 12th DOL, patient was observed to be less irritable, still with elevated liver enzymes, and no progression of cutaneous lesions were noted (Fig3).

DISCUSSION

Diffuse cutaneous is encountered almost exclusively in infants, rarely in neonates, and may persist into adult life. It has been associated with systemic mastocytosis particularly the indolent type. Deaths associated with extensive mast cell mediator release in both children and adults are rare but have been reported.[3]

The pathogenesis of mastocytosis reveals changes in the structure and activity of kit receptor expressed on mast cells (MC), melanocytes, and other cells. Stem cell factor (SCF) is the ligand for the transmembrane tyrosine kinase receptor c-kit, and is an important growth factor for the final maturation and development of mast cells. Uncontrolled proliferation of mast cells in mastocytosis seems to be secondary to abnormalities of ligand-receptor (c-kit ligand).[5]

Patients presenting with childhood CM may complain of pruritus and flushing, often exacerbated by exercise, heat or local trauma to skin lesions. They may also experience abdominal pain, diarrhea, palpitations, dizziness and syncope. When there is extracutaneous involvement, patients may present with fever, night sweats, malaise, weight loss, bone pain, epigastric distress, and cognitive disorganization. It is to be noted that in mastocytosis, there is a relative absence of pulmonary symptoms.[3]

Cutaneous presentation of diffuse cutaneous mastocytosis includes multiple erythematous to yellow-tan papules and plaques with leathery texture.[5] Some may describe it as peaud'orange appearance on the skin surface (Figure 4). cutaneous mastocytosis and urticariapigmentosa are associated with a non-scarring bullous eruption. The vesicles and bullae usually resolve when patient is about 3 to 5 years of age.[6] DCM presenting with generalized bullae has a relatively poorer prognosis and has been observed to have a higher rate of transformation to systemic mastocytosis (SM).[3] The blisters are believed to be due to serine proteases that are released from mast cells.

Basically, the diagnosis of childhood CM is based on the clinical presentation of the cutaneous lesions, a positive Darier sign and the presence of significant mast cell hyperplasia on histologic study.

Darier sign is the development of an urticarial wheal after firmly rubbing a characteristic lesion. The sign is more apparent in childhood urticarial pigmentosa and mastocytomas rather than in adult mastocytosis. This is elucidated by the fact that there is a 40 to 150 fold greater mast cell concentrations in childhood UP and mastocytomas than normal skin as compared to 8-fold greater content in adult mastocytosis.[6] Stains used to detect mast cells in tissues include Giemsa, toluidine blue, Leder, and monoclonal antibodies that recognize tryptase or CD117.[3]

Treatment for cutaneous mastocytosis is conservative and symptomatic. The goal is alleviation of symptoms using anti-mediator drugs such as antihistamines, cromolyn sodium, acetyl salicylic acid and ketotifen. The importance of emollients should be emphasized. To decrease histamine release associated pruritus, flushing and wheal formation, intake of H1 antihistamines such as hydroxyzine, cetirizine and fexofenadine is effective. H2 antihistamines for management of excess gastric secretion such as cimetidine and ranitidine can then be combined to H1 blocker to support control of symptoms of mastocytosis.[7,8]

Patients and their family members should be informed of potential mast cell degranulating stimuli such as ingested alcohol, anticholinergic preparations, aspirin and other NSAIDS, narcotics, polymyxin B sulfate, systemic anesthetics, heat and friction. A number of systemic anesthetic agents have been directly and indirectly linked in precipitating symptoms of mastocytosis. It is recommended to monitor patients 24 hours post operatively after undergoing surgery with general anesthesia to watch out for delayed anaphylaxis, although, injections of lidocaine can be used safely in these cases. Foods such as crawfish, lobster, spices, cheese and hot beverages should also be avoided.

Case reports showed good cutaneous response to application of psoralen plus PUVA, local corticosteroids with occlusion or intralesional triamcinolone acetonide injections.2 Under occlusion potent topical glucocorticoids for 8 h/day for 8-12

weeks decreases the number of lesional skin mast cells. However this method can cause skin atrophy and when the treatment is discontinued, recurrence of lesions are expected within the year. 1-2 months treatment of methoxypsoralen with ultraviolet A (PUVA) light given four times a week can aid in the pruritus and appearance of wheals of CM patients. Though, within 3-6 months of discontinuation of PUVA pruritus often reappears.

Prognosis of diffuse cutaneous mastocytosis is variable, though most bullous lesions spontaneously resolve before 5 years of age. DCM is also linked to have an increased risk of systemic involvement. Mast cell leukemia has been reported in persistence of diffuse cutaneous mastocytosis in adulthood that has developed to indolent systemic mastocytosis.

CONCLUSION

Diffuse cutaneous mastocytosis occurs most exclusive in infants but is rarely seen in neonates such as the case presented. Cutaneous presentation ranges from leathery papules and plaques as well as vesicles and bullae. Physicians and family members should be informed of the potential mast cell degranulating stimuli and also of the signs and symptoms for systemic involvement. Mainstay of treatment remains to be application emollients, and topical glucocorticosteroids plus addition of H1 with or without H2 antihistamines.

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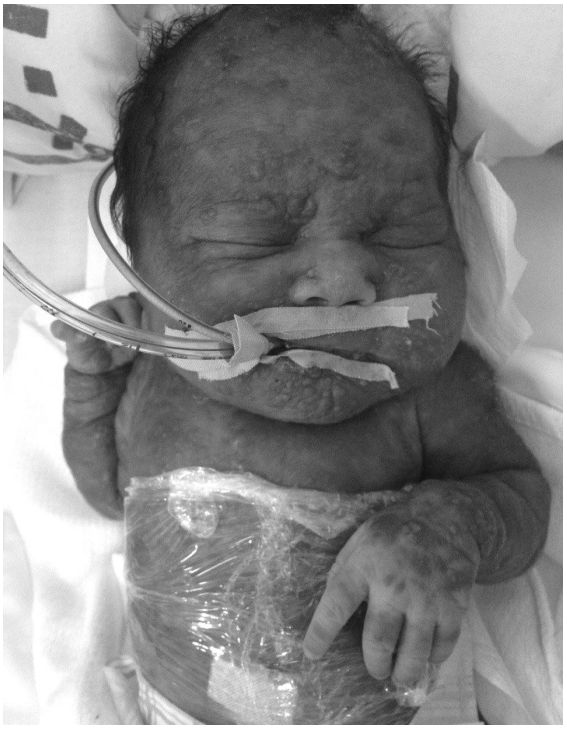

Figure 1

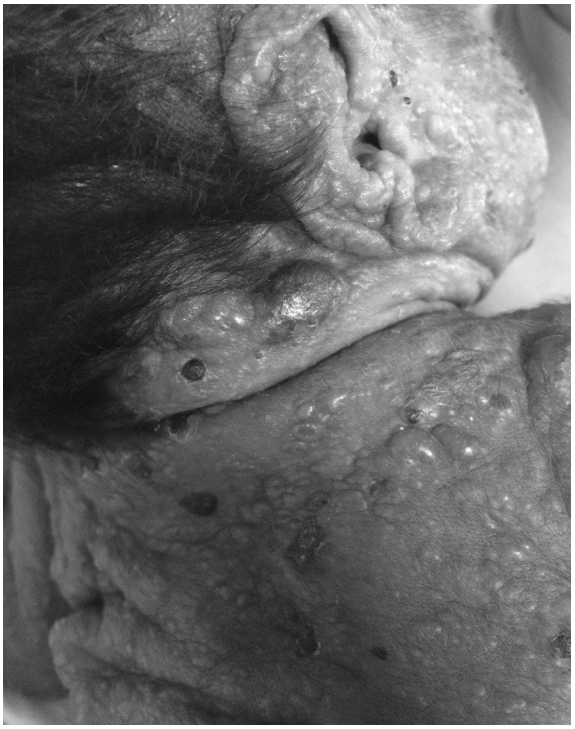

Figure 2

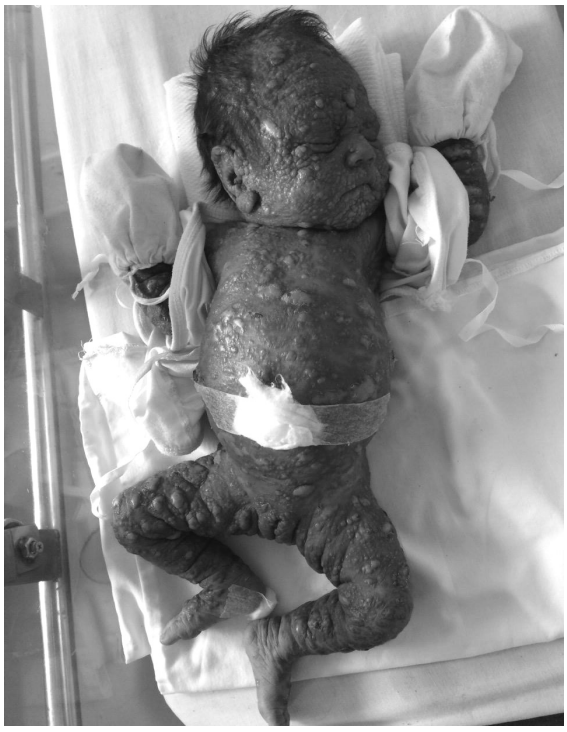

Figure 3

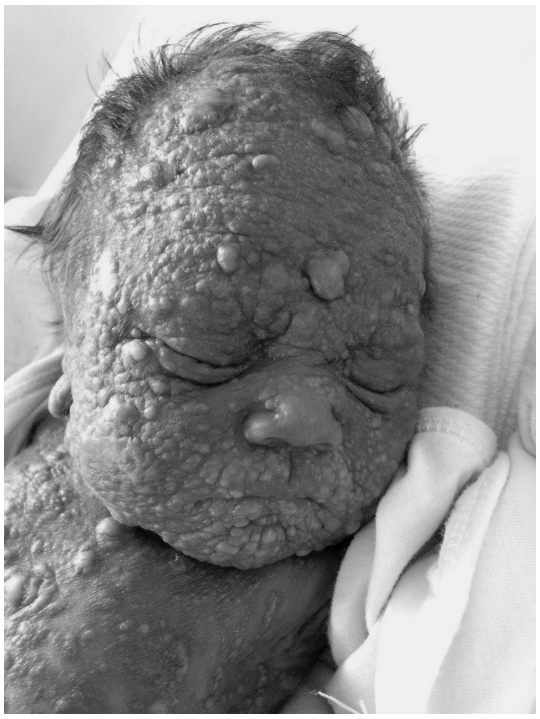

Figure 4

Bejeweled: Chronic Bullous Disease of Childhood in a 2-Year Old Treated with Colchicine: A Case Report*

Danielle Nicolle Dionisio Mejia, MD[1]
Mae Ramirez-Quizon, MD, FPDS[2]

ABSTRACT

Linear IgA bullous dermatosis, also known as chronic bullous disease of childhood when present in the pediatric age group, is a rare blistering disease more predominantly seen in females less than five years old. This case describes a 2-year old girl who presented with scattered, tense vesicles and bullae on an erythematous base forming the classic "cluster of jewels" appearance. This clinical picture is often mistaken as bullous impetigo, commonly seen in children, delaying diagnosis and prompt treatment. Histopathologic examination showed subepidermal blistering with a predominantly neutrophilic inflammatory infiltrate. The direct immunofluorescence studies revealed a linear band of IgA deposition in the basement membrane zone consistent with the diagnosis of CBDC. The patient was started on colchicine and oral prednisone at 1 mg/kg/day and complete resolution was achieved within two weeks of therapy.

Keywords

Linear IgA bullous dermatoses, Chronic bullous disease of childhood, colchicine

**First place, Case report category, Rizal Medical Center Annual Resident's Research Contest 2017*

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INTRODUCTION

Chronic bullous disease of childhood (CBDC) is a rare autoimmune blistering disease predominantly seen in children less than five years old with a slight female predominance.[1] This entity presents as multiple scattered tense vesicles and bullae on an erythematous base. These vesicles occur in clusters exhibiting a "cluster of jewels" or a "string of pearls" appearance. Fresh lesions are sometimes seen around older ones presenting as a "collarette of blisters". Histopathologically, it presents as subepidermal blistering confirmed through direct immunofluorescence, seen as a homogenous linear band of IgA1 deposition at the basement membrane zone.[2] Antibodies are said to target more than 1 antigen. IgA is bound to a 97 k-Da antigen present in the lamina lucida. This antigen is identical to the 180 k-Da BP antigen essential in anchoring basal keratinocytes to the epidermal basement membrane.[1] This disease will occur with spontaneous resolution of lesions within two years however, treatment is aimed at controlling flares and inducing remission. The standard of care involves the use of dapsone at 25-100 mg/day however, due to difficult access for this drug, colchicine was used and was noted to control the flare.

Case Report

A 2-year old female presented with a 1-month history of a solitary tense blister in the left lower leg that eroded upon scratching. There was subsequent spread to the lower extremities, trunk, and neck leaving erosions due to incessant scratching. The patient was given hydrocortisone cream applied twice a day for a week and oral antihistamines which provided no relief. Pulverized amoxicillin was later applied with an increase in the number of lesions. The blisters eventually spread to the face which prompted consult. The primary service diagnosed this as a case of bullous impetigo and referred to the dermatology service. Cutaneous examination revealed multiple well-defined, salmon pink-red annular plaques bordered by tense vesicles and bullae arranged in a cluster of jewels appearance. Some plaques appear with central erythematous erosions topped with hemorrhagic crusting. [Figure 1 A-D]

Histopathology revealed a subepidermal blister with a moderately dense superficial perivascular and interstitial infiltrate composed of neutrophils mostly, and occasional lymphocytes. [Figure 2 A-B] Direct immunofluorescence showed a homogenous linear band of IgA at the dermo-epidermal junction consistent with linear IgA disease. [Figure 3]

As dapsone is not locally available, the patient was started on oral prednisone at 1 mg/kg/day after breakfast. There was slight resolution of lesions, but new lesions erupted. [Figure 4 A-F]. Colchicine was started at 500 mg twice a day with resolution of lesions in two weeks. [Figure 5 A-J]

Discussion

This case of a 2-year old girl with a solitary blister on the left leg that progressed to tense vesicles and bullae within the border of erythematous annular plaques in a cluster of jewels appearance was treated with an oral corticosteroid to immediately suppress the inflammation coupled with a second line drug and noticeable improvement was seen. Most cases of CBDC are treated with dapsone at an initial dose of 25 mg to 100 mg per day. This can be given together with oral corticosteroids. The average treatment duration is 20 months.[5] In the Philippines, dapsone is only available as part of the multidrug treatment blister packs for the treatment of leprosy hence colchicine was given. Colchicine inhibits microtubule assembly through the formation of tubulin that interferes with mitosis and cellular migration. It also inhibits cellular adherence, motility, and chemotaxis. One of its off-label uses includes the treatment of CBDC at a dose of 0.5 mg/day. [6] This drug has been proven safe and well tolerated by children with a safety profile comparable to its use in adults. [7]. The most common side effects reported are gastrointestinal in nature. Diarrhea, abdominal pain, nausea and vomiting may be seen in patients taking high doses (about 4.6 mg in 6 hours). This patient was given a dose within the prescribed therapeutic dose per age and did not experience any of these side effects. A baseline complete blood count was taken and then monitored for agranulocytosis, anemia, and thrombocytopenia. The blood urea nitrogen, serum creatinine, aspartate amino transferase and alanine aminotransferase were also taken since dosing requirements are adjusted in cases of hepatic and renal impairment.[8]

According to Banodkar et al., CBDC, histopathologically, presents with a neutrophilic predominance and the action of colchicine against neutrophils was a clear indication for using this medication for this case. [7,8] Colchicine dosed at 0.5 mg twice a day with concomitant decrease in oral prednisone was said to achieve total remission with no relapse noted on maintenance. In the case reported by Zeharia et al., colchicine at the said dose was started twice daily and remission was achieved in two weeks without any side effects noted in the child.[9] Another case of CBDC was reported by Salud et al., wherein oral prednisone at 0.5 mg/kg/day tapered over a month resulted in resolution of the bullae within 2 weeks.[10]. Prednisone at 1 mg/kg/day may be also started initially as one waits for the histopathologic report and colchicine at 0.5mg twice daily be added once certain with the diagnosis. [11]

Conclusion

Chronic bullous disease of childhood or childhood linear IgA disease is a rare acquired autoimmune blistering disease in children less than 5 years old with a classic appearance of tense vesicles and bullae arranged seemingly like a cluster of jewels. Due to the neutrophilic nature of the disease, dapsone remains the first choice in treatment. Although mostly used in cases of G6PD deficiency, colchicine exhibits excellent action against neutrophils and is a viable option. This drug is readily available, accessible, and affordable. In the Philippines, literature is scarce in in terms of the use of colchicine as first line agent for linear IgA disease. We present this case to demonstrate the efficacy and safety of colchicine in chronic bullouse disease of childhood and to advocate its use as a first line agent.

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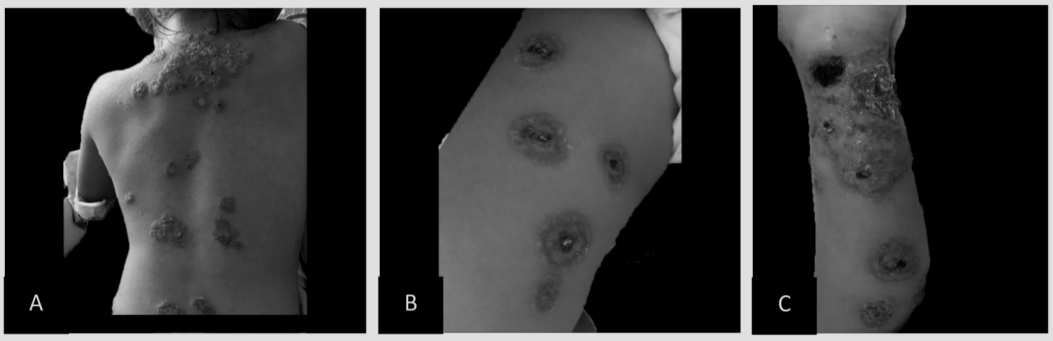
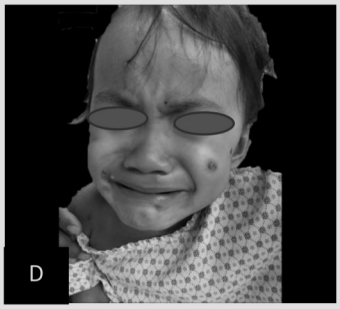
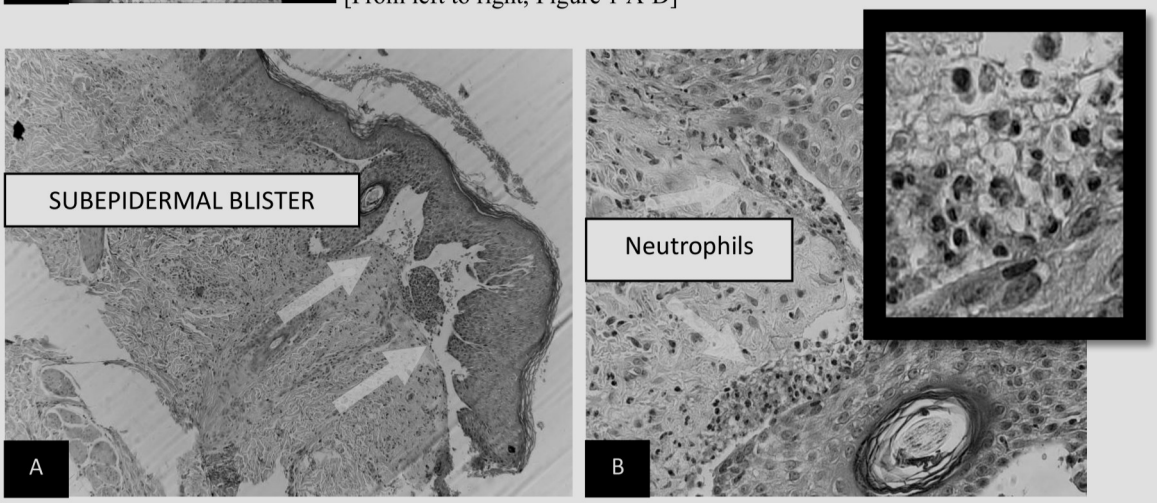
APPENDIX

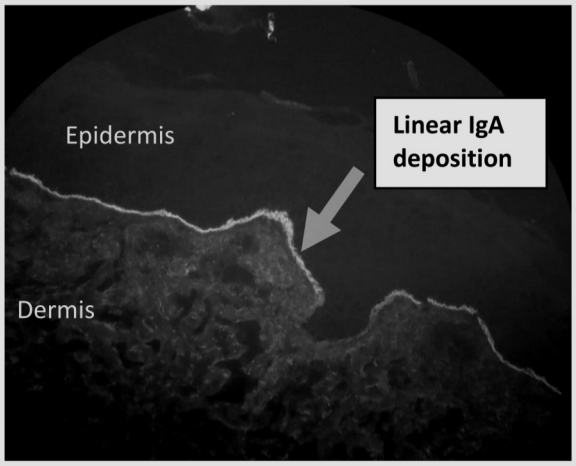




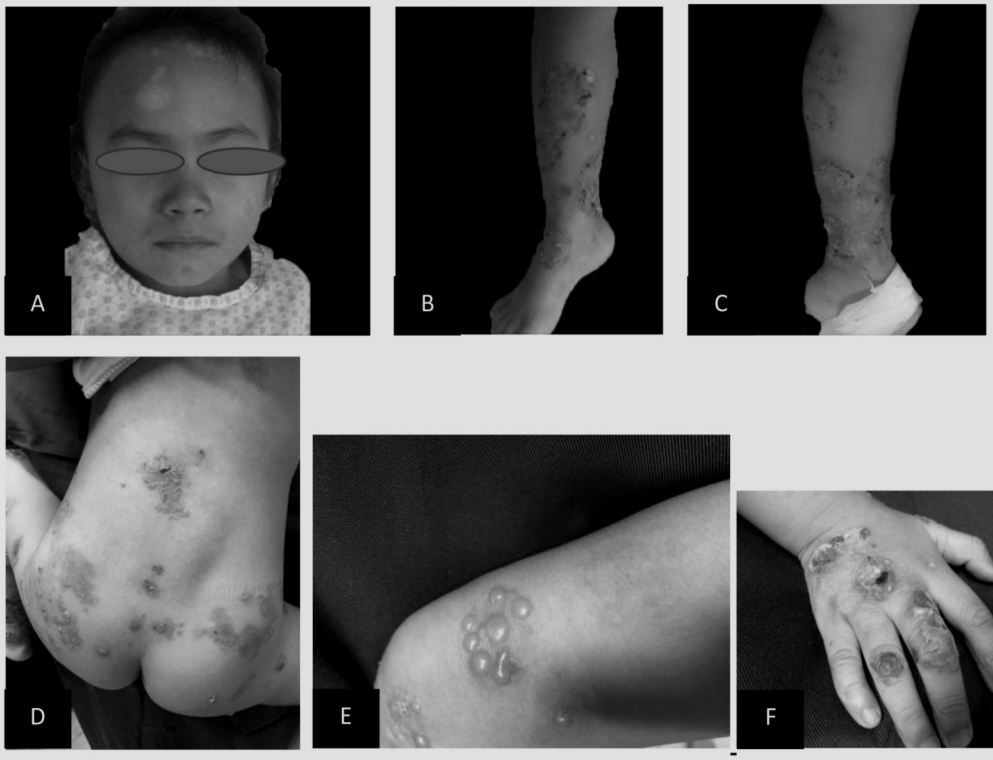
[From left to right, Figure 1 A-D]



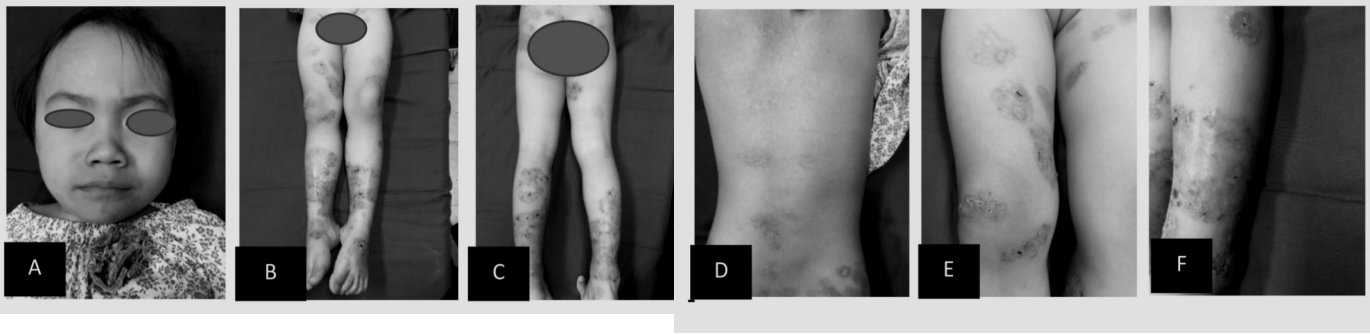
[Figure 2 A-B]

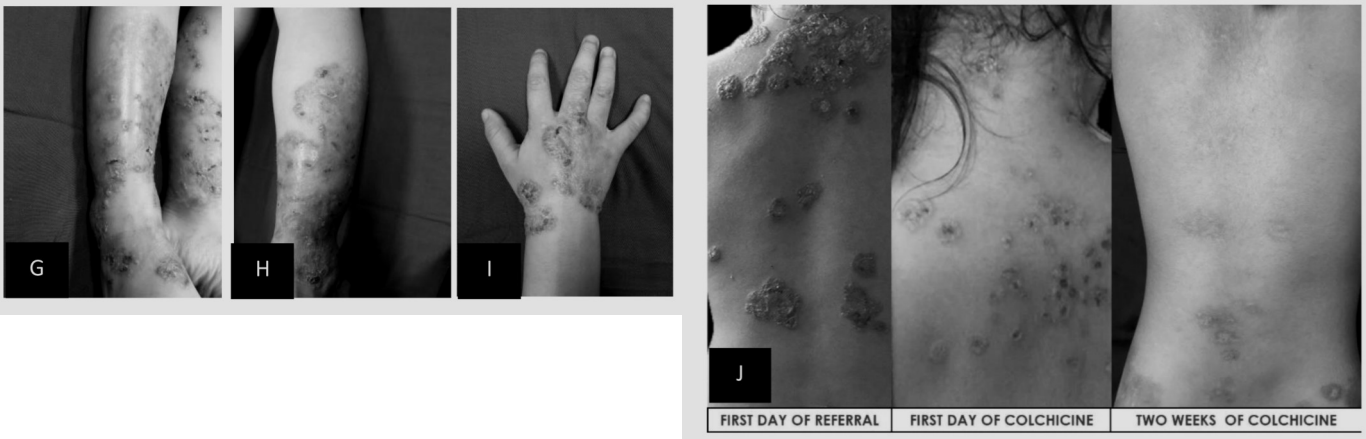


[Figure 3]



[Figure 4 A-F]





[Figure 5 A-J]

Recovery in Schizophrenia: Perspectives from Psychiatrists in the Philippines

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ABSTRACT

Background: A reliable and socially validated definition of recovery in schizophrenia is essential to decrease stigma associated with the illness. This study aimed to define recovery in schizophrenia in the Philippine context, determine its specific elements, and describe methods of assessment in clinical practice.

Methods*:* We invited a group of purposively selected Filipino psychiatrists to participate in six simultaneous roundtable discussions to gather their opinions and perspectives on recovery in schizophrenia. Transcripts of the discussions were then subjected to framework analysis.

Results and Conclusion: Most Filipino psychiatrists were of the considered opinion that recovery in schizophrenia is possible, and their vision of a recovered patient resembles a combination of psychological and medical models. The mini-FROGS tool was deemed generally applicable in the Philippine setting except for *self-esteem and sense of independence* primarily because it is difficult to evaluate. The SWN was received with mixed reactions among the psychiatrists. Spirituality as an element of recovery and the family-oriented culture of the Filipinos were emphasized as important considerations in assessing patients. Other suggestions were given to tailor-fit these tools to the Philippine context.

Keywords: schizophrenia; mental health recovery; mini-FROGS; Subjective Well-being Under Neuroleptics (SWN); Philippines

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INTRODUCTION

The Diagnostic and Statistical Manual of Mental Disorders Third Edition defined remission in schizophrenia as "free of all signs of the illness (whether or not on medication)".[1] Full remission or recovery, described as a complete return to premorbid functioning of patients, was considered possible but it was rare that the concept was met with rampant skepticism among clinicians.[1] Some of them even questioned the original diagnosis when such event was said to be occurring.[1] In the Fifth Edition of DSM, recovery in schizophrenia was given a more hopeful tone, with few reported cases to have recovered completely.[2] In the past, Emil Kraepelin described schizophrenia as the kiss of death.[3] More recently, patients and doctors have developed a more positive perspective on the course of schizophrenia to counter the stigma related with the illness.[3]

In a study by Andresen et al, four models of recovery were presented.[4] The medical model views recovery as "a return to a former state of health", and thus involves the symptoms, hospitalization, medication, and assessments of the functioning of the patients.[4] The rehabilitative model regards patients with schizophrenia as continuously disabled but are able to return to a semblance of their previous life through therapy.[4] The empowerment model sees mental illness as having no biological foundation and merely as "a sign of severe emotional distress in the face of overwhelming stressors."[4] Hence, medication is not necessary for recovery so long as patient remains optimistic.[4] Lastly, the psychological model focuses on the "establishment of a fulfilling, meaningful life and a positive sense of identity founded on hopefulness and self-determination."[4] This model identified four components: hope, self-identity, meaning in life, and responsibility.[4]

Given these different perspectives, Liberman and Kopelowicz called for a more inclusive and consensually validated definition because it was said that using reproducible and reliable terms on recovery decreases the stigma associated with the illness.[5] This definition should also be parallel with the normative behaviour of the community wherein it is to be applied.[5] Only then will this be socially valid.[5] Moreover, tools for diagnosis such as the Functional Remission of General Schizophrenia (FROGS) scale[6], the mini-FROGS scale[7], and the Subjective Well-Being Under Neuroleptics short form (SWN)[8] were developed by Western countries. Hence, these may not be socially valid in the Philippines.

This paper, then, aims to define recovery in schizophrenia in the Philippine context, to determine its specific elements, and to describe the methods of assessment in local clinical practice.

METHODS

To address the objectives, six simultaneous roundtable discussions participated in by a group of purposively selected Filipino psychiatrists were held on 28-29 April 2018 in Makati City. Participants were identified by a core group of practicing psychiatrists based on a) years of practice and b) venue of practice (i.e., public or private) to ensure diversity in perspectives on recovery in schizophrenia.

The core group, who also acted as facilitators, prepared a set of questions for discussion to address the forum objectives.

Table 1. Discussion guide questions

Objectives	Guide Questions
Define recovery in schizophrenia in the Philippine context	1. Do you believe that a patient with schizophrenia can recover?
	2. What is your vision of a patient with schizophrenia who has recovered?
Determine the specific elements of recovery	3. What are your thoughts about the applicability of the four items in the Mini-FROGS in the Philippine setting?
	4. Are there other elements that you look for that indicate recovery in your patient?
Describe method of assessment of recovery in local clinical practice	5. How do you determine your patient's level of functionality in each of the four items of the Mini-ROGS? a. Travel and communication b. Management of illness and treatment c. Self-esteem and sense of independence d. Respect for biological rhythms
	6. Would you be willing to use the SWN for your patients? Why or why not?
	7. How do you assess your patient's well-being?
	8. How do you assess recovery in your practice?

Proceedings of the discussions were audio-recorded for processing and analysis. Assigned facilitators and documentors also concurrently took notes of salient points of the discussion. At the end of the session, the facilitator, with support from the documentor, provided a recapitulation of major discussion points for validation by the participants. Discrepancies, errors, or refinements pointed out by participants were corrected on-site.

Documentors (CHT, JCM, DNO, MLR, ATS, CJT) prepared a transcription of audio-recordings and field notes from their respective groups. These were then validated by senior members of the team (CTA, MPS, CVB, MED, MAG, MSH, BSP, ELT).

Data derived from transcripts of discussions, together with field notes, were subjected to framework analysis where responses were coded to the discussion questions and objectives. This was done at two levels: first, by individual groups (coding performed by CHT, JCM, DNO, MLR, ATS, CJT, and validated by CTA and MPS), followed by analysis in the aggregate (coding performed by CHT and validated by CTA and MPS).

All small group discussion attendees provided prior consent for participation, and documentation of their responses.

This project was funded by Johnson & Johnson (Philippines), Inc. The funder did not have any direct role in the analysis and interpretation of data derived from the small group discussions.

Results

Profile of participants

A total of 47 Filipino psychiatrists participated in the round table discussions, with around seven to 10 participants in each small group. Among them, 23 came from the public sector, 19 from the private sector, and five from both.

Figure 1. Clinical experience of the participants

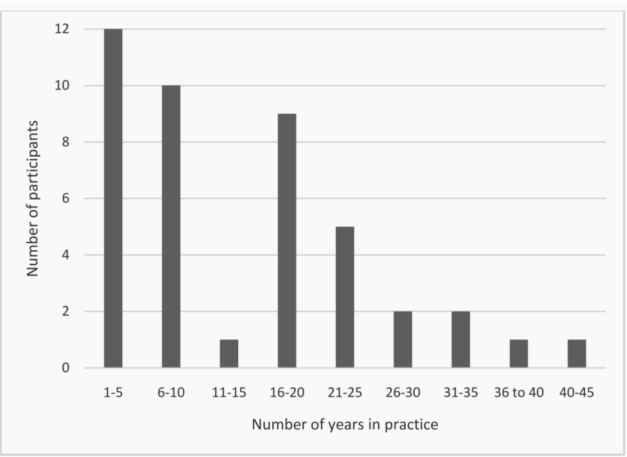

Figure 1 shows the frequency of participants in terms of their number of years in practice. Their clinical experience ranged from one year up to 42 years, with a mean of 14 years and mode of two and 20 years (n = four). Four participants did not give information on this.

Recovery in schizophrenia in the Philippines

Five of the six groups expressed their belief that recovery from schizophrenia is possible. In these groups, recovery was most often perceived as a combination of the elements of the medical and psychological models of recovery. Hence, the recovered patient was envisioned as follows:

- has symptoms at a minimum and under control (compliance to medication)
- has an understanding and insight of his/her illness
- can take responsibility for his/her illness with minimal assistance from others
- has returned to his/her normal level of functioning
- is productive and responsible enough to be reintegrated into the society
- can make decisions of his/her own and see self-actualization as the final goal

Simply put, a recovered patient can be described as "somebody like us" (Private, 42 years in practice). A private sector doctor in practice for 18 years believed that patients experiencing delusions can still be considered recovered as long as they do not act on them (i.e. he/she recognizes what is real

and what is not). Even patients who are not well-groomed can be considered recovered if they can redeem their reputation by explaining their unkempt appearance (Public, 27 years in practice).

Moreover, insight and acceptance were said to be insufficient in themselves to pronounce recovery because these only capture the patient's adaption to the illness. Adaptation to the environment should also be considered by measuring the everyday functionality (Private, eight years in practice). Another notable statement by a private sector doctor practicing for 35 years pointed out the importance of spirituality in recovery. He claimed that pastors and priests play a significant role to achieve this.

The importance of giving hope for recovery to patients and their families through psychoeducation was also emphasized. One doctor said that: "There is a need for doctors to level up their programs for the patients. Although they do believe that recovery is possible, it is not a common practice in the Philippines to target recovery for patients because most of them only settle on reducing the symptoms." (Private, 42 years in practice)

The only group which answered "No" defined full recovery as being free from any medications. Furthermore, a private sector doctor in practice for 14 years asserted that biopsychosocial recovery is possible but biological recovery is not. Given the genetic basis of the disease, she said that patients with schizophrenia will have the disease for a lifetime, in contrast with infectious diseases where elimination of the etiologic agent may be achieved.

There was also one doctor who "...believes that recovery is possible, but it cannot be helped to cast doubts on the diagnosis whenever a patient is said to be recovering." (Public, four years in practice)

Elements of recovery in schizophrenia

Two groups considered the Mini-FROGS[7] as generally applicable in the Philippines. The other three groups considered it applicable except for the third item (i.e. self-esteem and sense of independence) while the last group regarded it as overall inappropriate in the local setting.

Travel and communication. Besides being basic necessities of a person, these are considered good indicators of recovery from schizophrenia. Not only are they needed for consultation, but they are also important in evaluating the productivity and social life of the patient. However, it was suggested that travel and communication be separated because they are assessed differently. For travel, the distance, mode of transportation, purpose, and ease of navigation should be specified.

Management of illness and treatment. This will account for whether the patient has already gained insight on the illness through psychoeducation, and whether he/she is aware of warning signs of relapse. Compliance to medication is also affected by the financial capability of the patient, thus it was advised that this be asked in connection with the other.

Self-esteem and sense of independence. This item met mixed reaction among the participants. Self-esteem was said to be important because social stigma remains rampant in the country. However, it is a broad and a culturally dependent concept that makes it difficult to evaluate. The Philippines as an archipelago complicates it further because each region has a different view on how it is defined (Private, 10 years in practice).

Related to self-esteem is the ability to handle criticism. The participants thought that expecting this from patients may be too much because even normal people have difficulty doing it. Another issue raised was the inappropriateness of this question in the Philippines because families are usually the source of criticism for patients here. Since the tool is to be answered by relatives, there can be bias in the assessment (Public, four years in practice).

On the other hand, sense of independence may be influenced by the close family ties promoted by the Filipino culture. This criterion was made for a more individualist country rather than a collectivist country such as the Philippines, where family plays a big role in the patient's independence. For instance, patients at age 21 are not really expected to live by themselves already (Public, 20 years in practice). In some cases, the families themselves set restrictions on the functionality of the patients. The clinicians should first clarify whether the family permits the

patient to do activities of daily living before assessing them (Public, four years in practice & Private, six years in practice).

A clear local definition of self-esteem and sense of independence needs to be established first. It was also suggested that the former be replaced by adaptation to stress and the latter by initiative.

Respect for biological rhythms. This refers to the routine and structure of the patient. It was considered as one of the best indicators of recovery since it is related to functionality. To make it more thorough, it was proposed that exercise frequency, substance abuse, health choices and nutrition, and meal schedules be included in the criteria for this item.

Aside from these, the following elements were also identified as indicators for recovery:

- Spirituality
- Self-care and grooming
- Empathy (especially towards fellow patients)
- Anger management and impulse control
- Social network (long-term relationships)
- Sense of belongingness and integration to society
- Happiness and satisfaction of the patient and his/her family
- Initiative, motivation, and hope
- Adaptation to stress and environment
- School, work, and other psychosocial activities
- Judgment and decision-making skills

Assessment of recovery in local clinical practice

To assess recovery from schizophrenia, the patient is compared to the doctor's vision of a recovered patient. This is done by evaluating the specific elements of recovery identified earlier. Improvement of the patient can also be checked by asking the patient to rate how he/she feels during the first and the last day of consultation, and then comparing the answers.

Doctors assess the functionality of patients in the four items of the Mini-FROGS by employing the following methods.

Travel and communication. Functionality in travel is usually defined as the ability to go from one place to another. This is assessed by:

- How the patient went to the clinic
- Ability to travel alone without any difficulties
- Ability to travel with other people without causing them any burden
- Ability to follow simple rules while travelling
- Complexity of the transportation mode used
- How he/she responds to hypothetical situations given by the doctor (e.g. going to an unfamiliar place, getting lost)

One group had a different perspective on the functionality of travel. They said that it is not about checking whether patients can get from one place to another but about their thought process and decision-making. Basically, it is concerned about the complexity of travelling itself and how patients troubleshoot when necessary.

Functionality in communication is assessed by:

- Quantity and quality of conversation with the doctor (i.e. how the patient talks and how much information is shared)
- Ability to get the message across in any form of communication
- Ability to use different modes of communication (personal, text messaging, social media, etc.)
- How the patient feels when interacting with other people (Is he/she afraid to talk with them? Can he/she build new relationships?)
- How he/she responds to hypothetical situations (e.g. replying to overwhelming messages in social media)

Management of illness and treatment. The ability of the patient to manage the illness and treatment is assessed by:

- Attitude towards the illness (taking responsibility and initiative for his/her actions)
- Level of compliance to medications
- Level of knowledge and insight of the illness (recognizing signs of relapse)
- Level of openness to the doctor regarding symptoms
- Level of knowledge on his/her rights as a patient with schizophrenia and how he/she exercises them
- Health choices of the patient
- Patient's foresight/prediction of relapse and his/her response to this
- Proactive approach in the management of the illness (learning about it on his/her own, interest)

One of the important points on treatment was given by a public sector doctor practicing for more than 20 years. He said that compliance to medication does not necessarily mean the patient has already accepted the illness, and that sometimes, this is only done to relieve symptoms.

Meanwhile, to prove the possibility of gaining interest on one's illness, one doctor said that there are patients who become members of support groups for schizophrenia (Private, 18 years in practice).

Self-esteem and sense of independence. Many participants disagreed with the use of this item in the Philippine setting. Self-esteem and sense of independence are difficult to score, but they may be assessed relatively by:

- Patient's reaction to criticisms and stigma
- Level of self-sufficiency and financial independence
- Level of self-knowledge on his/her strengths and weaknesses
- Willingness to do things and make decisions on his/her own
- Interest [in the illness] is possible for high functioning patients, some of them are even members of support groups. (Private, 18 years in practice)

Respect for biological rhythms. This is assessed by:

- Patient's self-care and physical fitness (exercising)
- Patient's basic biological functionality (eating, sleeping, taking a bath)
- Ability to follow a schedule of activities
- Ability to follow or be incorporated in the "family routine" which is very applicable in the Philippines

Some patients prefer not to exercise, so for a public sector doctor in practice for 22 years, this is just a plus point but not a crucial factor to consider. On the other hand, the age and work of the patients should be regarded according to a public sector doctor with one year of experience. This is to account for normal variations in biological rhythms. For example, young patients tend to sleep later than the older ones. In terms of work, there are patients with night shift jobs.

Another tool that can be used to assess recovery of patients is the SWN[8]. Three groups expressed their willingness to use this for the following reasons:

1. It gives specific objectives during patient assessment.
2. It can be answered by patients while waiting for their consultation.
3. It can be used to assess the patient's progress.
4. It can serve as an avenue for further discussion, especially for patients who find it difficult to open up.

Meanwhile, the other three groups showed hesitation in using it because:

1. It is too Westernized.
2. Some of the items are abstract.
3. The measurement scale is quite difficult to operationalize.

The following suggestions on how to improve and tailor-fit it to the Philippine setting were given:

- Translate it to the native language of the patient
- Make it in question form
- Shorten the measurement scale into 3-4 points or simply "Yes" or "No"
- Group the items into physical, social, and cognitive
- Add more hypothetical family situations to make it sound more local (Public, 4 years in practice). Instead of saying "My body is a burden to me", rephrase it into "Am I a burden to my family?" (Public, 27 years in practice)
- Develop an SWN app that patients can answer using their devices (Private, 18 years in practice)

During consultations, the patient's well-being is not usually given much attention throughout the assessment. A private doctor practicing for 38 years called for her colleagues to rethink whether they truly consider in the assessment of the illness how patients really feel. Doctors tend to assess using their own sense of recovery, sometimes disregarding the actual well-being of the patients.

When they do assess patient's well-being, the following are done:

- Observing the physical appearance and grooming of the patient and his/her relatives
- Observing the verbal and non-verbal cues of the patient
- Asking the patient how he/she is or how his/her sleep was, and contextualizing his/her answer of "I'm okay" or "I'm good"
- Asking what he/she feels about himself/herself, mood, and relationships with others
- Asking whether he/she is happy or satisfied with his/her life

The ABC method (A for appearance, B for behavior, and C for communication) can be used first before proceeding to the symptomatic questions (Public, 28 years in practice).

DISCUSSION

The perspective of most psychiatrists in the Philippines that recovery in schizophrenia is possible is consistent with the recent trend of a more positive approach in the treatment of the illness. Leucht mentioned that despite recovery rates being low for patients with schizophrenia, it is still achievable through the support and hope given by clinicians.[9] In a study in Malaysia by Dahlan et al, it was found that good social support was the strongest factor to affect functional remission.[10] This, too, was emphasized during the discussion conducted for this paper. Through psychoeducation, clinicians can help patients not only to gain insight of the illness but to accept and own it as well. Acceptance will lead the patients towards recovery.

According to the findings of Andresen et al, the psychological model corresponds to most of the beliefs of consumers.[4] They enumerated five phases of psychological recovery: moratorium, awareness, preparation, rebuilding, and growth.[4] These phases involve learning about the illness, relationships with peers, taking responsibility for actions, and working towards personal goals.[4] In the growth phase, the patient can still show symptoms of the illness, but he/she knows how to manage them.[4] Meanwhile, the medical model takes into consideration the level of functionality of the patients.[4] Together, these two models resemble the vision of a recovered patient of the Filipino psychiatrists.

Recovery has also been described in relation with management of the illness. Compliance to medication was regarded as a basic indication of recovery because it helps the patients maintain their symptoms at a minimum. The role of medication was demonstrated in a study by Williams et al wherein patients got improved scores in both the patient- and

provider-rated surveys after receiving paliperidone palmitate (PP).[11] Anderson et al also found that patients treated with injectable paliperidone palmitate had improved adherence and were 2.5 times more likely to achieve remission than those under oral atypical antipsychotic therapy.[12]

Two of the most important findings of this study are the emphasis on spirituality as an element of recovery and the family-oriented culture of the Filipinos in connection with the sense of independence. Participating psychiatrists repeatedly suggested that these should be considered in assessing recovery of Filipino patients. Moreover, these two aspects are not commonly seen in any literature involving recovery in schizophrenia. Hence, this strengthens the need to localize the definition of recovery.

Time has also been noted an essential component of recovery. For Liberman et al and Whitehorn et al, good performance in terms of psychopathology and psychosocial functioning should be sustained for two years to regard a patient as recovered, while Torgalsboen et al set it to five years.[5] However, this has not been touched upon in this paper because the focus of the discussions was to establish a definition of recovery to be adopted in clinical practice where the goal is to maintain the patients in the state of recovery for as long as possible. For the sake of a clear-cut definition, further studies can be done to establish this.

This project utilized facilitated roundtable discussions to pool the opinions of psychiatrists in the Philippines. This method gave all participants an equal chance to voice out their stand about the topic in an unrestrictive manner while also having a structured flow of conversation. It also allowed them to highlight the key points of the discussion, to debate on particular ideas, and to resolve these conflicts right away. However, one of the disadvantages of using this method is the presence of a dominant personality in a group that can affect the judgment of the other participants and sway them to agree to his/her views. The discussion is also influenced by the seating arrangement of the participants. The first one to talk may convince the next ones to take a similar stand. Lastly, limited time given to answer all the questions could have prevented the group to exhaust all their ideas on the topic. These limitations, however, were managed through skilled facilitation of the discussion.

One of the strengths of this project lay on the equal representation of both the public and private sectors, and the wide range of clinical experience of the participants. Hence, it can be said that this pioneer undertaking on recovery in schizophrenia in the Philippines was able to provide a general overview of how clinicians in the country perceive recovery of patients from the illness. It also opens further discussion on the topic to address other issues raised during the forum. For instance, broad ways to assess patients using the mini-FROGS and SWN were given by the participants. Another discussion can be done to develop a standard way of assessing patients using these tools.

Declaration of Interest

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