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editorial

Medical education in dermatology in the 21st century

Teaching of dermatology in medical students varies in different universities worldwide. In Malaysia, medical students' interest in dermatology is dismal because of lack of exposure in medical college. There is a move to reinforce dermatology in medical school curriculum and standardise the teaching in most if not all universities in Malaysia. In the beginning of the 21st century, there were no in-house dermatology teaching staff in local universities. Since the inception of Advance Masters of Dermatology in 2002, there are now four public universities and two private medical schools with in-house dermatologists. In the pipeline, a common website for dermatology slide teaching is proposed. Similarly, common lecture notes shall be shared among universities even to those medical colleges without dermatology staff. We welcome you to share your views and feedback on the article on Dermatology education in this issue of the MJD.

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GENERAL DERMATOLOGY - Original Article

PATCH TESTING WITH PRESERVATIVE SENSITIZERS. A YEAR RETROSPECTIVE STUDY FROM SELAYANG HOSPITAL

Voo Sook Yee, *MRCP*, Rohna Ridzwan, *MRCP*

Abstract

Introduction: Other than nickel, fragrance and rubber, preservatives are well known sensitizers.

Objectives: To study the pattern of preservative allergy among patients patch tested at Patch Test Unit Selayang Hospital.

Materials & Methods: We conducted a retrospective analysis of the data of all the patients patch tested with preservative sensitizers present in the European Baseline Series and other commercial series in Selayang Hospital from January 2011 to December 2011.

Results: 243 patients were patch tested. 28.4% of the patients had a positive reaction to one or more of the preservative sensitizers. Paraben mix was the most frequently positive allergen (11.8%). 17.8% of the Indians had paraben allergy, as compared to 11.3% of Malays and 11.2% of Chinese. Females were more significantly associated with a positive reaction to one or more of the preservative sensitizers ($p=0.010$). A younger age group (<35) was more significantly associated with formaldehyde allergy. "Face and upper limbs combined" presentation was significantly associated with a positive reaction to formaldehyde and methylchloroisothiazolinone/ methylisothiazolinone ($p=0.042$ and $p<0.001$ respectively).

Conclusion: Our data differ from most other countries in that paraben mix was the most frequently positive preservative sensitizer and that younger age group was significantly associated with sensitization to formaldehyde.

Keywords *paraben mix, formaldehyde, contact allergy, Malaysia*

Introduction

Most cosmetics, household and industrial products contain preservatives. Its' function is to inhibit the growth of bacteria and fungus, thus enabling these products to have a longer shelf-life. Unfortunately, preservatives are also common sensitizers[1]. Studies have shown an increased in the prevalence of formaldehyde allergy in the 1960s due to exposure to cosmetics and textile finishes[2]. This is followed by methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI) in the 1970s and methyldibromo glutaronitrile (MDBGN) in the 1990s[3].

There are many studies on the prevalence and trends of preservative allergy from the western countries. Data from South East Asian countries is scarce. Malaysia is a multiethnic country comprising of Malay, Chinese, Indians and local indigenous groups, each with their own respective unique cultures and preferences.

Aim

The aims of this study are to study the demographic characteristic, frequency and pattern of preservative allergy among patients patch tested at Patch Test Unit Selayang Hospital.

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Materials and methods

This is a retrospective analysis of all the patients that underwent patch test in Selayang Hospital in 2011. Patients were patch tested with the European Standard Series (ESS) and additional series when indicated, using allergens from Chemotechnique Diagnostics (Malmö, Sweden). Preservative sensitizers are found in the ESS and the Cosmetic Series (CS) and Hairdressing Series (HDS).

The allergens were prepared by using the IQ Chambers and occluded at the back for 2 days. Readings were done on Day 4 and Day 7 in accordance to the International Contact Dermatitis Research Group recommendation.

The records of the patients patch tested to preservative sensitizers were recorded and analyzed, namely formaldehyde 1% aq., quaternium-15 1% pet., methyldibromo glutaronitrile (MDBGN) 0.3% pet., paraben mix 16% pet., methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI) 0.01% aq., diazolidinyl urea 2% pet., imidazolidinyl urea 2% pet., dimethylol dimethyl (DMDM) hydantoin 2% aq., sorbic acid 2% pet., triclosan 2% pet., 2-bromo-2-nitropropane-1,3-diol (bronopol) 2% pet., iodopropynyl butylcarbamate (IPBC) 0.1% pet., benzyl alcohol 1% pet., 4-chloro-3-cresol (PCMC) 1%pet., 2-phenoxyethanol 1% pet. and chloroacetamide 0.2% pet.

Patients' presentations were grouped into "face", "hands", "upper limbs", "face and upper limb combined", "trunk" and "lower limbs". Age of the patients were grouped into <20, 20-35, 36-50 and >50. Positivity is defined as positive reaction to at least one or more preservative sensitizers.

Statistics

Data obtained were analyzed using SPSS Version 12.0. Association between categorical variables was analyzed using the chi-squared test. Statistical significance was set at $p < 0.05$.

Results

243 patients were patch tested and the female to male ratio of 1.5:1. One patient had an angry back syndrome. 30 and 8 out of the 243 patients were also patch tested with CS and HDS respectively. Malays constituted 55.6%. There were younger (<36 years old) than older patients (Table 1).

28.4% of the patients had a positive reaction to at least one or more preservative sensitizers, with a female predominance (34.4% vs. 19.3%, p=0.010). The most frequently positive preservative sensitizer in this study was paraben mix 11.8%, followed by formaldehyde 8.6%, MCI/MI 8.6% and MDBGN 4.5% (Table 2).

Females had 3 times more frequent sensitization to MCI/MI as compared to males (11.7% vs. 4.0%, p=0.038). Proportionately more females had a positive reaction to paraben mix, formaldehyde, quartenium-15 and MDBGN. However, this is not statistically significant. The percentage of Malay, Chinese or Indian with a positive reaction to at least one or more of the preservative sensitizers was approximately equal. There were more Indian patients sensitized to paraben mix as compared to Malays and Chinese. However, this was not statistically significant. Younger patients (less than 36 years of age), had a significantly more positive reaction to formaldehyde (p=0.038) (Table 3).

"Face & upper limbs" presentation was significantly more associated with positive reaction to one or more preservative sensitizers (p=0.034). It was also significantly associated with positive reaction to formaldehyde and MCI/MI (p=0.042 and p<0.001 respectively). "Face" presentation was significantly associated with positive reaction to diazolidinyl urea (p=0.016) (Table 4). "Hands" presentation was significantly associated with sensitization to MDBGN (p=0.046)

Discussion

As only selected patients were patch tested with additional series (CS and HDS), the frequency of sensitization of different preservative sensitizers are not directly comparable. Almost a third of patients that underwent patch test in 2011 had positive reactions to at least one or more preservative sensitizers. It is important to note from this study that without doing the additional series, we would have missed 5% of preservative allergy in this cohort of patients.

The results show that paraben mix is the most frequently positive preservative allergen in our hospital in 2011. This is much higher than reported elsewhere. Paraben is an uncommon allergen across the Europe countries 0.1-2.2%[4], India 4%[5], meanwhile China (Beijing) has a sensitization rate

Table 1 Demographic characteristic of the patients.

Patient characteristics		n	%
Gender	Male	98	40.3
	Female	145	59.7
Ethnic	Malay	133	54.7
	Chinese	80	32.9
	Indian	28	11.5
	Others	2	0.8
Age group	<20	59	24.2
	20-35	66	27.2
	36-50	62	25.5
	>50	55	22.6

Table 2 Frequency of sensitization of common preservative sensitizers in various countries.

Allergen	Present study	Thailand[7]	China[5]	European[4] Countries
Paraben mix	11.8%	10.9%	20%	0.1-2.2%
Formaldehyde	8.6%	4.5%	15.8%	0.7-5.9%
Quaternium-15	2.1%	2.5%	-	0.1-3.2%
Imidazolidinyl urea	0.0%	1.7%	3.0%	0.4-1.0%
Diazolidinyl urea	0.8%	3.6%	-	0.7-1.1%
MCI/MI	8.6%	4.3%	-	1.2-4.2%
MDBGN	4.5%	5.6%	-	0.3-3.8%

Table 3 Frequency of sensitization to preservatives.

Allergen	Present study	Positivity*		Formaldehyde		MCI/MI		Paraben mix	
Gender	Male	19	(19.3%)	6	(6.1%)	4	(4.0%)	10	(10.2%)
	Female	50	(34.4%)	15	(15.3%)	17	(11.7%)	18	(12.4%)
	p-value		**0.010**		0.251		**0.038**		0.597
Age	<20	14	(23.7%)	7	(11.9%)	1	(1.7%)	8	(11.8%)
	20-35	23	(34.8%)	10	(15.2%)	9	(13.6%)	11	(16.7%)
	36-50	16	(25.8%)	2	(3.2%)	6	(9.6%)	9	(14.5%)
	>50	16	(28.5%)	2	(3.6%)	5	(9.0%)	2	(3.6%)
	p-value		0.534		**0.038**		0.123		0.140
Ethnic	Malay	35	(26.3%)	12	(9.0%)	12	(9.0%)	15	(11.3%)
	Chinese	25	(31.2%)	6	(7.5%)	8	(10.0%)	9	(11.2%)
	India	8	(28.6%)	3	(10.7%)	1	(3.5%)	5	(17.8%)
	Others	1	(50.0%)	0	(0.0%)	0	(0.0%)	1	(50%)
	p-value		0.786		0.919		0.720		0.304

**Positive reaction to one or more preservative sensitizers.*

Table 4 Frequency of sensitization to formaldehyde, MCI/MI, diazolidinyl urea, paraben mix with different presentations.

Patient characteristics	"Face " vs. others	"Face & UL combined" vs. others
Positive reaction to one or more preservative sensitizer	36.5% vs. 25.5%	46.2% vs. 26.2%*
p-value	0.097	0.034
Formaldehyde	12.6% vs. 7.2%	19.2% vs. 7.3%
p-value	0.183	0.042
MCI/MI	14.2% vs. 6.7%	26.9% vs. 6.4%
p-value	0.064	<0.001
Diazolidinyl urea	3.1% vs. 0%	0.0% vs. 0.9%
p-value	0.016	0.616
Parabens mix	9.5% vs. 12.2%	11.4% vs. 11.5%
p-value	0.564	0.895

**46.2% of the patients with "face and upper limbs" presentation has positive reaction to one or more preservative sensitizers compared to only 26.2% of the patients with other presentations.*

of 20%[6] and closer to home, Thailand 10.9%[7]. Other common allergens are formaldehyde 8.6% and MCI/MI 8.6% respectively. In contrast, a study from European countries recorded 0.7-5.9% and 1.2-4.2%[8] respectively whereas Thailand recorded 4.5% and 4.3% respectively[7] (Table 2). Another more recent study from Thailand[9] recorded sensitization rate of 3.5% and 4.3% respectively. On the other hand, North America recorded a higher frequency of sensitization rate of 9% to formaldehyde[10]

The mark difference in the positivity rate may be due to 1) Difference in legislation concerning the usage of these preservatives in cosmetics, household and industrial products in different countries 2) Difference in selection of patients to be patch tested. However, this is a finding from a single centre and may not reflect the whole country. Parabens are the most commonly used preservatives in cosmetic and industrial products, as they are less costly, odourless, colourless, stable and have a wide spectrum of antibacterial activity[11]. Cross-reactions with benzocaine and para-phenylenediamine have been reported, which are thought to be uncommon. Our study found none.

In Malaysia, parabens are found not only in the international, but also in the local domestic cosmetics and pharmaceutical products. Parabens are also found in certain fruits and vegetables for example olive, carrot and cucumber[14].

Cosmetic products in Malaysia are regulated by the National Pharmaceuticals Control Bureau[13], where the maximum concentration of formaldehyde and MCI/MI is similar to the European countries. However, there is no specific regulation with regards to paraben use. The European countries allow the maximum concentration of 0.4% of each paraben and a maximum total of 0.8% of all parabens in cosmetics, whereas MCI/MI use in cosmetics is permitted up to 100ppm[4]. The maximum concentration of free formaldehyde permitted in cosmetics is 0.2%. In addition, all finished products containing formaldehyde or formaldehyde releasers must be labelled "contains formaldehyde" whenever concentration exceeds 0.05%[15]. MDBGN is banned from being used in leave-on products in 2003 and in rinsed-off products in 2007 in Europe[8]. In the light of this result, perhaps a study to determine the paraben concentration in various consumer products should be carried out in the near future.

On the other hand, it is important to be aware of the concept of "paraben paradox"[12]. This concept refers to two phenomena 1) Patients who are sensitized to parabens may continue to use paraben containing products on intact skin; however, if the same products are applied to skin with impaired epidermal barrier, they may induce a dermatitis 2) Individuals who are sensitized to parabens have false negative patch test reactions when parabens are patch-tested on an intact skin.

Our study found that 14.2% of the patients who were allergic to formaldehyde had concomitant contact allergy to formaldehyde releasers (p=0.001). 14.2% of the patients who were allergic to formaldehyde had concomitant positive reaction to quaternium-15(p<0.001), whereas 60% of patients who were allergic to quaternium-15 were allergic to formaldehyde (p<0.001). These almost mirror the findings by Lundov et al[20] whereby concomitant allergy to quaternium-15 is found in 23% of patients allergic to formaldehyde, whereas 74% of patients allergic to quartenium-15 were found to be allergic to formaldehyde as well. This is mostly likely because quaternium-15 is a formaldehyde releaser that releases the greatest amount of formaldehyde[20].

Females had 1.5 times more frequent positive reaction to one or more preservative sensitizers as compared to males (34.4% vs. 19.3%, p=0.010). Proportionately more females are sensitized to formaldehyde, quaternium-15, MCI/MI, paraben mix and diazolidinyl urea;none of which reached statistical significance. These results are not surprising and most likely due to higher usage of cosmetics and other preservative containing household products in women. Furthermore, since females use more cosmetic products, they are more likely to seek medical attention than males. It is important to note that about one fifth of the males were sensitized to one or more preservative sensitizers. A study from UK found sensitization to paraben mix as significantly more frequent in men, whereas sensitization to diazolidinyl urea and quaternium-15 to be more frequent in women[8].

Interestingly, sensitization to paraben mix was found to be more frequent among Indians as compared to Malay and Chinese although it was not statistically significant. This finding may be related to higher use of domestic cosmetics and traditional/herbal liniments amongst the Indians.

Younger age groups of less than 20 and between 20-35 years old had significantly more frequent sensitization to formaldehyde as compared to age groups 35-50 and > 50 years old. This finding is in contrast to a Danish study[16] where formaldehyde allergy was significantly higher amongst the 41-60 year-old as compared to those less than 40 and more than 60 years old. A study done in Singapore[17] on children and adolescents as well as another study from Greece[18] done on the patients under 16 years old using the European Standard Series reported that formaldehyde and MCI/MI were not the common allergens. However, these two studies focused on the common allergens rather than preservative allergens. Lundov et al[20] found majority of the formaldehyde-allergic patients were exposed to cosmetic and household products containing formaldehyde (78% and 16% respectively).

Our study shows younger age group between 20-35 year-old has about 1.5 times higher rate of sensitization to MCI/MI compared to the older age group (35-50 and >50 years old), though this is not statistically significant. This again contrasts with the study done by Lundov et al[19] who found MCI/MI allergy to be significantly associated with those above 40 years of age, occupational dermatitis and hand eczema. We postulate that the MCI/MI allergy in our cohort of patients is mainly due to usage of cosmetics in that age group (working adults). We only had 9 cases of occupational dermatitis in 2011 and they were mainly related to rubber allergy.

Our study found “face and upper limbs combined” presentation to be significantly associated with a positive reaction to one or more preservative sensitizers, which is not surprising as these areas have the highest contact with cosmetics and household product. “Face and upper limb combined” presentation was significantly associated with formaldehyde and MCI/CI allergy as well. “Face” presentation was significantly associated with diazolidinyl urea allergy. This was similar with the findings of Schnuch et al[8] where diazolidinyl urea allergy was associated with face dermatitis. “Hands” presentation was significantly associated with MDBGN. Latorre et al[15] found the ‘hands’ to be the most common site of dermatitis in patients with a positive patch test only to formaldehyde, whereas the face and legs were the most usual sites in patients with positive patch test reactions to the formaldehyde releasers (quaternium-15, imidazolidinyl urea and diazolidinyl urea).

The limitation of our study includes 1) it is retospective in nature and 2) it does not represent the true prevalence of sensitization of Malaysian population. The population in this study consisted of selected patients with suspected contact allergy. Our centre, that is Selayang Hospital, mainly receive referral from Gombak, Rawang and Sentul, thus the results may differ from other centres in Malaysia.

Conclusion

Paraben mix is most frequently positive preservative sensitizer among our patients followed by formaldehyde and methylchloroisothiazolinone/ methylisothiazolinone (MCI/MI). The younger age groups were more frequently associated with sensitization to formaldehyde and MCI/MI.

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EDUCATION - Original Article

DEVELOPING A DERMATOLOGY CURRICULUM FOR MALAYSIAN MEDICAL UNDERGRADUATES: INITIAL RESULTS OF THE DELPHI METHOD

Adawiyah Jamil, *AdvMDerm*, Mazlin Mohd Baseri, *AdvMDerm*, Leelavathi Muthupalaniappen, *MMed (Fam. Med)*, Roshidah Baba, *FRCP*

Abstract

Background: Dermatology in the Malaysian undergraduate medical curriculum is included as a sub-specialty subject in Internal Medicine. The dermatology course content for undergraduate varies among the different teaching institutions. A standardized curriculum is required to prepare graduates for clinical dermatological practices in a tropical country and also applicable worldwide.

Methods: The Delphi method is used to reach a consensus on the curriculum's core content. A questionnaire with lists of dermatological conditions was developed by a panel of dermatologists and family physician. A total of 60 participants comprising of 20 dermatologists, 20 family physicians and 20 general practitioners are asked to rate the importance of each dermatological conditions stated in the questionnaire. The same participants then answers the questionnaire again with results of the first round made available to them. The final curriculum content will be identified based on the panel's collective opinions.

Results: We present the results of the first part of the study which is the (questionnaire development). Section 1 of the questionnaire lists 20 topics according to the classification of dermatological diseases and common dermatological diseases. Section 2 expands each classification by listing specific diseases or conditions. There are 4 to 13 diseases identified under each classification. This provides a total of 171 options to be graded by each participant. Section 1 aimed to identify important topics based on the classification and common dermatological diseases. The list of specific diseases aimed to identify the important dermatological conditions or diseases under each classification.

Conclusion: A standardized appropriate curriculum in dermatology is required for the Malaysian undergraduate teaching curriculum which is acceptable both locally and internationally. The finding of the study may be used to recommend a standard Malaysian medical undergraduate dermatology curriculum.

Keywords *education, medicine, Malaysia*

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Introduction

Dermatology as a subject in the Malaysian undergraduate medical curriculum is included as a sub-specialty subject in Internal Medicine. This sub-specialty area is formally taught in a few local universities depending on the content of the Internal Medicine programme.

The course content varies among the different institutions based on the individuals involved in the development of the academic programme and the model of the curriculum. There is lack of published data which looks at the suitability and effectiveness of the current undergraduate dermatology course content in Malaysia. Hence there is a need for a review and update of the dermatology curriculum.

There are few reports on the availability of a dermatology module as a component of the core medical curriculum and the content of the curriculum. In the United Kingdom in year 2000, 19 out of 24 medical schools had an integrated dermatology curriculum[1]. In 18 of these schools, students were exposed to patients with dermatological conditions in the hospital or primary care setting. In a survey conducted in India, 3 out of 7 colleges had formal assessments on dermatology knowledge[2]. A survey in the United States of America identified 33 medical schools without an undergraduate dermatology program[3]. In the schools that had a program, more than half allocated less than 10 hours to dermatology teaching.

The importance of including dermatology in the medical curricula was illustrated by a few reports. Seventy one percent of general practitioners surveyed in the United Kingdom agreed that dermatology is an essential part of the medical curriculum and should be included in postgraduate programs[4]. Thirty seven percent of primary care physicians thought their undergraduate training is adequate to prepare them to diagnose common dermatological diseases, but only 28% felt they were adequately prepared to treat these diseases[5]. Fifty-one percent who completed an undergraduate dermatology module felt they were adequately prepared to make a diagnosis. Of those who did not complete the module, only 25% felt they were adequately prepared to diagnose common dermatological diseases. In terms of the ability to treat common dermatological illnesses, 42% of those who completed their module felt adequate compared to 16% who did not complete their module[5].

In 2006, the British Association of Dermatologists (BAD) recommended an evidence based core undergraduate dermatology curriculum[6]. Following the introduction of the BAD recommendations, an audit of the core curriculum content in the United Kingdom medical schools was performed in 2009[7]. In terms of hours of exposure, the number of seminars or lectures ranged from 0 to 39 with a mean of 10, while the number of clinic sessions ranged from 0 to 18 with a mean of 5. Essential clinical skills, background knowledge, skin failure and emergency dermatology are included in most curricula. There were still gaps in the implementation of the recommended curriculum. The Canadian dermatology undergraduate curriculum was reviewed in 1983, 1987, and 1996[8]. The average number of hours dedicated to dermatology teaching in Canada improved by 7 hours to 20.5 hours between 1996 and 2008[8]. The main restriction identified in implementing the curriculum in Canada is the small number of dermatologists available as teachers.

Identification of the core contents is required to develop a standard medical undergraduate dermatology curriculum for the country. This has to be tailored to its usefulness in the local setting, especially taking into consideration the tropical climate, differences in the Asian population and skin of color. The curriculum in general must also be applicable worldwide. Additionally, a clearly defined curriculum is important given the very limited time available for the teaching of dermatology.

Aim

The objective of this study is to identify the appropriate course content for the Malaysian medical undergraduate dermatology curriculum.

Study design

This is a cross sectional study using the Delphi method to assess the appropriateness of a dermatology course content in the medical undergraduate curriculum.

Methodology

A questionnaire containing lists of dermatological conditions to be included in the curriculum was developed by 3 dermatologists (2 from an academic institution, 1 from the Ministry of Health Malaysia) and a family physician. The list was created based on the recommendations of the British Association of Dermatologists for a medical undergraduate curriculum[6], standard dermatology textbooks[9,10], published literature on the subject[2-5,8] and personal clinical experience. The topics were grouped under

accepted classifications of dermatological diseases. The limited time available for a dedicated dermatology teaching is taken into consideration. In general about two weeks is allocated for teaching of dermatology in a five-year undergraduate program. This is an important point to consider in deciding the curriculum content and it will be highlighted to the participants of this study. The questionnaire development is the first part of the study.

In the next part of the study, the questionnaire will be sent via email or snail mail to 20 members of the Dermatological Society of Malaysia, 20 family physicians and 20 general practitioners who are members of the Academy of Family Physicians of Malaysia. All the members of the Dermatological Society of Malaysia are qualified dermatologists while members of the Academy of Family Physicians of Malaysia consist of family physicians and general practitioners. Participants are asked to rate the importance of each disease or condition as part of the curriculum content based on a 5-point Likert scale (very important, fairly important, undecided, fairly unimportant, not important). They are given 6 weeks to return the completed questionnaire. Non responders will be reminded twice, at 2 weeks apart using both telephone call and mail. Responses from this questionnaire will be considered as Round 1. The responses will be analyzed and a summary of the results prepared. The results from Round 1 and the questionnaire will then be sent back to the respondents. They will be asked to look at the results from Round 1 and answer the questionnaire again (Round 2). They may change their answers or keep to their previous answers. Results from Round 2 will then be analyzed.

Sample size calculation

The Delphi group size does not depend on statistical power. It is based on group dynamics in order to achieve a consensus among experts. The literature recommends 10-18 experts in a Delphi panel[12]. We decided to have a group consisting of 20 dermatologists, 20 family physicians and 20 general practitioners, a slightly larger group size to account for drop outs. Dermatologists, family physicians and general practitioners are chosen as the responders in this study as they manage most dermatological cases.

Inclusion criteria consist of dermatologists who are members of the Dermatological Society of Malaysia and registered with the National Specialist Registry, family physicians who are members of the Academy of Family Physicians of Malaysia and registered with the National Specialist Registry, and general practitioners who are members of the Academy of Family Physicians of Malaysia.

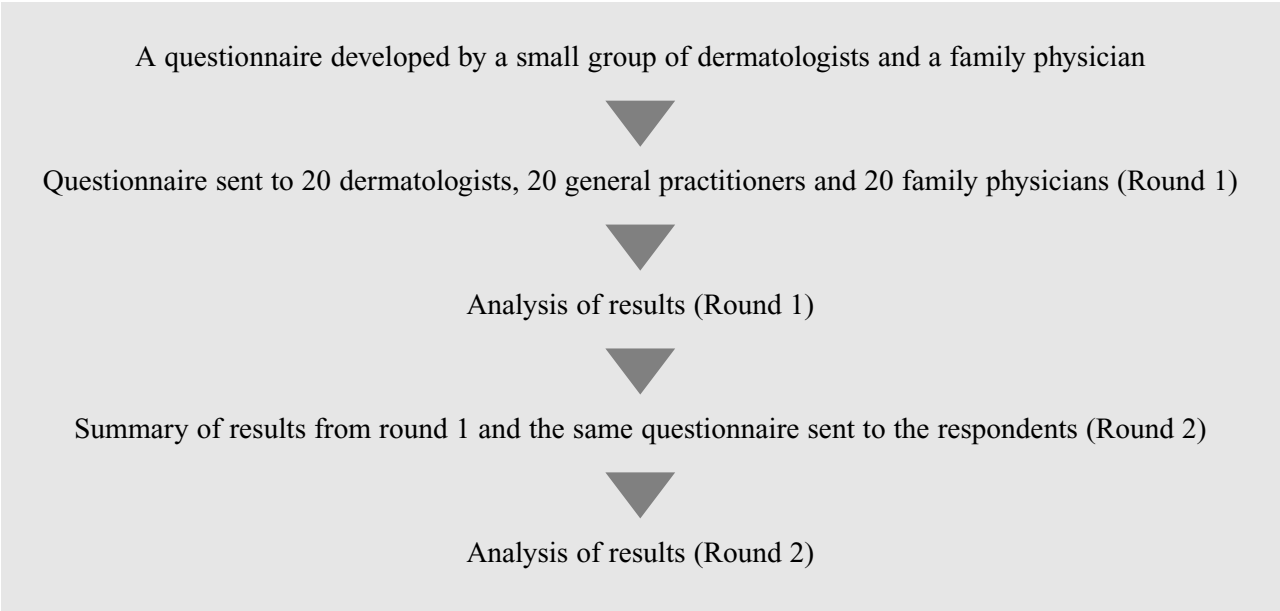

Figure 1 Flow chart of study methodology.

Statistical analysis

Statistical analyses will then be performed in the second part of the study. Analysis will be performed in both Round 1 and Round 2. Mode and median values of each topic will be calculated. Mode values that correlated with median values indicate that the results are a valid representation of the group's view. The level of agreement is determined by calculating the percentage of respondents that choose each answer scale. Responses from the three groups will be analyzed separately and compared. The responses from the groups will also be analyzed together.

Results

The questionnaire was developed by a small group of dermatologists and a family physician is shown in Appendix 1. Section 1 of the questionnaire includes 20 topics according to the classification of dermatological diseases and common dermatological diseases. The topics consist of skin structure and function, infection and infestations, skin tumours, skin signs of systemic diseases, dermatology emergencies, bullous diseases, drug eruptions, psoriasis, eczema, hair and nail disorders, pigmentary disorders, sexually transmitted infections, leprosy, acne, dermatosurgery, genodermatoses, phamacotherapy, clinical skills and diagnostic procedures. Section 2 expands each classification by listing specific diseases or conditions. There are 4 to 15 diseases identified under each classification. This provided a total of 175 options to be graded by each participant. Section 1 aimed to identify important topics based on the classification and common dermatological diseases. The list of specific diseases aimed to ascertain the important dermatological conditions or diseases under each classification. Respondents are given the opportunity to add conditions/diseases which they thought important to include in the curriculum. The questionnaire takes about 30 minutes to complete.

Discussion

Realizing the importance of identifying the core content of a standard dermatology curriculum for the country, the authors have decided to make the development process accessible to all interested parties. The Delphi method was chosen as it provides a systematic approach to identify and prioritize the curriculum content in order to achieve a consensus. In addition, it allows contributions of expertise, represents a collective judgment, gives an opportunity to revise views, anonymity and avoids direct confrontation[11]. In this study, Round 1 of the questionnaire will examine the depth and breadth of topics included. It will also narrow down the topics considered important by the multidisciplinary panel. Round 2 allows each responder to revise their answers from Round 1 after considering the panels' collective opinions. The questionnaire that has been developed (Appendix 1) provides a framework for these objectives.

The British Association of Dermatologists (BAD) had recommended an evidence based core undergraduate dermatology curriculum developed based on the Delphi method in 2006[12]. The opinion of a panel consisting of 26 consultant dermatologists, 9 dermatology specialist registrars, 33 medical and surgical specialties clinicians, 13 general practitioners, 8 junior doctors, 10 dermatology nurses, 4 undergraduate basic sciences tutors, 6 pharmacists and 2 members of the Skin Care Campaign were evaluated. In our study, we selected general practitioners and family physicians to be in the panel as invariably, primary care is the first point of patient contact with health professionals. They would be able to identify common and important dermatological conditions encountered in daily clinical practice. Furthermore, family physicians who supervise junior medical officers will be able to identify the knowledge lacking in these young doctors and what they should be taught in medical schools.

In conclusion, efforts are being made to improve the teaching of undergraduate dermatology in Malaysia. It is important to develop a curriculum to suit our country and at the same time is relevant globally. The final results of this study may be used to recommend a standard Malaysian medical undergraduate dermatology curriculum.

Malaysian Dermatology Curriculum for Medical Undergraduates
QUESTIONNAIRE

Please place a ✔ for each topic listed.
Scale:

1	2	3	4	5
Very important	Fairly important	Undecided	Fairly unimportant	Not important

Section 1

A. The topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

TOPIC	1	2	3	4	5
1 Skin: structure and function					
2 Infections and infestations					
3 Skin tumours					
4 Skin signs in systemic diseases					
5 Dermatology emergencies					
6 Bullous diseases					
7 Drug eruptions					
8 Psoriasis					
9 Eczema					
10 Hair and nail disorders					
11 Pigmentary disorders					
12 Sexually transmitted infections					
13 Leprosy					
14 Acne					
15 Dermatosurgery					
16 Genodermatoses					
17 Phamacotherapy					
20 Clinical skills and diagnostic procedures					

Please state if there are other very important topics which you think has not been listed.

Section 2

1. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Structure and function of the skin	1	2	3	4	5
1. Anatomy of the skin					
2. Physiology of the skin					
3. Functions of the skin					
4. Pathophysiology of skin diseases					
5. Histopathology of common skin diseases					

Please state if there are other very important sub-topics which you think has not been listed above.

2. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Infections and infestations	1	2	3	4	5
Bacterial infections					
1 Erythrasma					
2 Impetigo					
3 Ecthyma					
4 Folliculitis					
5 Abscess, furuncle, carbuncle					
6 Erysipelas					
7 Cellulitis					
8 Necrotizing fasciitis					
9 Mycobacterium infection					
Fungal infections					
10 Tinea pedis and manuum					
11 Tinea corporis, cruris					
12 Tinea capitits, kerion					
13 Pityriasis versicolor					
14 Cutaneous candidiasis					
15 Onychomycosis					
16 Subcutaneous mycoses					
17 Invasive mycoses					

Infections and infestations	1	2	3	4	5
Viral infections					
18 Molluscum contagiosum					
19 Viral exanthems					
20 Hand, foot and mouth disease					
21 Herpes labialis					
22 Varicella zoster					
23 Herpes zoster					
24 Verruca vulgaris					
Infestations					
25 Pediculosis					
26 Scabies					
27 Cutaneous larva migrans					
28 Insect bite reactions					

Please state if there are other very important topics which you think has not been listed above.

3. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Skin tumours	1	2	3	4	5
1 Nevomelanocytic nevi					
2 Blue nevus, Spitz nevus, Nevus spilus, Nevus of Ota, Nevus of Ito, Mongolian spot, Becker's nevus					
3 Vascular tumours & malformations					
4 Seborrhoiec keratoses, skin tags					
5 Lipoma, dermatofibroma					
6 Keloids, hypertrophic scar					
7 Syringoma, sebaceous hyperplasia, trichoepithelioma					
8 Actinic keratoses					
9 Cutaneous horn					
10 Squamous cell carcinoma					
11 Basal cell carcinoma					
12 Malignant melanoma					
13 Cutaneous T cell lymphoma, Sezary syndrome					

Please state if there are other very important topics which you think has not been listed above.

4. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	The skin in systemic diseases	**1**	**2**	**3**	**4**	**5**
1	Cutaneous lupus erythematosus					
2	Dermatomyositis					
3	Behcet's syndrome					
4	Scleroderma					
5	Sarcoidosis					
6	Skin signs of viral hepatitis					
7	Systemic vasculitides					
8	Diabetes mellitus					
9	Internal malignancy/paraneoplastic conditions					
10	Dermatitis herpetiformis					
11	Amyloidosis					

Please state if there are other very important topics which you think has not been listed above.

5. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Dermatology emergencies	**1**	**2**	**3**	**4**	**5**
1	Acute erythroderma					
2	Staphylococcus scalded skin syndrome					
3	Urticaria, angioedema and anaphylaxis					
4	Eczema herpeticum					
5	Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis					
6	Psoriasis von Zumbusch					

Please state if there are other very important topics which you think has not been listed above.

6. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Bullous diseases	**1**	**2**	**3**	**4**	**5**
1 Bullous pemphigoid					
2 Pemphigus vulgaris					
3 Hailey hailey disease					
4 Linear IgA disease					
5 Epidermolysis bullosa acquisita					

Please state if there are other very important topics which you think has not been listed above.

7. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Eczema	**1**	**2**	**3**	**4**	**5**
1 Atopic eczema					
2 Seborrhoiec eczema					
3 Discoid eczema					
4 Hand and feet eczema					
5 Asteatotic/ craquele					
6 Stasis eczema					
7 Juvenile plantar					
8 Allergic contact dermatitis					
9 Irritant contact dermatitis					
10 Photodermatitis					
11 Phytodermatitis					
12 Photophytodermatitis					

Please state if there are other very important topics which you think has not been listed above.

8. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Hair, nail and mucosal disorders	**1**	**2**	**3**	**4**	**5**
1	Alopecia areata					
2	Androgenetic alopecia					
3	Telogen afluvium					
4	Anagen effluvium					
5	Hirsutism, hypertricosis					
6	Primary cicatricial alopecias					
7	Paronychia					
8	Nail signs in systemic diseases					

Please state if there are other very important topics which you think has not been listed above.

9. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Pigmentary disorders	**1**	**2**	**3**	**4**	**5**
1	Vitiligo					
2	Albinism					
3	Melasma					
4	Post inflammatory hypo/hyper pigmentation					

Please state if there are other very important topics which you think has not been listed above.

10. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Sexually transmitted infections	**1**	**2**	**3**	**4**	**5**
1	Syphillis					
2	Gonorrhoea					
3	Genital herpes					
4	Genital warts					
5	Chlamydia trachomatis infection					
6	Lymphogranuloma venereum					

Sexually transmitted infections	1	2	3	4	5
7 Chancroid					
8 Granuloma Inguinale					

Please state if there are other very important topics which you think has not been listed above.

11. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Photodermatoses	1	2	3	4	5
1 Photodermatitis					
2 Porphyrias					
3 Polymorphic light eruption					
4 Photoexacerbated dermatoses					
5 Chronic actinic dermatitis					

Please state if there are other very important topics which you think has not been listed above.

12. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Drug eruptions	1	2	3	4	5
1 Exanthematous drug eruption					
2 Drug induced hypersensitivity syndrome					
3 Acute generalised exanthematous pustulosis					
4 Fixed drug eruption					
5 Erythema multiforme					
6 Drug induced lupus					
7 Drug induced vasculitis					
8 Drug induced photosensitivity					

Please state if there are other very important topics which you think has not been listed above.

13. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Genodermatoses	**1**	**2**	**3**	**4**	**5**
1	Ichthyoses					
2	Epidermolysis bullosa					
3	Congenital viral infection					
4	Congenital malformations					
5	Transient dermatoses of the neonate					
6	Vascular malformations/tumours/ lymphangiomas					

Please state if there are other very important topics which you think has not been listed above.

14. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Dermatosurgery/procedural skills	**1**	**2**	**3**	**4**	**5**
1	Laser					
2	Electrocautery					
3	Cyrotherapy					
4	IL triamcinalone					
5	Skin biopsy, excision					

Please state if there are other very important topics which you think has not been listed above.

15. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

	Dermatopharmacotherapy	**1**	**2**	**3**	**4**	**5**
1	Topical steroids					
2	Topical antibiotics					
3	Topical anti-fungals					
4	Topical tretinoin					
5	Keratolytics					
6	Topical immunomodulators					
7	Emollients					
8	Tar preparations					

Dermatopharmacotherapy	1	2	3	4	5
9 Astringents					
10 Wet wraps					
11 Wet dressing					
12 Isotretinoin					
13 Antihistamines					
14 Biologics					
15 Writing a prescription					

Please state if there are other very important topics which you think has not been listed above.

16. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Clinical skills and bedside investigations	1	2	3	4	5
1 Dermatology history taking					
2 Dermatology physical examination					
3 Identification and description of cutaneous lesions					
4 Counselling					
5 Tape test					
6 Skin scraping for fungal culture					
7 Microscopic examination with KOH					
8 Tzanck smear					
9 Slit skin smear					

Please state if there are other very important topics which you think has not been listed above.

17. The sub-topics listed must be included in the medical undergraduate dermatology curriculum. Please grade your opinion according to the scale.

Miscellaneous inflammatory disorders	1	2	3	4	5
1 Lichen planus					
2 Pityriasis rosea					
3 Pityriasis lichenoides					
4 Pyoderma gangrenosum					

Please state if there are other very important topics which you think has not been listed above.

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DERMATO-ONCOLOGY - Short Case

MARJOLIN'S ULCER SECONDARY TO CHRONIC BURN SCAR IN 2 PATIENTS

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Keywords *skin cancer, squamous cell carcinoma, chronic skin lesion*

Introduction

Marjolin's ulcer is a term used to describe a malignant transformation in a chronic scar, usually secondary to burn injury. The histopathology of the malignant change is usually squamous cell carcinoma. We reported two cases of Marjolin's ulcer arising from a chronic burn scar.

Case report

CASE 1

A 59 year-old Myanmar lady presented with 2 years history of verrucous plaque with ulceration over the right posterior ankle. She had no previous history of penetrating injury. She gave a history of burn secondary to fire 30 years ago, resulting in a chronic scar extending from the lower legs up to the thighs. There was a history of similar ulcer over the left leg, which resulted in a left below knee amputation 3 years ago. There was no family history of malignancy.

On examination, there was a verrucous plaque, with central ulceration on the right posterior ankle (Figure 1). The lesion measured 5x7 cm in diameter. The edges were raised and erythematous. There was also evidence of burn scar extending from the right lower leg to the thigh. Left leg was amputated below the knee level. There was no evidence of chronic arsenic ingestion.

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Skin biopsy from the ulcer edge showed marked parakeratosis, with malignant squamous cells infiltrating into the dermis, arranged in trabeculae and nests, surrounded by desmoplastic, inflamed stroma (Figure 2).

The malignant squamous cells were well differentiated. There were keratin pearls and intercellular bridging. The nuclei were enlarged, pleomorphic and vesicular, with prominent nucleoli. Mitotic figures were easily seen. The features were consistent with a well differentiated squamous cell carcinoma.

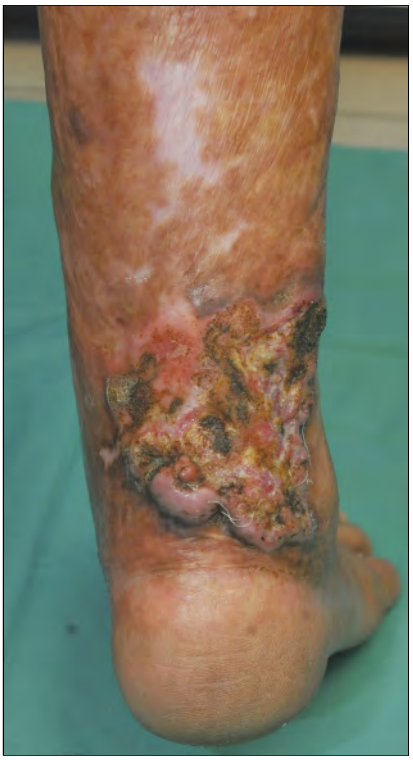

Figure 1
Ulcerated plaque, with raised margin on the postero-lateral aspect of the right ankle.

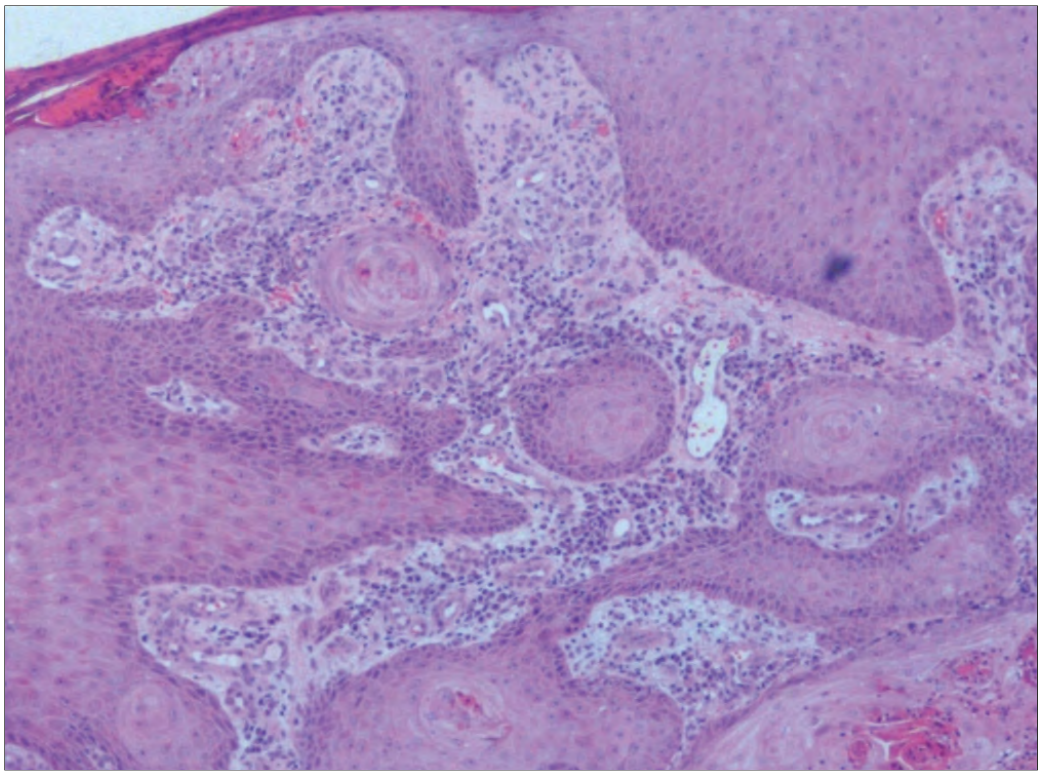

Figure 2
Malignant squamous cells infiltrating into the dermis, arranged in trabeculae and nests, surrounded by desmoplastic, inflamed stroma (haematoxylin & eosin, x4 magnification).

Tissue for bacterial culture grew Streptococcus Group B and Escherichia coli. Tissue cultures for fungus and mycobacterium were negative. Tuberculous and non-tuberculous mycobacterium Polymerase Chain Reaction (PCR) were also negative.

Computed tomography (CT) scan of the thorax, abdomen and pelvis showed focal area of lung fibrosis, with two calcified left lung nodules, likely to represent granuloma. There was no evidence of lung metastases and no lymphadenopathy.

Magnetic resonance imaging (MRI) of the right leg showed irregular, ill-defined exophytic skin lesion arising from the postero-lateral aspect of the right ankle. There was also evidence of local extension into the superficial fascia and superficial part of the subcutaneous fat. The muscles, vessels, bones and ankle joint were normal.

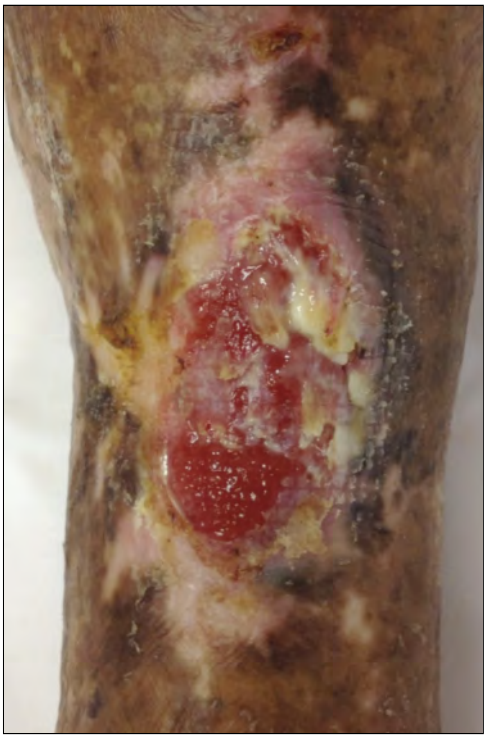

Figure 3
Ulcerated plaque, with fleshy erythematous nodule in the centre of the left forearm.

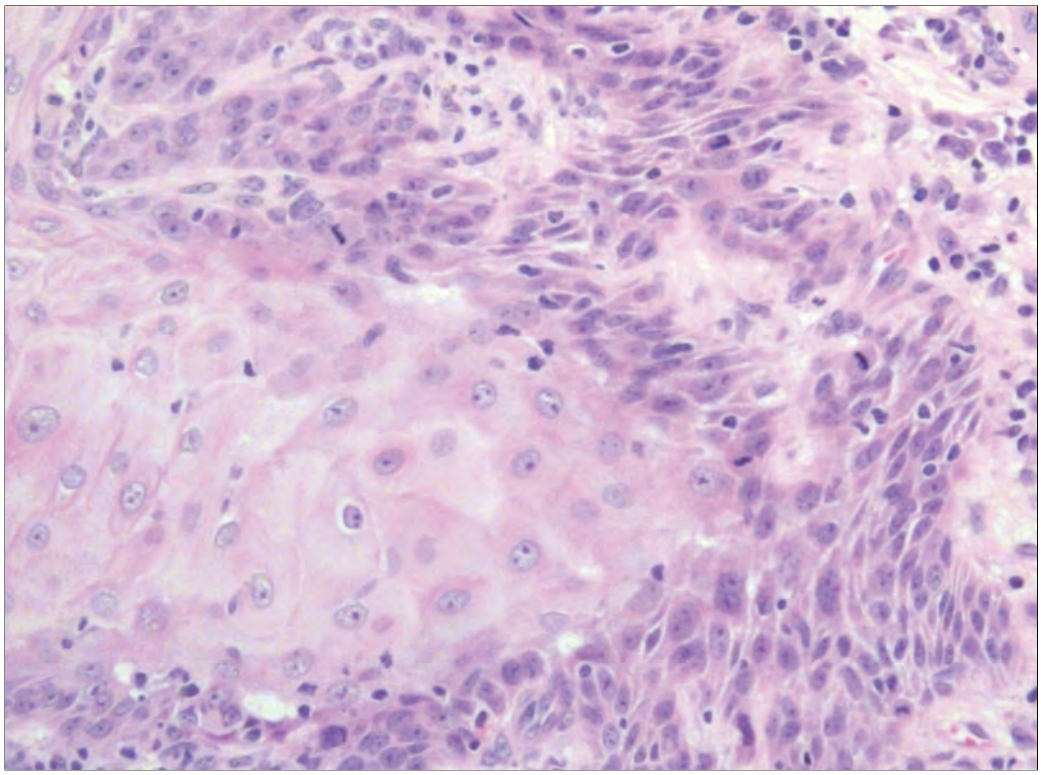

Figure 4
Large keratinocytes, with pleomorphic vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm. Mitoses also present (haematoxylin & eosin, x20 magnification).

As patient had amputation of the left leg, she was not keen for further surgical intervention. She was hence referred for radiotherapy and is currently undergoing treatment.

CASE 2

A 53 year-old Indian lady presented with 3 months history of ulcerated plaque over her left forearm. There was a history of burn injury secondary to hot water scalding at the age of 3 years old. On examination, there was an ulcerated plaque on her left forearm, measuring 5 x 3 cm diameter (Figure 3). There was no axillary lymphadenopathy.

Skin biopsy showed malignant squamous cell infiltration into the stroma. The cells were large in size, with pleomorphic vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm (Figure 4). Keratin pearls and intercellular bridges were also seen. The features were consistent with a well differentiated squamous cell carcinoma.

She was referred to the orthopaedic surgeon for excision and grafting.

Discussion

Burn injury occurs with varying depth and intensity. The healed burn injury, especially if it healed by secondary intention is at risk for continued injury during the course of daily activities. This is because the skin has lost the normal architecture of the dermis, nerves, vessels, and adnexa. It is less elastic, more easily injured and ulcerated compared to normal skin.

Studies have shown that major burn can lead to significant depression of both humoral and cell-mediated immunity[1]. The impairment of the immune system is dependent on the extent of burn, and increased with the occurrence of superimposed infections[2]. Individuals who experience chronic immunosuppression are at a greater risk of developing a malignancy[3].

Malignancies arising in burn scar tissue have been well documented. Kowal-Vern et. al reported 412 cases of cutaneous malignancies from 1923 to 2004[4]. In a recent study published by Duke J et.al, 759 cases of solid organ malignancies were reported in patients with previous history of hospitalization for burn between 1983 to 2008[5]. They also noted that there was a gender effect in relation to incidence of cancer after burn, with a significant risk of cancer for females[5]. Examination of total incident cancer notifications for females in the burn cohort from 1983 to 2008 found cancer of the breast (26.2%) to be the most common notification, followed by cancers of female genital system (12.7%), colorectal (9.8%) and lung (9.8%) cancers[5].

Historically, skin neoplasms are known to arise where chronic exposure to fire or heat injures the skin: the 'kangri' burn cancer in India, the 'kairo' of the Japanese, the 'kang' cancer of north-west China and erythema ab igne in the British[6-8]. Celsus was the first to note the development of cancer in burn scars[9]. In 1828, a French surgeon, Jean-Nicholas Marjolin, published his description of 'warty' changes of chronic ulcers[10]. It was only in 1903 that Da Costa coined the term 'Marjolin's ulcer'[11]. However, several authors have noted that Marjolin was not the first to describe the entity's neoplastic nature. It was probably Dupuytren, Marjolin's competitor, who first described the cancerous changes in an acid burn scar in 1839[9].

For many years the term Marjolin's ulcer was used as a synonym of burn scar neoplasm. However, there are several pathologies that contribute to Marjolin's ulcer development, such as osteomyelitis[12], decubitus ulcers[12], chronic fistulas[13], frost bite[14], chronic venous insufficiency[15], vaccination sites[16] and skin graft donor sites[17].

The histology of Marjolin's ulcer is usually squamous cell carcinoma (SCC), which accounted for 73% of cases, followed by basal cell carcinoma (BCC) in 10% of cases. Other less frequent histological changes are malignant melanoma, sarcomas (fibrosarcoma, liposarcoma, dermatofibrosarcoma protuberans, mesenchymal tumor) and mixed tumors (SCC-BCC and SCC-melanoma)[18].

There is usually a lag period between the development of Marjolin's ulcer in a scar tissue and the time of injury. The latency is inversely proportional to the patients' age. The older the patient at the time of injury, the shorter the lag period. The average latency period is 36 years and the average patients' age at the time of diagnosis is 52[18]. Male to female ratio is 2:1[18]. The commonest affected sites are the lower extremities, which accounted for 36% of cases. This is followed by the head & neck region, upper extremities and the trunk[18].

Marjolin's ulcer is commonly mistaken for an infected ulceration occurring at the scar tissue sites. Changes such as the appearance of painful, non-healing ulcers, enlarging in circumference, with elevated and indurated borders, foul-smelling, with exudate and bloody discharge suggest a malignant transformation. Biopsy is recommended to confirm the neoplastic transformation. Unfortunately diagnosis is often delayed. Marjolin's ulcer has a high metastatic potential and 30% of the cases have enlarged lymph nodes with possible distant metastasis at diagnosis[18].

Most researchers agree that the best prevention of these scar malignancies is primary skin grafting of the burn sites. Examination of the effects of burn severity and skin graft amongst burn survivors and cancer incidence identified a significant association for those with burns of total body surface area of 20% or greater, while a non-significant positive association was found for those who had skin graft[5]. On the basis that prolonged healing of wounds may be a potential risk factor for carcinoma, it has been suggested that early skin grafting may be important with respect to prevention of cancer.

To date, there has not been a consensus reached over the treatment protocol. Wide surgical excision seems to be the most preferred method. Defects are usually skin grafted either with free flaps or split-thickness skin grafts (STSG)[19]. If there is a clinically palpable lymphadenopathy, lymph node dissection is recommended with an exception for malignant melanoma, where the sentinel lymph node biopsy should be performed regardless of the presence of enlarged lymph nodes. CO_2 laser had also been tried successfully in some cases[20]. Inoperable cases and recurrences may be treated with radiotherapy alone or combined with chemotherapy.

Conclusions

Marjolin's ulcer may begin as an indolent lesion, but has the potential to become a very aggressive malignancy. Unfortunately the diagnosis and treatment are usually delayed. In order to reduce the malignant transformation, burns, especially full thickness burns, should be skin grafted. Patients suffering from burns or other skin pathologies leading to the formation of scar tissue must be monitored regularly. Any suspicious lesions or ulcerations must be biopsied. Surgical treatment is the mainstay treatment of Marjolin's ulcer. Radiotherapy and chemotherapy can be reserved for patients unsuitable for surgery.

Acknowledgement

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DERMATO-ONCOLOGY - Short Case

SQUAMOUS CELL CARCINOMA ARISING FROM HYPERTROPHIC LICHEN PLANUS: A CASE REPORT AND REVIEW OF LITERATURE

Tan Wooi Chiang, *MRCP*, Mohd Affandi, *AdvMDerm*, Dawn Ambrose, *MRCP*

Keywords *skin cancer, malignant transformation, Malaysia*

Introduction

Lichen planus (LP) is a common papulo-squamous disorder involving the skin, mucosa, nails and hair[1]. Although it is a benign disorder, malignant changes may occur. There are very few case reports on malignant transformation of cutaneous lichen planus[2].

We report a case of squamous cell carcinoma (SCC) which developed over a long standing hypertrophic lichen planus (HLP) lesion on the right shin of a young Indian male. Case is described for the rarity of complication arising from a common condition.

Case report

A 31-year-old Indian male presented with a chronic warty plaque over both leg since the age of 4. The lesion started as red itchy plaques that gradually enlarged over time. He was treated with potent topical steroid with or without occlusion and intermittent cryotherapy. The lesion improved significantly but did not disappear completely.

Twenty-seven years after the initial presentation, a 5-cent coin size warty growth had appeared at the centre of the plaque. The growth enlarged rapidly over 6 weeks and bled on touching. There was no history of trauma or contact with irritant substances. He was otherwise well and healthy. He is a non-smoker.

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Examination revealed a well defined, 5 cm by 3.5 cm, hypertrophic plaque on the anterior aspect of the right shin. There was an ulcerated exophytic growth measuring 1.5 cm by 1.5 cm seen at the centre of the plaque (Figure 1a & Ib). The mucous membranes, hair and nails were normal. Systemic examinations were unremarkable.

Wedge biopsy specimens were obtained from the hypertrophic plaque and the exophytic growth. Histopathology examination of the plaque lesion showed typical features of hypertrophic LP (Figure 2) while the section from the exophytic growth showed features suggestive of SCC (Figure 3). The neoplastic cells were stained positive for CK 5 and CK 6 but were negative for S100, HMB45 and CD34. MRI of the right lower limb revealed no extension into underlying muscle and bone. Other blood tests were normal.

The tumour was completely excised. Soft tissue reconstruction with flap and skin graft and transposition of the right inguinal dissection were done. Biopsy confirmed no inguinal lymph node involvement.

Follow up to 12 months noted, the patient to be well with no local recurrence or distant metastases. Other plaques on the left leg and ankle were treated with cryotherapy and potent topical steroid.

Discussion

Lichen planus (LP) is a chronic T cell mediated mucocutaneous disease. The actual cause of this condition remains unknown. It is characterized by pruritic, violaceous, polygonal, flat topped papules/ plaques which are distributed symmetrically over the extremities[1].

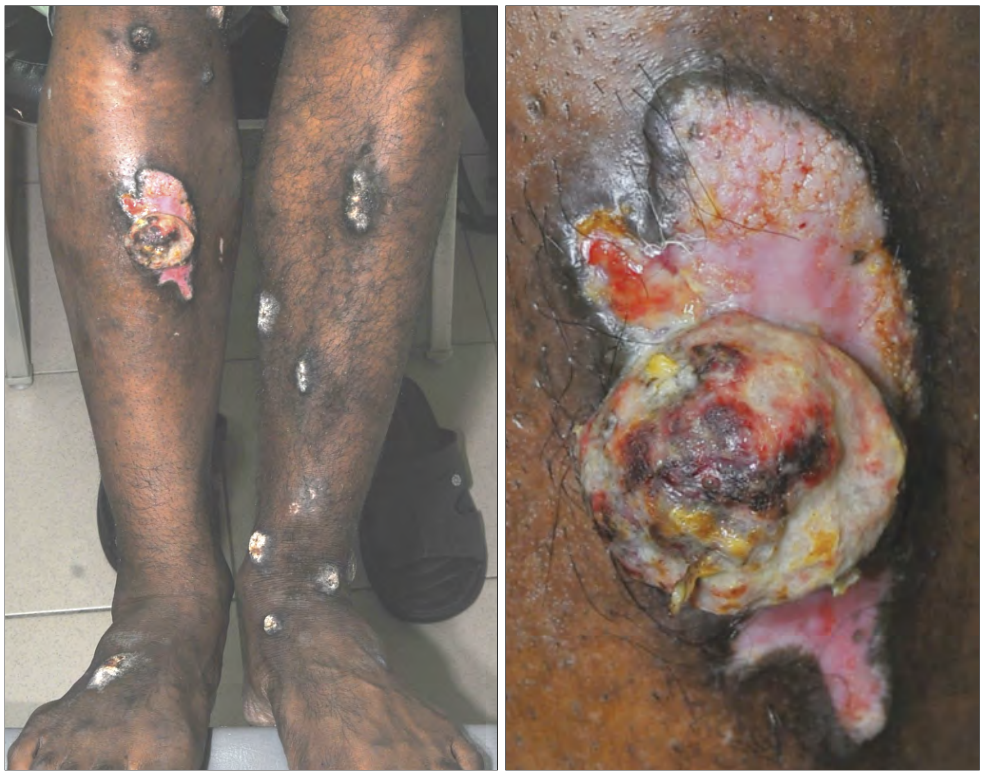

Figure 1a & 1b (close up view)
Ulcerated growth seen at the centre of the plaque. A few atrophic depigmented lesions were noted over both legs (previous site of hypertrophic LP).

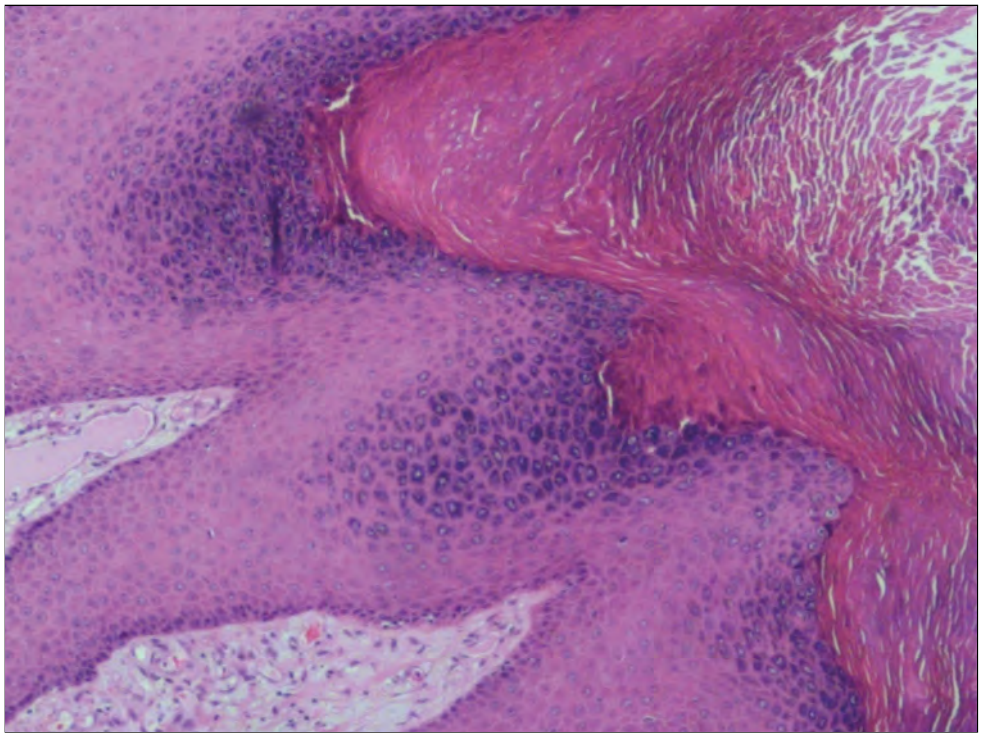

Figure 2
Marked hyperkeratosis, wedge-shaped hypergranulosis and acanthosis of the epidermis (hematoxylin and eosin stain; original magnification x4).

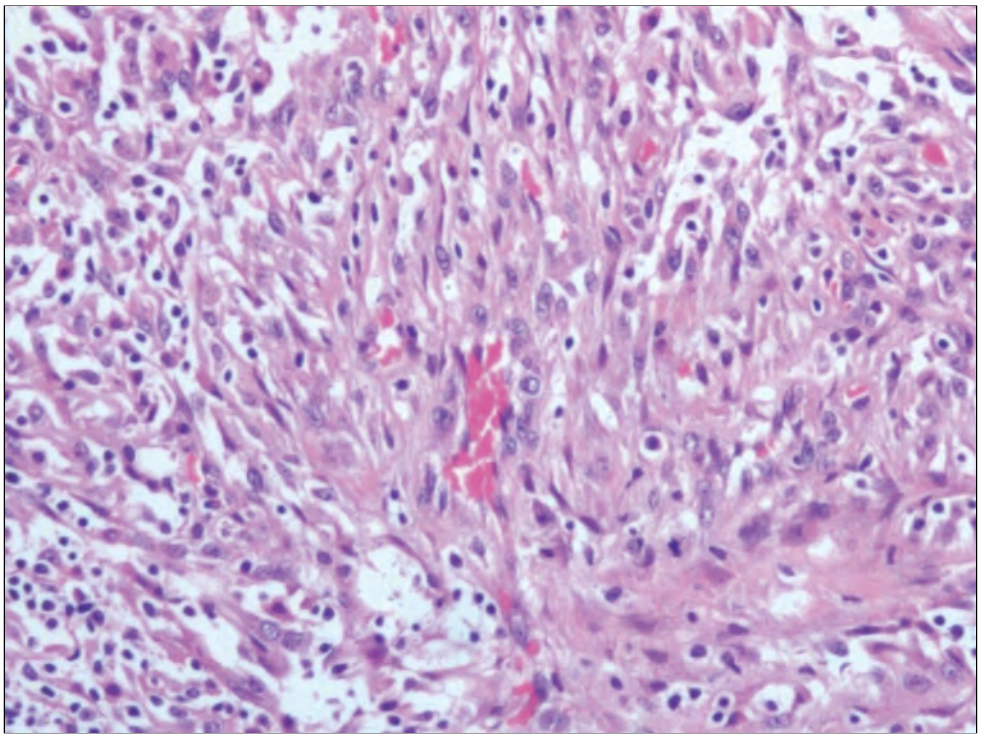

Figure 3
Focal ulcerated epithelium with a diffuse neoplastic cell infiltration within the underlying stroma. The neoplastic cells are polygonal to spindle shaped cells with pleomorphic vesicular nuclei, prominent nucleoli and variable amount eosinophilic cytoplasm. Mitoses are noted (hematoxylin and eosin stain; original magnification x4).

LP is a common benign inflammatory dermatosis. It occasionally clears within a few weeks. In 50% of the cases, the lesions subside within 9 months. Up to 70% of patients may experience spontaneous remission within 15 months. Only 12-20% of cases will develop recurrent disease later in life[3]. Since the first report of malignant transformation of LP in 1903, its malignant transformation potential remained a concern.

Malignant transformation rate of LP varies widely. It was reported in the literature to be between 0.4 and 6.5% but in most studies it do not exceed 1%. Meta-analysis of epidemiological studies by Sousa et al revealed a malignant transformation rate of 1.63% over 5 years (0.27% per year)[4].

The incidence of malignancy in LP actually depends on the anatomical site involved and the type of lichen planus. Malignant transformation can occur in mucosal lichen planus especially oral LP. The frequency of malignant transformation from oral LP ranges from 0% to 5.3% with the highest rate of 40-60%, noted in those with erythematous and erosive lesions[5]. World Health Organisation (WHO) had classified oral lichen planus as a pre-malignant condition[6].

A long term retrospective epidemiological study of malignancy in patients with LP has demonstrated a significant association between oral LP and SCC with a relative risk of 5.9%, especially among men and smoker. No significant risk of transformation of cutaneous LP into SCC had been reported[5]. However, the major limitation of this study is both chronic and acute LP was included in the review. The result may vary if only the chronic LP form were analyzed.

Malignant transformation in cutaneous LP is very rare[2]. To date, less than 100 cases of cancers were reported. Cutaneous LP related SCC has an incidence of 0.4%. Nearly all them arose from hypertrophic LP of the lower leg[7]. More recent reports suggest that the association may be greater with ulcerative LP.

Hypertrophic LP typically present as red brown or violaceous, firm, thick, verrucous plaques on the shins and around the ankle. It often persisted for many years and healed with area of pigmentation and scarring with degree of atrophy. The chronicity of LP appears to be a risk factor for the development of SCC.

All reported LP related malignant cases have long latency periods between the diagnosis of LP and the development of neoplastic transformation (range between 4 years and 35 years; mean of 12 years)[7]. Our patient also showed long latency period of 27 years before the development of malignant transformation.

There is a controversy as to whether the cancer complicating LP has been part of the natural history or the result of exposure to external factors like tobacco, radiation, arsenic or chronic irritation. Cancers do occur from the site of chronic inflammatory processes such as chronic venous stasis ulcer, discoid lupus erythematosus, lupus vulgaris or burn scars.

The actual mechanism of neoplastic transformation is not known. Some authors postulated the possible role of prolonged chronic inflammation in the development of cancer. Chronic inflammatory processes will lead to overdrive of the cytokines and growth factors, which will constantly stimulate epithelial cell proliferation and turn into neoplastic condition[8-9].

Very few data are available with regards to LP related SCC behaviour, although some authors suggest a bad prognosis[10]. We also observed an aggressive form of SCC in our patient with rapid progression, ulceration and of a poorly differentiated type of SCC.

Conclusion

Although cutaneous LP associated SCC is very rare, the awareness of the possibility of malignancy arising on cutaneous LP must be kept in mind. When treatment fails or new lesion appears, skin biopsy must be done for early diagnosis of malignant transformation. Careful and vigilant follow up for those with long standing hypertrophic lichen planus is necessary to allow early detection of SCC.

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DERMATO-ONCOLOGY - Short Case

CHRONIC ARSENIC POISONING ASSOCIATED WITH MULTIPLE SKIN MALIGNANCIES

Low Zhi Mei[1], Tey Kwee Eng[2], *MRCP*, Choon Siew Eng[2] *FRCP*

Keywords *basal cell carcinoma, squamous cell carcinoma, lung metastasis*

Introduction

Chronic arsenic poisoning is rarely seen nowadays. It may develop as a result of long term use of Chinese herbal medications, drinking high-arsenic artesian well water or occupational exposure. The most common manifestations of chronic arsenic poisoning are hyperpigmentation or classical "raindrop" melanosis, punctate hyperkeratosis and skin tumours.

Bowen's disease is the most common form of skin tumour induced by arsenic followed by squamous cell carcinoma and basal cell carcinoma. Chronic arsenic poisoning is also associated with internal malignancy such as carcinoma of lung, stomach, colon, kidney, bladder and hematopoietic system.

Recognizing signs of chronic arsenic poisoning allows early diagnosis and treatment of associated cutaneous and internal malignancy. We describe a man who developed multiple malignancies namely basal cell carcinoma, squamous cell carcinoma and Bowen's disease following exposure to arsenic-containing traditional Chinese medication given for his childhood asthma.

Case report

A 52-year old single Chinese man, first presented to the Department of Dermatology, Sultanah Aminah Hospital, Malaysia in 2003 with a three-year history of multiple brownish plaques on the trunk. Patient had severe childhood asthma which was treated with Sin Lak Pills, a traditional Chinese anti-asthmatic preparation, for more than 5 years. He had no history of drinking well water or living close to tin mines. There is no family history of malignancies. He was working in the family goldsmith business and stopped since 2003.

Clinical examination revealed a cutaneous horn on his chest and multiple mildly erythematous plaques with brownish adherent crusts of varying sizes ranging from 1x1 cm to 5x5 cm on his trunk and thighs (Figure 1). He also had multiple punctate hyperkeratoses on both the palms and soles (Figure 2). Raindrop-like hypomelanosis were noted on his thighs (Figure 3) and upper the back of the trunk. Biopsies from the plaque on the trunk, thigh and cutaneous horn confirmed diagnoses of Bowen's disease, basal cell carcinoma (BCC) (Figure 4) and squamous cell carcinoma (SCC).

The Bowen disease on the trunk, BCC on his left thigh and cutaneous horn with underlying SCC were totally excised while the smaller plaques assumed to be Bowen disease were treated with cryotherapy and acitretin 30mg daily. In spite of the acitretin prophylaxis, he continued to develop more SCCs. In May 2005, total excision of a fungating mass on his right palm by orthopedic team was confirmed to be SCC and in 2006, another SCC on the posterior aspect of the left thigh was removed. At the same time, an enlarged axillary lymph node with metastasis was removed, followed by radiotherapy to the affected area.

In 2008, after one month history of cough, contrast-enhanced CT scan (CECT) of thorax was done. It showed sub-pleural thickening in the left lateral chest, associated with fibrosis, likely secondary to radiotherapy. Bilateral multiple areas of consolidation were also noted. He sought treatment in Singapore and was diagnosed and treated for

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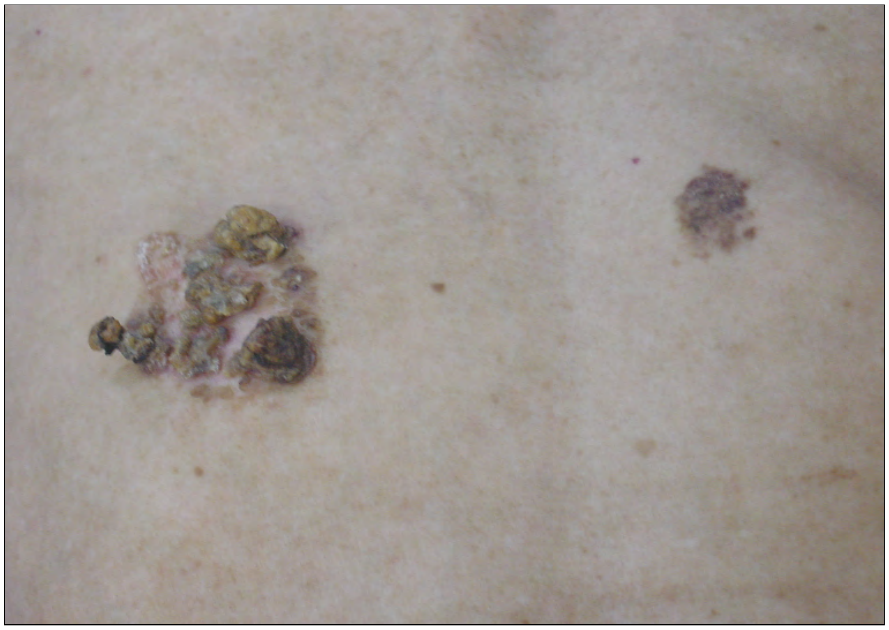

Figure 1
Lesion on patient's back.

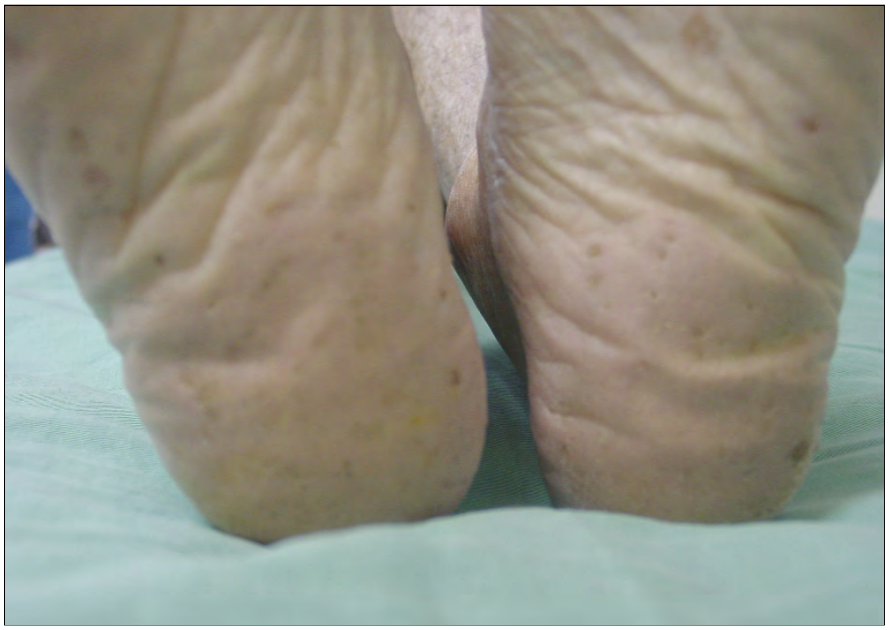

Figure 2
Punctate hyperkeratosis on patient's soles.

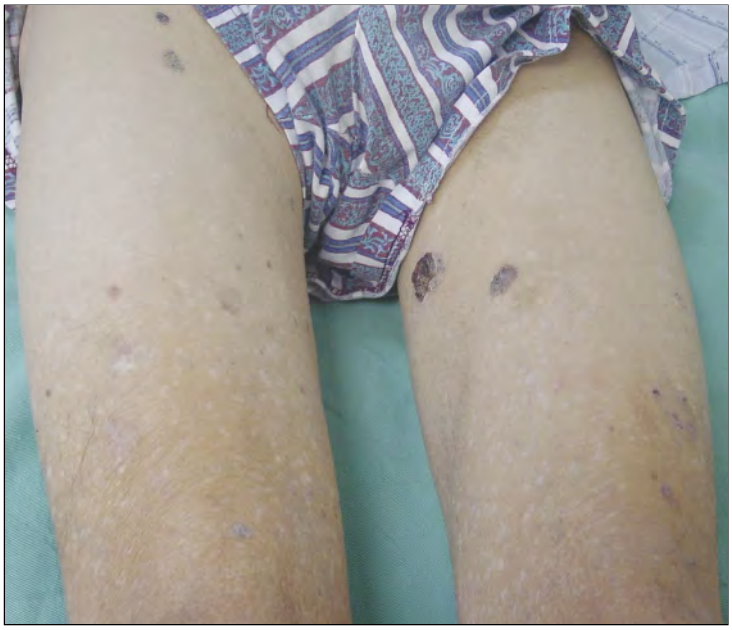

Figure 3
Raindrop-like hypomelanosis on patient's thighs.

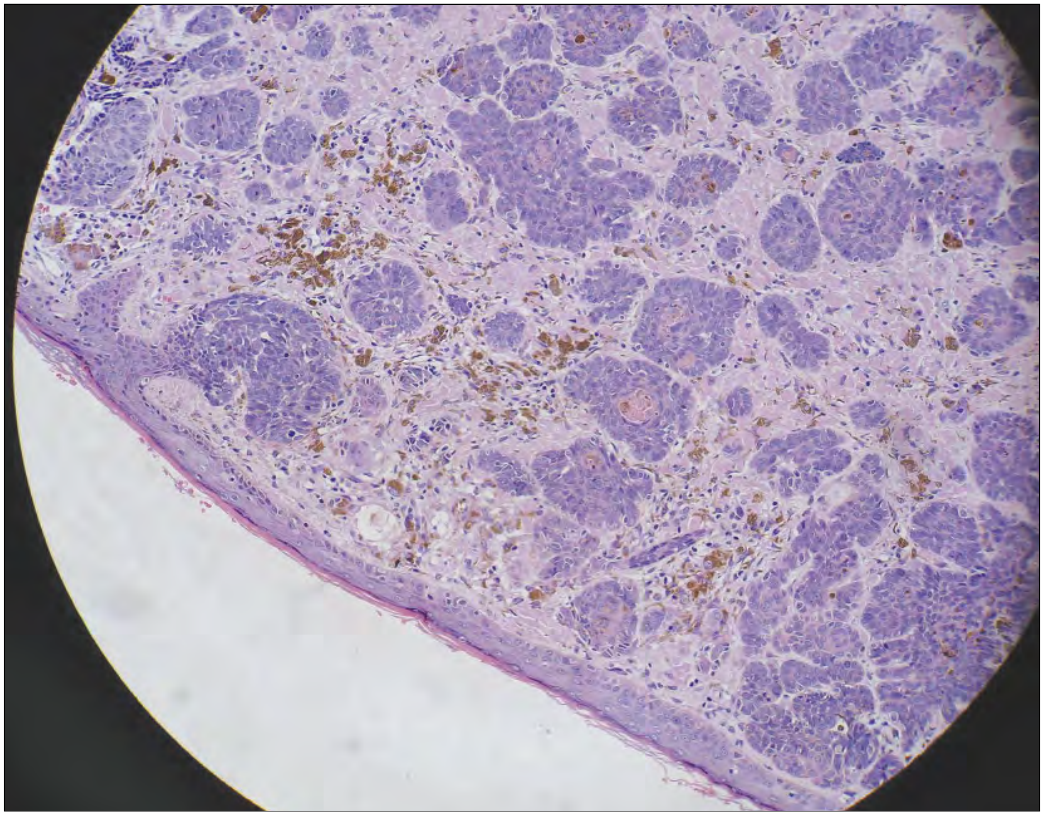

Figure 4
Basal cell carcinoma.

pulmonary tuberculosis. He stopped taking acitretin for more than a year but was well till December, 2011 when he started losing weight again.

CECT of the thorax showed bilateral upper lobe fibrosis, bronchiectasis with scattered small nodules and right lung base interlobular septal thickening. Tuberculosis workup was negative but patient declined bronchoscopy to rule out primary or metastatic lung carcinoma and succumbed to his illness in May 2012.

Discussion

Arsenic is classified as a Class I human carcinogen by the International Agency for Research on Cancer, because of its association with skin and visceral cancers[1]. Chronic arsenicism is defined by WHO as a chronic health condition arising from prolonged ingestion of arsenic above a safe dose for at least 6 months, usually manifested by characteristic skin lesions, with or without the involvement of internal organs[1]. Visceral malignancies usually manifest after cutaneous onset[2].

Arsenic can be found in naturally contaminated drinking water and landfills, traditional Chinese or herbal medicines and in occupational settings (agricultural chemicals, mining, carpentry and manufacture of gallium arsenide computer microchips)[3,4]. Taiwan reported effects of arsenic on the skin in an area with high arsenic concentrations in well water[5]. Ayurvedic and Chinese medicines are also known to contain high level of arsenic. Skin lesions occurring after the treatment of asthma with inorganic arsenic was reported in the United States in 1952[5].

Chronic arsenicism from Sin Lak Pills (Traditional Chinese medicines) was reported in Singapore[6-8]. These pills were used to treat asthma and its usage had been linked to various systemic and skin diseases. It was banned in 1972, due to the excessive content of inorganic arsenic sulfide. The National Skin Centre of Singapore reviewed patients with cutaneous lesions related to chronic arsenic intake. Out of 17 patients, 14 took Chinese herbal remedies contaminated with inorganic arsenic[8].

Our patient had severe childhood asthma and was treated with Sin Lak Pills for more than 5 years in Singapore. He had no history of drinking well water and no history of living close to tin mines. The source of arsenic was likely from the Sin Lak Pills.

Chronic exposure to arsenic can lead to the development of internal malignancies such as lung and urinary tract carcinomas, and cutaneous malignancies such as Bowen's disease, arsenical keratosis, BCC and SCC[9-11]. Skin manifestations of chronic arsenicism include spotted melanosis interspersed with hypopigmentation (raindrop appearance), Bowen's disease, BCC and SCC and hyperkeratotic corns or warts on the palms and soles. Lung is a common major site for arsenic-related cancers.

Based on WHO 2005 field guide for the detection of arsenic poisoning, a urine sample with concentration of arsenic higher than 50µg/L confirms recent exposure. Since arsenic is rapidly cleared from the blood, it is only useful to assess recent high concentration exposures[1]. Since this patient was exposed to arsenic in Sin Lak Pills many years ago, performing the urine test to detect arsenic would be of no significance.

Hyperkeratosis, hyperpigmentation, and hypopigmentation may disappear with time, and this may conceal the possible exposure to arsenic. A diagnosis of arsenic poisoning must be considered when multiple keratoses or multiple lesions of BCC, Bowen's disease and SCC are found in sun-protected part of the body. Arsenicism has become rare, but should still be kept in mind due to persistent environmental, occupational exposure and the reintroduction of arsenic trioxide as a rescue treatment for promyelocytic leukaemia[12].

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DERMATOLOGY THERAPEUTIC - Short Case

SUCCESSFUL MANAGEMENT OF CUTANEOUS POLYARTERITIS NODOSA WITH INFECTED ULCERS WITH CLOFAZIMINE AND EPIDURAL ANALGESIA

Michelle Voo Sook Yee[1], *MRCP*, Ng Kim Swan[2], *MMed (Anaes)*, Mary Suma Cardosa[2], *FFPMANZCA*, Salmi Abdullah[3], *MMed (Path)*, Rohna Ridzwan[1], *MRCP*

Keywords *vasculitis, regional anaesthesia, anti-inflammatory drug*

Introduction

Cutaneous polyarteritis nodosa is an uncommon form of cutaneous vasculitis affecting small and medium size arteries. We describe a case of infected cutaneous polyarteritis nodosa in a 30-year-old man who responded to antibiotics, steroids and clofazimine together with aggressive dressing which was possible due to effective pain relief.

Case report

A 30-year-old Chinese man presented to the Dermatology clinic with painful ulcers on the ankle and dorsum of both feet for one month. There was no history of photosensitivity, joint or muscle pain or oral ulcers.

Physical examination revealed multiple stellate shaped ulcers on the dorsum of both feet, which were covered with slough. There was also lace-like purplish reticulated rash at both calves suggestive of livedo reticularis. There were no subcutaneous nodules, oral ulcers nor malar rash. Cardiovascular, respiratory and abdominal examinations were unremarkable. There was no sign of peripheral neuropathy.

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A working diagnosis of cutaneous polyarteritis nodosa (cPAN) was made with differential diagnosis of livedoid vasculopathy. Skin biopsy showed leucocytoclastic vasculitis, fibrinoid necrosis of the medium size vessel walls and luminal thrombi at the capillaries (Figure 1a & b). There was C3 staining along the basal layer and blood vessel, with IgM positive at the vessel walls.

Blood investigations revealed a total white cell count of 13 x103/L , hemoglobin 16g/dL, platelet count 277 x 103/L. Inflammatory markers were within normal range: Erythrocyte sedimentation rate (ESR) 8mm/hr, C-reactive protein 0.4 mg/L. Renal profile, liver function and complement levels were normal. Hepatitis B surface antigen, Anti Hepatitic C antibody, HIV, antinuclear antibody (ANA), Anticardiolipin antibody, anti neutrophil cytoplasmic antibody (c-ANCA) and cryoglobulin were negative.

He was initially treated as outpatient with oral prednisolone 1mg/kg/day, oral cloxacillin and celecoxib. However, he returned a week later and was admitted to the ward for a week because of unbearable ulcer pain, which was treated with oral Tramadol 50mg QID. On discharge he was given azathioprine 1mg/kg/day which was subsequently titrated to 2mg/kg/day. Pus swab for culture taken during admission grew no organism.

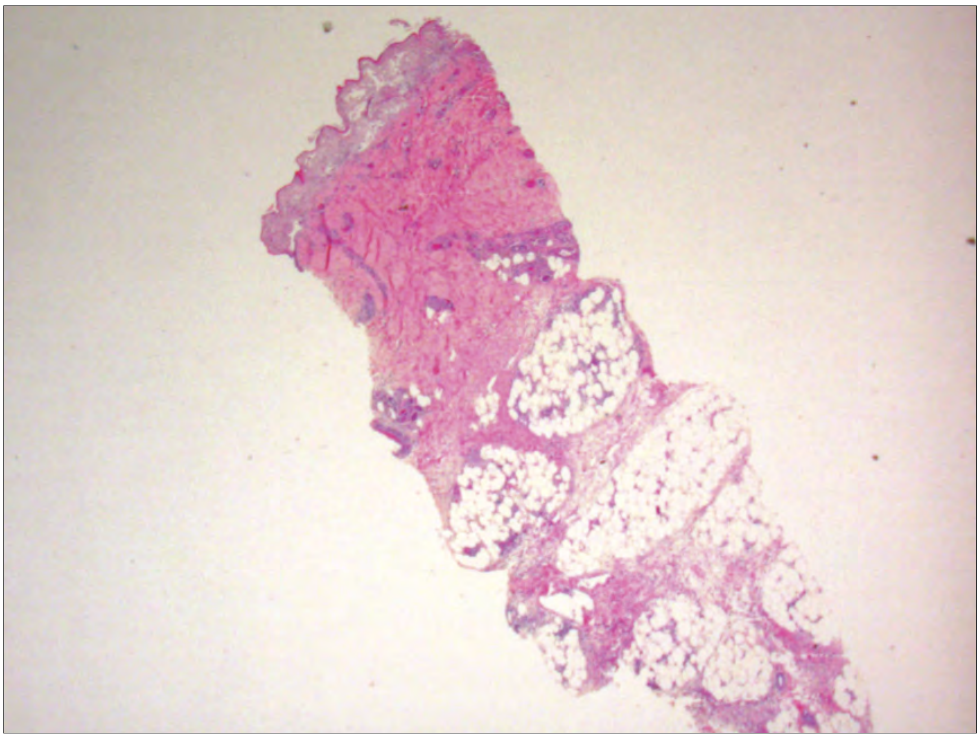

Figure 1a
Epidermal necrosis and subcutaneous infiltrates 10x H&E.

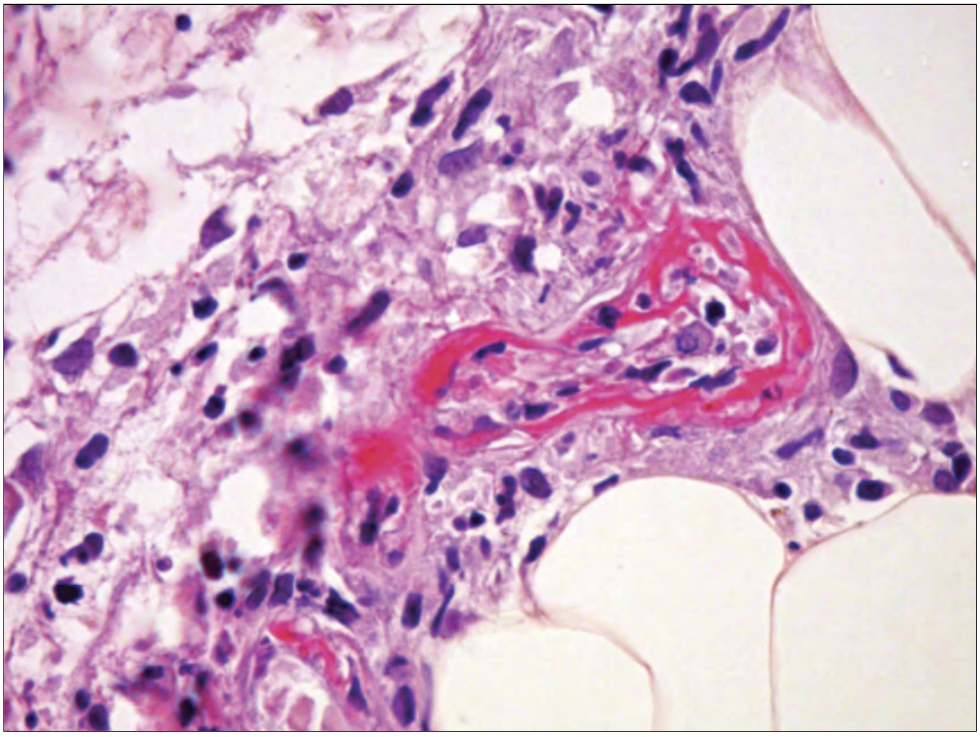

Figure 1b
Fibrinoid necrosis in the vascular wall 400x H&E.

He was readmitted to hospital one month after discharge because of emergence of new ulcers which were infected (Figure 2a & b). As the pus from the ulcers grew Pseudomonas aeruginosa, he was given a 10-day course of intravenous ceftazidine. Ulcers were dressed daily with alginate dressing preceded by acetic acid 3% soak and potassium permanganate 5% 1:10000. His pain score reached 8 (on a scale of 0 to 10) especially during dressing, despite being given oral dihydrocodeine 60mg BD and morphine 15mg subcutaneously prior to dressing. He was also started on gabapentin, which was gradually titrated up to 300 mg TDS as he had features of neuropathic pain (burning pain, allodynia and dysaesthesias on both feet). The pain during dressing was so severe that it was not possible to do effective dressing and the ulcers did not show any sign of healing despite two-week inpatient treatment.

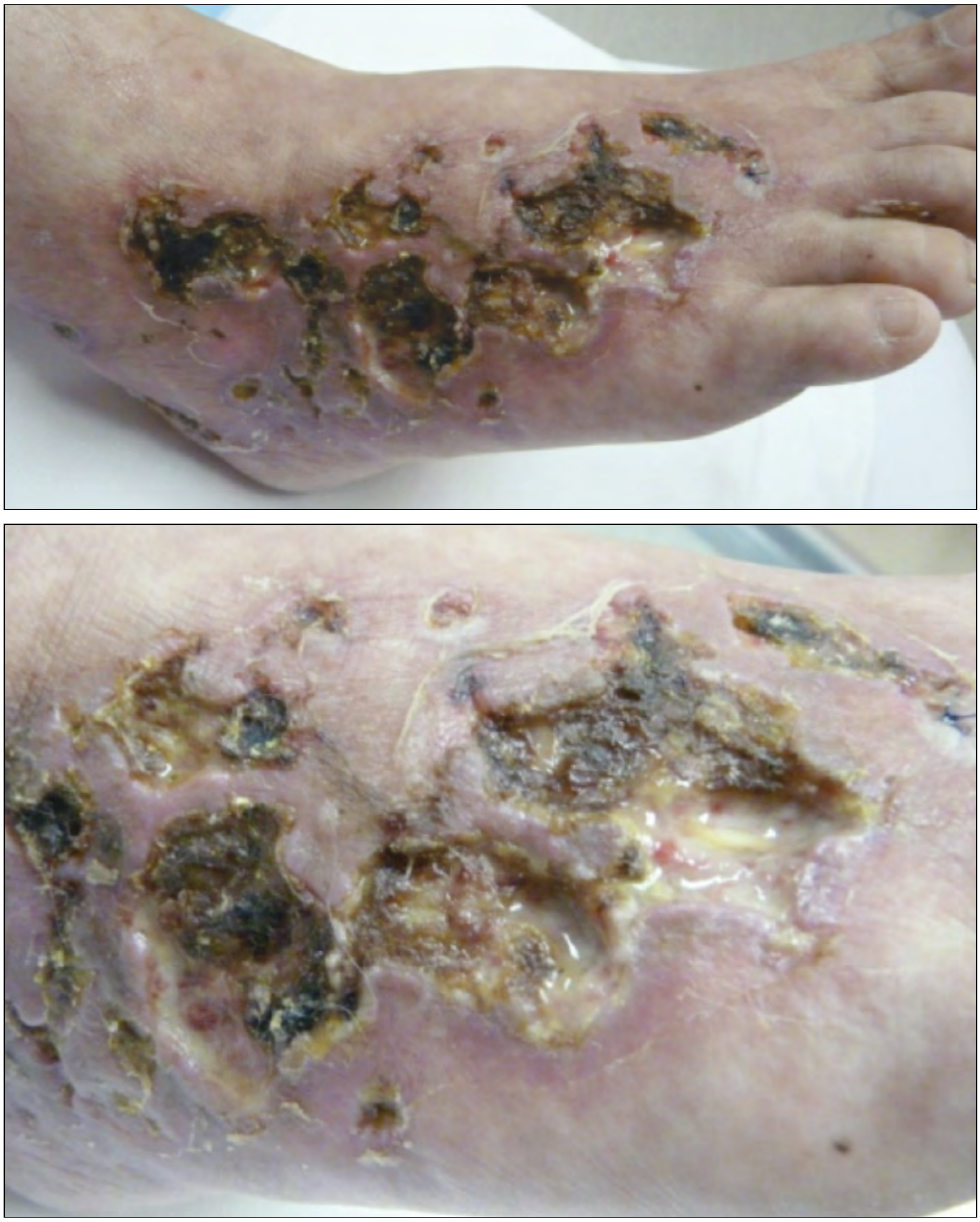

Figure 2a & 2b
Infected ulcers following treatment with oral prednisolone 60mg daily and azathioprine 150mg daily for 6 weeks.

The Pain Management Team, who had been consulted earlier on the management of his pain, decided to start epidural analgesia using a mixture of 0.1% ropivacaine and fentanyl 1mcg/ml at 5mls/hour using an ambulatory pump. This was subsequently changed to patient controlled epidural analgesia (PCEA) using a mixture of 0.2% ropivacaine and fentanyl 2 mcg/ml, running as a background infusion of 3 ml/hour with a 5 ml bolus on demand, which was mainly used just before and during dressing. Only after starting the epidural analgesia was analgesia adequate to allow aggressive dressing of the ulcers, which then began to heal.

Azathioprine was stopped as there was no improvement after two-months therapy, and also because of the active bacterial infection. As he was not suitable for other immunosuppressive agents due to ongoing infection, oral clofazimine 100mg once daily was started as a steroid-sparing agent.

With the combination of clofazimine and aggressive dressing of the ulcers the patient improved rapidly. The ulcers appeared to be clean with healthy granulation tissue within two weeks of new treatment (Figure 3). Epidural analgesia was ceased after 16 days and analgesia was provided by aqueous morphine 20 mg before dressing.

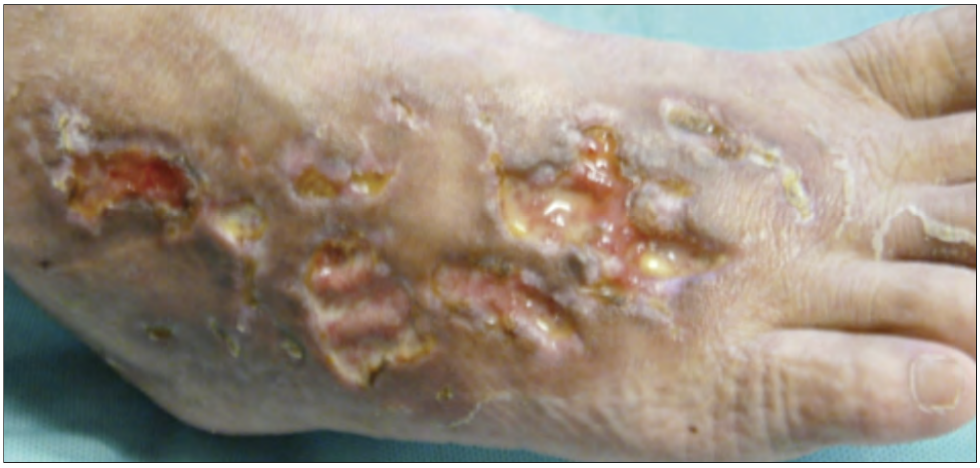

Figure 3
Day 13 of clofazimine and epidural analgesia.

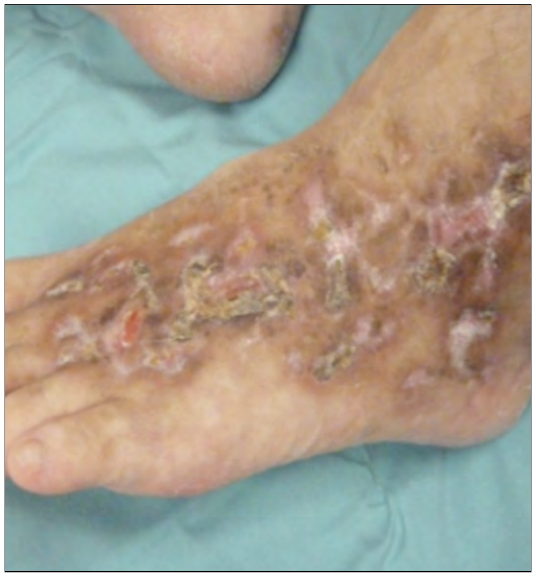

Figure 4
After 6 weeks of clofazimine and prednisolone 25mg daily.

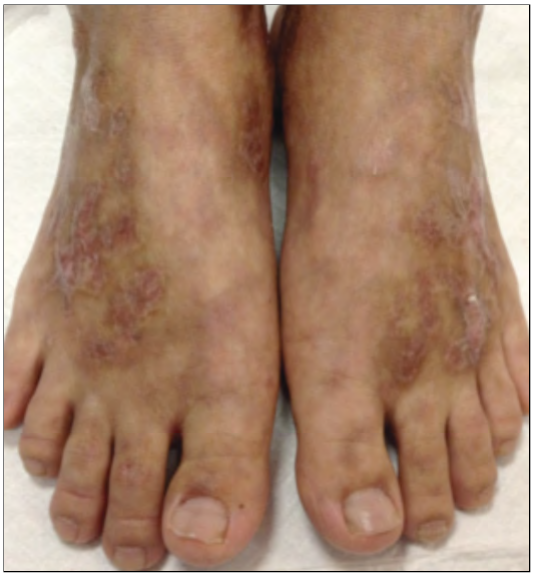

Figure 5
After 2 months of clofazimine and while on prednisolone 5mg daily.

The patient was discharged from the ward one month later with clofazimine 100mg once daily, dihydrocodeine 60mg twice daily, gabapentin 600mg three times a day, aqueous morphine 20mg as needed and prednisolone 1mg/kg/day. His prednisolone was tapered off by 5mg every two weeks. The ulcers continued to reduce in size and were fully healed 6 weeks after discharge (Figure 4).

Cutaneous polyarteritis nodosa (PAN) is an uncommon form of cutaneous vasculitis. It runs a chronic relapsing and remitting benign course. Most common presentations are tender subcutaneous nodules, livedo reticularis, necrosis and ulceration. Most of this features occurs on the lower limbs[1,2]. In a retrospective study of 79 cases, 80% had painful nodules, 56% had livedo reticularis and 49% had ulcers[1].

Extracutaneous manisfestations include myalgia (31.2%), arthralgia (69%), neuropathy (22%) and fever (25%)[1]. Our patient presented with livedo reticularis, painful ulceration and necrosis at the ankle and dorsum of both feet as well as neuropathic pain; however he denied myalgia or arthralgia. Common laboratory abnormalities include mild anemia, moderate leucocytosis and elevated ESR[2]. Our patient had mild leucocytosis (WBC 13 x103 u/L), but hemoglobin and ESR were normal.

Diagnosis of cPAN requires clinicopathological correction. Clinical presentations such as livedo reticularis, tender subcutaneous nodules and or cutaneous ulceration and necrosis should prompt suspicion. Skin biopsy shows vasculitis involving small and or medium sized arteries. The diagnosis of cPAN can only be made after the exclusion of systemic PAN. In a series of skin biopsies done on 9 cases of cutaneous PAN, direct immnunofluorescence showed C3 and IgM in 77.8% and 33.3% of the cases respectively[3]. Another case series reported IgM deposition within the vessel wall in 60%, C3 deposition in 40% and both C3 and IgM deposit in 20%[4]. Our patient's histopathology stained positive for both IgM and C3.

Mild cPAN responds to topical corticosteroids, non steroidal anti-inflammatory drugs and colchicine[2]. Severe cases require systemic corticosteroids and steroid sparing agents. Drugs reported in the literature that have been used as steroid sparing agents are colchicine, hydroxychloroquine, dapsone, methrotrexate, sulphapyridine, pentoxyphyline and intravenous immunoglobulin[2]. However there are no prospective randomized controlled trials evaluating the efficacy of these agents.

Our patient's ulcers were refractory to 3 months of prednisolone 1mg/kg/day and 2 months of azathioprine 2mg/kg/day. This may have been contributed to by the ongoing infection. Clofazimine as a steroid sparing agent was started as he was deemed not suitable for other immunosuppressant because of the ongoing infection.

Clofazimine is a lipophilic rimino-phenazine dye with antimicrobial, anti-inflammatory and immunosuppressive activity. In 1974, a randomized, double blind controlled trial[5] comparing clofazimine (100mg per day) with chloroquine (250mg per day) in 33 patients with systemic lupus erythromatosus with active skin disease showed a good response observed between the clofazimine group (82.4%) compared with the chloroquine group (75%). More studies need to be done to evaluate the efficacy of clofazimine as a possible steroid sparing agent in cutaneous vasculitic ulcer.

Incident pain during wound dressing is challenging to manage especially when it is severe. Good pain control allows proper wound dressing and promotes wound healing. A careful history will reveal the characteristic of pain whether it is nociceptive or neuropathic. Successful pain control relies on the identifying the underlying pain mechanism and continuous pain assessment[7]. However, pain management in chronic leg ulcers maybe suboptimal. In a cross-sectional study of 520 patients with chronic leg ulcers[8], although 26.5% of the subjects reported pain on change of dressing, only 8.6% were given analgesia prior to dressing. Mild to moderate pain can be easily managed by oral analgesics. Parenteral strong opioids like morphine may also be necessary to relieve the severe pain during dressing. In this patient however, the wounds were deep and dirty and some desloughing had to be done at each dressing, resulting in intolerable pain.

Epidural infusion of local anaesthetics and opioids, which is commonly used for postoperative analgesia, was started for this patient because of its ability to provide the necessary somatic block to allow dressing to take place without pain. The practical problem of requiring additional bolus doses before and during dressing was overcome by providing the patient with the possibility of self-administered bolus doses through a patient-controlled device. This provided excellent analgesia for dressing and was also useful for post-dressing pain, thus allowing patient to ambulate at ease.

In this patient, good pain control enabled the slough and pus to be cleared during wound dressing, thus allowing the wounds to heal. An additional benefit of the epidural analgesia with continuous infusion of low concentration of the local anesthetics was sympathetic block of the lower limbs, resulting in vasodilatation and improved circulation, which might also have contributed to better wound healing[9].

Conclusion

This patient who had cPAN with severely infected ulcers of both feet was successfully managed by addressing all aspects of disease management. This includes optimal pain control using epidural analgesia which enabled aggressive wound dressing and ulcer healing. We advocate using a multidisciplinary approach when managing challenging cases like this. The use of clofazimine as steroid sparing agent in cPAN needs further study.

Acknowledgement

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ADDENDUM

1. In reference to article on Pseudocyst of Ear in MJD 2012 Dec; 29
   It should read as: **Pseudocyst of Ear**
   Sumit Kar, Atul Mohankar, Ajay Krishnan, Nitin Gangane

2. In reference to back cover of MJD 2012 Dec; 29
   It should read as: 27 Case Report
   Pseudocyst of Ear
   Sumit Kar, Atul Mohankar, Ajay Krishnan, Nitin Gangane

1ST FELLOWSHIP ASIAN ACADEMY OF DERMATOLOGY AND VENEROLOGY (DERMATOPATHOLOGY) EXAMINATION

FAADV (Dermapathology) Examination

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Venue: Medical Academies of Malaysia, Kuala Lumpur
Organizer: Malaysian Dermatological Society (PDM) & Asian Academy of Dermatology and Venerology (AADV), in collaboration with St John's Institute of Dermatology (London)

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Dr Dawn Ambrose (Malaysia)
Dr Noor Zalmy Azizan (Malaysia)

Candidates:
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Dr Diah Mira (Indonesia)
Dr Norashikin Shamsudin (Malaysia)
Dr Khalid Al-Aboud (Middle East)

DAY 1
Written - 60 MCQs (60 minutes)
20 Short answer questions (90minutes)
Slide reading session - 60 slides (120minutes)

DAY 2
Viva session - 20 minutes each

Results of 1st FAADV (Dermapathology) examination:
1. Dr Norashikin Shamsudin (Distinction)
2. Dr Khalid Al-Aboud (Distinction)

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