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*No abstract required

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For example:

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For example:

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GENERAL DERMATOLOGY - Original Article

DERMATOMYOSITIS: CLINICAL PROFILE AND ASSOCIATION WITH MALIGNANCIES IN 43 PATIENTS

Yap EWY¹, Lee BS², San VE², See CKL², Wong NKL², Choon SE¹

Abstract

Introduction: Dermatomyositis is a rare idiopathic inflammatory myopathy with distinctive cutaneous manifestations. This study aims to determine the demographic characteristics, clinical features and associated malignancies in patients with dermatomyositis.

Materials & Methods: Dermatomyositis is a rare idiopathic inflammatory myopathy with distinctive cutaneous manifestations. This study aims to determine the demographic characteristics, clinical features and associated malignancies in patients with dermatomyositis.

Results: Forty-three cases were identified, with female to male ratio of 1.26:1. Mean age of onset was 47.8 +18.0 years. Malay and Chinese patients made up the bulk of the patients, contributing 53.5% and 44.2% respectively. Photosensitive rash was the commonest clinical presentation, occurring in 55.8% of the patients, followed by Gottron's papules (46.5%), heliotrope rash (44.2%), alopecia (23.3%) and calcinosis (9.3%). Median Creatinine Kinase level was 293IU/L (interquartile range 89-1166), Lactate Dehydrogenase 641IU/L (interquartile range 459-986) and Aspartate Transaminase 70.5IU/L (interquartile range 41.5-156.25). Concomitant malignancies occurred in 14 patients (32.5%), the commonest being nasopharyngeal carcinoma (6 patients), followed by gastrointestinal tumours (3 patients), breast cancer (2 patients) and lymphoproliferative disorders (2 patients) and lung cancer (1 patient). Of these 14 patients, malignancies were detected in 10 patients within the first year, and 2 patients within the second year after diagnosis of DM. Two patients had malignancies diagnosed within 6 months prior to the diagnosis of DM. Malignancy accounts for 64.7% of the 17 mortalities recorded. The proportion of Malay patients with paraneoplastic dermatomyositis with respect to the total number of Malay new clinic attendees over the past 13 years is 7 in 10,000 persons whereas in Chinese patients, the proportion is 15 in 10,000 persons.

Conclusion: Malignancy is found in about a third of all patients, with Chinese predisposition seen. This could explain why nasopharyngeal carcinoma is most prevalent in our centre.

Keywords: Dermatomyositis, paraneoplastic, malignancy

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Introduction

Dermatomyositis (DM) is an idiopathic inflammatory myopathic condition with cutaneous findings as distinguishing feature. Classical skin manifestations include Gottron’s papules, heliotrope rash, photodermatitis, periangual telangiectasias and calcinosis. Amongst these, pruritus is the commonest initial symptom. Muscle involvement is characterized by symmetrical proximal muscle weakness, with or without myalgia or tenderness. Distal muscle weakness may occur late in the course
of disease. In addition, patients may also present with systemic manifestations. It is estimated that 35-40% of patients with DM suffers from interstitial lung disease.\textsuperscript{1, 2}

The most commonly used criteria for the diagnosis of DM is the Bohan and Peters criteria, which consists of: (1) symmetrical proximal muscle weakness (2) elevated muscle enzymes such as creatinine kinase and aldolase (3) pathological features of myositis on muscle biopsy (4) evidence of myositis on electromyogram (EMG), e.g. polyphasic, short, small motor unit potentials, fibrillation, positive sharp waves, increased insertional irritability, and repetitive high-frequency discharge (5) classical cutaneous features. Presence of cutaneous features is mandatory to diagnose DM. Along with cutaneous features, presence of 3 out of criteria 1-4 fulfilled will render the diagnosis of DM ‘definite’, ‘probable’ if 2 criteria are fulfilled and ‘possible’ if only 1 criteria is fulfilled.\textsuperscript{3}

Many studies have highlighted the rarity of this disease with incidences ranging from 7.1 to 9.63 per million populations.\textsuperscript{4, 5} Despite its rarity, DM continues to be a major concern due to its association with a wide range of malignancies. The types of malignancies associated vary across different population, and include nasopharyngeal, ovarian, lung, gastric, colorectal, breast, pancreatic cancers and non-Hodgkin’s lymphoma.\textsuperscript{1, 6}

This study aims to look at the clinical profile of patients with DM in Dermatology Clinic, Hospital Sultanah Aminah, Johor Bahru, which is a tertiary referral centre for the state of Johor, Malaysia. Over the past 13 years, the Dermatology clinic has total new patient load of 57,655 patients with Malay patients making up 34,491 (59.8%), 22.7% Chinese patients 13,071 (22.7%), 14.9% Indian patients 8,568 (14.9%) and 1525 (2.6%) in patients of other ethnicities. The types of malignancies associated will be studied as well.

Materials & Methods
This is a retrospective review of all patients with DM followed up in the Department of Dermatology Hospital Sultanah Aminah, Johor Bahru from 1st February 2000 to 31st October 2013. The diagnosis of DM was made using the Bohan and Peter criteria, whereby patients have to fulfill at least 1 other criterion in addition to presence of cutaneous features. Demographic information, clinico-laboratory features, and outcome are collected and analysed. Outcome is defined as either alive or deceased. For patients who were lost to follow up, a search was done at the Registry of Life and Death to verify their life/death status and identify the causes of death for the deceased. All data collected were tabulated using Microsoft Office Excel 2007 and then analysed using SPSS statistical software. Statistical significance is determined using T-test, Pearson Chi-Square, Fischer’s Exact Test and Mann-Whitney U Test. Ethical clearance is obtained from Ethics Committee of the Ministry of Health Malaysia (NMRR-13-1451-17317).

Results
A total of 43 patients were identified. The demographic characteristics and clinico-laboratory features are summarized in Table 1. Figure 1 illustrates some of the cutaneous features commonly encountered in our centre. There is slight predisposition towards females. Mean age of onset was 47.8 ± 18.0 years. Malay and Chinese patients made up the bulk of patients, contributing 53.5% and 44.2% respectively.

Table 1 Demographic and clinic-laboratory characteristics of DM patients (n=43)

<table>
<thead>
<tr>
<th>Demographic characteristics</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age* (years)</td>
<td>47.8 ± 18.0</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>44.2</td>
</tr>
<tr>
<td>Female</td>
<td>55.8</td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>53.5</td>
</tr>
<tr>
<td>Chinese</td>
<td>44.2</td>
</tr>
<tr>
<td>Indian</td>
<td>0</td>
</tr>
<tr>
<td>Others</td>
<td>2.3</td>
</tr>
<tr>
<td>Clinical features (%)</td>
<td></td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>55.8</td>
</tr>
<tr>
<td>Gottron papule</td>
<td>46.3</td>
</tr>
<tr>
<td>Heliotrope rash</td>
<td>44.2</td>
</tr>
<tr>
<td>Alopecia</td>
<td>23.3</td>
</tr>
<tr>
<td>Calcinosis</td>
<td>9.3</td>
</tr>
<tr>
<td>Muscle enzymes</td>
<td></td>
</tr>
<tr>
<td>Creatinine Kinase (CK)</td>
<td>293 (89-1166)</td>
</tr>
<tr>
<td>Aspartate Transaminase (AST)</td>
<td>641 (459-986)</td>
</tr>
<tr>
<td>Lactate Dehydrogenase (LDH)</td>
<td>70.5 (41.5-156.25)</td>
</tr>
</tbody>
</table>
Concomitant malignancies occurred in 14 patients (32.5%). Figure 2 illustrates the types of malignancies encountered.

There were 17 mortalities recorded, and malignancy accounts for 64.7% of total mortalities (11 patients). Other causes of death include sepsis (3 patients), acute pulmonary edema (1 patient), dissecting aortic aneurysm (1 patient) and interstitial lung disease (1 patient).

Out of the 14 patients with paraneoplastic DM, malignancies were detected in 10 patients within the first year, and 2 patients within the second year after diagnosis of DM. Two patients had malignancies diagnosed within 6 months prior to the diagnosis of DM. These findings are summarized in Table 2. The proportion of Malay patients developing paraneoplastic dermatomyositis with regards to the total Malay new clinic attendees is 7 in 10,000 persons. This finding is similar in patients of other ethnicities, whereas Chinese patients report a higher proportion of 15 in 10,000 persons.

Table 3 illustrates possible indicators of occurrence of malignancies. A statistical significant association was found between raised C-reactive protein (CRP) and malignancy (p <0.05).
Table 2  Characteristics of patients with paraneoplastic dermatomyositis

<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Sex†</th>
<th>Race§</th>
<th>Malignancy*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.</td>
<td>26</td>
<td>F</td>
<td>Viet</td>
<td>Breast Ca</td>
<td>Died</td>
</tr>
<tr>
<td>2.</td>
<td>49</td>
<td>M</td>
<td>Mly</td>
<td>Lung Ca</td>
<td>Died</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
<td>47</td>
<td>M</td>
<td>Chi</td>
<td>NPC</td>
<td>Died</td>
</tr>
<tr>
<td>4.</td>
<td>47</td>
<td>F</td>
<td>Mly</td>
<td>Gastric Ca</td>
<td>Died</td>
</tr>
<tr>
<td>5.</td>
<td>53</td>
<td>F</td>
<td>Mly</td>
<td>Thymoma</td>
<td>Died</td>
</tr>
<tr>
<td>6.</td>
<td>57</td>
<td>F</td>
<td>Chi</td>
<td>Breast Ca</td>
<td>Alive</td>
</tr>
<tr>
<td>7.</td>
<td>57</td>
<td>F</td>
<td>Mly</td>
<td>Gall bladder Ca</td>
<td>Died</td>
</tr>
<tr>
<td>8.</td>
<td>59</td>
<td>M</td>
<td>Mly</td>
<td>NPC</td>
<td>Died</td>
</tr>
<tr>
<td>9.</td>
<td>66</td>
<td>M</td>
<td>Mly</td>
<td>NPC</td>
<td>Died</td>
</tr>
<tr>
<td>10.</td>
<td>67</td>
<td>M</td>
<td>Chi</td>
<td>NPC</td>
<td>Died</td>
</tr>
<tr>
<td>11.</td>
<td>70</td>
<td>M</td>
<td>Chi</td>
<td>NPC</td>
<td>Died</td>
</tr>
<tr>
<td>12.</td>
<td>74</td>
<td>M</td>
<td>Mly</td>
<td>Gastric lymphoma</td>
<td></td>
</tr>
</tbody>
</table>

Malignancy detected within 2 years after diagnosis

<table>
<thead>
<tr>
<th>No</th>
<th>Age</th>
<th>Sex†</th>
<th>Race§</th>
<th>Malignancy*</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>13.</td>
<td>41</td>
<td>M</td>
<td>Mly</td>
<td>Pancreatic Ca</td>
<td>Alive</td>
</tr>
<tr>
<td>14.</td>
<td>57</td>
<td>M</td>
<td>Chi</td>
<td>NPC</td>
<td>Died</td>
</tr>
</tbody>
</table>

† F = Female, M = Male
§ Chi = Chinese, Mly = Malay, Viet = Vietnamese
* Ca = Cancer, NPC = Nasopharyngeal carcinoma

Table 3  Possible indicators for development of malignancy

<table>
<thead>
<tr>
<th>Possible indicators</th>
<th>With malignancy (n=14)</th>
<th>Without malignancy (n=29)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender * (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>64.3</td>
<td>34.5</td>
<td>0.102</td>
</tr>
<tr>
<td>Female</td>
<td>35.7</td>
<td>65.5</td>
<td></td>
</tr>
<tr>
<td>Ethnicity b (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>57.1</td>
<td>51.7</td>
<td>0.369</td>
</tr>
<tr>
<td>Chinese</td>
<td>35.7</td>
<td>48.3</td>
<td></td>
</tr>
<tr>
<td>Others</td>
<td>7.2</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Clinical Features (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heliotrope rash</td>
<td>28.6</td>
<td>51.8</td>
<td>0.199</td>
</tr>
<tr>
<td>Photosensitivity</td>
<td>78.6</td>
<td>44.8</td>
<td>0.052</td>
</tr>
<tr>
<td>Gottron papulea</td>
<td>42.9</td>
<td>48.3</td>
<td>0.758</td>
</tr>
<tr>
<td>Alopecia</td>
<td>7.1</td>
<td>31.0</td>
<td>0.128</td>
</tr>
<tr>
<td>Calcinosiss</td>
<td>0.0</td>
<td>13.8</td>
<td>0.286</td>
</tr>
<tr>
<td>Age of diagnosis (years)</td>
<td>51.1 ± 7.3</td>
<td>46.4 ± 7.7</td>
<td>0.432</td>
</tr>
<tr>
<td>ESR † (mm/hr)</td>
<td>72.1 ± 39.5</td>
<td>70.2 ± 29.4</td>
<td>0.929</td>
</tr>
<tr>
<td>CRP ‡ (mg/L)</td>
<td>122.90</td>
<td>6.44</td>
<td>0.016</td>
</tr>
<tr>
<td>Muscle enzymes (U/L)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>76.0</td>
<td>61.0</td>
<td>0.303</td>
</tr>
<tr>
<td>LDH</td>
<td>565.0</td>
<td>677.0</td>
<td>0.377</td>
</tr>
<tr>
<td>CK</td>
<td>335.0</td>
<td>143.0</td>
<td>0.573</td>
</tr>
</tbody>
</table>

* Variables were analysed using Pearson Chi-Square test, with values reported in percentages.
† Variables were analysed using Fisher’s Exact test, with values reported in percentages.
‡ Variables were analysed using Mann-Whitney test, with values reported in median.
Discussion

Dermatomyositis (DM) is an autoimmune condition, likely due to a combination of environmental and genetic susceptibility. It appears to be more prevalent in Asians as compared to the Western community, signifying the role of ultraviolet radiation in their pathogenesis, as previously described by Okada et al.7 Recent advances also revealed the role of HLA gene polymorphisms in the pathogenesis of DM. This may be partly attributed to the influence of HLA molecules on T-cell receptor development, peripheral tolerance, and immune response to environmental agents. To support this, a recent study by Gao et al concluded that presence of HLA-DRB1*07, DQA1*01, DQB1*02, DRB1*07 and DQA1*0104 alleles increase risk of DM amongst Han Chinese population.8

Since the first case of paraneoplastic DM reported by Stertz in 1916, there has been a lot of attention drawn to the relationship between DM and cancer. Although the association of malignancies in patients with DM is well established, the exact mechanism remains elusive. Some parties believe environmental carcinogens and bioactive mediators produced in paraneoplastic conditions are responsible for the immune reactions against the muscle fibers and skin. Others believe that the immunocompromised state triggers development of both malignancies and myositis.9-11

Cancer diagnosis can precede, parallel, or follow DM diagnosis. The risk of malignancy in patients with DM declines steadily with increasing years since initial diagnosis of DM. The cancer risk is six fold during the first year, 2.5 fold during the second year, with no significant increase in subsequent years of follow-up.12 The grave outcome in paraneoplastic DM patients emphasises the importance of predicting those at risk of developing cancer. Over the years, many attempts have been made to identify these predictors. A meta-analysis by Wang et al reported age, male sex, cutaneous necrosis and dysphagia as indicators of malignancy. The same study also found arthritis and interstitial lung disease to be protective.13 In a separate study by Trallero-Araguas involving 312 patients, the presence of anti-p155 autoantibody is linked with malignancies. Anti-p155/140 has a high negative predictive value (89-100%) and therefore, a negative result reasonably exclude the presence of occult malignancy (14). Other features identified by smaller studies in the past as predictors of malignancies include necrotic skin ulcerations, pruritus, elevated ESR and periungual erythema.15,16

Our centre reports raised C-reactive protein (CRP) as a marker of cancer. C-reactive protein (CRP) is a sensitive inflammatory biochemical marker, frequently elevated in infections, inflammatory diseases, traumas, myocardial infarctions, surgeries, and cancers.17 Malignancies that have been implicated with raised CRP include lung, colorectal, and pharyngolaryngeal carcinoma.18,19 The biological reason between malignancies and elevated CRP is unclear. Two theories have been postulated. The first suggests that the growth of a tumour and its surrounding tissue inflammation is responsible. Tumour cells produce various cytokines and chemokines that attract leukocytes and secrete interleukin-6 and interleukin-8, which stimulate CRP production in the liver. The second hypothesis on the contrary, postulates that chronic inflammation, of which CRP is a marker, plays a pivotal role in carcinogenesis by inducing DNA damage and promoting angiogenesis, propagating neoplastic spread and further metastasis.

The range of malignancies seen in paraneoplastic DM is vast, and encompasses from nasopharyngeal carcinoma, to gastrointestinal, gynaecological and breast malignancies. Amongst Chinese patients, nasopharyngeal carcinoma is the leading associated malignancy, with consistent reports seen in south China, Hong Kong, Taiwan and Singapore.20-26 Gastric cancer, on the other hand is most prevalent amongst Japanese patients.27 In Europe, Hill et al reported ovarian, lung, pancreatic, gastric, colorectal cancers and non-Hodgkin’s lymphoma in Scandinavian patients with paraneoplastic DM. A previous study from Hospital Kuala Lumpur, Malaysia reported nasopharyngeal carcinoma as the commonest malignancy, which is consistent with our results.28 These findings suggest that the type of malignancy associated parallels the expected probability of that cancer within each ethnic or regional population. This should be taken into consideration while screening for malignancy in DM patients.

Several weaknesses were identified in this study. Firstly, as this is a retrospective review, data deficit was encountered. The study sample size is small, and possibly underestimated as general physicians and rheumatologists also manage DM patients in our region. In addition, a large number of patients were not screened for interstitial lung disease, either via a lung function test or high resolution computed tomography (HRCT) of thorax due to resource limitations. Despite these shortcomings, our results are in agreement with many of the earlier studies.
Malignancy is seen in 32.6% of our patients. Although lower than the reported 47.4% from Hospital Kuala Lumpur, Malaysia, this is in keeping with the rates reported overseas, which range from 13–42%. Nasopharyngeal carcinoma is the commonest malignancy seen, possibly due to Chinese predisposition seen amongst our clinic new attendees.

In conclusion, the high mortality rates amongst paraneoplastic DM patients warrant thorough search for malignancy. Basic workup should include complete history taking and physical examination together with inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). In patients with high risk features, more aggressive screening strategies, such as positron emission tomography (PET)/CT scan should be considered. PET/CT scan had been proven to be comparable in sensitivity and specificity to thoracic / abdominal CT, mammography, gynecologic examination, ultrasonography, and tumor marker analysis. In addition, due to the high incidence of nasopharyngeal carcinoma in this region, patients should also be referred to the ear, nose and throat (ENT) assessment, which include a blind biopsy of the fossa of Rosenmuller even when there’s no apparent abnormality seen.

References


LEARNING POINTS FROM THIS STUDY

1. Dermatomyositis has a typical dermatologic features e.g. heliotrope rash, Gottron’s sign and papules, shawl sign, poikiloderma and musculoskeletal features e.g. proximal muscle weakness. Practising clinician must have a high index of suspicion when seeing patients with these features. Early diagnosis portends better clinical outcome.

2. In this study, 32.5% of patients with dermatomyositis seen in Hospital Sultanah Aminah Johor Bahru was diagnosed to have concomitant malignancies. The age range of these patients were between 26 and 74 years with a mean of 55 years. Thus, it is imperative that all adult patients with dermatomyositis be screened for underlying malignancies.

3. The commonest malignancy detected was nasopharyngeal carcinoma. This has been shown in this study and another in Hospital Kuala Lumpur. Nasopharyngeal carcinoma is more commonly seen among the Chinese and also the Bidayuhs of Sarawak. Hence, it is important that clinician refer all adult patients with dermatomyositis for assessment of their fossa of Rosenmuller for the presence of nasopharyngeal carcinoma. A blind biopsy of the area is advised to allow early diagnosis.

4. In this study, malignancies were detected 6 months prior to and within 2 years of the diagnosis of dermatomyositis. Majority of malignancies were diagnosed with a year. Screening for underlying malignacies should be done early in the diagnosis to allow early management and stratification of the patients.

5. An interesting finding from this study is the association of paraneoplastic dermatomyositis with elevated C reactive protein (CRP). This finding might suggest the use of CRP as a risk predictor for underlying malignancy. Those with increased CRP should be more aggressively screened especially for pharyngeal, colonic and lung malignancies.

6. Medical professionals from all disciplines must be educated on this association of dermatomyositis and cancer so as to allow better multidisciplinary collaboration in the management of the patients.

Yap FBB
Editor-in-Chief, Malaysian Journal of Dermatology
A 5 YEAR RETROSPECTIVE STUDY ON THE CLINICAL PATTERNS AND TREATMENT OUTCOMES OF SEVERE CUTANEOUS ADVERSE DRUG REACTIONS (SCARS) IN HOSPITAL TENGKU AMPUAN RAHIMAH, MALAYSIA

Tee SH, Ng TG

Abstract

Introduction: Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) are severe cutaneous adverse drug reactions (SCARs) related to a variety of medications.

Objectives: We aim to document the epidemiological features, the causative drugs and clinical outcomes of patients with SCARs treated in Hospital Tengku Ampuan Rahimah (HTAR) between January 2009 and December 2013.

Materials & Methods: A retrospective review of the data of all patients with SJS, TEN and DRESS treated from January 2009 to December 2013 was retrieved and analyzed.

Results: A total of 33 SCARs patients were seen, which included SJS (25), TEN (3) and DRESS (5). The mean age was 42.8 years. The male-to-female ratio was 1.36:1. Allopurinol (33.3%) was the commonest offending drug, followed by antibiotics (30.3%), anticonvulsants (12.1%), non-steroidal anti-inflammatory drugs (12.1%) and traditional medications (6.1%). Eighty percent of SJS and all TEN and DRESS patients were given systemic corticosteroids. One patient with TEN (33.3%) was concurrently given intravenous immunoglobulin. All SJS patients survived. Two patients with TEN (66.7%) and one patient with DRESS (20%) succumbed due to sepsis.

Conclusion: The commonest drugs implicated for SCARs in our study were allopurinol and antibiotics. Inappropriate use of these drugs leads to increased risk of SCARs. Early recognition and prompt treatment of patients with SCARs may improve their outcome.

Keywords: Severe cutaneous adverse drug reactions (SCARs), Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS).

Introduction

Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and drug reaction with eosinophilia and systemic symptoms (DRESS) are severe cutaneous adverse drug reactions (SCARs) which are rare but associated with significant morbidity and mortality. TEN has an estimated incidence of 0.4 to 1.9 million people annually worldwide.\(^1\)\(^,\)\(^3\)

The overall combined incidence of SJS, SJS/TEN overlap and TEN is estimated to be 2 to 7 per million per year.\(^4\)\(^,\)\(^8\) SJS has an annual incidence of 1.2 to 6 per million people,\(^9\) approximately outnumbering TEN by three folds. A prospective seven-year study in a West Indian general population estimated an annual incidence of DRESS to be 0.9 per 100,000.\(^10\)
The overall mortality rate among patients with SJS and TEN is approximately 25 percent, ranging from approximately 10 percent for SJS to more than 30 percent for TEN.\textsuperscript{11,12} Retrospective studies have reported mortality rates for DRESS to be 5 to 10 percent.\textsuperscript{13,14}

Clinically, SJS and TEN are characterized by polymorphic lesions characterized by erythematous macules, papules, plaque, vesicles, and bullae. It usually affects the distal extremities with positive Nikolsky’s sign. Oral, genital, and conjunctival mucosae are often involved in the form of erosion or ulceration. The basic difference between SJS and TEN is the percentage of body surface area (BSA) involved: <10\% in SJS; >30\% in TEN and 10 to 30\% in SJS-TEN overlap. DRESS is a drug-induced hypersensitivity reaction that includes skin eruption, hematologic abnormalities (eosinophilia and atypical lymphocytosis), lymphadenopathy, and internal organ involvement (liver, kidney and lungs). There is no highly sensitive and specific \textit{in vivo} or \textit{in vitro} tests available for identifying offending agents in SJS and TEN.\textsuperscript{15}

Furthermore, a drug challenge in a case of SCARs is not ethically justified as these are the life-threatening reactions. So, to identify the drugs associated with risk of causing severe skin reactions, retrospective epidemiological data are required.

This study aims to determine the demography, causative drugs and clinical outcomes of patients with SCARs in Hospital Tengku Ampuan Rahimah (HTAR), Selangor, Malaysia during a five-year period between 2009 and 2013.

**Materials & Methods**

A retrospective review of all cases admitted to the ward or seen in the dermatology clinic in HTAR with a diagnosis of SJS, TEN and DRESS was done for a period of 5 years between 1st January 2009 and 31st December 2013. Data were retrieved from clinical notes in the Medical Records Department. Data studied included the age, gender, ethnic group, medical history, presenting complaints, causative drugs, duration between the initial consumption of the drug and the onset of symptoms, and score for toxic epidermal necrolysis (SCORTEN). Treatment regimes, duration of hospitalization, complications and mortality were also recorded.

The diagnosis was made by clinicians or dermatologists based on clinical features. A clinical diagnosis of SJS and TEN was made based on criteria proposed by Bastuji-Garin \textit{et al.} The diagnosis of DRESS was established according to RegiSCAR (European Registry of Severe Cutaneous Adverse Reaction) and J-SCAR (Japanese Research Committee on Severe Cutaneous Adverse Reaction) criteria. SCARs in this study included only SJS/TEN spectrum of cutaneous adverse drug reaction and DRESS.

SCORTEN is a score of 7 independent risk factors for high mortality i.e. age, heart beat, serum blood urea nitrogen, percentage of detached body surface area, serum bicarbonate and serum glucose. The mortality rate is dependent on the number of risk factors with 1 risk factor portending a risk of 3.2\% and 5 or more risk factors giving a mortality rate of >90\%.

Data collected were compiled on a Microsoft Excel\textsuperscript{\textregistered} sheet and subjected to descriptive statistical analysis.

**Results**

**Epidemiology**

There were 25 patients with SJS (75.8\%), 3 with TEN (9.1\%), 5 with DRESS (15.1\%) (Figure 1). This study showed a slight male preponderance with a male-to-female ratio of 1.36:1. Mean age was 42.8 years ranging between 7 and 81 years. The majority of the patients were in the age group of 20-59 years. The gender, ethnic and age distribution of the patients for each diagnosis are shown in Table 1.

**Drugs implicated for SCARs**

Drugs implicated in the various SCARs patterns are shown in Table 2. Allopurinol (33.3\%) was the most common implicated drug, followed by antibiotics (30.3\%) and anti-convulsants (12.1\%). Cotrimoxazole (3 patients) was the commonest causative drug among the antibiotics, followed by erythromycin and amoxicillin (2 patients each). Among the anticonvulsants, carbamazepine (2 patients) was the commonest drug followed by lamotrigine and phenytoin (1 patient each).

**Interval between the drugs taken and onset of symptoms and duration of hospital stay**

The mean incubation period i.e. the interval between commencement of the drug and onset of symptoms of SCARs were 10.7 days, 14 days and 14.7 days for SJS, TEN and DRESS respectively. The duration of hospital stay in patients with TEN was longer with a mean of 11 days compared to only 8.8 days in patients with SJS (Table 3).
Treatment
For patients with SJS, 5 (20%) of them were treated with supportive therapy only whereas 20 (80%) of them were given systemic corticosteroids (either intravenous hydrocortisone 300 - 400mg/day or oral prednisolone 0.5 – 1mg/kg/day). Intravenous hydrocortisone was changed to oral prednisolone once the patients were able to tolerate orally well. All TEN and DRESS cases were treated with corticosteroids. Out of 3 patients with TEN, one patient was also treated with intravenous immunoglobulins (IVIG).
Table 2  Drug groups and individual drugs implicated for SCARs

<table>
<thead>
<tr>
<th>Drugs</th>
<th>SJS (n=25) No (%)</th>
<th>TEN (n=3) No (%)</th>
<th>DRESS (n=5) No (%)</th>
<th>Total (n=33) No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-gout (Allopurinol)</td>
<td>8 (32.0)</td>
<td>1 (33.3)</td>
<td>2 (60.0)</td>
<td>11 (33.3)</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>8 (32.0)</td>
<td>1 (33.3)</td>
<td>1 (20.0)</td>
<td>10 (30.3)</td>
</tr>
<tr>
<td>Co-trimoxazole</td>
<td>3 (12.0)</td>
<td>0</td>
<td>0</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>2 (8.0)</td>
<td>0</td>
<td>0</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>Amoxycillin</td>
<td>2 (8.0)</td>
<td>0</td>
<td>0</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>Fansidar</td>
<td>1 (4.0)</td>
<td>0</td>
<td>0</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Ciprofloxacain</td>
<td>0</td>
<td>0</td>
<td>1 (20.0)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>0</td>
<td>1 (33.3)</td>
<td>0</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>3 (12.0)</td>
<td>0</td>
<td>1 (3.0)</td>
<td>4 (12.1)</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>2 (8.0)</td>
<td>0</td>
<td>0</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>Lamotrigine</td>
<td>1 (4.0)</td>
<td>0</td>
<td>0</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>0</td>
<td>0</td>
<td>1 (3.0)</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>3 (12.0)</td>
<td>0</td>
<td>0</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>Traditional medications</td>
<td>1 (4.0)</td>
<td>1 (33.3)</td>
<td>0</td>
<td>2 (6.1)</td>
</tr>
<tr>
<td>Others</td>
<td>2 (8.0)</td>
<td>0</td>
<td>1 (3.0)</td>
<td>3 (9.1)</td>
</tr>
</tbody>
</table>

SCORTEN, morbidity and mortality
Score for toxic epidermal necrolysis (SCORTEN) was calculated in patients with SJS or TEN to evaluate patients’ prognosis. Thirteen patients had SCORTEN of 0, 9 patients had SCORTEN of 1, 3 patients had SCORTEN of 2 and 3 respectively. Two out of three patients with SCORTEN of 3 succumbed to their illness. One of them was a 57-year-old Malay man who received cloxacillin for cellulitis. He developed TEN which was then complicated by septicaemia secondary to pneumonia. He died 13 days after onset of TEN. Another patient with SCORTEN of 3 was an Indonesian man who developed TEN due to traditional medication, which was taken to boost his energy. This patient also had concomitant leptospirosis infection. He succumbed 7 days after the onset of TEN due to septicaemia with multiorgan failure.

Table 3  Incubation period and duration of hospital stay

<table>
<thead>
<tr>
<th></th>
<th>SJS</th>
<th>TEN</th>
<th>DRESS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation period</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>10.7</td>
<td>10.3</td>
<td>14.7</td>
</tr>
<tr>
<td>Range</td>
<td>1 - 35</td>
<td>7 - 14</td>
<td>1 - 30</td>
</tr>
<tr>
<td>Duration of stay</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>8.8</td>
<td>11.0</td>
<td>9.3</td>
</tr>
<tr>
<td>Range</td>
<td>0 - 21</td>
<td>9 - 13</td>
<td>6 - 12</td>
</tr>
</tbody>
</table>
Discussion
This study showed an overall slight male preponderance with a male-to-female ratio of 1.38 to 1 and a ratio of 1.4 to 1 for SJS and TEN only. This finding is in contrast with earlier studies showing females are affected twice as often as males in SJS and TEN.16,17 A study conducted in Dr. Hasan Sadikin General Hospital Bandung also reported similar finding as our study with a slight male preponderance (male-to-female ratio of 1.11 to 1)18, while a study conducted in Changi General Hospital in Singapore showed equal numbers of males and females affected with SJS/TEN.19

In our series, we reported 25 cases of SJS (75.8%), 3 TEN (9.1%) and 5 DRESS (15.1%) over a 5-year period between 1st January 2009 and 31 December 2013. In our neighboring country, Indonesia, 39 cases of SJS, 7 cases of SJS-TEN overlap and 11 cases of TEN were reported in Dr. Hasan Sadikin General Hospital Bandung during the same period of time.18 In Singapore, there were 18 cases of SJS, 7 SJS/TEN and 3 TEN reported in Changi General Hospital over a 7-year period between January 2004 and November 2010.19 Local data reported 88 cases of SJS, 21 cases of TEN and 34 cases of DRESS in Hospital Sultan Aminah, a tertiary hospital in Johor, Malaysia over a 10-year period between January 2001 and December 2010.20

In our study, the majority of the patients were aged between 20 and 59 years. The mean age of 42.8 years is similar to other Asian studies which reported younger patients' cohort compared to studies from Europe and US.20 The most common drug implicated in our hospital was allopurinol, accounting for 32% of SJS and TEN patients; and 40% of DRESS patients. Several recent reports suggested that allopurinol is the drug most commonly responsible for SJS/TEN in European and Asian countries.21,22 A study involving 30 patients with DRESS in Taiwan also showed that allopurinol was the main culprit in DRESS.23

Similar to the findings in our study, a local study at Hospital Sultan Aminah Johor Bahru reported that allopurinol, carbamazepine and cotrimoxazole were the top three main culprit drugs for SCARs which accounts for 38 cases (26.3%), 25 cases (17.4%) and 17 cases (11.8%) respectively.20 A 4-year (January 2004 to December 2007) review of SJS and TEN in Sarawak reported that allopurinol was the commonest drug implicated which accounts for 7 cases (36.8%); followed by carbamazepine (26.3%) and phenytoin (10.5%).24 Study in Changi Hospital Singapore showed that the commonest implicated drugs for SJS and TEN were carbamazepine, followed by beta-lactam antibiotics and NSAIDS.19 In Indonesia, paracetamol (16.56%), carbamazepine (7%), amoxicillin (5.73%) were the main causative drugs in 57 cases of SJS/TEN reported in Dr Hasan Sadikin General Hospital from 2009-2013.18

The commonest implicated drug for SCARs in our study which is allopurinol is similar to studies done locally in Hospital Sultan Aminah and Sarawak General Hospital as well as studies in European and Asian countries. All the patients with SCARs due to allopurinol in our study survived. The analysis of cutaneous adverse drug reactions (cADRs) in Hospital Sultan Aminah Johor Bahru showed that the majority of allopurinol-induced cADRs (78% of 50 cases) were SCAR with 5 fatalities yielding a mortality rate of 10%.20

Risk factors for SCARs attributed to allopurinol are presence of HLA-B*5801, older age, renal impairment, concomitant use of diuretic and recent initiation of the drug.25 High allopurinol dose, previously suggested to be a risk factor, was not confirmed as such in a recent systematic review of all published cases on allopurinol hypersensitivity.25

In Malaysia, the number of allopurinol-induced adverse drug reactions reported to our National Pharmaceutical Control Bureau (NPCB), increased from 16 cases in 2001 to 80 cases in 2008. After an alert issued by our NPCB in 2008, the number of cases reported dropped to about 50 cases per year. Allopurinol was prescribed for asymptomatic hyperuricemia in 34% of treated patients.26 A 10-year observational survey in Italy on ADRs to allopurinol reported that 95% of allopurinol was prescribed for asymptomatic hyperuricemia and 12 patients were under allopurinol dosage adjustment according to creatinine clearance.27 Other published studies also revealed inappropriate indications for allopurinol in up to 86% of patients.28,29 Our study showed that allopurinol was prescribed in asymptomatic hyperuricemia in 36% of patients (4 out of 11 cases), which is consistent with our local reported data but lower that of the data reported in Italy, Australia and New Zealand. Despite the availability of allopurinol usage guidelines in the Malaysian Clinical Practice Guideline in Management of Gout published in October 2008, it is evident from our data that a significant proportion
of clinicians remain perplexed about the preferred management of asymptomatic hyperuricaemia. It is of utmost importance that clinicians should justify the use of allopurinol on the basis of a favorable benefit/risk assessment for the patients. Therefore, we recommend judicious prescription of allopurinol for only accepted indications and the dose adjusted to patient’s renal function. Our data indicate the continuing need to disseminate information regarding the appropriate use of allopurinol in treating patients to minimize the unnecessary morbidity and mortality which may occur with allopurinol-induced ADRs.

Our study reported two cases (6%) of SCARs due to traditional medicines. One patient took traditional medicines for energy boosting developed TEN and succumbed due to sepsis with multiorgan failure. Another patient was a 22-year-old Malay man who developed SJS due to traditional medicine and had complete recovery. A retrospective study done in Peking University Third Hospital, Beijing on SCARs over a 8-year period (from January 1994 to December 2002) reported that Chinese traditional medicines were the third most common offending drugs for SCARs.30 The study included cases of exfoliative dermatitis on top of SJS/TEN and DRESS.29 In Singapore, 7.1% of SJS and TEN cases treated in Changi General Hospital were due to Chinese traditional medicines19 SCARs to traditional medicines can be a reaction to naturally-occurring medicinal compounds, natural toxins, or to contaminants or adulterants in these medicines. The problem of SCARs to traditional medicines will become more significant as the use of traditional medicines becomes more widespread and of increasing healthcare and economic importance. Already, in many parts of the world, expenditure on traditional medicine is growing rapidly. Therefore, it is important that the public, traditional practitioners and qualified doctors be cognizant of potential adverse reactions of traditional medicines. Awareness will help in dispensing the appropriate advice and therapy, which will in turn prevent unnecessary complications and fatalities. This may also reduce unwanted readmissions, prolonged hospital stays or inappropriate labeling of drug allergy to other medicines.31

Currently, no treatment modality has been established as standard for patients with SJS and TEN. Out of 25 cases of SJS, 20 cases were treated with corticosteroids, whereas 5 cases were given supportive therapy only. Out of these 5 cases, one patient had retroviral disease and sepsis secondary to pneumonia while another patient had late presentation to dermatology clinic. Out of 20 patients treated with systemic corticosteroids, one patient who had underlying bronchial asthma who developed pneumonia during the hospitalization. All patients with SJS treated with corticosteroids or supportive therapy survived. The controversy over whether systemic corticosteroids should be used to curtail progression remains unresolved. A large multicenter European study, suggested that a short course of moderate to high dose of systemic corticosteroids (e.g. prednisone 1 to 2 mg/kg per day for three to five days) may not be harmful and may have a beneficial effect if given early in the course of the disease (i.e. within 24 to 48 hours of symptom onset).32,33 However, an updated mortality analysis of the RegiSCAR cohort and a systematic review of case series did not confirm a survival benefit for patients treated with systemic corticosteroids.34,35 The patient outcome in our study showed that it appears reasonable to initiate corticosteroids as early as possible before significant tissue damage occurs. Nevertheless, patients should be monitored for immunosuppression-related infections, and antimicrobial agents should be used accordingly if there is evidence of infection.

IVIG contains anti-Fas antibodies that can abrogate the Fas-mediated keratinocyte apoptosis. A systematic review and meta-analysis on the efficacy of IVIG for the treatment of TEN concluded that although high-dose IVIG exhibited a trend towards improved mortality and children treated with IVIG had a good prognosis, the evidence does not support a clinical benefit of IVIG.36 Randomized controlled trials are necessary.

In our series, one out of three cases with TEN was given IVIG. He was a 53 year-old Indonesian who developed TEN secondary to traditional medicines. He had concomitant leptospirosis which was complicated with multiorgan failure resulting in his death 7 days after the onset of TEN. He was planned for IVIG 0.4g/kg over 5days (2g/kg total dose). However, only 2 doses were given as he died before the administration of the third dose of IVIG. We could not make any conclusion about the use of IVIG in treatment of SJS and TEN as it was used only in one patient in our study. Two out of three patients with TEN succumbed due to sepsis.
For all patients with DRESS, systemic corticosteroids were given. Four patients (80%) with DRESS survived. One out of 5 patients died of multiple complications including sepsis, perforated gastric ulcer, acute renal failure, atrial fibrillation 8 days after the onset of DRESS. The early administration of systemic steroids is generally recommended for all cases of DRESS syndrome.37 Systemic steroid therapy should be given with a minimum dose of 1.0 mg/kg/day of prednisone or equivalent. Gradual taper after clinical and laboratory stabilization is recommended to avoid relapse.38 There is often significant improvement of symptoms and laboratory abnormalities within several days after initiating steroid treatment.38,39,40 A consensus group of the French Society of Dermatology has published recommendations for the management of DRESS syndrome which recommended the use of corticosteroids equivalent to 1 mg/kg per day of prednisone on top of multidisciplinary evaluation in DRESS with the presence of signs of severity (transaminases > 5 times normal, renal involvement, pneumonia, hemophagocytosis, cardiac, etc.).41

Conclusion
In conclusion, the commonest drugs implicated for SCARs in our study were allopurinol, antibiotics, NSAIDS, and anticonvulsants. Inappropriate use of these drugs leads to increased risk of SCARs. Early recognition and prompt treatment of patients with SCARs may improve their outcome.

References
26. Choon SE. Allopurinol hypersensitivity in Malaysia. Regional Conference of Dermatology 2014; 51
LEARNING POINTS FROM THIS STUDY

1. SJS is the commonest SCARs seen in Tengku Ampuan Rahimah Hospital, Klang, Selangor. All clinicians should identify SCARs early and refer them to Dermatologist urgently to prevent associated morbidity and mortality.

2. Allopurinol is the commonest offending drug causing SCARs. Most cases are due to inappropriate use of allopurinol to treat asymptomatic hyperuricaemia. Judicious use of allopurinol is of utmost importance to prevent SCARs. Education of healthcare professionals about risks of allopurinol should be done nationwide. Identification of HLA-B*5801 as shown by study by Chang et al in Hospital Kuala Lumpur will help stratify patients who require antigout medications in the near future.

3. Antinbiotics namely co-trimoxazole is also a common offending agent causing SCARs in Klang. This antibiotic should be use appropriately for specific indications e.g. treatment and prophylaxis of Pneumocystis jiroveci pneumonia.

4. Anticonvulsants namely the aromatic anticonvulsants (carbamazepine, phenytoin and phenobarbitone) were the third commonest cause of SCARs in Klang. It is essential that health care providers prescribe these medications with caution. Proper justification of their use is very important. Their use in treatment of neuralgias should be replaced with newer and safer medications. Identification of HLA-B*1502 as shown by Chang et al in Hospital Kuala Lumpur will in the near future help clinicians decide on the use of carbamazepine in their potential patients.

5. The high mortality rate of SCARs in which 66.7% of TEN patients and 20% of SJS patients in Klang succumbed due to the drug related allergy should warrant proper education of the health care professionals and general public about proper prescription of oral and systemic medications. It is imperative that all junior healthcare professional namely medical, dental, pharmacy and paramedical students be exposed to the dangers prescription medications early in their medical profession.

Yap FBB
Editor-in Chief, Malaysian Journal of Dermatology
COST OF MEDICATIONS IN THE TREATMENT OF MODERATE TO SEVERE ACNE IN SARAWAK, MALAYSIA

Yap FBB¹, Pubalan M²

Abstract

Introduction: Acne is a common problem causing impairment in quality of life requiring topical and oral treatment. The objective of this study is to determine the cost of medications for the treatment of an episode of moderate to severe acne vulgaris in patients attending the dermatology clinics in Sarawak.

Materials & Methods: This cross-sectional study was conducted between June 2008 and January 2009 in all the 3 dermatology clinics in Sarawak. Data were collected from 165 patients with moderate to severe acne and analysed using SPSS ver 15. Statistical significance was set at p < 0.05.

Results: The mean cost of medications to treat 1 episode of acne was RM 1170.48 per patient. The government and patients spent an average of RM 519.41 and RM 651.07 respectively. The cost to treat 1 episode of severe acne (mean RM 1861.75) was significantly higher than to treat moderate acne (mean RM 470.79, p < 0.001). Working patients paid more for their acne medications (mean RM 1624) compared to students (mean RM 732.21, p = 0.001). In patients with moderate acne, patients with tertiary education spent more (mean RM 657.54) on their medications compared to those with primary/secondary education (mean RM 338.50, p = 0.04) There was no association between the cost of medications and the socio-demographic variables of gender, ethnic group and economic background.

Conclusion: Cost of treating moderate to severe acne in Sarawak is high and comparable to Western societies. This data might help in formulating and optimizing resource allocations for the treatment of acne.

Keywords: Acne vulgaris, costing, medications

Introduction

Acne vulgaris is a common problem, affecting more than 80% of the population in their lifetime.¹ It causes psycho-social disabilities and significant morbidities among its sufferers, requiring optimal treatment.²⁻⁵ Multiple anti-acne medications are available for the treatment of acne. These consist of facial cleansers, topical agents and oral agents. Moreover, there are also multiple types of cosmetic agents and traditional medications for the treatment of acne.

The cost of anti-acne medications vary widely. The cost of these medications are lower in the government clinics compared to the private institutions and local pharmacies/chemists in Malaysia. The cost also varies with the practice of the treating clinicians. This costing is important for clinicians and health care administrators for the optimal resource allocation and utilization.
Data on the cost of medications for the optimal treatment of acne vulgaris is lacking. Health care providers and administrators depended heavily on regional and international studies. Nevertheless, the relevance of these data are frequently questioned because of the difference in the socio-cultural background of the population studied and the practice of the treating clinicians.

The objective of this study is to determine the cost of medications for the treatment of an episode of moderate to severe acne vulgaris in patients attending the dermatology clinics in Sarawak, Malaysia.

Materials and Methods
This cross sectional study was conducted between June 2008 and January 2009 in all the 3 dermatology clinics in Sarawak (Sarawak General Hospital, Miri Hospital and Sibu Hospital). All the patients with moderate and severe acne on initial presentation to the dermatology clinics were invited to participate in the study. All the consecutive patients who consented were included. Data on socio-demography, number and duration of each episode of acne vulgaris and the anti-acne treatment given were recorded in the case report forms. The type, cost (Table 1) and duration of each anti-acne medication given in the clinics were recorded. This constituted the government cost of the anti-acne medications. For patient cost of the anti-acne medications, the patients were required to recall the type, duration and cost of all the anti-acne medications used before attending the government dermatology clinics.

Data collected were analyzed with SPSS ver. 15 (SPSS Inc, Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD). Categorical data were expressed as frequencies and percentages. Analysis was done to determine the relationship between cost of medications and socio-demographic variables using student t test for comparison of means.

Results
A total of 165 patients consented for the study. Of these, 82 (49.7%) patients had moderate acne and 83 (51.3%) patients had severe acne on presentation to the dermatology clinics. Females constituted 61.8% (n= 102) of the patients. The mean age was 23.1 ± 6.72 years ranging between 10 and 46 years. Chinese make up 41.8% (n = 69), Malays 39.4% (n = 65) and Sarawakian natives 18.7% (n = 31).

<table>
<thead>
<tr>
<th>Anti-acne medications</th>
<th>Cost (RM)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Topical medications</strong></td>
<td></td>
</tr>
<tr>
<td>2% Sulphur in calamine</td>
<td>3.63/100mL</td>
</tr>
<tr>
<td>Benzoyl peroxide 5% gel</td>
<td>11.85/40gm</td>
</tr>
<tr>
<td>Benzoyl peroxide 10% gel</td>
<td>13.90/40gm</td>
</tr>
<tr>
<td>Tretinoin 0.05% cream</td>
<td>16.40/20gm</td>
</tr>
<tr>
<td>Tretinoin 0.01% gel</td>
<td>19.20/15gm</td>
</tr>
<tr>
<td><strong>Facial cleansers</strong></td>
<td></td>
</tr>
<tr>
<td>2% Cetrimide lotion</td>
<td>2.63/1L</td>
</tr>
<tr>
<td><strong>Oral medications</strong></td>
<td></td>
</tr>
<tr>
<td>Spironolactone 25 mg tablet</td>
<td>0.08/tablet</td>
</tr>
<tr>
<td>Doxycycline 100 mg capsule</td>
<td>0.08/capsule</td>
</tr>
<tr>
<td>Erythromycin ethyl succinate 400 mg</td>
<td>0.19/tablet</td>
</tr>
<tr>
<td>Desogestrol 150 mcg/ethinylestradiol 30 mcg tablet (Marvelon)</td>
<td>0.45/tablet</td>
</tr>
<tr>
<td>Cyproterone acetate 2 mg/ethinylestradiol 0.035 mg tablet (Diane-35)</td>
<td>1.13/tablet</td>
</tr>
<tr>
<td>Isotretinoin 10 mg capsule (Nimegen)</td>
<td>1.58/capsule</td>
</tr>
</tbody>
</table>

There were 159 (96.4%) patients who had 1 episode of acne, 5 (3.0%) patients had 2 episodes of acne and 1 (0.6%) patient had 3 episodes. Of the patients with 1 episode of acne, 109 (68.6%) patients were successfully treated with 1 complete course of oral anti-acne treatment and 50 (31.4%) patients required 2 complete courses. Of the patients who had 1 complete course of anti-acne medications, 91.7% had incomplete course of oral anti-acne antibiotics. The mean duration of treatment per episode was 8.4 months ranging from 3 to 24 months.

Oral anti-acne agents were utilized in all the 165 patients. Isotretinoin was utilized in 89 episodes of acne, antibiotics in 128 episodes, oral contraceptive agents in 10 episodes (Table 2). Of the patients who had 1 episode of acne successfully treated with 1 course of oral anti-acne medications, 72 (66.0%) patients had doxycycline, 33 (30.3%) patients had isotretinoin and 4 (3.7%) patients had oral contraceptive agents (1 had Diane-35, 2 had Marvelon and 1 had spironolactone). There were 8
patients who used traditional Chinese medications for the treatment of their condition before attending the dermatology clinics.

Topical agents and facial cleansers were used by 150 (90.9%) and 160 (94.7%) patients respectively. The most common topical agent used was benzylperoxide (67.9%), tretinoin (45.4%) and clindamycin (18.8%). Multiple types of facial cleanser of various prices were used, mostly of major cosmetic brands.

The mean cost of medications in the treatment of 1 episode of acne per patient was RM 1170.48 ± 1654.69. The government and patients spent a mean of RM 519.41 ± 650.44 and RM 651.07 ± 1377.32 per patient per episode on the anti-acne medications respectively. The mean cost of medications for the treatment of 1 episode of severe acne was RM 1861.75 ± 2023.13 per patient, significantly higher than the mean cost of RM 470.79 ± 644.02 per patient for the treatment of 1 episode of moderate acne (p < 0.001). This trend was seen in both the patients with moderate and severe acne. The breakdown of medication costs showed that for working patients, the government cost was RM 602.92 ± 715.31 per patient per episode and the patient cost was RM 1022.07 ± 1756.05 per patient per episode. For students, the costs were RM 438.89 ± 573.94 and RM 293.32 ± 738.88 respectively. The patient cost for working patients was significantly more than that of students (p = 0.001) whereas the government cost was not different between the two groups of patients (p = 0.11).

In patients with moderate acne, patients with tertiary education spent a mean of RM 657.54 ± 811.11 per patient per episode. This was significantly more than the mean of RM 338.50 ± 458.01 for those with primary or secondary education (p = 0.04). However, this trend was not noted in patients with severe acne. There was no association between the cost of medications and the socio-demographic variables of gender, ethnic group and economic background.

Discussion
There are very few studies examining the cost of medications in the treatment of acne. Such studies are difficult to conduct because of the differences in practice among dermatologists. In Sarawak, the average cost of treating one episode of acne was RM 1170.48 (USD 374.55). In comparison, the mean cost was USD 463.61 per episode in the United States and USD 99.75 per annum in South Africa.6,7 This difference might be related to the anti-acne preferences of the dermatologists, patient factors and the socio-economic factors.

It is interesting to note that the cost of treating one episode of acne in Sarawak is almost comparable to a developed nation of United States. This is despite the differences in the per capita income of both nations. This might be attributed by the study being done in the tertiary dermatological clinics in Sarawak, where the treatment of acne is optimal compared to treatment in the primary health care settings where the number of topical agents is limited and isotretinoin is not available. Another possible reason for the high cost of acne treatment in this study is the estimation of cost for patients with only moderate and severe acne. These patients required the use of oral anti-acne especially isotretinoin, thus, escalating the medication cost.

<table>
<thead>
<tr>
<th>Oral anti-acne</th>
<th>Number of courses used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isotretinoin</td>
<td>89</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>128</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>127</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>1</td>
</tr>
<tr>
<td>Ethylsucinate</td>
<td></td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>10</td>
</tr>
<tr>
<td>Diane-35</td>
<td>5</td>
</tr>
<tr>
<td>Marvelon</td>
<td>3</td>
</tr>
<tr>
<td>Spironolactone</td>
<td>2</td>
</tr>
</tbody>
</table>

Table 2 Oral anti-acne agents used

Table 3 shows the relationship between the cost of medications and the socio-demographic variables. The mean cost of medications for the treatment of acne in students was significantly less than working patients. The mean cost for working patient was RM 1624.99 ± 2026.44 per patient per episode, significantly more than the mean of RM 732.21 ± 1027.63 per patient per episode for students (p = 0.001).
It was interesting to note that only occupational status was associated with cost of medications. The cost was significantly higher in working patients compared to students. The higher cost in working patients might be due to the fact that these patients are more willing to spend for their condition as they are more cosmetically concerned. It is surprising to note that the cost was not associated with gender and socio-economic status. Male patients attending dermatology clinics are more cosmetically concerned and more aware of their condition, thus demanding optimal treatment. The treatment of acne is not dependent on the socio-economic status of the patients as all the patients are treated optimally in the dermatology clinics in Sarawak.

In conclusion, cost of medications for the treatment of one episode of moderate and severe acne vulgaris in Sarawak is high, with patient cost higher than the government cost. Working patients were more likely to spend more on their condition compared to students. This finding is likely to help the health administrators in Malaysia and other regional countries in allocating the optimal resources and utilization for the treatment of acne vulgaris.
References


LEARNING POINTS FROM THIS STUDY

1. Acne is a common problem affecting not only adolescence but also adults. It causes significant impact on the quality of life. Moderate to severe acne are commonly treated with combination of oral and topical medications. This study have shown that these medications are not cheap and comparable with Western societies.

2. The average cost of treating 1 episode of acne in the government service is RM 1170.48 per patient. The government spend an average of RM 519.41 per patient. It has to be stressed that cost of medications in the government setting is many times cheaper than in the private setting. So, this cost is only relevant in the government setting.

3. Patients with acne who are working are more conscious about their outer appearance and would spend more on anti-acne products. Facial appearance is very important for the working class especially those involved in human relations. A better facial appearance translate to better self esteem and confidence.

4. This study provide a baseline costing on treatment of acne. Hopefully, this data can be utilized by hospital administrators to optimize resource allocations for patients with acne in Malaysia.

Yap FBB
Editor-in-Chief, Malaysian Journal of Dermatology
GENERAL DERMATOLOGY - Original Article

STUDY OF AWARENESS AND MISCONCEPTIONS REGARDING ACNE AMONG NON-MEDICAL COLLEGE STUDENTS

Ti T1, Romemacedonia JC1, Oh YL1, Wong HX1, Mariette DS1, Theingi MM1

Abstract

Introduction: Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous apparatus of certain body areas like face and trunk and is characterized by the formation of comedones (blackheads and whiteheads), erythematous papules, pustules, nodules and cysts. This skin disorder is more common among the young people. Nonetheless, it occurs in everyone. The age group affected by acne is 10 to 17 years old for females and 14 to 19 years old for males.1 It is found to be more severe in males (71.1%) compared to females (64.6%) in adolescents.2 It also affects 3% of male and 12% of female adults.3

Although acne is a widely studied disease, the misconception and myths about acne are still prevalent in our population. This study aimed to evaluate the awareness and misconceptions of acne among non-medical college students.

Objectives: A cross-sectional study was conducted among the AIMST University Foundation students in March 2014.

Materials & Methods: A retrospective review of the data of all patients with SJS, TEN and DRESS treated from January 2009 to December 2013 was retrieved and analyzed.

Results: 200 students ranging from 18 to 21 years participated in the study. The female to male ratio was 2:1. 83.3% agreed that acne is curable. 48.5% understood that acne is not a serious health problem. 51.8% believed that acne is not contagious. Regarding the risk factors, 59.3% attributed acne to genetics. Many agreed that acne affects adolescents (52.8%) and teenage boys have more severe acne (57.8%). 92% believed that dirt causes blackheads. Most students claimed that poor hygiene (58.3%), stress (94.9%), sleep (96.4%), diet (92%), shaving (74.4%) and sunlight (81.9%) cause acne formation. Greasy hair products (52.5%) and cosmetic products (85.9%) can aggravate acne. As to the treatment, 52.6% suggested that acne should be treated. Popping/squeezing pimples with pus rapidly heals acne (53.6%). Those with history of acne agreed that acne could lead to scarring without picking (61.4%), and that acne scars is treatable (65.8%).

Conclusion: The misconceptions of acne are prevalent among the non-medical college students. This issue has to be addressed with the collective effort from all parties to dispel the misconceptions and myths of acne.

Keywords: acne vulgaris, misconception, myths

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3 Department of Population Medicine, Faculty of Medicine and Health Sciences, Universiti Tunku Abdul Rahman

Introduction
Acne vulgaris is a chronic inflammatory disorder of the pilosebaceous apparatus of certain body areas like face and trunk and is characterized by the formation of comedones (blackheads and whiteheads), erythematous papules, pustules, nodules and cysts. This skin disorder is more common among the young people. Nonetheless, it occurs in everyone. The age group affected by acne is 10 to 17 years old for females and 14 to 19 years old for males.1 It is found to be more severe in males (71.1%) compared to females (64.6%) in adolescents.2 It also affects 3% of male and 12% of female adults.3
Acne vulgaris is a multifactorial disease. The four main factors in the ethiopathogenesis of acne are increased sebum secretion, follicular plugging, bacterial colonization and inflammation. It is also noted that majority of the individuals who suffer from acne have a positive family history.1

There have been extensive researches on the ethiopathogenesis, treatment and psychosocial impact of acne but there is a paucity of data regarding the beliefs and misconceptions about acne among the general public.4,5 A local study done in UKM has shown that the prevalence of acne among medical students is high.6 Therefore, a survey was conducted among the Foundation students of AIMST University to help us to have a better understanding of the misconceptions of acne among the non-medical college students.

Materials and methods
This was a cross-sectional study carried out at AIMST University in March 2014. The Foundation students from April, May and July batches were enrolled in the study. All students regardless of their sex, age and students with or without acne were included in the study. The exclusion criteria included students who voluntarily excluded themselves, those who were ill on the day of the survey and refused to participate in the survey.

A set of specially designed questionnaire (as attached in the Appendix) was formulated with reference to several creditable sources and validated by a dermatologist. Three choices were given for each question, namely ‘agree’, ‘disagree’ and ‘not sure’. The questionnaire addressed three main issues on acne, namely the risk factors, causative factors and general measures to combat acne.4 A verbal consent was obtained prior to the distribution of the questionnaire. The questionnaire was distributed unannounced to the students and completed during their classes. Upon completion of the questionnaire, pamphlets were disseminated to all the participants to enhance their understanding and correct their misconceptions about acne. The identification of the students was kept confidential. The data obtained was interpreted and tabulated to evaluate the participant’s awareness of acne. The data was tabulated using Microsoft Excel while data analysis was done by using Epi Info Version.3,5,4 Data was subjected to descriptive analysis and presented as number (percentages).

Results
A total of 200 AIMST Foundation students, randomly selected from April, May and July batches were enrolled in this study. The students’ age ranges from 18 to 21 years old. The ratio of female to male students is 2:1, as shown in Figure 1. The gender of the remaining 14 students is not known.

Of the total subjects, 83.2% of the students had previous history of acne while 16.8% remained as non-sufferers. According to the 83.2% of the acne sufferers, only 24.2% of them have sought treatment for acne. 83.3% of the students were aware that acne is a curable disease. However, approximately half of the students (48.5%) agreed that acne is not a serious systemic health problem (Table 1).

The first part of the questionnaire intended to evaluate the awareness of the subjects regarding the risk factors of acne (Table 1). Most of the students (59.3%) are not aware that acne is not purely attributable to genetic factor. 52.8% of the students also thought that acne is only seen in adolescents. 57.8% of the students either believed or are not sure that acne is more severe in teenage boys than in teenage girls.

The second part of the questionnaire was about the students’ awareness and misconceptions on the causes of acne (Figure 2). 92% of the students believed that blackheads are due to the accumulation of dirt. 58.3% of the students thought that acne is purely due to poor hygiene. 94.9%, 96.4%, 92% and 74.4% of the students either believed or are not sure that acne is contributed by stress, sleep, diet and shaving respectively. Only 18.1% of the students were aware that sunlight does not worsen acne. Most students agreed that greasy hair products (52.5%) and cosmetic products (85.9%) can aggravate acne. About half of the students (51.8%) gave a negative response for the statement ‘acne is contagious’.

Fifty three point six percent of the students believed that popping/squeezing pimples with pus allows acne to heal rapidly4. 52.6% agreed that acne should be treated whereas 13.4% believed acne should run its course and that no treatment is required. 11.9% did not know that treatment options are available for acne scars. 61.4% of the students who have had acne before agreed that acne could lead to scarring without picking. 65.8% of the acne sufferers gave a positive response that acne scars are treatable.
Table 1  Impression on acne and risk factors for acne

<table>
<thead>
<tr>
<th></th>
<th>Agree No (%)</th>
<th>Disagree No (%)</th>
<th>Not sure No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impression on acne (N = 198)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curable disease</td>
<td>165 (83.3)</td>
<td>8 (4.0)</td>
<td>25 (12.6)</td>
</tr>
<tr>
<td>Serious systemic health problem</td>
<td>55 (27.8)</td>
<td>90 (48.5)</td>
<td>47 (23.7)</td>
</tr>
<tr>
<td>Risk factors (N = 199)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Genetic factor</td>
<td>55 (27.6)</td>
<td>81 (40.7)</td>
<td>63 (31.7)</td>
</tr>
<tr>
<td>Adolescence age group</td>
<td>67 (33.7)</td>
<td>94 (47.2)</td>
<td>38 (19.1)</td>
</tr>
<tr>
<td>Severity in boys</td>
<td>61 (30.7)</td>
<td>84 (42.2)</td>
<td>54 (27.1)</td>
</tr>
</tbody>
</table>

Figure 1  Gender distribution

Figure 2  Perception on causes of acne
Discussion

Nowadays, societal norms have placed perpetual emphasis on an individual’s outer appearance and having clear, beautiful skin is a trait that is highly esteemed in many cultures. Many have consequently sought treatment for skin conditions such as acne. Acne vulgaris is one of the commonest skin disorders with profound psychosocial impact. For many years, the understanding of society on acne has been guided mostly, if not entirely, by misconceptions/myths which have been passed down from generation to generation, circulated among peers and published in the mass media. Therefore, it is of no surprise that the misconceptions about acne remain prevalent to this day.

This research aims to study the misconceptions of acne among the Foundation students in AIMST University and at the same time, educating them about the facts of acne as well as correcting their misconceptions. The selection of sample was made to ensure adequate representation of different demographic groups in Malaysia. Foundation students are selected for this study because they are more representative of the general population as they are not yet exposed to the medical education.

Of the 200 respondents, 124 are females, 62 are males and the remaining 14 did not specify their gender. Therefore, analysis of data cannot be performed based on gender because it would be questionable.

With reference to the results obtained from this study, it is confirmed that the misconceptions about acne remains prevalent among the Foundation students. The 83.2% who reported having suffered from acne in this study supports the already known fact that acne is a common problem affecting adolescents. Some students still have the wrong belief about acne as evidenced by the fact that despite 83.3% correctly identified acne as a curable disease, less than half of the students (48.5%) believed that acne is not a systemic health problem. The misconceptions have also been passed down from generations to generations, and whatever that is held over many generations is often difficult to be dispelled.

Unfortunately, a significant number of students (92%) thought that blackheads are caused by dirt accumulation and more than half of them (58.3%) attributed acne to poor hygiene alone. The findings that majority of them did not truly understand the fact that acne is not caused by stress (94.9%), sleep deprivation (96.4%), diet (92%) and shaving (74.4%) further reflects the poor awareness of the subjects on the etiologies of acne. Furthermore, about half of the students (48.2%) are not aware that acne is not a contagious disease. This shows that the misconceptions of acne are highly prevalent among students despite the high availability of information.

Most of the students (53.6%) failed to understand that popping or squeezing pimples with pus will not hasten the recovery of this skin condition. We found that of the 83.2% acne sufferers in this study, only 24.2% of them have sought treatment for acne. Majority of the students (61.4%) who have suffered from acne agreed that acne could lead to scarring without picking. From the figures regarding the treatment of acne, we can deduce that the treatment utilization for acne is still very low and the misconceptions about acne are prevalent among the AIMST Foundation students.

The booming beauty industries like beauty parlours, together with beauty and cosmetics magazines, skincare websites have indirectly encourage a growing trend of seeking advice and treatment of acne from non-health professionals, rather than consulting a dermatologist. These non-health professionals have inadequate understanding about acne and have been offering advices that may further propagate the misconceptions about acne.

This study confirms that the prevalence of the misconceptions of acne among the AIMST Foundation students is significantly high. The students’ misconceptions towards acne could stem from their repetitive exposure to beauty magazines written by non-health experts that further strengthen the already existing misconceptions they have. In addition, the existence of the already large group that hold the misconceptions tend to enhance and promote the misconceptions through counter confirmation of the same ideas from members of the peers that hold the same misconceptions. The misconceptions have also been passed down from generations to generations, and whatever that is held over many generations is often difficult to be dispelled.
Such misconceptions about acne can lead to improper or under-treatment of acne, which could result in poor response and complications such as acne scarring that can potentially affect the quality of life of the affected adolescents. Therefore, corrective actions should be taken to address this issue. Further studies on different populations are necessary to highlight this issue so that proper measures can be taken to correct the misconceptions of acne among students.

It is a common old wives saying: ‘Acne is a sign of adolescence and will wear out with time.’ While it is true that acne usually occurs during the adolescence period, it may persist in some long after teenage days are gone, creating a considerable psychological impact on the quality of life of the adolescents. Therefore, treatment of acne should always take into consideration this important aspect of life caused by acne.

Early treatment should be instituted for acne because a proactive approach towards acne can minimize the risk of scarring. The widely held misconceptions about acne among adolescents can be corrected through promotion of public education about the facts of acne. It is time to look into these myths and scientifically remove the hurdle surrounding one of the most treatable skin disorders.

**Conclusion**

In conclusion, the result of our study revealed that acne and the misconceptions of acne among adolescents are both common. The findings from our study were consistent with other studies on similar populations elsewhere. The prevalence of misconceptions of acne among students remains high in spite of the availability of information about acne in the media. There is a need to understand the reason behind this so that appropriate and effective actions can be constructed to overcome this problem effectively.

**References**

LEARNING POINTS FROM THIS STUDY

1. Misconception of acne is common among the lay person. Many still believe the myths linked to acne.

2. Acne is not only a disease of adolescence as perceived by 52.8% of respondents. It is also commonly seen in adults especially females. Knowledge that acne still persist in adults is important as it will allay anxiety about having other facial skin diseases and allow for proper treatment seeking behaviour.

3. Only 24.2% of respondent in this study seek treatment for their acne and 52.6% think that acne should be treated. This might be due to the perceived notion that acne will heal itself with time. Those with severe acne who don’t seek treatment will eventually end up having severe facial scarring.

4. Many respondents perceived acne to be due to dirt and poor hygiene. This will lead to stigmatization of those with acne being dirty and unkempt.

5. Proper education should be given to the general public about acne and its treatment to dispel all these myths and wrong perception about this condition.

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Appendix

Misconception of Acne Questionnaires

Please fill in your details and tick on the choice you agree with.
Age:
Sex:
Did you experience acne before?
[ ] Yes [ ] No

If yes, please answer the next question.
Did you seek medical attention for the acne breakout?
[ ] Yes [ ] No

Please tick on the choice you agree with:

1. Acne is a curable disease.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

2. Acne is a serious systemic health problem.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

3. Acne is purely attributable to genetic factor.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

4. Acne is seen only in adolescence.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

5. Acne is always more severe in teenage boys than in girls.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

6. Blackheads are formed by dirt.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

7. Acne is caused by poor hygiene alone.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure
Questions related to the treatment of acne:

16. Squeezing/popping pimples with pus will help them go away faster.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

17. Topical steroid alone is a treatment option.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

18. One should allow acne to run its course without treatment.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

19. Severe acne can lead to scarring even without picking.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure

20. There’s no treatment for acne scars.
   a. [ ] Agree
   b. [ ] Disagree
   c. [ ] Not sure
MULTIPLE HYPOPIGMENTED PATCHES ON THE SKIN

A 35 year old Indian lady presented with multiple hypopigmented macules and patches on the whole body concentrated mainly on the trunk and proximal limbs. She started to notice the skin lesions since her teenage years. The skin lesions were neither itchy nor painful. She has seen many doctors over the years without much improvement.

Questions

1. What is the most likely diagnosis?
   a. Pityriasis alba
   b. Lichen planus
   c. Pityriasis versicolor
   d. Epidermodysplasia verruciformis (EV)

2. What is the investigation of choice?
   a. Tape test
   b. Skin biopsy
   c. Skin scraping for fungal culture
   d. None

3. What is the expected histological finding?
   a. Interface dermatitis
   b. Presence of spores and short ‘cigar-butt’ hyphae in stratum corneum
   c. Large keratinocytes with perinuclear haloes and blue-gray pallor
   d. Non specific finding

4. What treatment can be prescribed for this patient?
   a. Acitretin
   b. Phototherapy
   c. Oral antifungal
   d. Topical steroids

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Discussion
Epidermodysplasia verruciformis (EV) is a rare autosomal recessively inherited disease. Patients with EV are susceptible to infection by specific types of human papillomavirus (HPV).¹ The disease was first described by Lewandowsky and Lutz.²

The increased susceptibility to certain HPV infections is caused by a defective cell mediated immunity. This in turn is due to mutation in the EVER1 and EVER2 genes located in the EV1 locus on chromosome 17. Another EV susceptibility locus is the EV2 locus on chromosome 2.¹ ³ The HPVs that are specific to EV are usually referred to as “EV-HPVs”. They are HPV 3, 5, 8, 9, 10, 12, 14, 15, 17, 19 to 25, 28, 29, 36, 46, 47, 49 and 50.¹

There are 2 clinical forms of EV based on potential malignant transformation. The commoner benign form presents with pityriasis versicolor like hypopigmented flat wart-like macules and patches on the trunk and proximal limbs. It usually manifests in infancy and early childhood. On the other hand, the potentially malignant form presents with verrucous and seborrheic warts-like lesions. The lesions are commonly seen on the sun exposed areas.¹ The transformation to skin malignancy usually occurs in the forth to fifth decade. Malignant transformation is seen in 30% to 60% of patients.⁵

Invasive squamous cell carcinoma is the commonest skin cancer detected. Other malignancies include Bowen’s disease and adnexal carcinomas.

The diagnosis of EV must be suspected in patients with pityriasis versicolor-like lesions who failed to respond to treatment or patients with multiple verrucous skin lesions. The key to diagnosis is typical clinical features, histopathological examination and HPV typing (this is not widely available).¹

The histopathological examination of skin lesion in EV is mainly focused on the epidermis. Hematoxylin and eosin staining reveals moderate hyperkeratosis of the stratum corneum with presence of acanthosis and koilocytes (vacuolated keratinocytes) that have blue-gray pallor and perinuclear haloes.¹ These are the typical features of planar warts. There is no definitive treatment for EV. Preventive measure namely sun avoidance and protection is of utmost importance.

Treatment for warts are employed for each individual lesions and this include destructive treatment e.g. cryotherapy and immunomodulating treatment e.g. imiquimod. Treatment with retinoids e.g. acitretin are also useful. They are believed to down regulate HPV transcription and up regulate Langerhans cells.¹

References

Answers: 1.d, 2.b, 3.c, 4.a
GENERAL DERMATOLOGY - Short Case

PITFALLS IN DIAGNOSIS AND TREATMENT OF PEMPHIGUS FOLIACEUS IN A YOUNG BOY

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Introduction
Pemphigus foliaceus (PF) is due to loss of malphigian cell coherence through binding of IgG +/- C3 antibody directed against a polypeptide antigen complex on the keratinocyte surface. Childhood PF typically causes erythema and scalp scaling that slowly progresses to involve the trunk and limbs. It is rare in children.1

Herein we report a case of a young boy with PF complicated with allergic contact dermatitis, sepsis & erythroderma.

Case Report
A 9 year old boy presented with scaly scalp lesions associated with crusting & oozing (Figure 1). He was initially treated as impetiginized scalp psoriasis. Differentials were tinea capitis & seborrheic dermatitis. Mucosal surfaces, joints & nails were spared. No blisters were seen. Oral cephalixin, acitretin & topical steroids was initiated. His lesions progressed unto his face despite those treatments. Specimens taken were positive for Trichophyton & Pseudomonas. He was treated with oral terbinafine for 4 weeks. Acitretin was stopped due to intolerable itch.

Lesions progressed rapidly to erythroderma. Patient developed MRSA sepsis after immunosuppression with cyclosporin & prednisolone. First skin biopsy (right arm) showed spongiotic dermatitis with eosinophilia suggestive of allergic contact dermatitis. Papillary dermis had perivascular inflammation with prominent eosinophilic infiltrate. Adnexa & subcutis was unremarkable with no blister formation. PAS stain was negative. No immunofluorescence was done at that time. Repeat open

Figure 1A At initial presentation with dominant scalp involvement and few scattered lesions on the trunk.

Figure 1B Erythrodermic with generalized scales and underlying erythema.
application test (ROAT) on a unilateral arm showed patient’s skin lesions worsened on Aqueus cream & Betamethasone. The positive ROAT coupled with the skin biopsy findings strongly suggested the possibility of ongoing allergic contact dermatitis although a patch test could not be performed at that point of time.

Discussion

PF usually presents with erythematous scaly plaques and superficial erosions resembling an exfoliative dermatitis. If a child is seen in the early stage of the disease with only scalp involvement, lesions can be mistaken for the commoner causes of childhood scalp scaliness such as tinea capitis, seborrheic dermatitis or scalp psoriasis. Intact blisters may not be seen as blisters are superficial with too thin a blister roof to allow fluid accumulation.

As lesions progress to the erythrodermic stage, differential diagnoses include severe or disseminated forms of impetigo, seborrheic dermatitis, psoriasis, and staphylococcal scalded skin syndrome. In an erythrodermic child, it is important to consider the diagnosis of PF & biopsy lesions early before treatment complicates the clinical picture. Diagnosis is confirmed by histo-pathological findings, mainly the presence of a sub corneal blister with positive direct immunofluorescence for IgG and C3. PF in children is rare with only 7 cases in the pediatrics population reported over a period of 12 years (1986-1997). Given its rarity, treatment guidelines for juvenile pemphigus foliaceus are lacking.

Severe PF are usually treated with systemic steroids & immunosuppressants. Multiple studies have shown Dapsone to be effective in PF in children. The potential toxicity (methaemoglobinaemia & hemolysis, life threatening neutropenia & agranulocytosis) of this well known product at this age calls for very close hematological monitoring.

PF should be suspected in erythematous scalp lesions. Concomittant allergic contact dermatitis & superimposed fungal/bacterial infection can blur clinical picture & delay diagnosis.
References


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GENERAL DERMATOLOGY - Short Case

PERIANAL BASAL CELL CARCINOMA: REPORT OF A CASE

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Introduction
Basal cell carcinoma (BCC) is the most common human malignancy in the world. Ultraviolet light exposure is an established risk factor of BCC, which explains its predilection for sun-exposed areas. BCCs occurring in sun-protected areas are rare and other etiologies must be considered.

Case synopsis
A 68-year-old Chinese male presented with a painful perianal nodule for more than 1 year. He had a past medical history of hypertension with no prior note of basal cell carcinoma or immunosuppression. He also denied any radiotherapy, chronic irritation or trauma to the anus. Physical examination revealed an indurated area at the perineum measuring 1.8 by 0.9 cm. (Fig. 1). Incisional biopsy performed showed nodular BCC. Magnetic resonance imaging of the pelvis showed no deep extension or lymph node involvement. The patient underwent wide local excision (WLE) and reconstructive surgery. No metastasis was observed in the 2-year follow-up period.

Discussion
Basal cell carcinoma in non sun-exposed areas is rare. In the largest study of 18 943 cases of BCC, only 15 perianal BCCs (0.08%) were reported. Nodular BCC was the commonest histological subtype.¹

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Figure 1 The patient presented with an indurated area with irregular margins in the perianal region measuring 1.8 by 0.9cm. There was no inguinal lymphadenopathy.

Figure 2 Infiltrating basaloid tumour composed of nests, cords and islands with peripheral palisading. The tumour cells had oval hyper-chromatic nuclei with frequent mitotic activity. There was invasion into the reticular dermis to a depth of 3 mm. (Haemotoxylin and Eosin stain, magnification x20).

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Factors implicated in development of BCC include familial syndromes (neviod basal cell carcinoma syndrome), radiotherapy, immune deficiencies and chronic irritation. The human papilloma virus is not a proven etiological factor in the pathogenesis of BCC in non sun-exposed areas. In situ hybridization failed to detect the human papilloma virus in the specimens from patients with perianal and genital BCC.2,3

Perianal BCC accounts for only 0.2% of the anorectal tumors. Squamous cell carcinoma (SCC) is the most common tumour of the anal canal and the basaloid variant is the most common phenotype.3

BCC and basaloid SCC show overlapping histological features that pose diagnostic challenges. Both comprise nests of oval cells with moderate amount of eosinophilic to basophilic cytoplasm and peripheral nuclear palisading. The only significant distinguishing factor is retraction artifacts suggestive of BCC. Immunohistochemistry patterns can aid in diagnosis. Diffuse Ber-EP4 and BCL2 expression are features of BCC. CDKN2A and SOX2 expression characterize basaloid SCC.3

BCCs are locally invasive with little metastatic potential. Lesions <2 cm can be treated by wide local excision with 1 cm margins.4 The recurrence rates after surgery vary. Paterson et al5 followed 19 patients treated with local excision (LE) (17/19), electrocautery (1/19) and Moh's microsurgery (1/19). All patients were free of recurrence 72 months after excision. Nielson had 34 cases of perianal BCC managed with LE (27/34), abdominoperineal resection (4/34) and radiotherapy (3/34).5 There was a recurrence rate of 24 % following LE. They underwent a repeated LE with no recurrence in 5 years.

BCCs in sun-protected areas present late. Gibson et al reported perianal BCC with an average size of 1.95 cm and ulceration in 30% of cases.1 Paterson et al reported average perianal BCC size as < 2cm and ulceration in 29% of cases.2 Although no correlation between tumour size and metastatic potential exists, larger tumours require reconstructive surgery and cause greater morbidity. It is conceivable that the poor visualization of such areas by patients could contribute to its late detection. It is thus imperative for clinicians to increase surveillance in these areas.

This case illustrates that BCC can occur in sun-protected areas and suspicious lesions should be biopsied with immunohistochemistry analysis.

References