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editorial

WORLD SKIN HEALTH DAY 2013

The Malaysian Dermatological Society celebrates its World Skin Health Day by welcoming patients to join as partners with health care providers in promoting patient safety. Patients and their family members can improve patients' outcome by learning to recognise skin reactions caused by medications and alert their health care providers promptly. They can play an important role in preventing medical errors and adverse events. This article is published in Malaysian English Daily newspaper.

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editorial **WORLD SKIN HEALTH DAY 2013**

RECOGNISING SKIN ADVERSE DRUG REACTIONS

Medications have relieved many symptoms, cured some and rarely caused unwanted skin reactions and suffering. Although most of these skin side effects resolve on stopping the medications, severe forms of drug reaction can cause a temporary disfigurement and even death especially in those who present late and have other medical illnesses. Patients and their family members should learn to recognise the different forms of adverse drug reactions and seek medical assistance as soon as possible. They also have the social obligation to inform and educate their family members and friends to prevent others from suffering from adverse drug reactions.

Measles-like rash

Inform your doctor if you were started on any medication days or weeks before the occurrence of itchy red spots. It may be medication for infection, pain or traditional complementary medication and health supplements taken for general well being. The rash usually starts on the face and gradually extends to the trunk and limbs. After stopping the offending medication, the rash usually settles by turning brown with superficial peeling of the skin. This is the commonest and least dangerous form of skin adverse drug reaction.

Red eyes with either mouth or/and genital ulcers associated with painful skin rash

This is one of the severe forms of drug reaction which necessitates inpatient care and nursing in the hospital. If the patient has not taken any medication prior to the illness, this condition may be associated with a herpes viral infection.

Swollen eyelids or lips

This usually occurs within minutes or 1 to 2 days after taking medication. Itchy skin wheals may be present. Danger signs include difficulty in swallowing, breathing or fainting. Although these symptoms can rapidly improve with treatment, they may recur between 4 and 16 hours later. If you are staying very far from the health centres and have difficulty in reaching the hospital promptly, it is best to be observed in the hospital.

Other signs of drug reaction

- Measles-like rash with pustules
- Generalised red itchy swollen skin or generalised dry scaly skin
- Painful reddish-blue round patches that heals with a blue-black stain

Patient's role in his/her own safety

1. Inform the doctor if you have
   a. History of rash after taking medication
      i. itchy or painful red rash
      ii. swelling of eyelids and lips
      iii. painful red eyes with oral and/or genital ulcers
      iv. round painful reddish-blue patches that heals with a blue-black stain
   b. Your face and forearms becomes itchy and red after being exposed to the sun (photosensitivity/ photodermatitis)
   c. Developing rash after using gloves, costume jewellery, skin care products etc. (Contact dermatitis)
   d. Family members with allergy to penicillin, sulphur drugs or anti-epileptic medications (familial drug reactions)

2. If you are given a specimen bottle or a wrist tag, check whether it has your name on it.

3. Inform the nurse before any injections or transfusion if
   a. Your doctor has not indicated that you are going to receive this therapy.
   b. You are given a medication that you are allergic to (e.g. penicillin group).
   c. You suspect that the medication may cross react with the drug you are allergic to.
   d. The blood group stated on the blood pack is different from your own blood group.

4. Inform the pharmacist if
   a. You are given medication that you are allergic to.
   b. You suspect that the medication may cross react with the drug you are allergic to.
   c. You are given more than the usual dose of your regular medication but you have not been informed by the doctor.
   d. You are given medication which the doctor does not ask you to take.

5. Know your medications and their possible side effects. Return to the clinic and inform the doctor if any side effects occur.

6. If you are on moisturizing soap and ointment, be careful when you are walking on tiles especially in the bathroom. Have a stool, anti-slip mat and hand railing in the bathroom to prevent fall. Otherwise, get your family members to assist you in walking in and out of the bathroom.

7. If you are given an ointment to apply on your lesions, ask the pharmacist
   a. The correct sites to apply it.
   b. The correct way to apply it.
   c. When to stop applying it.
      i. Stop if the lesion worsens after application
      ii. Stop when lesion has resolved.
      iii. Stop after 2 weeks if lesions does not improve with topical steroid

8. If you are given a solution to apply on the skin lesions, ask
   a. The correct sites to apply it.
   b. The correct way to apply it.
   c. Does the solution need to be diluted before use?
   d. Does the solution need to be washed off after application? If yes, when to wash off.

9. If you do not understand what your health care provider tells you, bring along a family member to talk to them.

FAMILY MEMBER / CARE PROVIDER'S ROLE IN PATIENT SAFETY

1. Accompany patient if the patient has
   a. Difficulty in communicating with the health provider.
   b. Hard of hearing or visual difficulty.

2. Check with patient whether medication is taken or applied as instructed.

3. If patient has difficulty in applying topical medication, learn from the health care provider

   a. How to apply them properly especially shampoo and solution that require dilution.
   b. The correct site for each cream/ointment/ solution/solution.
   c. When to stop the treatment, prolonged usage of certain medication may cause adverse effect.

4. Ask the doctor about possible side effects that can occur and what family/care taker should do
   a. When side effects occur.
   b. To prevent the side effects. E.g.
      i. Avoid fragrant or scented skin care products if the patient has eczema or psoriasis.
      ii. Protect patient from direct sunlight if the drug can cause photosensitivity e.g. isotretinoin, neotigason and doxycycline.
      iii. Protect the patient from direct sunlight and apply sunblock if patient has skin disease that is aggravated by sunlight e.g. lupus erythematosus, photodermatitis etc.
      iv. Do not allow the patient to drive if he/ she is taking a sedating antihistamine.
      v. Have a stool and anti-slip mat in the bathroom if the patient is on moisturizing soap or ointment.
      vi. Bring the patient for investigation as instructed to check for blood / urine abnormality caused by the medication.

5. Inform doctor if patient/sibling has history of allergies to medication or contact to a particular substance/object.
   a. If patient has allergy to
      i. black dye, patient can also react to sulfur drug.
      ii. penicillin, patient may also react to cephalosporin.
      b. If patient's sibling has allergy to anti-epileptic medication, patient may also be allergic to this medication.

6. Alert the nurse if the patient's name tag / medication slip / appointment card does not belong to the patient. This is to prevent medical error.

A little effort made by patient and family as illustrated above may evade costly medication error and improve patient safety and health while on medical treatment. Let's work together for a better and safer health care.

DERMATOLOGY THERAPEUTICS - Original Article

ADHERENCE TO TOPICAL MEDICATION IS POOR AMONG PATIENTS WITH ATOPIC ECZEMA

Mazlin MB[1], Aniza I[2], Jong YF[2], Chia SL[2], Mohd Ikhwan NMS[2], Noramira A[2]

Abstract

Background: Non-adherence is a major hindrance to treatment success in any disease. In chronic diseases, adherence to long term treatment is about 50% but existing data on adherence to topical treatment in dermatological diseases are limited. In atopic eczema (AE), adherence to topical therapy is essential to control inflammation and maintain adequate moisturization but these treatment aims will not be achieved without optimal adherence.

Objectives: To assess the frequency of treatment adherence among our patients with AE and to identify the influencing factors.

Methods: We carried out a questionnaire-based study involving dermatology outpatients with AE. Demographic data were collected and patients or carers were interviewed to assess steroid phobia, knowledge, perception on treatment and use of alternative treatment.

Results: Out of 75 patients included in the study, only 14.7% were adherent to treatment. 58.7% of patients had steroid phobia but this did not significantly affect adherence. 41% of patients who use alternative treatment had poor adherence compared to patients who did not.

Conclusion: Adherence to topical treatment is poor among our AE patients and multi-pronged intervention is needed to improve adherence. For clinicians, non-adherence should be considered when managing patients who appear 'resistant' to optimized treatment.

Keywords: *dermatitis, compliance, alternative therapy*

Introduction

Adherence to treatment is defined as "the extent to which a patient's behaviour - taking medication, following a diet and/or executing lifestyle changes - corresponds with agreed recommendations from a health care provider."[1]. The term 'compliance' is no longer used due to its submissive connotation and has largely been replaced by 'adherence'; which suggests that patients are equal partners in decision-making concerning their health.

The adherence rate to long-term therapy for chronic illnesses in developed countries is on average 50%[2] and is even lower in developing countries. Poor adherence not only affect treatment efficacy, it also leads to wastage, increase in disease-related medical cost, additional consultations and delayed disease control.

Adherence to topical therapy poses additional challenge as it is affected by day-to-day issues such as the time available for application, patient's acceptability to the type of vehicle used i.e. ointment

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or creams, patient's application habits resulting in irregular dosaging, etc. Chronic dermatological disease such as atopic eczema (AE) for instance, requires prolonged and regular use of topical treatment and discipline in applying medications is essential to ensure treatment success. In AE, two main aims of topical therapy are: (i) to maintain adequate moisture using emollients[3] and (ii) to control inflammation with anti-inflammatory agents[4]. Topical corticosteroid (TC) is the main anti-inflammatory agent used and treatment is often required for months or years[5].

Prolonged use of TC and its side effects can make patients become non-adherent towards treatment. Steroid phobia is characterized by irrational fear and anxiety of patients about using TC preparations and it is a common problem among dermatology patients. In a study which included 200 AE patients, 72.5% were worried about using TC and 24% admitted to be non-adherent towards treatment because of their worries. The main concerns were the side effects of the TC such as skin thinning (34.5%), growth and development disturbance (9.5%); making them non-adherent towards treatment leading to more frequent relapses in the future[6].

Patients with AE attending outpatient government dermatology clinics are often prescribed various types of topical medications in generous amounts in order to control their disease and patients' adherence to treatment is often taken for granted. In this study, we aim to determine the frequency of treatment adherence to topical medications among AE patients with the hope of understanding the magnitude of this problem among our patients. We would also like to identify the associated factors to help us formulate some interventions which may be applied in order to improve treatment adherence among AE patients.

Methods

This cross-sectional study was conducted in the outpatient dermatology clinic Universiti Kebangsaan Malaysia Medical Centre (UKMMC). The study was conducted from April to May 2013. Patients were identified from the clinic database and universal sampling method was applied. The inclusion criteria include: patients with confirmed AE, able to communicate in Bahasa Malaysia and English and consented to the study. Patients who did not complete the questionnaire or did not consent to the study were excluded. Ethics approval was obtained from the ethics committee of Universiti Kebangsaan Medical Centre (UKMMC).

Data was collected using guided self-administered questionnaire in both English and Bahasa Malaysia. The questionnaire consist of 33 questions covering 5 domains: adherence (8 questions based on Morisky score), steroid phobia (6 questions), perception on treatment (5 questions), knowledge (9 questions) and complimentary/alternative treatment (5 questions). Socio-demographic data include gender, age, race, educational level, family income, disease duration and severity. Direct questions with yes or no responses were used to explore about steroid phobia and use of alternative treatments. Patient's knowledge on types of medications used in AE and strengths of the TC were assessed. Statements such as "I am using too many creams/ ointment on my skin", "creams/ointment make my skin sticky and shiny", "doctors give me too many types of cream" are examples of questions used to evaluate patient's perception towards treatment. Patient's perceptions towards severity of their disease were recorded as mild, moderate and severe. Data was analysed using Statistical Package for Social Science (SPSS) program version 21. Chi-square test and Mann-Whitney U test were used to analyse the data.

Results

Total of 95 patients with AE were given questionnaires but only 75 respondents were included in the study (83.3%). Forty three (57.3%) patients were male. Majority of the patients were Malays (72%) followed by Chinese (25%), Indian and other races. The mean age was 18.6 years with ages ranging from 1 to 72 years. Thirty four (45.3%) respondents studied until secondary level and the mean family income per month was RM3746 (ranging from RM950 to RM50,000). The mean disease duration was 8.23 years. Thirty eight (50.7%) patients had co-existing atopic diseases such as asthma, allergic rhinitis, keratoconjunctivitis, hypertension and diabetes mellitus. Patients' perception of disease severity was classified into mild (22.7%), moderate (48%) and severe (29.3%). Detailed sociodemographic data are shown in Table 1.

The overall adherence rate was approximately 14.7% (Table 2). Sixty four (85.3%) patients had poor adherence to treatment. Malay patients had the highest rate of poor adherence (87%) compared to patients from other ethnicity but the difference was not statistically significant. This may be explained by sampling bias as our patients were mostly Malays. Similar to earlier studies we found no significant relationship between genders with treatment adherence[6,16]. (Table 3)

Table 1 Sociodemographic data of study patients.

Variables	Frequency (n)	Percentage (%)
Gender		
Male	43	57.3
Female	31	41.3
Age (years)	18*	18**
Race		
Malay	54	72
Chinese	19	25
Indian	1	
Others	1	
Educational Level		
Primary	9	12
Secondary	34	45.3
Matriculation	1	1.3
Diploma	23	30.7
Degree	8	10.7
Family Income	2500*	2000-4000**
Disease duration	5*	2-11**
Perceived disease severity		
Mild	17	22.7
Moderate	36	48.0
Severe	22	29.3

** median ** Inter quartile range (IQR:25-75)*

Table 2 Summary of results on treatment adherence among AE patients.

Adherence	Frequency (n)	Percentage (%)
Good	11	14.7
Poor	64	85.3

In contrary to what we postulated, there was no significant association in adherence between patients who felt that they had severe disease to those who did not (p = 0.925); we interpret this lack of difference due to the habits of our patients adjusting the dosages/frequency of the topical treatment on their own based on the response to treatment, such as reducing the use of cream once the disease improves - and this data is captured as non-adherence because it was done outside of prescribed practice. Conflicting data exists regarding disease severity influencing adherence but most studies were on non-dermatological diseases[7,8]. There was no significant difference between the rate of adherence in patients with negative attitude towards therapy and those without (Table 3). Patients' perception towards treatment was not demonstrated to affect adherence significantly. (p = 0.855)

Good parental knowledge about their children's disease has been shown to be one of the determining factors for improved adherence towards the treatment in AE patients[9]. Our study did not demonstrate significant relationship between treatment adherence and knowledge (p=0.930) but several studies have shown improved adherence among AE patients after intervention[10,11]. Education alone is not enough to improve adherence; patient must also be informed, motivated and skilled in the use of cognitive approaches[12].

Forty-four patients (58.7%) had steroid phobia but we found no significant association between steroid phobia and treatment adherence ($p > 0.005$). However, percentage of poor adherence among our patients with steroid phobia (88.6%) was higher compared to those without steroid phobia (80.6%)

Table 3 Summarize data on influencing factors on adherence with *P* Value.

Variables	Adherence *n* (%)		*P* value
	Good	Poor	
Gender			
Male	6 (14.0)	37 (86.0)	1.000
Female	5 (15.6)	7 (84.4)	
Race			
Malay	7 (13.0)	47 (87.0)	
Non Malay	4 (19.0)	17 (81.0)	0.760
Perceived Eczema Severity			
Mild	3 (17.6)	14 (82.4)	
Moderate	5 (13.9)	31 (86.1)	0.925
Severe	3 (13.6)	19 (86.4)	
Steroid Phobia			
Yes	5 (11.4)	39 (88.6)	
No	6 (19.4)	25 (80.6)	0.527
Perception on Treatment			
Poor	5 (13.9)	31 (86.1)	
Good	6 (15.4)	33 (84.6)	0.855
Knowledge			
Good	6 (15.0)	34 (85.0)	
Poor	5 (14.3)	30 (85.7)	0.930
Use of Alternative Treatment			
Yes	2 (6.5)	29 (93.5)	
No	9 (20.5)	35 (79.5)	0.175
Family Income			
	3000* (3000-4000)**	2500* (2000-4000)**	0.307#
Disease duration			
	3.00* (1.00-10.00)**	5.00* (2.25-11.75)**	0.195#

** Median ** Interquartile range (IQR: 25-75) # Mann Whitney Test = Z*

but the difference was not statistically significant (p = 0.527). Reasons for their worry about using steroids include skin thinning, worsening of the disease or exacerbation of itch. Half of the patients did not know or remember why they worry about using steroids. Hon et al reported fear of side effects such as skin thinning, effect on growth and development (poor weight gain) were patients' main concerns[13]. Misconceptions and lack of knowledge may be corrected by improving patient education and counselling.

Thirty one respondents (41%) admitted to using alternative medications/supplements for their skin condition. Most received recommendations from relatives, friends and pharmacists. The mean amount of money spent on supplements was RM155 per month and some of the supplements named include Gel Gamat, vitamin and spirulina. Out of this group, 93.5% had poor adherence compared to 79.5% of patients who did not use alternative medications. (p = 0.175). Even though the difference was not statistically significant, we felt that the small sample size may have influenced this finding. In a study by Anderson et al, 42.5% of patients with AE used alternative treatment and became non-adherent to modern medicine treatment[14]. This might be due to fears of the side effects, poor knowledge and influence from family, friends, television, internet and other sources. Lack of satisfaction towards steroid treatment and improvements of a friend's condition with alternative treatment are also among the known factors which encourage the use of alternative treatment compared to modern medicine[15].

Discussion

Adherence to topical medications is poor among patients with AE in our clinic. Keeping in mind this study is based on self-reported questionnaire, the actual adherence rate may be even lower. In a study by Krencji-Manwaring et al using electronic monitors to determine adherence 'stealthily' among children with AE, mean adherence of 32% was reported[16]. The prevalence of adherence in our study is lower than other studies conducted in the west and this is a real cause for concern.

Topical treatment poses extra challenges as compared to oral treatment because it is affected by various factors. Patients' or carer's personality, occupation and hence, time available to apply medications, extent of skin involvement, patients' or carers' perception/acceptability towards the vehicle of the medications, chronicity of the illness, adequacy of prescribed medications, are just among the few factors which can influence adherence. Serrup et al found that the percentage of adherence toward dermatological treatment varies from 55% to 66% and the adherence to topical treatment is lower compared to other treatment form[16]. Popping a pill on a daily basis is often perceived as easier as and more convenient than to apply medication to a large extent of skin surface[19].

The outcome of this study has been limited by several factors. Measuring adherence to topical medications accurately in a research setting is not an easy task. In our study, interviews and questionnaires are subjected to recall and response bias which make them susceptible to over - or under-estimates of adherence but it remains the cheapest and most convenient method of assessment. Other methods commonly used in research include treatment logs, prescription renewals monitoring, weighing of medications as well as electronic monitoring devices which enable researchers to monitor both frequency and time of bottle opening. Each method has its own advantages and disadvantages.

Another important limitation is the lack of validated questionnaire to measure adherence to topical treatment. There are various validated tools measuring adherence to oral medications such as Drug Attitude Inventory (DAI)[20], Medication Adherence Questionnaire (SMAQ)[21], Medication Adherence Rating Scale (MARS)[22], etc. but none was designed to assess adherence to topical medication. We used a modified version of SMAQ to suit the objectives of our study and found certain issues unique to topical treatment which remained unaddressed. For instance, in managing AE, it is accepted practice to 'step down' or reduce the frequency of application of TC when the disease improves. Such practice can reduce the side effects without making the disease worse. Reducing the dose or frequency of treatment is considered as non-adherent behaviour in the questionnaire and therefore, gives a higher percentage of non-adherence. Asking patients the reasons they reduce/stop treatment may be able to shed more light into this matter and self-regulated 'step down' approach to treatment should not be considered as non-adherence.

A standardized, universally acceptable target for treatment adherence is also lacking. In a clinical trial which assessed adherence among psoriasis patients over 8-week period using combination of patients' log, weighing of medications and electronic monitoring devices, despite being aware that their medication use was being monitored, patients' adherence rate was merely 55%[23]. At what level is considered acceptable adherence rate to topical medication? For oral treatment, it is defined as acceptable when consumption is 80-120% of the recommended doses[24] but no similar level exists for topical medication. Achieving 100% adherence rate to topical medications is unrealistic and admittedly, near perfect adherence would be more plausible but currently there is no specified acceptable level of adherence.

Methods used to measure adherence to topical treatment are still far from perfect. Adherence is often assessed by determining the quantity and frequency of medications used, but assessing whether application was performed in the correct way at the correct time for the prescribed duration is rarely measured in clinical research. This will also affect the outcome of adherence studies.

Despite limitations of this study, there are important clinical implications. Since the adherence rate in our clinic; which is a university-based tertiary care centre with doctor to patient ratio of about 1: 12.5-15 is poor, the adherence rate of AE patients in a busier clinic with lower doctor to patient ratio may be even lower because of shorter consultation time per patient. Patients' adherence to treatment plans is essential for treatment success. Good communication is key to a good doctor-patient relationship and this will be affected by duration of consultation as well as the communication skills of the health care provider.

Communication skills of a health care provider should not be underestimated as it has been shown that patients adhere to treatment 2.16 times greater if their doctor is a good communicator[25]. Since majority of AE patients are in the paediatric age group, parental factors such as time availability, dynamics of parent-child relationship, parents' understanding about the disease and treatment must be taken into consideration. Steroid phobia should be identified early so any misconceptions can be corrected. Parents' fears can be allayed by good doctor-patient (parent) relationship and this has been shown by Ohya et al[26].

Patients and carers should be allowed to actively participate in formulating their treatment plans and a clinician-patient alliance should be formed. This will encourage trust between patients and doctor, empower the patient/carer and hence, improve adherence. Use of individualized AE written action plans or instructions tailored to patient's/carer's lifestyle, for instance, would be easier for patients to follow and this will improve adherence.

Adherence to topical treatment can also be affected by complicated treatment regimes. Simplifying the daily regimes by minimizing number and frequency of topical medications may lead to improved compliance. 'Hit hard' approach to initial treatment would lead to greater initial efficacy and patients may be encouraged to continue treatment to achieve and maintain good disease control.

'White coat compliance' is a term used to describe the behaviour pattern when patient's adherence improves around the time of office visits and it has been demonstrated in studies using electronic monitoring devices[16,23,27]. We can capitalize on this behaviour pattern by having early follow-up visit after initiating treatment - it may be an effective way to boost patient's use of medication to achieve better treatment outcome[27].

Patient education sessions by doctors and specialized nurses can be incorporated as part of management strategy at the clinic. When possible, waiting time at the clinics can be utilized for patient education to save time. Distribution of informative pamphlets with explanation by health care provider, supervised video screenings or internet are possible sources of information for AE patients and should be recommended. Memberships and regular meetings in AE clubs or associations may be used as another platform to educate patients.

Lastly, it is crucial that clinicians be made aware of how dismal the rate of treatment adherence is among AE patients. In our dermatology practice, if a patient does not improve despite adequate and appropriate treatment, we should consider the findings of this study. Instead of escalating treatment, non-adherence may be a more likely explanation.

Conclusion

Adherence towards topical treatment among our patients with AE is unsatisfactory and intervention is needed to improve this in the clinic setting. Individualized patient education, improved health care provider-patient relationship and communication are essential to ensure good adherence and hence, treatment success.

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References

1. Sabate E. Adherence to long-term therapies. Evidence foraction. Geneva: World Health Organisation, 2003.
2. Haynes RB. Interventions for helping patients follow prescriptions for medications. Cochrane Database of Systematic Reviews 2001: Issue 1.
3. Knownacki S. The Important of Emollients in Treating the Increasing Incidence of Atopic Eczema. Nurs Times 2009; 105(28):18-22.
4. Levy M.L. Atopic dermatitis: Understanding the Disease and its Management. Curr Med Res Opin. 2007; 23:3091-3103.
5. Aubert-Wastiaux H, Moret L, Le Rhun A et al. 2011. Topical corticosteroid phobia in atopic dermatitis: a study of its nature, origins and frequency. Br J Dermatol 2011; 165: 808-814.
6. Charman CR, Morris AD, Williams HC. Topical corticosteroid phobia in patients with atopic eczema. Br J Dermatol 2000; 142(5): 931-936.
7. Seo MA, Min SK. Development of a structural model explaining medication compliance of persons with schizophrenia. Yonsei Med J. 2005; 46:331-40.

8. Matthews D, Hingson R. Improving patient compliance: a guide for physicians. Med Clin North Am 1977; 61(4):879-89.
9. Beattie PE, Lewis-Jones MS. Parental knowledge of topical therapies in the treatment of childhood atopic dermatitis. Clin Exp Dermatol 2003; 28(5):549-53.
10. Cork MJ, Britton J, Young S et al. Comparison of Parent Knowledge, Therapy Utilization and Severity of Atopic Eczema Before and After Explanation and Demonstration of Topical Therapies by a A Specialist Dermatology Nurse. Br J Dermatol 2003; 149(3):582-589.
11. Agner T. Compliance among patients with Atopic Eczema. Acta Derm Venereol 2005; 215:33-35
12. Balakrishnan R. The Importance of Medication Adherence in Improving Chronic-Disease Related Outcomes: What We Know and What We Need to Further Know. Med Care 2005; 43(6):517-520.
13. Hon KLE, KamWY, Leung TF et al. Steroid fears in children with eczema. Acta Pediatr 2006; 95(11):1451-5.
14. Anderson PC, Dinulos JG. Atopic Dermatitis and Alternative Management Strategies, Curr Opin Pediatr 2009; 21 (1):131-8.
15. Zhang W, Leonard T, Bath-Hextall FJ et al. Chinese Herbal Medicine for Atopic Eczema The Cochrane Skin Group Cochrane Library 2009.
16. Krejci-Manwaring J, Tusa MG, Carroll C et al. Stealth monitoring of adherence to topical medication: Adherence is very poor in children with atopic dermatitis. J Am Acad Dermatol 2007;56: 211-216
17. Jing J, Sklar GE, Oh VMS, Li SC. Factors affecting therapeutic compliance: A review from the patient's perspective. Ther Clin Risk Manag 2008; 4(1): 269-286.
18. Serup J, Lindblad AK, Maroti MI et al. J. 2006. To follow or not to follow dermatological treatment. Acta Derm Venereol. 56(2): 211-217.
19. Krejci-Manwaring J, McCarthy MA, Camacho F et al. Adherence with topical treatment is poor compared with adherence with oral agents: implications for effective clinical use of topical agents. J Am Acad Dermatol 2006;54: S235-36.
20. Hogan TP, Awad AG, Eastwood R. A self-report scale predictive of drug compliance in schizophrenics: reliability and discriminative validity. Psychol. Med 1983; 13, 177-183.
21. Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Medical Care 1986;24:67-74.
22. Thompson K, Kulkarni J, Sergejew AA. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. Schiz Res 2000; 42(3):241-247.
23. Carroll CL, Feldman SR, Camacho FT et al. Adherence to topical therapy decreases during the course of an 8-week psoriasis clinical trial: Commonly used methods of measuring adherence to topical therapy overestimate actual use. J Am Acad Dermatol. 2004;51(2):212-216.
24. Cramer J. ISPOR Medication Compliance and Persistence Special Interest Group. www.ispor.org/ signs / medication. asp (accessed May 20, 2013).
25. Zolnierek KB, Dimatteo MR. Physician Communication and Patient Adherence to Treatment: A Meta-analysis. Medical Care 2009, 47:826-834.
26. Ohya Y, Williams H, Steptoe A et al. Psychosocial factors and adherence to treatment advice in childhood atopic dermatitis. J Invest Dermatol. 2001; 117(4):852
27. Feldman SR, Camacho FT, Krejci-Manwaring J et al. Adherence to topical therapy increases around the time of office visits. J Am Acad Dermatol 2007; 57:81-83.

GENERAL DERMATOLOGY - Original Article

LICHEN PLANUS AND HEPATITIS C INFECTION: EXPLORING THE ASSOCIATION AMONG MALAYSIAN PATIENTS

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Abstract

Background: The association between chronic hepatitis C infection with lichen planus (LP) remains controversial. Geographical and immunogenetic factors may play a role in this association.

Objectives: We sought to compare the prevalence of hepatitis C in patients with LP with healthy blood donors at our centre.

Materials & Methods: We conducted a retrospective study in Hospital Kuala Lumpur, Malaysia. All patients with biopsy- proven LP who had undergone hepatitis C serology screening from January 2007 to June 2012 were recruited. The prevalence of Hepatitis C seropositivity among healthy blood donors in Malaysia was used as comparison.

Results: Thirty five patients with LP were included in the study. Majority of the patients were Indians (71.4%) followed by Malays (14.3%), Chinese (8.6%) and other ethnicity (5.7%). 82.6% of patients had classical cutaneous LP out of which 17% had oral involvement. Anti-HCV was reactive in 2.9% patients. Among the healthy blood donors, anti-HCV was positive in 1.5% of patients. There was no significant difference between the prevalence of hepatitis C seropositivity between the two groups (p=0.431).

Conclusion: There is no significant association between chronic hepatitis C infection and LP among our patients. We recommend screening for hepatitis C in LP patients should be limited to those with risk factors.

Keywords: *lichen planus, viral hepatitis, Malaysia*

Introduction

Lichen planus (LP) is an idiopathic mucocutaneous dermatosis involving the scalp, skin mucous membranes and nails. Classically, it is characterised by markedly pruritic, polygonal, flat- topped papules with Wickham's striae and it exhibits koebnerization. The association of LP and chronic hepatitis C virus (HCV) infection was firstly described in 1989 by Mokni et al[1]. A link between these two diseases was postulated by the fact that LP was frequently associated with chronic liver disease[2].

This was later supported by studies demonstrating the presence of hepatitis C viral RNA via polymerase chain reaction from lesional biopsies of oral LP and its absence from biopsy of non-lesional area within the same individuals[3]. Despite these findings, the association seemed to vary with different geographical regions[4]. Whilst studies in Mediterranean countries had demonstrated such association, several studies from Europe had refuted this finding.

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In HCV-related LP, the condition tends to be more generalised, prolonged and has high incidence of mucosal involvement[5]; suggesting a more severe presentation compared to the non HCV-related LP.

In Malaysia, where the prevalence of hepatitis C viral (HCV) infection is estimated to be 1.5%[6,25] such association has yet to be established. In our heterogenous and multiethnic country, the HCV-LP association may vary to other countries where the population is more homogenous. We sought to determine if the HCV-LP association exist among our patients.

Methods

This retrospective observational study was conducted at the Dermatology Department Hospital Kuala Lumpur. All patients with biopsy-proven LP who had undergone hepatitis C serology screening at diagnosis from January 2007 to June 2012 were included in the study. Hepatitis C serology screening was performed using Enzyme-Linked ImmunoSorbent Assay (ELISA).

The prevalence of HCV seropositivity in the LP group was compared to the prevalence among healthy blood donors in Blood Services Centre, Kuala Lumpur. Patients' demographical and clinical data were analysed using Statistical Package for Social Sciences (SPSS) version 21. The differences in hepatitis C seropositivity between the two groups were analysed using Chi square test. P value of less than 0.05 was considered statistically significant.

Results

A total of 69 patients with LP were identified. Thirty four patients were excluded due to unavailability of hepatitis C serology results. Thirty five patients were eligible for analysis; 19 males and 16 females with mean age of 46.9 years. Majority of the patients were of Indian ethnicity (71.4%) followed by Malays (14.3%), Chinese (8.6%) and other ethnics (5.7%). This finding is in contrast to the ethnic proportions of our clinic attendees during this period, which were predominantly Malays.

Twenty nine (83%) patients had classical LP, 5 (14%) had hypertrophic LP and 1 patient had lichen planopilaris (Figure 1). Only 6 (17%) patients also had oral mucous membrane involvement. Out of 35 patients, only 1 (2.9%) patient showed hepatitis C seropositivity and the patient had hypertrophic LP without oral mucosal involvement. In the blood donor group, 53 out of 3540 (1.5%) patients were HCV positive[19]. The difference of hepatitis C seropositivity observed between the two groups was not statistically significant ($p = 0.431$).

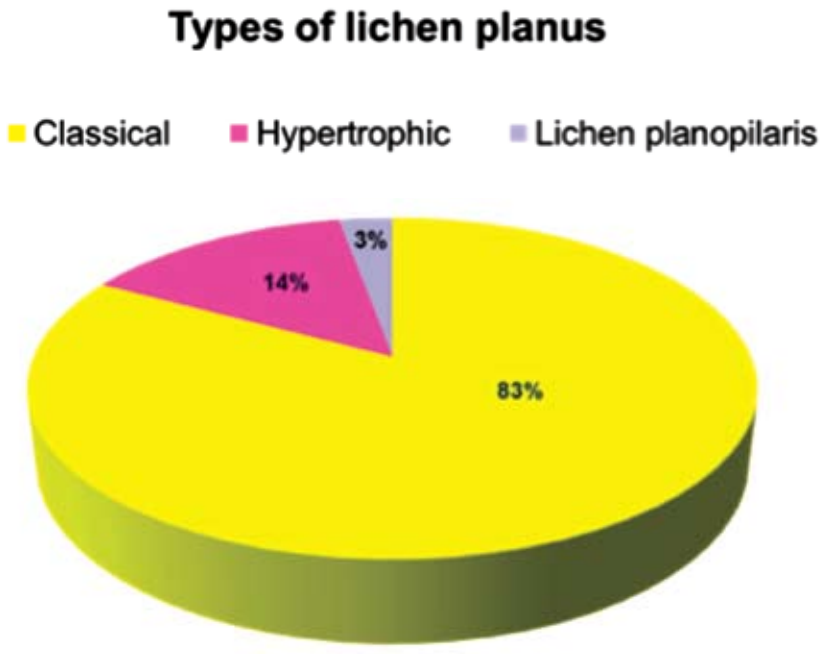

Figure 1 Distribution of clinical subtypes of lichen planus.

Table 1 Comparison to other studies.

Study	Current	Stojanovic *et al (12)*	Lodi *et al (4)*	Klantrit *et al (13)*	Gimenez-Garcia *et al (14)*	Udayashankar *et al (9)*	Ibrahim *et al (8)*
Country	Malaysia	Slovenia	Italy	Thailand	Spain	India	Egypt
Year	2012	2008	2004	2003	2003	2003	1999
No of patients	35	173	303	60	101	40	43
Local prevalence of HCV infection (%)	1.5	<1	0.5	5.6	0.7	4.8	18.1
Reactive anti-HCV (%)	2.9	1.2	19.1	8.3	8.9	0	6.9
Oral LP present	6	71	303	60	53	7	not stated
Association shown	no	no	yes	Yes	yes	no	no

Discussion

In our study, we did not find significantly higher prevalence of anti-HCV antibodies among patients with LP as compared to the historical control group. The prevalence of hepatitis C seropositivity in LP patients ranges from 3.8 % to 65 % worldwide[4]. Its prevalence is lower in our study at 2.9%. Our finding is consistent with other studies from Slovenia, India and Egypt, where no association between LP and HCV infection was found[7,8,9]. Meta-analyses have shown significant association between the two diseases mainly in the Mediterranean, Japan and USA[10] but not in South Asia, Africa and North America[11]. These meta-analyses also suggest that the variable findings may be explained by variation in HCV prevalence in different regions, differences in viral characteristics and genetic susceptibility for HCV infected individuals to develop LP[10].

In a meta-analysis by Shengyuan et al, the authors found important association between Hepatitis C and LP but there is a difference when the association between the two diseases are analysed reciprocally[11]. The odds ratio (OR) for HCV exposure among patients with LP was 5.4 (95% confidence interval [CI], 3.5-8.3) when compared to control but OR for prevalence of LP among HCV patients was 2.5 (95% CI, 2.0-3.1). There was no significant association in isolated cutaneous LP ($p = 0.17$)[11]. A summarized comparison between the findings in our study and other similar studies worldwide is shown in Table1.

High HCV endemicity does not equate to higher LP prevalence. This is suggested by studies conducted in African countries with the highest HCV prevalence in the general population which did not show significant association between the two diseases[8,15]. Hepatitis C may not be the primary aetiology of LP, but its interaction with the host immune system had resulted in LP. Hence, LP probably represents a cell-mediated response to an antigenic trigger from HCV infection[16,17]. This also suggests that other factors such as genetics or immunological factors play a more important role in the pathogenesis of HCV-related LP.

HCV-related LP has also been shown to be associated with certain LP subtypes. The association of HCV was demonstrated to be present in erosive LP and not in other form in certain studies[18]. Majority of our patients were of the classical type, which may explain the lack of HCV-LP association. At present, there is a much stronger association between oral LP compared to cutaneous LP with HCV infection[7,10,19]. Carozzo et al had demonstrated that oral LP may be influenced by genetic allele involving HLA-DR6 in Italy[20]. This could partially explain the peculiar geographic heterogeneity of the association between HCV and oral LP. In our study, only 6 patients had oral lesions. Such a small number of patients with oral involvement can be explained by the fact that most of purely oral LP cases is often managed by the maxillofacial specialist and will only be referred to dermatologist if there is associated cutaneous involvement.

LP appears to be more common among Indian patients. In our study, we found a striking predominance of Indian patients (71.4%) compared to other ethnicity. Similar finding was described by Vijayasingam et al in Singapore in which 69% of patients with LP in his study were Indians[21]. This strongly suggests some genetic predisposition to develop LP among certain ethnicity.

HCV related LP may be associated with certain HCV genotypes but data on this postulation is rather scarce. HCV possesses high genomic variability and various genotypes have been reported. Certain HCV genotype may influence its ability to induce LP in susceptible individuals. Different genotypes are more prevalent in different parts of the world. Lodi et al and Imhof et al compared the geno/subtype distribution of patients with chronic hepatitis C with and without LP in Italy and Germany respectively[23,24]. The HCV genotype isolated in their LP patients were mostly of 1b, 2a[23] and 1b[24]. However, no convincing correlation between geno/subtype and the presence of LP were found and the studies were limited by its small sample size[23,24]. In Malaysia, the commonest genotype is type 1a and 3[22], which may explain the reason for lack of association shown in our study population.

There are several limitations in this study. To avoid selection bias, only patients with histologically confirmed LP were recruited in the study. This limited the number of patients who fulfilled the study criteria because biopsy was not performed in almost half of patients diagnosed as LP. This may be because of its pathognomonic morphology at presentation, unintentional omission by the attending doctor and patient refusal. This study is also limited by its retrospective nature. Thus, each individual risk factor for acquiring HCV infection was not completely available for analysis.

Lastly, we recommend a larger, controlled, prospective study to confirm our findings and a comparison between prevalence of HCV in Malaysian patients with oral VS cutaneous LP may also be explored. A parallel HCV genotype studies will also be beneficial to investigate whether our specific local HCV genotypes is associated to LP.

Conclusion

The association between LP and HCV infection is lacking among our patients and currently, there is not enough data to support routine screening for HCV infection in every patient with LP without any risk factors.

References

1. Mokni M, Rybojad M, Puppin D Jr et al. Lichen planus and hepatitis C virus. J Am Acad Dermatol 1991;24:792.
2. Carrozzo M. Oral diseases associated with hepatitis C virus infection.Part 2: lichen planus and other diseases. Oral Dis 2008; 14: 217-228.
3. Erkek E, Bozdogan OE, Olut AI. Hepatitis C virus infection prevalence in lichen planus: examination of lesional and normal skin of hepatitis C virus-infected patients with lichen planus for the presence of hepatitis C virus RNA. Clin Exp Dermatol, 26: 540-44.
4. Lodi G , Giuliani M, Majorana A et al. Lichen planus and hepatitis C virus: a multicentre study of patients with oral lesions and a systematic review. Br J Dermatol2004; 151: 1172-1181.
5. Stephanos J. Hadziyannis. Skin diseases associated with hepatitis C virus infection. JEADV 1998; 10: 12-21.
6. Lavanchy D. Evolving epidemiology of hepatitis C virus. Clin Microbiol Infect 2011;17:107-115.
7. Stojanovi L, Lunder T, Poljak M et al.. Lack of evidence for hepatitis C virus infection in association with lichen planus. Int J Dermatol2008;47: 1250-1256.
8. Ibrahim HA, Baddour MM, Morsi MG et al. Should we routinely check for hepatitis B and C inpatients with lichen planus or cutaneous vasculitis? East Mediterr Health J 1999;5: 71-78.
9. Udayashankar C, Nath A.K, M. D'Souza.Hepatitis C Virus serology in patients with lichen planus. The Internet Journal of Dermatology. 2009; 7(2).
10. Lodi G, Pellicano R, Carrozzo M. Hepatitis C virus infection and lichen planus: a systematic review with meta-analysis. Oral Dis 2010; 16:601-612.
11. Shengyuan L, Songpo Y, Wen W et al. Hepatitis C virus and lichen planus: a reciprocal association determined by a meta-analysis. Arch Dermatol. 2009;145(9):1040-7.
12. Larisa Stojanovic L, Lunder T, Poljak M et al. Lack of evidence for hepatitis C virus infection in association with lichen planus. Int J of Dermatol 2008; 47, 1250-1256.
13. Klanrit P, Thongprasom K, Rojanawatsirivej S. Hepatitis C virus infection in Thai patients with oral lichen planus. Oral Dis 2003; 9: 292-7.
14. Gimenez-García R, Pérez-Castrillón JL Lichen planus and hepatitis C virus infection. JEADV2003; 17: 291-295.
15. Daramola OOM, George AO, Ogunbiyi AO. Hepatitis C and Lp in Nigerians: any relationship? Int J Dermatol 2002; 41:217-219.
16. Roy KM, Bagg J. Hepatitis C virus and oral disease: a critical review. Oral Dis 1999; 5 :270-277.
17. Lodi G, Porter SR. Hepatitis C virus infection and lichen planus: a short review. Oral Dis 1997; 3:77-81.
18. R Gimenez-García, JL Pérez-Castrillón. Lichen planus and hepatitis C virus infection. JEADV 2003 17(3): 291-295.
19. Nagao Y, Sata M. Hepatitis C virus and lichen planus. J Gastro Hepatol 2004;19:1101-1113.

20. Carrozzo M, Brancatello F, Dametto E t al. Hepatitis C virus-associated oral lichen planus: is the geographical heterogeneity related to HLA-DR6?. J Oral Pathol Med 2005; 34: 204-8.
21. Vijayasingam SM, Lim KB, Yeoh KH et al. Lichen planus: a study of 72 cases in Singapore. Ann Acad Med Singapore. 1988 Oct;17(4):541-4.
22. Davidson F, Simmonds P, Fergson JC et al. Survey of major genotypes and subtypes of hepatitis C virus using RFLP sequences amplified from the 5' non-coding region. J Gen Virology 1995;76:1197-1204.
23. G. Lodi, M. Carrozzo, R. Hallett et al. HCV genotypes in Italian patients with HCV-related oral lichen planus. J Oral Pathol & Med 1997; 26 (8):381–384.
24. Imhof M ,Popal H, Lee J.H et al. Prevalence of Hepatitis C Virus Antibodies and Evaluation of Hepatitis C Virus Genotypes in Patients with Lichen planus. Dermatology 1997;195:1-5.
25. G. Duraisamy, Zuridah MY Ariffin.Prevalence of hepatitis C antibodies in blood donors in Malaysia. Med J Malaysia 1993; 48 (3) :313-316.

GENERAL DERMATOLOGY - Original Article

PATTERN OF ALLERGIC CONTACT DERMATITIS IN SCHOOL CHILDREN IN SELAYANG HOSPITAL, MALAYSIA

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Abstract

Background: Allergic contact dermatitis (ACD) was thought to be infrequent in children. However, there was an increasing number of case reports and cross-sectional studies in the past three decades indicating that ACD is not as rare as previously thought. Understanding the pattern of allergic contact dermatitis in children would help with the diagnosis and prevention of this disease.

Aim: This study explored the spectrum of contact allergens in schoolchildren.

Methodology: This is a retrospective analysis of all primary and secondary schoolchildren who underwent patch test at the Department of Dermatology, Hospital Selayang, Malaysia between January 2012 and March 2013. Patch tests were performed with European Baseline Series and other additional commercial series from Chemotechnique Diagnostics in IQ chambers. The parameters studied included sites of dermatitis, positive patch test reactions and sources of the allergens. Readings were recorded according to the International Contact Dermatitis Research Group recommendation. Results were analyzed using the SPSS Version 12.0.

Results: 84 out of 327 (25.7%) patients who underwent patch tests were primary and secondary schoolchildren. Of the 84 schoolchildren, 60.7% had at least one positive patch test reaction. The most common allergens were preservatives found in cosmetic series (51%), rubber chemicals (47.1%), nickel sulfate (31.3%), fragrances (19.6%) and topical medicaments (19.6%). The majority (86%) of patients with facial dermatitis were positive to allergens in dental series, whereas 41.9% of patients with dermatitis involving the upper limbs and 50% of patients with dermatitis involving the lower limbs had positive patch test to rubber chemicals. Patients with dermatitis involving the trunk mostly had positive patch test to fragrances (50%). Sources of fragrances were mainly found in toiletries, topical medicaments and cosmetics.

Discussion: This results of this study were interesting because of the high rate of sensitization to preservatives, mainly paraben mix. There were also high sensitization rates to rubber chemicals, which could be due to contact with rubberized shoes, sports equipment and stationery.

Conclusions: Schoolchildren with face, limbs or trunk dermatitis should be patch tested with additional dental, rubber and fragrance series respectively.

Keywords: *preservative allergy, rubber chemical allergy, fragrance allergy, nickel allergy*

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Introduction

Allergic contact dermatitis (ACD) was thought to be infrequent in children and most of the cases of dermatitis in children are mainly of atopic dermatitis[1].

It cannot be determined whether the prevalence of allergic contact dermatitis is truly low or whether ACD is not sufficiently considered in children with dermatitis.

The incidence and prevalence of ACD in the population of schoolchildren are largely unknown because only a few systematic studies in unselected populations have been undertaken. Most of the studies did not provide the relevance of positive patch test results, and therefore an accurate estimate of ACD could not be determined[2]. The most frequent patch test reactions were to metals, fragrances, preservatives, neomycin, rubber chemicals and more recently also colourings[3]. Detecting ACD in children may help these patients in making decisions regarding occupation as they enter adulthood.

It is thought that sensitization rate increases with cumulative environmental exposures. With modernization, children are increasingly exposed to a variety of allergens including fragrances, cosmetics, preservatives and dental braces[4]. However, studies also reported that the rate of sensitization to different allergens varies over time and also according to geographical distribution[3,5].

The standard diagnostic procedure for allergic contact dermatitis includes clinical history and patch testing. Patch test consists of a screening series, which will pick up approximately 80% of allergens[6,7]. However, considerable variations exist between centres and the series employed are often adapted to include allergens of local importance.

Aim

The aim of this study is to explore the spectrum of contact allergens in schoolchildren.

Methods

This is a retrospective analysis of all primary and secondary schoolchildren who underwent patch test at the Department of Dermatology, Hospital Selayang, Malaysia. Primary schoolchildren were defined as children from the age of six to twelve years while secondary schoolchildren were from the age of 13 to 19 years. Schoolchildren who underwent patch testing for allergic contact dermatitis from January 1, 2012 to March 31, 2013 were identified from medical records.

Patch tests were performed with European Baseline Series and other additional commercial series from Chemotechnique Diagnostics (Malmo, Sweden) in IQ chambers. Patches were applied to the patients and removed after 48 hours. Initial reading was done at 48 hours and final reading was recorded at 96 hours after patch application. The parameters studied included sites of dermatitis, positive patch test reactions and sources of the allergens. Readings were recorded according to the International Contact Dermatitis Research Group recommendation: negative reaction, + (erythema, infiltration, discrete papules), 2+ (erythema, papules, infiltration, discrete vesicles) and 3+ (coalescing vesicles, bullous reaction).

Patients' clinical presentation were grouped according to site(s) of involvement, i.e. face, trunk, upper limbs and lower limbs. Positivity was defined as a positive reaction to at least one or more of the allergens tested.

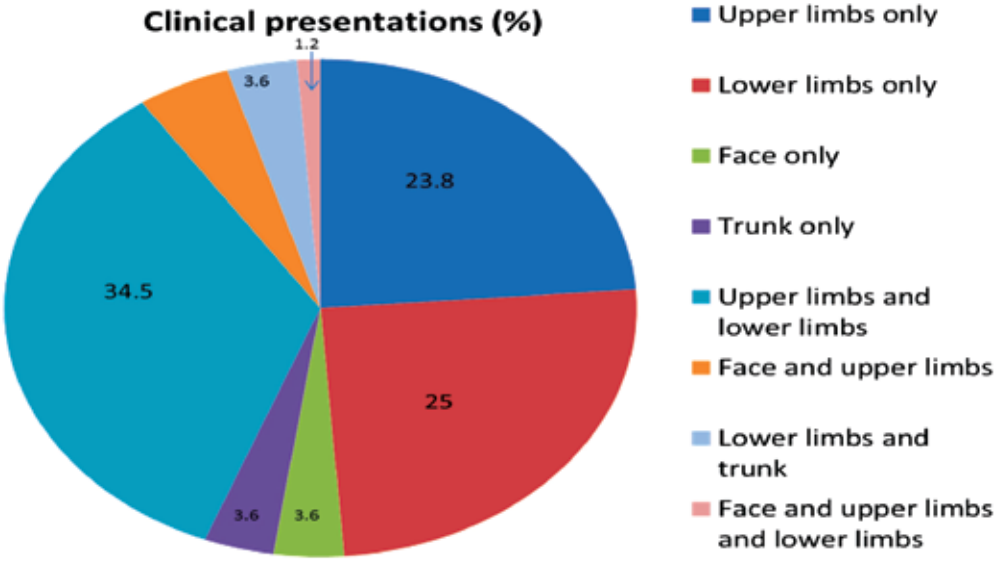

Figure 1 Clinical presentations of schoolchildren with suspected allergic contact dermatitis.

Table 1 Frequency of sensitization to preservatives, rubber chemicals, nickel sulfate, fragrances and topical medicaments.

	Patch test		
	Positive n (%)	**Negative n (%)**	**p-value**
Preservatives			
Gender	13 (50.0%)	19 32.8%)	0.151
Male	13 (50.0%)	39 (67.2%)	
Female			
Age			0.225
6 -12 year-old	7 (26.9%)	25 (43.1%)	
13 -19 year-old	19 (73.1%)	33 (56.9%)	
Race			0.000
Malay	14 (53.8%)	33 (56.9%)	
Chinese	11 (42.3%)	21 (36.2%)	
Indian	1 (3.8%)	4 (6.9%)	
Rubber chemicals			
Gender			0.000
Male	12 (50.0%)	20 (33.3%)	
Female	12 (50.0%)	40 (66.7%)	
Age			0.000
10 6 -12 year-old	10 (41.7%)	22 (36.7%)	
13 -19 year-old	14 (58.3%)	38 (63.3%)	
Race			0.000
Malay	10 (41.7%)	37 (61.7%)	
Chinese	14 (58.3%)	18 (30.0%)	
Indian	0 (0.0%)	5 (8.3%)	
Nickel sulphate			
Gender			0.776
Male	7 (43.8%)	25 (36.8%)	
Female	9 (56.3%)	43 (63.2%)	
Age			0.151
6 -12 year-old	9 (56.3%)	23 (33.8%)	
13 -19 year-old	7 (53.8%)	45 (66.2%)	
Race			0.013
Malay	5 (31.3%)	42 (61.8%)	
Chinese	8 (50.0%)	24 (36.5%)	
Indian	3 (18.8%)	2 (2.9%)	
Fragrances			
Gender			1.000
Male	4 (40.0%)	28 (37.8%)	
Female	6 (60.0%)	46 (62.2%)	
Age			0.735
6 -12 year-old	3 (30.0%)	29 (39.2%)	
13 -19 year-old	7 (70.0%)	45 (60.8%)	
Race			0.02
Malay	2 (20.0%)	45 (60.8%)	
Chinese	8 (80.0%)	24 (32.4%)	
Indian	0 (0.0%)	5 (6.8%)	
Topical medicaments			
Gender			0.495
Male	5 (50.0%)	27 (36.5%)	
Female	5 (50.0%)	47 (63.5%)	
Age			0.735
6 -12 year-old	3 (30.0%)	29 (39.2%)	
13 -19 year-old	7 (70.0%)	45 (60.8%)	
Race			0.04
Malay	2 (20.0%)	45 (60.8%)	
Chinese	7 (70.0%)	25 (33.8%)	
Indian	1 (10.0%)	4 (5.4%)	

Table 2 Frequency of sensitization to preservatives, rubber chemicals, nickel sulfate, fragrances and topical medicaments with different presentations.

	Patch test		
	Positive n (%)	**Negative n (%)**	**p-value**
Facial			
Preservatives	4 (40.0%)	6 (60.0%)	0.717
Rubber chemicals	2 (20.0%)	8 (80.0%)	0.717
Nickel sulfate	4 (40.0%)	6 (60.0%)	0.091
Fragrances	1 (10.0%)	9 (90.0%)	1.000
Topical medicament	1 (10.0%)	1 (90.0%)	1.000
Upper limbs			
Preservatives	14 (25.0%)	42 (75.0%)	0.133
Rubber chemicals	15 (26.8%)	41 (73.2%)	0.798
Nickel sulfate	11 (19.6%)	45 (80.4%)	1.000
Fragrances	5 (8.9%)	51 (91.1%)	0.200
Topical medicament	5 (8.9%)	51 (91.1%)	0.200
Lower limbs			
Preservatives	18 (34.6%)	34 (65.4%)	0.467
Rubber chemicals	18 (34.6%)	34 (65.4%)	0.141
Nickel sulfate	10 (19.2%)	42 (80.8%)	1.000
Fragrances	8 (15.4%)	44 (84.6%)	0.305
Topical medicament	9 (17.3%)	43 (82.7%)	0.081
Trunkal			
Preservatives	1 (16.7%)	5 (83.3%)	0.661
Rubber chemicals	1 (16.7%)	5 (83.3%)	0.669
Nickel sulfate	0 (0.0%)	6 (100%)	0.349
Fragrances	3 (50.0%)	3 (50.0%)	0.021
Topical medicament	0 (0.0%)	6 (100%)	0.604

Statistics

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

Results

A total of 84 out of 327 (25.7%) patients who underwent patch tests were primary and secondary schoolchildren. Female to male ratio was 1.6 : 1. The majority (56%) of the patients were Malay, followed by Chinese (38%) and Indian (6%). Of the 84 schoolchildren, 60.7% had at least one positive patch test reaction. The most common allergens were preservatives found in cosmetic series (51%), rubber chemicals (47.1%), nickel sulfate (31.3%), fragrances (19.6%) and topical medicaments (19.6%).

There was no statistically significant difference in the sensitization to these allergens with regards to gender and age. Compared to Malay and Indian patients; Chinese patients were found to be more likely to develop ACD to rubber (58.3%, p=0.042), nickel sulphate (50.0%, p=0.013), fragrances (80%, p=0.02) and topical medicaments (70%, p=0.04).

Of the patients who had positive patch test reactions; 86% of patients with facial dermatitis were positive to allergens in dental series whereas 41.9% of patients with dermatitis involving the upper limbs and 50% of patients with dermatitis involving the lower limbs had positive patch test to rubber chemicals. 60% of the patients with facial dermatitis had dermatitis involving the perioral region. Patients with dermatitis involving the trunk mostly had positive patch test to fragrances (50%, p=0.021).

Discussion

Most of the studies pertaining to allergic contact dermatitis in children were based on the population of children in the United States and Northern European countries[8]. The results of our study differ from the majority of these studies in terms of the most common allergens. Preservatives, which are included in the European Baseline Series and Cosmetic Series, were found to be the most common sensitizers in this study. This finding may be due to the difference in legislation concerning the usage of preservatives in cosmetics and household products in different countries. Paraben mix is the most frequently positive preservative allergen in this study. Currently, there is no specific regulation with regards to the maximum concentration of parabens that can be used in consumer products in Malaysia[9]. Geographically closer to our study population, there is only one study from India which showed similar findings whereby the most common allergen was also found to be paraben mix[10].

Rubber chemicals were found to be the second most common allergen in our study and it is the most common sensitizer for patients presented with dermatitis involving the upper and lower limbs. Although rubber is ubiquitous in the environment, it is likely that this trend is due to contact with rubber containing products such as sports equipment and stationery including rubber erasers. Rubber is used in handles of badminton and tennis rackets and also in squash balls. Additionally, increased sensitization to rubber chemicals in patients presented with lower limb dermatitis may also be due to the increasing trend for sports shoes. In particular, one study showed that allergic contact dermatitis due to shin guards were most commonly caused by rubber chemicals i.e. thiurams and mercaptobenzothiazole[11]. Increased sweating during sports activities and occlusion from the sportswear may also alter the skin barrier and facilitate the entrance of allergens into the skin causing ACD.

Nickel sulfate was found to be the third most common sensitizer in this study and this is in agreement with our knowledge of the epidemiology of ACD in paediatric and adult populations[1]. Sources of nickel sensitization include jewelry, belt buckles, metal fasteners, spectacle frames and ear rings. Although there is a general opinion that more girls than boys are sensitized because girls are more likely to have their ears pierced at a young age, we found no statistically significant difference in the frequency of nickel sensitization between girls and boys in this study. It is perhaps useful to investigate whether ear piercing was performed in those who showed positivity towards nickel sulfate to understand more about the relevance of sensitivity to nickel in this study.

Fragrances were the fourth most common allergens found in our study and this could be contributed by the increased production of perfumed toiletry products made specifically for children. In younger children, toys are another potentially important source of exposure to fragrance and these include cosmetic-toy sets which contain products such as perfumes, lipstick and eyeshadow. One study found that levels of fragrance in some selected cosmetic-toy sets sold in retail outlets were higher than the recommended industrial guidelines[12]. Fragrances are also found in topical medicaments.When these products are applied on diseased skin such as wounds, leg ulcers or eczema, there is a higher chance for the allergens to cross the skin barrier and cause sensitization.

Patients presented with facial dermatitis were mostly found to be positive to allergens contained in dental series. This could be explained by the fact that most cases of facial dermatitis in this study were specifically perioral dermatitis. Exposure to metal and acrylates used in dental fillings could be the cause of sensitization in these patients[13]. However, contact with metal can also happen through playing musical instruments. Thus it is important to obtain a thorough history that includes such hobbies and activities.

In this study, the subset of Chinese patients were found to be more at risk of developing allergic contact dermatitis to rubber, nickel sulphate, fragrance and topical medicaments. There may be a true risk associated with this if they are more frequently exposed to allergens found in traditional topical Chinese medications[14]. Fragrance, colophony, rubber mix and nickel have been found in these topical preparations[15]. Alternatively, this finding may only be an apparent risk. Parents of Chinese schoolchildren may have different perception about the seriousness of skin diseases and may seek treatment earlier; making the Chinese schoolchildren more likely to be identified earlier compared to the other races. Further studies would be needed to elucidate this difference between the three main racial groups in Malaysia.

From our study, we find ita ppropriate to use the European Baseline Series supplemented with allergens according to the child's history. Children and adults can be tested with equal concentrations of patch test allergens[16]. Adolescents may be exposed to occupational allergens from part time jobs and thus it is important that history should consider exposure in such activities[17].

The limitations of our study include the retrospective nature of the study and that it is conducted only in a single centre. Selayang Hospital receives referral from areas surrounding Gombak and the population studied may not be fully representative of the Malaysian schoolchildren population.

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References

1. Mortz CG, Andersen KE. Allergic contact dermatitis in children and adolescents. Contact Dermatitis. 1999: 41(3): 121-30.
2. Lee PW, Elsaie ML, Jacob SE. Allergic contact dermatitis in children: commonallergens and treatment: areview. Curr Opin Pediatr. 2009 Aug:21(4) :491-8.
3. Flora B. de Waard-van der Spek, Klaus E. Andersen, Ulf Darsow et al. Allergic contact dermatitis in children: which factors are relevant? (review of the literature). Pediatr Allergy Immunol 2013: 24: 321-329
4. Bonitsis NG, Tatsioni A, Bassioukas K et al. Allergensresponsible for allergic contact dermatitis among children: a systematic review and meta-analysis. Contact Dermatitis. 2005 May:64(5): 245-257
5. Seidenari S, Giusti F, Pepe P, Mantovani L. Contact sensitization 1094 children undergoing patch testing over a 7-year period. Pediatr Dermatol 2005: 22: 1-5.
6. Sheretz E F, Swartz S M. Is the screening patch test tray still worth using? J Am Acad Dermatol. 1993: 36: 1057-1058.
7. Menné T, Dooms-Goosens A, Wahlberg J E, White I R, Shaw S. How large a proportion of contact sensitivities are diagnosed with the European standard series? Contact Dermatitis.1992: 26: 201-202.
8. Goon AT, Goh CL. Patch Testing of Singapore Children and Adolescents: Our Experience over 18 Years. Pediatr Dermatol. 2006: 23(2): 117-20
9. Voo SY, Ridzwan R. Patch Testing with Preservative Sensitizers. A Year Retrospective Study from Selayang Hospital. Malaysian Journal of Dermatology. 2013: 30: 1-6.
10. Sarma N, Ghosh S. Clinico-allergological pattern of allergic contact dermatitis among 70 Indian children. Indian J Dermatol Venereol Leprol 2010: 76: 38-44.
11. M T Ventura, MDagnello, M G Matino et al. Contact dermatitis in students practicing sports: incidence of rubber sensitisation. Br J Sports Med 2001; 35: 100-102.
12. Rastogi SC, Johansen JD, Menne T et al. Contents of fragrance allergens in children'scosmetics and cosmetic-toys. Contact Dermatitis.1999: 41(2): 84-8.
13. Bakula A, Lugovic-Mihic L, Situm M et al. Contact allergy in the mouth: diversity of clinical presentations and diagnosis of common allergens relevant to dental practice. Acta Clin Croat. 2011: 50(4): 553-61.
14. Sen P, Ho MS, Ng SK et al. Contact dermatitis: a common adverse reaction to topical traditional medicine. Int J Dermatol. 2010: 49(11): 1255-60.
15. L.-F. Li et al. Patch testing in allergic contact dermatitis caused by topical Chinese herbal medicine. Contact Dermatitis. 2002 47(3): 166-8.
16. Zug KA, McGinley-Smith D, Warshaw EM et al. Contact allergy in children referred for patch testing: North American Contact Dermatitis Group data, 2001-2004. Arch Dermatol. 2008: 144(10): 1329-36.
17. Milingou M, Tagka A, Armenaka M et al. Patch tests in children : a review of 13 years of experience in comparison with previous data. Pediatr Dermatol. 2010: 27(3): 255-9.

GENERAL DERMATOLOGY - Short Case

TRIGEMINAL TROPHIC SYNDROME. A CASE REPORT AND LITERATURE REVIEW

Esther A[1], Tang JJ[1], Norain K[2]

Keywords: *cranial nerve, skin atrophy, trigeminal anaesthesia, facial paraesthesia*

Introduction

Trigeminal trophic syndrome is a rare cause of chronic ulceration of the face[1,2]. These chronic ulceration in the trigeminal pathway was first described by Wallenberg in 1901[1]. It is usually a complication after an injury to the trigeminal sensory nuclei, spinal trigeminal tract, ganglion, or peripheral nerve branches. It is characterized by unilateral trigeminal anaesthesia, facial paraesthesia, crescent-shaped ulceration of the ala nasi[1,3]. We report a case of Trigeminal trophic syndrome in a 50 year old gentleman with ulcerative plaque on his scalp, left upper eyelid, left inner canthus and left ala nasi for the past 6 months. It is important to be aware of this disfiguring condition to ensure prompt diagnosis and further management.

Case report

A 50 year-old man presented to us with ulcerative plaque on the scalp and left side of the face for 6 months. He has diabetes mellitus, hypertension and history of cerebral vascular accident with right hemiparesis a year ago. CT brain showed cerebral infarct involving the left internal capsule. The ulcerative lesions started on the left side of scalp and then involved the left upper eyelid, left inner canthus and the left ala nasi. These lesions were painless and associated with contact bleeding. The old lesion on the scalp and left inner canthus eventually healed but ulcer on the left ala nasi and upper eyelid progressively increased in size.

He also complained of numbness over the left side of his face due to previous stroke. There was no history of preceding trauma, fever, photosensitivity or joint pain. There was no burning or crawling sensation over these area. He denied scratching or rubbing on the affected area.

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On examination, there were new and old ulceration confined to left side of his face (Figure 1, 2, 3). There were two ulcerative plaques on left upper eyelid and left ala nasi. The ulcer on left ala nasi had eroded the nasal cartilage leaving a triangular shape of ulcer with punch out appearance. The ulcer was clean with healthy granulation tissue. There was also another similar ulcer on left upper eyelid with clean base and minimal crust. He also had two healed crescentic ulcers with scarring over left side of scalp and left inner canthus. There were no lesions elsewhere in the body. He did not have any oral, genital or nail involvement. Examinations of other systems were all unremarkable. Our initial differential diagnosis included Erosive Discoid Lupus Erythematous, Erosive Lichen Planus, Lupus Vulgaris, Lethal Midline Granuloma, Deep Fungal Infection and Wegener's Granulomatosis.

His full blood count, liver and renal function, ESR, urine analysis were within normal limits. Syphilis, Hepatitis B and C serology and HIV screening were negative. The ANA, ENA, pANCA, cANCA were negative too. Mantoux test and Chest radiography were normal. Multiple skin biopsies were done but all revealed epidermal ulceration with inflammatory infiltrates without evidence of vasculitis, malignancy or granulomas (Figure 4). Special staining for fungi and acid fast bacili were all negative. Tissue cultures for mycobacteria tuberculosis and fungi were also negative. Immunofluorescence study was negative. The skin biopsy findings ruled out all of the above differential diagnosis and the final diagnosis of Trigeminal trophic syndrome was made. He was started on amitriptyline and carbamazepine with daily occlusive dressing for the ulcer on the face. The old lesions slowly dried up but he developed new lesion over scalp and left lower eyelids after 3 months of treatment. He was also referred to psychiatrist for co-management.

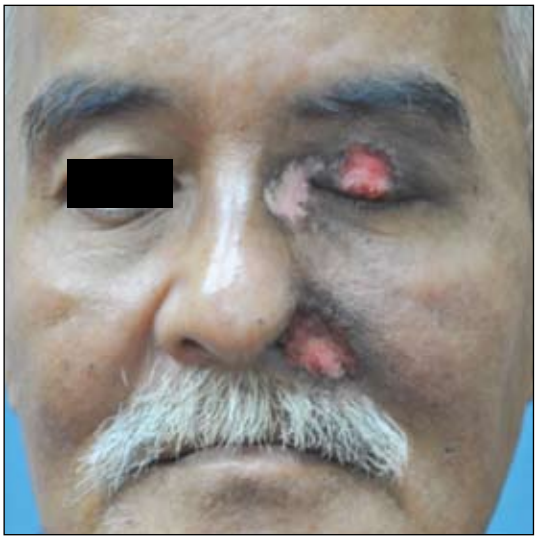

Figure 1 Ulcerative plaques with clean base and minimal crust over the left upper eye lid and left ala nasi with destruction of nasal cartilage.

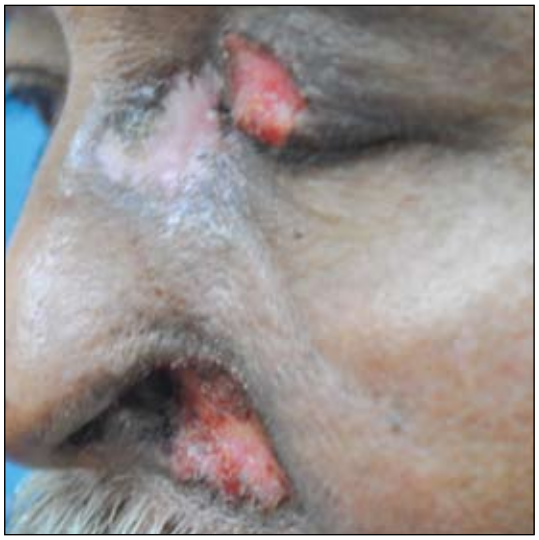

Figure 2 Close view of the ulcers over the left upper eye lid and left ala nasi with healed ulcer on left inner canthus.

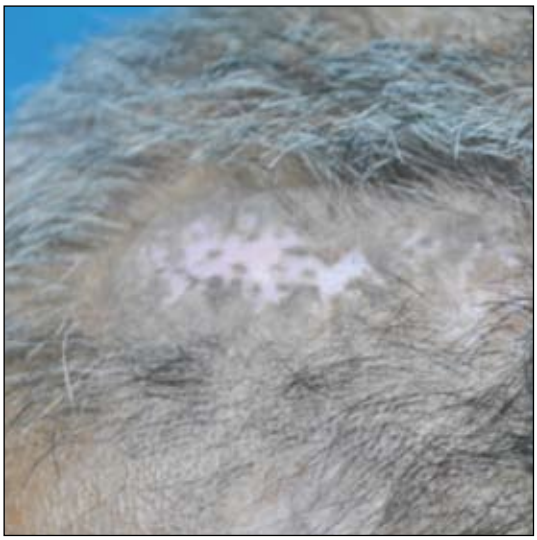

Figure 3 Close view of the healed ulcer with scarring over scalp.

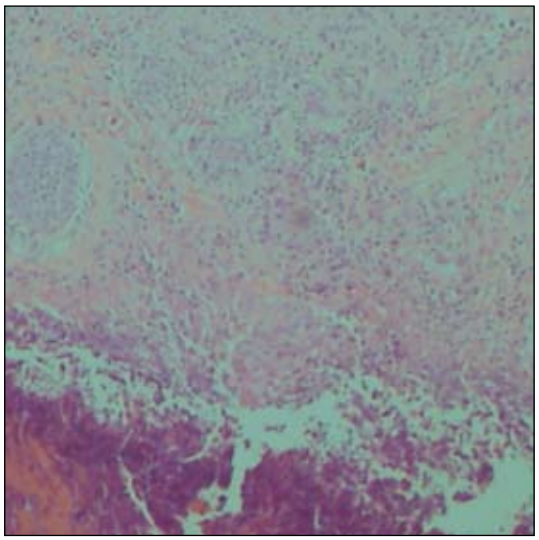

Figure 4 Skin biopsy showed epidermal ulceration with inflammatory infiltrates without evidence of vasculitis, malignancy or granulomas.

Discussion

Trigeminal trophic syndrome is rare cause of chronic ulceration of the face[1,2]. These chronic ulceration in the trigeminal pathway was first described by Wallenberg in 1901[1]. Trigeminal trophic syndrome occurs as a complication after an injury to the trigeminal sensory nuclei, tract, ganglion, or peripheral nerve branches. It is reported that two third of all cases is due to the damage from trigeminal nerve ablation (33%), or as result from cerebrovascular accident (33%). Other causes may include trauma, craniotomy, herpes zoster infection, astrocytoma, leprosy and complicated birth neurological deficit[2,5]. The age of onset ranges from 14 months to 94 year, with mean of 57 to 60 year and has a female to male ratio of 2.2-1[1,2]. The duration between the injury and the onset of the ulceration can be from weeks to years, with a average of 1 year[1,3].

Trigeminal trophic syndrome manifest as an unilateral trigeminal anaesthesia, facial paraesthesia, crescent-shaped ulceration of the ala nasi[1,3]. Even though the most common location of the ulceration is at the ala nasi, lesions has also been reported to involve scalp, ear, cheek, temple, palate or cornea[2,4]. The tip of the nose is typically spared due to its innervation by the ethmoidal branch of the ophthalmic division of the trigeminal nerve[2]. These lesions is usually self induced due to repeated manipulation like scratching or rubbing of the involved area which ulcerates and or rubbing of the involved area which ulcerates and heals with scarring[2]. The diagnosis of trigeminal trophic syndrome is based on clinical presentation of the ulcers, anaesthesia and facial paraesthesia in the distribution on trigemal nerve with a history of iatrogenic or non iatrogenic injury to the trigeminal nerves[1,2].

Skin biopsy for histopathology is needed to exclude other diseases that can mimic similar facial ulceration such as Erosive Discoid lupus Erythematous, Wegener's granulomatosis, Destructive Lethal Midline granuloma, Lupus vulgaris, Basal cell carcinoma, Subcutaneous fungal infection, Syphilis and other facial dermatitis[2,3,4]. Histopathology of trigeminal trophic syndrome is nonspecific as it only shows chronic ulceration with minimal inflammatory infiltrate and no granuloms or vasculitic lesions[1]. Other investigations may include autoimmune screening, infective screening and cultures.

Trigeminal trophic syndrome is a very challenging problem to treat. Patient education about self manipulation of the lesions is crucial to prevent further disfiguring of the ulceration. Wound care should be initiated and secondary bacterial infection can be treated with oral and topical antibiotics[2,4]. Pharmacologic medications like carbamazepine, amitriptyline, diazepam, pimozide, clonazepam, vitamin B supplements is believed to reduce paraesthesia and patients urge to pick on the lesions[1,3]. Using a protective barrier to cover the affected area helps to reduce manipulation of the lesion[2,4]. Cervical sympathectomy and transcutaneous electrical nerve stimulation have been used to improve blood supply and promote wound healing of this condition[1,3]. Surgical reconstruction using innervated cross face flaps that included nasal, nasolabial and forehead neurovascular flaps has been tried with a good long term prognosis[1,2]. New options are being explored to treat trigeminal trophic syndrome. In vitro cultured epidermal cell has been used recently to induce tissue regeneration in the treatment of neurotrophic ulceration of the face[1,6]. In a single case report, Schwerttner et al used a transplant of autologous cultured epidermal cell taken from retroauricular skin with excellent cosmetic result[1]. The other treatment option includes the use of thermoplastic dressings. Preston et al reported using thermoplastic dressing to treat two cases of trigeminal trophic syndrome with promising outcome[6]. Thermoplastic dressing is believed to interrupt the cycle of perceived irritation and secondary compulsive rubbing.

Conclusion

In conclusion, Trigeminal trophic syndrome is a rare cause of chronic ulceration of the face due to injury to the trigeminal nerves. The report of this case is to increase awareness to recognize this disfiguring condition to ensure prompt diagnosis and further management. Skin biopsy is essential to exclude other causes of facial ulceration. Treatment is very challenging and the aims include controlling of the paraesthesia, pain management, behavior modification, medical and surgical management of the wound.

References

1. Rashid RM, Khachemoune A. Trigeminal Trophic Syndrome. Eur Acad Dermatol and Ven 2007;21:725-731
2. Parrish S, Francis A, Allison TV. Trigeminal Trophic Syndrome: Report of Four Cases and Review of the Literarture. Dermatol Surg 2004;30:807-812
3. Anil MK, Diona LD, Fergal JM. Trigeminal Trophic Syndrome treated with Thermoplastic Occlusion. Australian J Dermatol 2011; 52:1-4
4. Seetha UM, Jeffrey ET, David MA. The Trigeminal Trophic Syndrome: An Unusual Cause of Nasal Ulceration. J Am Acad Dermatol 2004; 50:949-52.
5. Andrew JR, Anjela M, Stuart B, Anngela R. Reconizing Trigeminal Trophic Syndrome. J Am Acad Dermatol, Volume 55,2: 359-361
6. Preston PW, Orpin SD, Tucker WFG, Zaki I. Successful use of themoplastic dressing in two cases of the Trigeminal Trophic Syndrome. Clin and Exp Dermatol 2006; 31:525-527