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Original Article

Risk factors for secondary infection in foot eczema: a multicentre study

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Abstract: Little is known about the prevalence of foot eczema and its underlying bacterial infection in outpatient dermatology clinics in China. The aim of this study was to explore the clinical epidemiology of foot eczema, the causative bacterial infection, and the risk factors for secondary infection. Outpatients with foot eczema were studied at 31 tertiary hospitals of 16 cities in China mainland during spring 2014. Multilevel models were used for analyzing the hierarchical data. The data were divided into two levels; the first level included individual foot eczema patients, while the second level was based on the cities in which the patients were residing. The variables were screened by univariate analysis and multivariate analysis. Finally, the statistically significant variables were included in the two level logistic model. 703 (11.3%) had foot eczema (male, 45.9%). The average age was 42.91±16.86 years (age range, 1-90 y). The duration of disease in the majority of patients was between 1-5 years (N=336, 47.8%), while in 241 (34.3%) patients the duration was <1 year. 430 patients (61.2%) developed secondary infection. In univariate analysis, all variables were significantly associated with secondary infection, except gender. On multivariate analysis, moderate and severe itch intensity was significantly associated with secondary infection. In addition, history of allergies, infantile eczema and involvement of flexor surfaces were independently associated with a higher risk of secondary infection. We concluded that the prevalence rate of secondary infection is high among patients with foot eczema in China, and is aggravated by moderate itch and a history of flexor eczema.

Keywords: Foot eczema, secondary infection, multilevel model

Introduction

Eczema is a common, chronic, pruritic (itchy) inflammatory skin disease that belongs to a group of atopic disorders that include allergic rhinitis and asthma. Atopy refers to a genetic predisposition to develop immunoglobulin E (IgE)-mediated reaction in response to a wide variety of internal and external allergens. The disease typically presents with incessant pruritus and has a chronic relapsing course. Morbidity associated with eczema imposes a significant disease burden worldwide [1-3]. The estimated prevalence of eczema in China and United States of America is 7.5% and 10.7%, respectively [4, 5]. A study reported a 15-40% prevalence of atopy among children in the UK in the mid-1990s; the prevalence is reported to have increased in recent years [1, 6-8]. The pathophysiology of eczema remains poorly understood. Two major hypotheses have been forwarded regarding the progression of inflammation that leads to eczema, i.e., IgE-mediated sensitization to allergens due to a primary dysfunction of the immune system, and impaired integrity of the epithelial-barrier. The disorder appears to be the result of a complex interaction between defects in skin barrier function, immune abnormalities, and environmental and infectious agents. The successful management of eczema requires a multifaceted approach that involves patient and caregiver education [9, 10]; optimal skin care practices; anti-inflammatory treatment with topical corticosteroids (first-line) and/or topical calcineurin inhibitors (TCIs); first-generation antihistamines to help manage sleep disturbances, and the treatment of skin infections. Systemic corticosteroids may also be considered in severe cases that cannot be controlled with appropriate skin care and topical therapy [11].

Foot eczema, a common dermatosis, is mostly caused by leather processing chemicals, metal

buckles, black dyes of shoes and socks, adhesives, plastic, rubber shoes and polishing agents in that order of frequency [12, 13]. Secondary infection further aggravates foot eczema [14, 15]. A recent study reported an association of male sex, atopic hand eczema, hyperhidrosis and tobacco smoking, with an increased prevalence of foot eczema [16].

However, many researchers pay minimal attention to foot eczema, especially the secondary infection, compared to hand eczema. Secondary infection of eczema is a common and often neglected complication. Recurrence of bacterial infection is common, and is attributed to impaired cell-mediated immunity in these patients [17, 18]. In a study, 32% children were reported to have suffered from recurrent infection within a 3-month period [19].

Studies have shown that environmental factors (group environment and individual micro environment) contribute to the increased prevalence of eczema [20-22]. Group environment includes air, water, soil, radioactive sources and other bacterial sources. The individual small environment refers to the sedentary life style which appears to be a greater determinant of eczema than the group environment. Further research on prevalence and various risk factors associated with secondary infection in foot eczema in Chinese population is required.

The aim of this study was to explore the prevalence of foot eczema among Chinese population, and to elucidate risk factors for secondary infection in a multicenter study, which might populate data with hierarchical structure. The classical regression model is not ideally suited to the assessment of inter-regional differences from data having a hierarchical structure [23, 24]. A multilevel model can further decompose the residual after fitting the traditional model according to the level of data, which reduces the proportion of unexplained residual. Therefore, this study on foot eczema with secondary infection has been designed as a multicenter study that uses a multilevel model for ensuring a higher accuracy of results.

Materials and methods

Study design

This study was conducted from March 14 to May 29, 2014, in 31 tertiary hospitals of 16 cities of China mainland. One or two doctors from each hospital were selected to systematically analyze all patients with a diagnosis of eczema in that hospital during the study period. Field data collection was conducted using a questionnaire which was developed by professionals and adopted after a satisfactory field-test (pre-survey).

Study population and diagnosis

Patients with foot eczema accessed outpatient services of the Department of Dermatology in the 31 hospitals included in this study. Teaching hospitals and Class III Grade I hospitals were selected for study, which represented the highest quality of medical care in China. All clinicians managing these patients had >5 years of experience. The diagnosis and treatment were according to the *Prognosis of unclassified eczema: a follow-up study*, which was published in 2008 [25]. Diagnosis of eczema was primarily clinical (using the United Kingdom diagnostic criteria) [26]; atopic eczema and seborrheic eczema were clinically diagnosed and labeled as eczema, while the remaining unspecified eczema cases was labeled as unclassified eczema. Laboratory examination was conducted only if felt necessary. The various types of eczema such as xerotic eczema, nummular eczema, and auto sensitization eczema were diagnosed based on the clinical presentation.

Quality control

A comprehensive formal training of field investigators was conducted for this study (10.1, 2013-12.15, 2013). Specialist supervisors monitored the field data collection. The authors also conducted data quality checks by random verification of a sample of filled questionnaires.

Statistical methods and data analysis

Multilevel model: Multilevel models, also referred to as hierarchical linear models, are statistical models whose parameters vary at more than one level. The model is appropriate for analyzing data that is organized at more than one level. In this study, the patients with foot eczema comprised the first level; their city of residence served as the second level.

Null model: Initially, the null model was developed to detect aggregation of secondary infec-

Table 1. The fitting results of null model

	Estimates	Standard error	χ^2	*P*
Fixed effect				
$ß_0$	-0.054	0. 333	0.026	0.871
Random effect				
Level 2 μ_{0j}^2	4.659	1.243	14.051	<0.001
Level 1	1.000	0.000		

μ_{0j} refers to the two-level random effect of the mean of logit, whose variance μ_{0j}^2 was defined as random coefficient.

tion by city. Null model was a component of multilevel model which did not include any variables, and was used to verify the existence of hierarchical features, and to ensure that the minimum requirement for the application of multilevel model for data analysis was met.

Two-level model: The dependent variable was defined as the secondary infection among patients with foot eczema (no =0, yes =1). According to the principle of two levels of Logistic model, the basic form of the model was as follows:

$$\text{logit}(p_{ij}) = (ß_0 + \mu_{0j}) + ß_1 x_{ij}$$

$$\mu_{0j} \sim N(0, \mu_{0j}^2)$$

ß1 refers to effective parameters of independent variables, μ_{0j} refers to two-level random effect of the mean of logit, whose variance μ_{0j}^2 was defined as random coefficient. If the random coefficient of null model was not statistically significant, univariate analysis and traditional logistic model was applied. However, if the two-levels of random coefficient were statistically significant in the null model (indicating the aggregation of secondary infection of the patients with foot eczema at the city level), the two-level logistic model was applied.

Variable selection: Initially, the independent variables were subjected to univariate analyses. The statistically significant (*P*<0.05) independent variables on univariate analysis were included in the traditional logistic regression model. Finally, the statistically significant variables determined by traditional logistic regression were included in the two-level logistic model.

Data processing

In this study, MLwiN2.31 was used to develop a two-level logistic model; SAS 9.2 software was used for other analyses. Quantitative data are expressed as mean ± standard deviation; *P*<0.05 was considered as the criteria for statistical significance.

Ethical considerations

Written informed consent was obtained from all patients before enrollment. Written informed consent was obtained from all patients before enrollment. The study was approved by the ethics committee of the participating hospitals.

Results

Basic information

A total of 703 patients with foot eczema in 31 hospitals across 12 provinces (including 16 cities) in China were enrolled in this study. Among these patients, 323 (45.9%) were male. The average age was 42.91±16.86 years (age range, 1-90 y). The average age at onset of foot eczema was 39.67±16.37 years (age range, <1-80 y). In majority of the patients the disease duration was between 1-5 years (N=336, 47.8%), while in 241 (34.3%) patients the duration was <1 year. The incidence of secondary infection was 61.2% (N=430).

Lesions

Erythema was the most common clinical manifestation (61.1%) in the subjects followed by papules (55.2%) and dry skin (31.7%).

Null model

The null model was applied to assess any aggregation of foot eczema with secondary infection at the city level, and subsequently it was determined whether or not to apply the two-level logistic model. As shown in **Table 1**, the random coefficient at city level was 4.659 (χ^2=14.051, *P*<0.001), implying a significant aggregation of eczema with foot infection at city level; hence the data qualified for application of the two-level logistic model.

Univariate analysis

A higher age group; increased itch intensity; longer duration of illness; history of allergic disease, dry skin, infantile eczema or involvement of flexor aspects were significantly associated with secondary infection (**Table 2**).

Table 2. Distribution of secondary infection and influencing factors on univariate analysis

	Secondary infection			
	No (%)	Yes (%)	χ^2	*P*
Gender				
Male	135 (41.79)	188 (58.21)		
Female	138 (36.31)	242 (63.69)	2.207	0.137
Age				
≤18 years old	25 (51.02)	24 (48.98)		
18< and ≤49 years old	136 (34.69)	256 (65.31)		
≥50 years old	112 (42.74)	150 (57.26)	7.582	0.023
Itch intensity				
No	6 (85.71)	1 (14.29)		
Mild	47 (87.03)	7 (12.97)		
Moderate	191 (36.10)	338 (63.9)		
Severe	29 (25.66)	84 (74.34)	69.209	<0.001
Course of disease				
≤1 year	119 (49.37)	122 (50.63)		
1< and ≤5 year	114 (33.92)	222 (66.08)		
5< and ≤10 year	25 (30.12)	58 (69.88)		
>10 year	15 (34.88)	28 (65.12)	17.618	0.001
History of allergic disease within three generations				
No	241 (49.89)	242 (50.11)		
Yes	32 (14.54)	188 (85.46)	79.524	<0.001
History of dry skin				
No	210 (44.77)	259 (55.23)		
Yes	63 (26.92)	171 (73.08)	20.947	<0.001
History of infantile eczema				
No	265 (46.73)	302 (53.27)		
Yes	8 (5.882)	128 (94.118)	77.078	<0.001
History of the flexor side of eczema				
No	266 (46.58)	305 (53.42)		
Yes	7 (5.303)	125 (94.697)	76.922	<0.001

Multivariate analysis (traditional logistic model)

The statistically significant variables on univariate analysis were included in the traditional logistic analysis. Mild itch intensity was found to be protective against secondary infection, while moderate and severe itch intensity were significantly associated with secondary infection (**Table 3**). Duration of illness had no bearing on the occurrence of secondary infection. History of dry skin was found to be protective, while history of allergies, infantile eczema and involvement of flexor surfaces were independently associated with a higher risk of secondary infection.

Two-level logistic model

On applying the two-level logistic model, the individual level variables such as history of allergy or infantile eczema were no longer significantly associated with risk of secondary infection when compared with the results of traditional logistic model (**Table 4**). Compared with no itching, moderate itch intensity was still a risk factor, but severe and mild itch intensity were no longer a risk factor and protective factor, respectively for secondary infection. History of involvement of flexor surfaces was still significantly associated with an increased risk of secondary infection. The random coefficient at city level was little lower than the value in null

Table 3. Multivariate analysis for secondary infection using a traditional logistic model

	Estimates	Standard error	χ^2	*P*	*Odds Ratio*	95% Confidence Interval
Intercept ($ß_0$)	0.9040	0.3852	5.5073	0.0189		
Itch intensity						
No						
Mild	-1.2439	0.4219	8.6923	0.0032	0.2882	(0.1261, 0.6590)
Moderate	0.8287	0.3103	7.1319	0.0076	2.2903	(1.2467, 4.2076)
Severe	1.5861	0.3439	21.2705	<0.0001	4.8846	(2.4894, 9.5845)
Course of disease						
≤1 year						
1< and ≤5 year	0.3088	0.1613	3.6656	0.0555	1.3617	(0.9927, 1.8681)
5< and ≤10 year	0.1818	0.2272	0.6400	0.4237	1.1993	(0.7683, 1.8722)
>10 year	-0.2292	0.3073	0.5563	0.4558	0.7951	(0.4354, 1.4522)
History of allergic disease within three generations						
No						
Yes	0.5346	0.1381	14.9840	0.0001	1.7067	(1.3020, 2.2373)
History of dry skin						
No						
Yes	-0.4775	0.1273	14.0833	0.0002	0.6203	(0.4834, 0.7961)
History of infantile eczema						
No						
Yes	0.8105	0.2289	12.5412	0.0004	2.2490	(1.4360, 3.5224)
History of flexor eczema						
No						
Yes	0.7837	0.2359	11.0363	0.0009	2.1895	(1.3790, 3.4766)

model (4.64), which indicated a reduced aggregation when individual level variables were included (**Table 4**).

Discussion

In this study, we adopted a two-level logistic model for assessing the prevalence of foot eczema and the associated risk factors for secondary infection in China. Overall, 430 (61.2%) out of 703 patients suffered from secondary infection, which is higher than what was reported in a pediatric population from a study conducted in 1986 [19].

In addition to foot eczema, patients also developed other types of lesions, most commonly, erythema and papules, while nodular lesions and yellow scabs were less common. Although eczema may present with different symptoms, swelling and itching are the commonest manifestations, which often leads to oozing, scarring and aggravation of the rash [27]. 83.3% of foot eczema patients had ≤4 lesions, which might have been a contributing factor to the development of secondary infection.

On univariate analysis, except gender, all other variables such as higher age group; increased itch intensity; longer duration of illness; history of allergic disease, dry skin or infantile eczema; and involvement of flexor surfaces, were significant risk factors for secondary infection.

Multivariate regression is usually the preferred method for analysis of risk factors. However, the traditional multivariate regression model requires the individual variables to be independent of each other. When this presumption does hold true, results obtained by traditional regression model are vulnerable to bias. In the present study, the random coefficient was statistically significant, thus a two-level logistic model was deemed to be reliable, though the clustering of secondary infection was not completely eliminated in our study.

Patients with eczema are known to develop a higher threshold for itch. Secondary infection may, however, lead to an exacerbation of itch [28]. In the present study, the traditional logistic model showed that mild itching was a significant risk factor for secondary infection when

Table 4. The fitting results of two-level logistic model

	Estimates	Standard error	χ^2	*P*	*Odds Ratio*	95% Confidence Interval)
Intercept (ß0)	-4.454	1.486	8.988	0.002		
Itch intensity						
No						
Mild	-0.690	0.917	0.566	0.451	0.5015	(0.0831, 3.0262)
Moderate	2.064	0.731	7.969	0.004	7.8774	(1.8799, 33.0083)
Severe	-1.024	0.812	1.592	0.207	0.3591	(0.0731, 1.7639)
Course of disease						
≤1 year						
1< and ≤5 year	-0.276	0.303	0.831	0.361	0.7588	(0.419, 1.3742)
5< and ≤10 year	-0.389	0.442	0.772	0.379	0.6777	(0.285, 1.6117)
>10 year	0.736	0.580	1.608	0.204	2.0875	(0.6698, 6.5065)
History of allergic disease						
No						
Yes	0.644	0.396	2.816	0.093	1.9040	(0.8762, 4.1378)
History of dry skin						
No						
Yes	0.040	0.352	0.013	0.909	1.0408	(0.5221, 2.0749)
History of infantile eczema						
No						
Yes	1.340	0.706	3.604	0.057	3.8190	(0.9572, 15.2375)
History of eczema of flexor aspect						
No						
Yes	1.374	0.581	5.602	0.017	3.9511	(1.2652, 12.3389)
Random effect						
Level 2 (μ_{0j}^2)	4.641	1.292	12.895	0.0003		
Level 1	1.000	1.000				

compared with no itching. However, mild itch intensity was found to be a protective factor in the 2-level logistic model, although not statistically significant. Combined with the reduction of random coefficient, the 2-level logistic model yields more reliable results than that obtained with traditional multivariate regression. Moderate itch was 7.87 times likely to be associated with secondary infection than no itching. However, the influence of severe itching was opposite in the two models. Severe itching naturally induces more scratching, but also attracts more intensive medical treatment, which may be the reason for this interesting finding in our study.

When compared with disease of ≤1 year duration, presence of disease for >10 years was more commonly associated with secondary infection (OR=2.0875) in the 2-level model. However, the difference was not statistically significant. Similarly, a family history of allergic disease, infantile eczema or dry skin, though more commonly found in patients of foot eczema with secondary infection, did not have a significant association with secondary infection.

A population-based study in US revealed an increased risk of infection in childhood atopic eczema [29], which is consistent with our results. A plausible explanation for this association may be the role played by barrier disruption, immune disruption (or both) in the development of infection in eczema. In a pilot study conducted in young infants, regular oil baths appeared to reduce the risk of atopic eczema

[28]. Furthermore, in a representative cross-sectional study, the history of dry skin and eczema were significantly associated with chronic itch in hemodialysis patients [29]. In both these studies the persistence of symptoms appears to predict the increased risk of infections.

The relationship between involvement of flexor surfaces and risk of secondary infection has not been adequately researched. However, a case study documented the relationship between infection and hyperpigmentation in a 7 year old child [30]. In the present study, the involvement of flexor surfaces was associated with an increased risk of secondary infection. However, a cohort study is better equipped to confirm this relationship.

To the best of our knowledge, this is the first multicenter study exploring the risk factors associated with secondary infection among foot eczema patients in China.

Some limitations of our study need to be noted. Firstly, more definitive conclusions could have been drawn by a cohort study. Secondly, we had taken multi-level data and aggregation into account by using two-level logistic model, but the reduction of the random coefficient model was limited. A multi-center cohort study to explore the variables at a higher level could provide more definitive evidence. Thirdly, use of questionnaire for data collection in the field is known to be affected by recall bias on the part of the subjects. However, this possibility was minimized by a comprehensive formal training of the field investigators prior to the commencement of the study, in addition to meticulous quality control measures.

In conclusion, we found a high prevalence of secondary infection among Chinese patients with foot eczema. Moderate itch and the involvement of flexor surfaces were significant risk factors for secondary infection in these patients.

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Disclosure of conflict of interest

None.

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References

[1] Allen SJ, Jordan S, Storey M, Thornton CA, Gravenor MB, Garaiova I, Plummer SF, Wang D and Morgan G. Probiotics in the prevention of eczema: a randomised controlled trial. Arch Dis Child 2014; 99: 1014-1019.

[2] Silverberg JI, Garg NK, Paller AS, Fishbein AB and Zee PC. Sleep disturbances in adults with eczema are associated with impaired overall health: a US population-based study. J Invest Dermatol 2015; 135: 56-66.

[3] Agner T, Andersen KE, Brandao FM, Bruynzeel DP, Bruze M, Frosch P, Goncalo M, Goossens A, Le Coz CJ, Rustemeyer T, White IR, Diepgen T; EECDRG. Hand eczema severity and quality of life: a cross-sectional, multicentre study of hand eczema patients. Contact Dermatitis 2008; 59: 43-47.

[4] Hanifin JM, Reed ML; Eczema Prevalence and Impact Working Group. A population-based survey of eczema prevalence in the United States. Dermatitis 2007; 18: 82-91.

[5] Xueyan L LL, Yanming Y. Prevalence of and risk factors for skin diseases in a community of Lishui City. China J Lepr Skin Dis 2008; 24.

[6] Odhiambo JA, Williams HC, Clayton TO, Robertson CF, Asher MI; ISAAC Phase Three Study Group. Global variations in prevalence of eczema symptoms in children from ISAAC Phase Three. J Allergy Clin Immunol 2009; 124: 1251-1258, e23.

[7] Flohr C. Recent perspectives on the global epidemiology of childhood eczema. Allergol Immunopathol (Madr) 2011; 39: 174-182.

[8] Asher MI, Montefort S, Bjorksten B, Lai CK, Strachan DP, Weiland SK, Williams H; ISAAC Phase Three Study Group. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. Lancet 2006; 368: 733-743.

[9] Krakowski AC, Eichenfield LF and Dohil MA. Management of atopic dermatitis in the pediatric population. Pediatrics 2008; 122: 812-824.
[10] Krakowski AC and Dohil MA. Topical therapy in pediatric atopic dermatitis. Semin Cutan Med Surg 2008; 27: 161-167.
[11] Leung TN and Hon KL. Eczema therapeutics in children: what do the clinical trials say? Hong Kong Med J 2015; 21: 251-260.
[12] Febriana SA, Soebono H, Coenraads PJ and Schuttelaar ML. Contact allergy in Indonesian patients with foot eczema attributed to shoes. J Eur Acad Dermatol Venereol 2015; 29: 1582-1589.
[13] Chougule A and Thappa DM. Patterns of lower leg and foot eczema in South India. Indian J Dermatol Venereol Leprol 2008; 74: 458-461.
[14] Gilje O. [Virus infection as a secondary infection in eczema (Kaposi's varicelliform eruption)]. Tidsskr Nor Laegeforen 1951; 71: 611-613; passim.
[15] Nemkaeva RM. [Foot mycoses complicated by secondary infection]. Vestn Dermatol Venerol 1985; 55-56.
[16] Brans R, Hubner A, Gediga G and John SM. Prevalence of foot eczema and associated occupational and non-occupational factors in patients with hand eczema. Contact Dermatitis 2015; 73: 100-107.
[17] David TJ. Infection and prevention: current controversies in childhood atopic eczema: a review. J R Soc Med 1989; 82: 420-422.
[18] Rystedt I, Strannegard IL and Strannegard O. Recurrent viral infections in patients with past or present atopic dermatitis. Br J Dermatol 1986; 114: 575-582.
[19] David TJ and Cambridge GC. Bacterial infection and atopic eczema. Arch Dis Child 1986; 61: 20-23.
[20] Ronmark EP, Ekerljung L, Lotvall J, Wennergren G, Ronmark E, Toren K and Lundback B. Eczema among adults: prevalence, risk factors and relation to airway diseases. Results from a large-scale population survey in Sweden. Br J Dermatol 2012; 166: 1301-1308.
[21] Bohm D, Stock Gissendanner S, Finkeldey F, John SM, Werfel T, Diepgen TL and Breuer K. Severe occupational hand eczema, job stress and cumulative sickness absence. Occup Med (Lond) 2014; 64: 509-515.
[22] Behroozy A and Keegel TG. Wet-work Exposure: A Main Risk Factor for Occupational Hand Dermatitis. Saf Health Work 2014; 5: 175-180.
[23] Greco T, Edefonti V, Biondi-Zoccai G, Decarli A, Gasparini M, Zangrillo A and Landoni G. A multilevel approach to network meta-analysis within a frequentist framework. Contemp Clin Trials 2015; 42: 51-59.
[24] Efendi A and Molenberghs G. A multilevel model for hierarchical, repeated, and overdispersed time-to-event outcomes and its estimation strategies. J Biopharm Stat 2013; 23: 1420-1434.
[25] Li LF, Liu G and Wang J. Prognosis of unclassified eczema: a follow-up study. Arch Dermatol 2008; 144: 160-164.
[26] Williams HC, Burney PG, Pembroke AC and Hay RJ. Validation of the U.K. diagnostic criteria for atopic dermatitis in a population setting. U.K. Diagnostic Criteria for Atopic Dermatitis Working Party. Br J Dermatol 1996; 135: 12-17.
[27] Ferreira e Vasconcellos Ede C, Pimentel MI, Valete-Rosalino CM, Madeira Mde F and Schubach Ade O. Resolution of cutaneous leishmaniasis after acute eczema due to intralesional meglumine antimoniate. Rev Inst Med Trop Sao Paulo 2014; 56: 361-362.
[28] Hong J, Buddenkotte J, Berger TG and Steinhoff M. Management of itch in atopic dermatitis. Semin Cutan Med Surg 2011; 30: 71-86.
[29] Silverberg JI and Silverberg NB. Childhood atopic dermatitis and warts are associated with increased risk of infection: a US population-based study. J Allergy Clin Immunol 2014; 133: 1041-1047.
[30] Pfau A and Landthaler M. Recurrent inflammation in incontinentia pigmenti of a seven-year-old child. Dermatology 1995; 191: 161-163.