Clinical Features of Adult/Adolescent Atopic Dermatitis and Chinese Criteria for Atopic Dermatitis

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Abstract

Background: Atopic dermatitis (AD) is an inflammatory skin disease characterized by chronic recurrent dermatitis with profound itching. Most patients have personal and/or family history of atopic diseases. Several criteria have been proposed for the diagnosis of AD. Although the clinical features of childhood AD have been widely studied, there has been less large-scale study on adult/adolescent AD. The aim of this study was to investigate the clinical features of adult/adolescent patients with chronic symmetrical eczema/AD and to propose Chinese diagnostic criteria for adult/adolescent AD.

Methods: A hospital-based study was performed. Forty-two dermatological centers participated in this study. Adult and adolescent patients (12 years and over) with chronic symmetrical eczema or AD were included in this study. Questionnaires were completed by both patients and investigators. The valid questionnaires were analyzed using EpiData 3.1 and SPSS 17.0 software.

Results: A total of 2662 valid questionnaires were collected (1369 male and 1293 female). Of all 2662 patients, 2062 (77.5%) patients had the disease after 12 years old, while only 600 (22.5%) patients had the disease before 12 years old, suggesting late-onset eczema/AD is common. Two thousand one hundred and thirty-nine (80.4%) patients had the disease for more than 6 months. One thousand one hundred and forty-four (43.0%) patients had a personal and/or family history of atopic diseases. One thousand five hundred and forty-eight (58.2%) patients had an elevated total

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Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.178960

Received: 09-11-2015 **Edited by:** Yi Cui
How to cite this article: Liu P, Zhao Y, Mu ZL, Lu QJ, Zhang L, Yao X, Zheng M, Tang YW, Lu XX, Xia XJ, Lin YK, Li YZ, Tu CX, Yao ZR, Xu JH, Li W, Lai W, Yang HM, Xie HF, Han XP, Xie ZQ, Nong X, Guo ZP, Deng DQ, Shi TX, Zhang JZ. Clinical Features of Adult/Adolescent Atopic Dermatitis and Chinese Criteria for Atopic Dermatitis. Chin Med J 2016;129:757-62.

serum IgE and/or eosinophilia and/or positive allergen-specific IgE. Based on these clinical and laboratory features, we proposed Chinese criteria for adult/adolescent AD. Of all 2662 patients, 60.3% were satisfied with our criteria, while only 48.2% satisfied with Hanifin Rajka criteria and 32.7% satisfied with Williams criteria, suggesting a good sensitivity of our criteria in adult/adolescent AD patients.
Conclusion: Late-onset of eczema or AD is common. The clinical manifestations of AD are heterogeneous. We have proposed Chinese diagnostic criteria for adolescent and adult AD, which are simple and sensitive for diagnosis of adult/adolescent AD.

Key words: Adolescents and Adults; Atopic Dermatitis; Clinical Features; Diagnostic Criteria; Eczema

Introduction

Atopic dermatitis (AD), also known as atopic eczema, is a chronic inflammatory skin disease characterized by eczematous dermatitis and itching.[1-3] The prevalence of childhood AD ranged from 15% to 30% while adult AD from 2% to 10% in industrialized countries.[4] AD is often associated with other allergic conditions. Patients with AD often have personal and/or family history of other atopic diseases such as asthma, allergic rhinitis, and allergic conjunctivitis.[5-7] The clinical manifestations of AD are heterogeneous. Three stages are proposed including infantile AD, childhood AD, and adolescent/adult AD. The clinical features vary with stages. Elevation in total serum IgE level, eosinophilia, and allergen-specific IgE are main laboratory abnormalities of AD. Although the etiology and pathogenesis of AD remain unknown, mounting evidences have suggested that genetic predisposition such as defect of filaggrin synthesis[8] and environmental factors such as allergen exposure[9] contribute to the formation of AD. Studies have shown that dysfunction of skin barrier[10] and Th2 predominant immunity[11] play vital roles in the pathogenesis of AD.

In China, the symmetrical eczematous dermatitis is often diagnosed as eczema. We have performed a survey in 3016 Chinese dermatologists about the diagnosis in patients with symmetrical eczematous dermatitis. About half dermatologists claimed that more than 90% of these patients were diagnosed as eczema and <10% was diagnosed as AD (unpublished data), indicating an over-diagnosis of eczema and under-diagnosis of AD in China.

Several diagnostic criteria for AD have been proposed, including Hanifin and Rajka criteria,[12] Williams criteria,[13-15] and Japanese Dermatological Association (JDA) criteria.[16] Hanifin and Rajka criteria include 4 major features and 23 minor features and the diagnosis of AD requires 3 major features and 3 minor features, which are rather complicated. Williams criteria include six features. JDA criteria are composed of only 3 clinical features. The differences in diagnosis criteria may explain the variability of the prevalence of AD reported in different studies. In clinical practice, we found that Hanifin and Rajka criteria and Williams criteria were not easy for clinical use while some suspected the specificity of JDA criteria because they contained only 3 clinical features.

Although AD occurs both in children and adults, the studies in childhood AD are much more than that in adult AD. In China, there has been no large-scale study on adult/adolescent AD. We performed a hospital-based study to analyze the clinical features of adult/adolescent AD and tried to propose Chinese diagnostic criteria for these patients based on the clinical and laboratory findings.

Methods

Patients

This study was performed in 42 dermatological centers. Patients older than 12 years with symmetrical eczematous dermatitis for more than 2 months were included in this study regardless of the clinical diagnosis (eczema or AD). The informed consents were obtained from each patient.

Questionnaires and dermatological examinations

All investigators were trained for completing the questionnaire and for dermatological examinations. The study was performed from September 2013 to September 2014. The standardized questionnaires were completed by patients and investigators. The investigators also performed dermatological examination for characterization of the skin manifestations. In some patients, the complete blood count, total serum IgE level, and allergen-specific IgE were measured.

Data entry and statistical analysis

All the valid data were input by EpiData 3.1 software (The EpiData Association, http://www.epidata.dk/, Denmark) and analyzed by Statistical Package for Social Science 17.0 software (SPSS Inc., Chicago, IL, USA). Counting and ranked data were performed with number or constituent ratio (*n* or %), and measurement data were performed with mean ± standard deviation (SD). Comparison of counting data were analyzed using Pearson Chi-square test, comparison of ranked data were analyzed using Wilcoxon test, and comparison of measurement data were analyzed using independent sample *t*-test. Pearson and Spearman correlation index were applied to describe the correlation between ranked data and measurement data. A $P < 0.05$ was considered significant.

Results

Demographical features of the patients

A total of 2662 valid questionnaires were collected (1369 male and 1293 female). The mean age of the patients was 40.6 ± 18.9 years old (12.1–93.0 years old). Among them, 88.0% patients were older than 18 years old; 84.1% of patients were from urban areas while 15.9% patients were from rural areas [Table 1].

Clinical and laboratory features

Of all the patients, 600 (22.5%) had the disease before

Table 1: Demographic characteristics of the 2662 patients

Variables	Results
Gender, *n* (%)	
Male	1369 (51.4)
Female	1293 (48.6)
Age	
Mean age (years, Mean ± SD)	40.6 ± 18.9
12≤ age <18 years old, *n* (%)	320 (12.0)
≥18 years old, *n* (%)	2342 (88.0)
Height (cm, Mean ± SD)	166.5 ± 23.4
Weight (kg, Mean ± SD)	61.6 ± 13.6
Body mass index (kg/m^2, Mean ± SD)	22.5 ± 3.9
Residence, *n* (%)	
Urban area	2240 (84.1)
Rural area	422 (15.9)

12 years old, while 2062 (77.5%) patients had the disease after 12 years old. Approximately one-third (34.5%) patients were diagnosed as AD and 65.5% were diagnosed as eczema by investigators. The clinical features of these patients are summarized in Table 2. The laboratory findings are summarized in Table 3.

Propose of Chinese criteria for adult/adolescent atopic dermatitis

Based on the clinical and laboratory findings in these patients, we proposed a set of criteria for adult/adolescent AD [Table 4].

Sensitivity of Chinese criteria for diagnosis of adult/adolescent atopic dermatitis

By our criteria, 60.3% of these patients were diagnosed as AD while only 48.2% were diagnosed as AD by Hanifin and Rajka criteria and 32.7% by Williams criteria, suggesting a good sensitivity of our criteria in adult/adolescent AD patients although our criteria were less sensitive than JDA criteria (79.4%) [Table 5]. The clinical features of AD and non-AD patients are summarized in Table 6.

Discussion

Eczema and dermatitis are the most common skin diseases. AD is regarded as a special form of eczema with characteristic clinical manifestations and laboratory findings. Hence, AD is also called atopic eczema. In nearly all textbooks of dermatology, eczema and AD were described as two skin diseases.[17] In China, the diagnosis of eczema was much more common than AD.

According to the definition, AD is characterized by dermatitis with personal and/or family history of atopic diseases, increased serum IgE level and/or eosinophilia. Some regarded that AD is a syndrome rather than a simple skin disease. Several diagnostic criteria for AD have been proposed. Hanifin and Rajka criteria were proposed in 1980 and were widely used.[12,18] Brenninkmeijer *et al*.[19] reported that the sensitivity of Hanifin and Rajka criteria was 87.9–96.0%, and the specificity was 77.6–93.8%.

Table 2: Clinical manifestations of the 2662 patients with symmetrical dermatitis/eczema

Clinical manifestations	*n* (%)
Pruritus	2628 (98.7)
Chronic course (>6 months)	2139 (80.4)
Disease influenced by environmental/emotional factors	1904 (71.5)
Xerosis	1786 (67.1)
Itching upon sweating	1395 (52.4)
Personal or family history of atopic diseases	1144 (43.0)
Personal history of atopic diseases	725 (27.2)
Family history of atopic diseases	801 (30.1)
First-degree relative	694 (26.1)
Second-degree relative	231 (8.7)
Third-degree relative	108 (4.1)
Flexural dermatitis	1123 (42.2)
Visible flexural dermatitis	961 (36.1)
Food intolerance	900 (33.8)
Facial pallor/facial erythema	847 (31.8)
Intolerance to wool	695 (26.1)
Urticaria/angioedema	652 (24.5)
Scalp eczema/pityriasis	611 (23.0)
Eczema/AD before 12 years old	600 (22.5)
Periauricular fissuring/eczema	542 (20.4)
Hand and/or foot dermatitis	535 (20.1)
Ichthyosis/palmar hyperlinearity/keratosis pilaris	521 (19.6)
White dermographism	506 (19.0)
Perifollicular accentuation	436 (16.4)
Eyelid eczema	436 (16.4)
Nummular eczema	413 (15.5)
Pompholyx of hand/foot	405 (15.2)
Eczema/AD history before 2 years old	387 (14.5)
Liable to skin infections	387 (14.5)
Anterior neck folds	364 (13.7)
Cheilitis	341 (12.8)
Perineum eczema	313 (11.8)
Orbital darkening	262 (9.8)
Pityriasis alba	215 (8.1)
Breast eczema	177 (6.6)
Recurrent conjunctivitis	146 (5.5)
Dennie–Morgan infraorbital fold	145 (5.4)
Anterior subcapsular cataracts	73 (2.7)
Keratoconus	31 (1.2)

AD: Atopic dermatitis.

However, Hanifin and Rajka criteria had 27 clinical features (4 major features and 23 minor features), which were rather complicated for clinical use. William's criteria were relatively simple with 6 items. However, the "flexural dermatitis" and "onset before 2 years old" would exclude those who did not have flexural dermatitis and those who had the disease after 2 years old. JDA criteria were much simpler with only three clinical features. However, this may lower the specificity because the three features were just from four major features of Hanifin and Rajka criteria.

According to our findings in 2662 patients, we proposed three features as the criteria for adult/adolescent AD: (1) eczema for more than 6 months; (2) personal and/

Table 3: Laboratory findings of the 2662 patients with symmetrical dermatitis/eczema

Laboratory findings	*n/N* (%)
Elevated total serum IgE	1303/2496 (52.2)
Eosinophilia	740/2327 (31.8)
Positive allergen-specific IgE	355/1153 (30.8)
Elevated total serum IgE and/or eosinophilia and/or positive allergen-specific IgE	1548/2662 (58.2)

Table 4: Chinese criteria for adult/adolescent AD

Must have
Symmetrical eczema (dermatitis) for more than 6 months*
Plus one or more of the following
Personal† and/or family history‡ of atopic diseases
Elevated total serum IgE level and/or positive allergen-specific IgE and/or eosinophilia

*More than 6 months: Persistent or recurrent eczema/dermatitis for more than 6 months; †Personal history of atopic diseases: Allergic rhinitis and/or allergic asthma and/or allergic conjunctivitis; ‡Family history of atopic diseases: Eczema/AD and/or allergic rhinitis and/or allergic asthma and/or allergic conjunctivitis in first-, second- or third-degree relatives. AD: Atopic dermatitis.

Table 5: Comparison of sensitivity of different criteria for diagnosis of adult/adolescent AD

Criteria	AD/total	Percentage
Our criteria	1605/2662	60.3
Hanifin and Rajka criteria	1184/2455	48.2
Williams criteria	866/2648	32.7
JDA criteria	2110/2656	79.4

AD: Atopic dermatitis; JDA: Japanese Dermatological Association.

or family history of atopic diseases; (3) elevated total serum IgE level and/or positive allergen-specific IgE and/or eosinophilia. Because it has only 3 features, it is much easier for clinical use although it requires some laboratory tests. The pruritus is not included in our criteria because it is not specific for AD. Many other skin diseases also have pruritus. Similarly, "dry skin" is also not included in our criteria because it is rather subjective.

"Eczema for more than 6 months," "personal and/or family history of atopic diseases" and "elevated total serum IgE level and/or positive allergen-specific IgE and/or eosinophilia" are much specific for AD. As is well-known, the concept of atopy has been widely accepted for a long time,[17,20] focusing on the familial hypersensitivity of skin/mucosa and increased IgE level.[2] The definition of atopy has been revised in recent years as follows: Atopy is a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, and to develop typical symptoms such as asthma, rhinoconjunctivitis, or eczema/dermatitis.[5] From this perspective, the three features we have chosen meet the meaning of atopy properly.

"Eczema for more than 6 months" represents to the chronic course of AD and has been widely accepted. "Chronic or chronically relapsing dermatitis" was required in Hanifin and Rajka criteria proposed in 1980, but there was no explanation of specific course for "chronic." Later in 1994, the JDA developed diagnostic criteria for AD, which was partly revised in 2008, defined the "chronic or chronically relapsing course" as "more than 6 months in childhood, adolescent, and adulthood."[16] At the same time, the International Study of Asthma and Allergies in Childhood proposed a widely-used questionnaire for AD diagnosis in 1995, which also adopted the chronic course as 6 months.[21] Therefore, we consider that "eczema for more than 6 months" is necessary for the diagnosis of AD.

"Personal and/or family history of atopic diseases" stands for the importance of genetic factor and syndrome nature of the disease. As we all know, this feature has been accepted in AD diagnosis for many years by lots of criteria, such as the Hanifin and Rajka criteria and Williams criteria. Meanwhile, a revised Hanifin and Rajka criteria proposed by the American Academy of Dermatology, also chose "personal and/or family history" as one of the important features of AD.[22,23] However, Hanifin and Rajka criteria and the revised version did not mention the the degree of relatives for family history, and Williams criteria just suggested a history of atopic disease in the first-degree relative in children under 4 years old. However, in our patients, 8.7% of the second-degree relatives and 4.1% third-degree relatives had atopic diseases [Table 2], so the family history in our criteria included not only the first-degree relatives but also the second-, and third-degree relatives.

Elevation in total serum IgE level and/or positive specific IgE and/or eosinophilia are all the characteristics of "atopy." The elevated total serum IgE is one of the diagnostic features in Hanifin and Rajka criteria. In our patients, 52.2% had increased serum IgE level. In millennium criteria proposed by Bos *et al*.,[24] the presence of allergen-specific IgE was a mandatory criterion.[25] In our patients, 30.8% had specific IgE to at least one allergen. Eosinophilia is another characteristic of AD and was found in 31.8% of our patients. Because eosinophils are very sensitive to systemic corticosteroid treatment, so if eosinophil is normal, careful history taking, especially about the systemic use of steroid is necessary.

It has been widely accepted that AD is a systemic disease, and the skin manifestations are only a part of the disorder.[26,27] The European Academy of Allergology and Clinical Immunology (EAACI) task force proposed the term "atopic eczema/dermatitis syndrome" instead of the current "atopic eczema/dermatitis,"[5] underlining the fact that "AD" is a syndrome with certain clinical characteristics in common.[28] In keeping with the EAACI nomenclature, we agree that AD is a syndrome involving both skin and other organs such as respiratory tract, and is usually associated with elevation of total serum IgE and eosinophils. On the other hand, eczema is often a descriptive diagnosis, often referring to a broad range of conditions that begin as spongiotic dermatitis and may progress to a lichenified

Table 6: Clinical features of adult/adolescent AD

Clinical features	AD (n = 1605), n (%)	Non-AD (n = 1057), n (%)	χ^2	P
Pruritus	1582 (98.6)	1046 (99.0)	0.778	0.378
Xerosis	1190 (74.1)	596 (56.5)	89.332	0.000
Disease influenced by environmental/emotional factors	1186 (73.9)	718 (68.1)	10.834	0.001
Personal or family history of atopic diseases	986 (61.4)	158 (14.9)	561.936	0.000
Itching upon sweating	898 (56.0)	497 (47.2)	19.739	0.000
Flexural dermatitis	833 (52.0)	290 (27.6)	154.481	0.000
Visible flexural dermatitis	686 (42.8)	275 (26.2)	75.785	0.000
Food intolerance	613 (38.2)	287 (27.2)	34.527	0.000
Facial pallor/facial erythema	569 (35.5)	278 (26.4)	24.142	0.000
Intolerance to wool	484 (30.2)	211 (20.0)	34.281	0.000
Eczema/AD before 12 years old	473 (29.5)	127 (12.1)	110.266	0.000
Scalp eczema/pityriasis	461 (28.8)	150 (14.2)	75.579	0.000
Urticaria/angioedema	430 (26.8)	222 (21.1)	11.462	0.001
Periauricular fissuring/eczema	413 (25.8)	129 (12.3)	71.453	0.000
Hand and/or foot dermatitis	396 (24.7)	139 (13.2)	52.327	0.000
Ichthyosis/palmar hyperlinearity/keratosis pilaris	374 (23.3)	147 (13.9)	35.434	0.000
Eyelid eczema	333 (20.8)	103 (9.8)	55.963	0.000
Eczema/AD history before 2 years old	323 (20.2)	64 (6.1)	101.396	0.000
Perifollicular accentuation	313 (19.5)	123 (11.7)	28.466	0.000
White dermographism	305 (19.0)	201 (19.1)	0.001	0.975
Nummular eczema	295 (18.4)	118 (11.2)	25.296	0.000
Pompholyx of hand/foot	275 (17.2)	130 (12.3)	11.376	0.001
Liable to skin infections	270 (16.8)	117 (11.1)	16.648	0.000
Anterior neck folds	267 (16.7)	97 (9.2)	30.138	0.000
Cheilitis	240 (15.0)	101 (9.6)	16.462	0.000
Perineum eczema	230 (14.3)	83 (7.9)	25.558	0.000
Orbital darkening	182 (11.4)	80 (7.6)	10.262	0.001
Pityriasis alba	152 (9.5)	63 (6.0)	10.475	0.001
Breast eczema	126 (7.9)	51 (4.8)	9.288	0.002
Recurrent conjunctivitis	117 (7.3)	29 (2.7)	25.391	0.000
Dennie–Morgan infraorbital fold	97 (6.1)	48 (4.5)	2.799	0.094
Anterior subcapsular cataracts	54 (3.4)	19 (1.8)	5.848	0.016
Keratoconus	21 (1.3)	10 (0.9)	0.731	0.393

AD: Atopic dermatitis.

stage.[17] Moreover, AD is a chronic or chronically-relapsing disease while the eczema could be acute, subacute, or chronic.

It has been reported that approximately 45% AD patients had the disease within the first 6 months of life, 60% had AD during the 1st year and 85% before 5 years of age.[4] Ingordo *et al*.[29] reported that 8.8% of eczema were adult-onset AD. Ozkaya[30] reported that adult-onset AD account for 16.8% of total AD patients. While in our study, 77.5% patients had eczema or AD after 12 years old, indicating late-onset eczema/AD is quite common.

We compared the sensitivity between our criteria and other criteria. Of all 2662 patients, 60.3% satisfied our criteria, 48.2% satisfied Hanifin and Rajka criteria, 32.7% satisfied Williams, suggesting that our criteria have higher sensitivity in adult/adolescent AD patients. Although our criteria were less sensitive than JDA criteria (79.4%), they might increase the specificity with inclusion of personal/familial atopy history and laboratory evidence for atopy. With regard to the fact that the current AD clinical diagnostic rate was only 34.5%, our criteria could increase the diagnosis of AD by 25.8% in these patients.

Our study was a hospital-based retrospective clinical study, including only eczema and AD patients, and the population were restricted to adolescents and adults. Therefore, it is only for adult and adolescent. This is the limitation of our criteria. Furthermore, our criteria need more large-scale study for verification.

While our criteria are helpful for the diagnosis of adult/adolescent AD, it is necessary to differentiate some diseases that might satisfy this set of criteria such as hyper-eosinophilic syndrome, Wiscott–Aldrich syndrome, Netherton syndrome, hyper-IgE syndrome, Sezary disease and other diseases.

Acknowledgments

The authors thank all investigators from forty-two study sites for their contributions and also thank Dr. Chun-Fang Zhang from Peking University People's Hospital for her assistance in the design of the questionnaires.

Financial support and sponsorship

This work was supported partly by the Public Welfare Research Fund for Healthcare (No. 201202013).

Conflicts of interest

There are no conflicts of interest.

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