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Adult-Onset Atopic Dermatitis: A Cross-Sectional Study of Natural History and Clinical Manifestation

Kanokvalai Kulthanan, Pailin Samutrapong, Sukhum Jiamton and Papapit Tuchinda

SUMMARY The previously reported prevalence of adult-onset atopic dermatitis (AD) varied from 13% to 47%. There were a few reports of clinical features of adult-onset AD**.** The purpose of this article was to study the clinical features of Thai patients with adult-onset AD. We recruited prospective patients from the outpatient Department of Dermatology, Siriraj hospital, Mahidol University in Bangkok, Thailand, from June, 2006 to May, 2007. The diagnosis of AD was made according to the criteria of Hanifin and Rajka and the severity of AD in each patient was assessed using the Rajka and Langeland score. Fifty nine patients were enrolled. The majority of the patients developed their dermatitis during their third decade. Typical lichenified/exudative lesions were found in all cases. Non-typical morphologic variants were found in 76.3%. The most common were nummular lesions**.** The main sites of involvement were the flexural area. The common sites of non-flexural involvement were the trunk, extensors and hands. The severity of AD was moderate in 64.4% of cases. A personal history of atopy was found in 84.7% of cases. Skin prick testing showed positive results (mostly to multiple allergens) in 25 of 29 patients (86.2%). Elevated serum total immunoglobulin E was detected in 6 of 10 patients (60%). It is concluded that adult-onset AD is not a rare but under-recognized eczematous condition.

Atopic dermatitis (AD) is a chronic pruritic inflammatory skin disease which predominantly affects children. Surveys on the natural history of AD have reported clearance rates of about 30-90% from infancy to young adult life.[1-5] However, patients who have the onset of disease in adult life are sometimes seen. Bannister *et al.*[6] reported that 245 of 2604 patients (9%) who attended a contact clinic were diagnosed with AD which began for the first time at 20 years of age or older with no contact factor present. Tay *et al.* [7] reported the clinical onset was after the age of 21 years in 13.6 % of 492 AD patients. Ingordo *et al.*[8] used the age of 18 years as the cut-off mark and reported 8.8% of 502 adults affected by eczematous dermatitis were adult-onset AD. Similarly Ozkaya *et al.*[9] reported 63 of 376 patients (16.8%) were allocated to the adult-onset AD with the age of 18 years as the cut-off mark.

The prevalence of AD has been increasing worldwide during the last decade, especially in industrialized countries.[10] Several genetic analyses have identified different chromosome regions with a linkage to AD features.[11,12] A few reports of the clinical features of adult-onset AD have been done, mostly in Australia and Western countries.[6,8,9] Be-

From the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.
Correspondence: Kanokvalai Kulthanan
E-mail: sikkt@mahidol.ac.th

cause of the different genetic, dietary habits and environment between Asian and Caucasian people may cause different allergen sensitization, it is interesting to know the clinical features of Asian patients with adult-onset AD. The purpose of this article was to study the clinical features of Thai patients with adult-onset AD.

MATERIALS AND METHODS

Patients

This study was approved by the ethical committee on research involving human subjects of Siriraj Hospital, Mahidol University. We recruited prospective patients from the outpatient Department of Dermatology, Siriraj hospital, Mahidol University in Bangkok, Thailand, from June, 2006 to May, 2007. The diagnosis of AD was made according to the criteria of Hanifin and Rajka[13] and the severity of AD in each patient was assessed using the Rajka and Langeland score.[14] Written informed consent was obtained from all individuals. We used the age of 18 years as the cut-off mark to determine the adult-onset AD. Subjects who had other skin diseases that might interfere with the clinical features of AD or who were unwilling to participate in the study were excluded.

Data analysis

Demographic data, a complete history including personal and family history of atopy, onset and activity of personal atopy, course of dermatitis, previous treatment, contact and irritant factors were recorded. Physical examination, morphology and distribution of dermatitis were studied. The numbers of Hanifin–Rajka and UK working party's criteria were recorded. The UK working party's criteria[3] include an itchy skin condition plus three or more of the followings: history of flexural involvement, a personal history of asthma or hay fever, a history of generalized dry skin in the last year, onset of rash under the age of two years or visible flexural dermatitis.

On the examining day, patients were also asked about pruritus severity using a Visual Analog Scale, with a minimum score of 0 and maximum score of 10. While "0" means "doesn't itch at all" and "10" means "itch is worse than ever".

Appropriate investigation including skin prick testing using 28 allergens (13 aeroallergens and 15 food allergens) , patch testing using European standard series (Chemo technique Diagnosis, Sweden) were done. Serum total IgE levels were determined using the Nephelometry method (Dade Behring; Marburg, Germany). Levels of more than 100 IU/ml were regarded as high.

RESULTS

Demographic data

All patients were willing to participate in this study. No subject was excluded. Fifty nine patients were enrolled (50 females, 9 males) with an age range of 18 to 72 years (mean 34 ± 12.9 years). The age of onset ranged from 18 to 57 years (mean 29.4 ±10.8 years). The majority of the patients developed their dermatitis during their 3rd decade (18-29 years), as in Fig. 1. Most of our patients (27 cases, 45.8%) worked in offices.

Distribution of skin rashes

At the onset, one third of patients (35.6%) had dermatitis on both the flexural and non-flexural areas. The main sites of involvement were the flexural area in 47 cases (79.7%); the flexural area alone in 3 cases (5.1%), flexural and other sites in 44 cases (74.6%), whereas another 12 cases (20.3%) had only non-flexural involvement. The common sites of non-

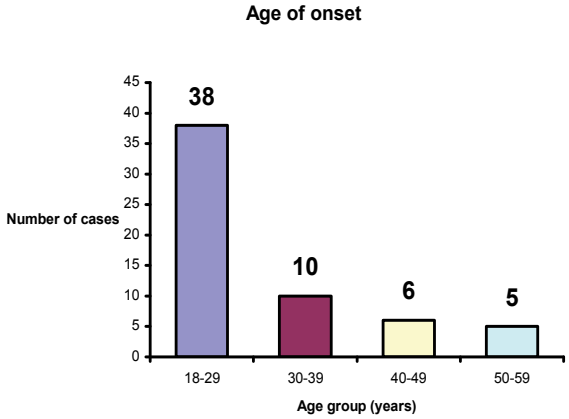

Fig. 1 The age onset of patients with adult-onset atopic dermatitis

flexural involvement are the trunk, extensors and hands as shown in Table 1.

Table 1 Distribution of lesions in patients with adult-onset atopic dermatitis

Sites	Cases (%)
Flexural (total)	47 (79.7)
- Neck	31 (52.5)
- Antecubital	28 (47.5)
- Popliteal	20 (33.9)
- Axilla	14 (23.7)
- Ankle	12 (20.3)
- Wrist	8 (13.6)
Nonflexual (total)	56 (94.9)
- Trunk	33 (55.9)
- Extensors (elbows + knees)	32 (54.3)
- Hands	24 (40.7)
- Seborrheic area (scalp + retroauricular area)	21 (35.6)
- Face	17 (28.8)
- Eyelids	16 (27.1)
- Feet	16 (27.1)
- Generalized	9 (15.3)
- Nipple	8 (13.6)
- Lips	4 (6.8)

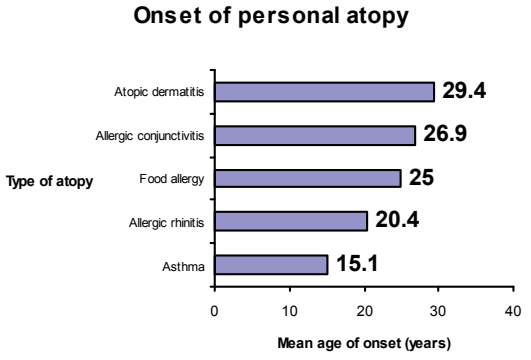

Fig. 2 The mean age of onset of personal atopy

Personal history of atopy

A personal history of atopy was found in 84.7% of the patients. Forty-four patients (74.6%) had allergic rhinitis, most of which were still active (28 of 44 cases). The mean age of onset of allergic rhinitis was 20.4 years (range 3-52 years). Allergic rhinitis preceded AD in 36 of 44 cases (81.8%). Eleven patients (18.7%) had asthma, most of which were not active (8 of 11 cases). The mean age of the onset of asthma was 15.1 years (range 3-30 years). Twenty-three patients (39%) had allergic conjunctivitis, most of which were still active (15 of 23 cases). The mean age of the onset of allergic conjunctivitis was 26.9 years (range 4-60 years). Forty-five of 59 (76.3%) had respiratory allergies (allergic rhinitis and/or asthma). Eleven of 59 (18.6%) had both allergic rhinitis and asthma**.** Five of 59 patients (8.5%) had all mucosal atopy (allergic rhinitis, asthma and allergic conjunctivitis). Sixteen patients (27.1%) had a history of food allergies, most of which were still active (15 of 16 cases) and seafood was the most common food allergy (14 of 16 cases). The mean onset of food allergies was 25 years (range 5 to 65 years). Fig. 2 shows the sequence of the age of onset of each atopic condition. Thirteen patients (22%) had a history of drug reaction. The most common drug reaction was to penicillin (7 cases), followed by cotrimoxazole (2 cases).

Family history of atopy

Thirty-two patients (54.2%) had at least one first degree family member with atopy. Of this group, a majority (22 of 32 cases, 68.8%) had allergic rhinitis and 10 cases (31.3%) had asthma. In 27 patients (45.8%), there was no family history of atopy. In total, there were 5 patients (8.5%) who had neither a personal nor a family history of atopy.

Severity of AD

The severity of AD was moderate in 64.4% of cases, mild in 33.9% of cases and severe in 1.7% of cases. The mean of the Visual Analog Scale evaluating pruritus severity on the examining day was 4.1 ± 2.5 (range 0-10). The mean body surface area affected was 5.7% (0.3-20%).

Type of lesions

Typical lichenified/exudative lesions were found in all cases. Nontypical morphologic variants were found in 45 of 59 cases (76.3%). The most common were nummular lesions which were found

in 22 cases (37.3%), followed by prurigo-like lesions in 19 cases (32.2%), seborrheic dermatitis-like lesions in 16 cases (27.1%) and follicular lesions in 14 cases (23.7%). Typical lichenified/exudative lesions alone were found in 14 cases (23.7%).

Results of patch testing

Forty-seven percent of patients had a history of dermatitis aggravated by irritant factors. Among these, detergents (24 of 28 cases, 86%) and soap (8 of 28 cases, 29%) were frequently reported. Patch testing was performed in 10 patients to rule out possible contact factors. Positive results were obtained in 9 cases. Eight of these had relevant past clinical histories. However, the current dermatitis could not be related to the contact allergens in any patients. The most frequently positive allergen was fragrance (4 of 8 cases, 50%), followed by nickel (3 of 8 cases, 37.5%). The others were paraben, gold, potassium dichromate, para-phenylenediamine, thimerosol, coal tar, neomycin and quaternium-15. Concerning the morphology among this group, typical lichenified was presented in all cases. Five cases (62.5%) had nummular lesions, 3 cases each (37.5%) had prurigo-like, and seborrheic dermatitis-like lesions, and 1 case (12.5%) had follicular lesions. No fungal or bacterial infections were detected in the nummular lesions.

Results of skin prick testing

Skin prick testing showed positive results in 25 of 29 patients (86.2%). Regarding the number of positive allergens in the skin prick testing, the range was from 1 up to 15 allergens (mean 6 ± 4.1). The most frequent allergen was *Dermatophagoides pteronyssinus* mites (16 cases; 64%). The others were dog epithelium (11 cases; 44%), mosquitos (11 cases; 44%), house dust (10 cases; 40%), Bermuda grass (7 cases; 28%), careless weed (7 cases; 28%), cat hair (7 cases; 28%) and cockroaches (6 cases; 24%).

Serum total immunoglobulin E (IgE)

Serum total IgE levels were measured in 10 patients. Among these, six patients (60%) had elevated IgE levels with a range from 162 to 1150 IU/ml (mean 669 IU/ml). Skin prick testing was performed in 4 of 6 patients who had high serum total IgE. All 4 patients showed positive results: two had 3 positive allergens, one had 2 positive allergens, the other one had 1 positive allergen. However skin prick testing was also done in 3 of the 4 patients who had normal serum total IgE, all 3 patients had positive results.

Diagnostic criteria

Regarding the frequency of the diagnostic criteria of Hanifin & Rajka, 59.3% of the patients had 4 major criteria whereas 40.7% had 3 major criteria. The most frequent major criterion was typical morphology and distribution which were presented in 45 of 59 cases (76.3%). The most frequent minor criteria was a course influenced by environmental or emotional factors (76.3% of cases), followed by itching when sweating (67.8%), periorbital darkening (61%) and xerosis (52.5%). The number of positive minor features ranged from 3 to 9 (mean 5.7 ± 1.6). Patients with 4 or lower minor criteria had mainly mild disease whereas patients with more than 4 minor criteria had moderate to severe AD (specificity 40%, sensitivity 82%, negative predictive value 53.3%, positive predictive value 72.7%; Tables 2 and 3).

Twelve patients (20.3%) with a diagnosis of AD according to the criteria of Hanifin and Rajka could not fulfill the UK working party's criteria (Table 4). In this group; 11 cases had no dry skin, 7 cases had no visible flexural eczema, 7 cases had no allergic rhinitis or asthma. The number of minor features of Hanifin and Rajka in these 12 patients ranged from 3-7 (mean 5.6 ± 1.4).

Management

Besides emollient, all of our patients were treated with topical medications. The most common was topical corticosteroids (54 cases, 91.5%) followed by tacrolimus (6 cases, 10.2%), pimecrolimus (5 cases, 8.5%), and topical antibiotics (2 cases, 3.4%). Systemic medications were prescribed to 55 patients (93.2%): antihistamine was the most common drug (54 patients, 98%), followed by prednisolone (26 patients, 44.1%) and oral antibiotics (5 patients, 8.5%). One patient was also treated by UVA1 phototherapy and cyclosporin.

Course

Mean duration from the onset of AD to recruitment was 5.1 years with a range of 6 months to 30 years. During this time, 38% of our patients experienced better disease course and another 38% had worse course. Subjectively, the average of the improvement was 63.6% with a range of 10 to 100%. One quarter of patients did not show any change in the course of disease.

DISCUSSION

According to the criteria of Hanifin and Rajka, the reported prevalence of adult-onset AD varied between 13% to 47%.[6-8, 15] According to previous reports on adult-onset AD, the majority of patients developed AD between 20 and 40 years of age, with the oldest age at onset being 79 years.[6, 7] However, Bannister reported peaked onset of adult-onset AD in the fifth decade. In the present study, the ages of AD onset ranged from 18 to 57 years with the majority having developed their dermatitis within the 3rd decade.

In general, childhood AD has no sex preponderance. In our study, adult-onset AD predominantly affected females. This is similar to the studies of Ozkaya *et al.*[9], Bannister *et al.*[6] which reported slight female predominance (54%, 65% respectively) in contrast to the previous study of Oranje *et al.*[16]

One third of our patients had dermatitis simultaneously on both the flexural and non-flexural areas. Ozkaya *et al.*[9] reported the sites of onset were mainly flexural areas (mainly antecubital/popliteal)(58.7%), followed by hands (14.3%) and eyelids (12.7%).

In our study, a typical lichenified/exudative

Table 2 Number of patients according to severity and number of minor criteria

Number of minor criteria*	Number of patients			
	Mild	Moderate	Severe	Total
3	2	3	0	5
4	6	4	0	10
5	2	11	0	13
6	2	6	0	8
7	6	10	0	16
8	2	3	1	6
9	0	1	0	1
Total	20	38	1	59

**Minor criteria*, number of Hanifin and Rajka minor criteria in each patient.

Table 3 Comparison of specificity, sensitivity, negative predictive value and positive predictive value with number of minor criteria

Minor criteria	Percent			
	Specificity	Sensitivity	NPV	PPV
≤ 3	10	92.3	40	66.7
≤ 4	40	82.1	53.3	72.7
≤ 5	50	53.8	35.7	67.7
≤ 6	60	38.5	33.3	65.2

Minor criteria, number of Hanifin and Rajka minor criteria in each patient; *NPV*, negative predictive value; *PPV,* positive predictive value.

pattern was found in all cases. Nontypical morphologic variants were found in 76 % of cases. The most common variant was nummular lesions, which was similar to previous reports in the literature that the nummular pattern was the most common type in children and adults.[16, 17] Prurigo-like lesions which were reported in some studies as the most frequently morphologic variant in adults was found in one third of our patients.[18, 19]

In our patients, the most common site of involvement was the trunk (55.9%), followed by the neck (52.5%). Hands were affected in 40.7% of the patients. Ingordo *et al.*[8] reported that the hands were the most affected site in their adult-onset AD patients. Bannister *et al.*[8] reported that 34% of their adult-onset AD patients had generalized lesions and the hands were the most affected site (28%).[6] It should be noted that these two studies used data derived from contact dermatitis clinics. Other studies also reported that hands are a greatly involved site in adult AD.[1, 2, 20]

Ingordo *et al.*[8] reported that the mean SCORAD indexes, according to the age-of–onset groups decreased when the age of onset increased. In our study, for nearly two thirds of the patients with adult-onset AD, the severity of AD was moderate and for one third it was mild. The severity of pruritus measured by the Visual Analog Scale on the examining day was moderate.

A personal history of atopy was found in 84.7% of our patients, (74.6% had allergic rhinitis, 18.7% had asthma). In 2001, Vichyanond *et al.*[21] reported the prevalence of allergic rhinitis and asthma in Thai university students was 26.3% and 8.8% respectively. This data implied the increased prevalence of other atopy in our adult-onset AD patients. In general, AD patients have an increased risk of developing other atopic conditions (atopic march), *i.e.* asthma and allergic rhinitis.[1] These conditions may arise when AD is active or has disappeared. Patients with severe AD or the early onset of AD have increased susceptibility to developing atopic respiratory disease later in their lives.[22-24] The sequence of mean age of onset of atopic conditions in our adult-onset AD were asthma, allergic rhinitis, allergic con-

Table 4 Characteristics of 12 patients with adult-onset atopic dermatitis not covered by the United Kingdom Working Party's criteria

Patient	Sex	Age (years)	Age of AD onset (years)	Morphology	Localization	Xerosis	AR and/or asthma	AD according to Hanifin and Rajka criteria (major + minor)	AD according to UK Working Party criteria
1	Female	18	18	Lichenified/exudative	Flexural, generalized	No	No	Yes (3 + 6)	No
2	Female	67	50	Lichenified/exudative, Follicular	Flexural, elbow, arm	No	No	Yes (4 + 3)	No
3	Female	27	25	Lichenified/exudative, Nummular, Prurigo-like	Flexural, trunk, extremities	No	No	Yes (4 + 4)	No
4	Female	28	24	Lichenified/exudative, Nummular	Flexural, eyelid, arm	No	No	Yes (3 + 7)	No
5	Female	20	18	Lichenified/exudative, Prurigo-like, follicular	Elbow, face, trunk, extremities, hand, foot	No	No	Yes (3 + 4)	No
6	Female	40	28	Lichenified/exudative	Trunk, foot	No	No	Yes (3 + 7)	No
7	Female	29	24	Lichenified/exudative, Prurigo-like	Trunk, knee, extremities, foot	No	No	Yes (3 + 6)	No
8	Female	53	52	Lichenified/exudative	Extremities	No	Yes	Yes (3 + 7)	No
9	Female	32	24	Lichenified/exudative	Eyelid, trunk, arm	No	Yes	Yes (3 + 7)	No
10	Female	19	18	Lichenified/exudative	Hand, foot	No	Yes	Yes (3 + 5)	No
11	Female	47	42	Lichenified/exudative, Nummular, Prurigo-like	Extremities, trunk	Yes	Yes	Yes (3 + 5)	No
12	Female	39	38	Lichenified/exudative	Eyelid, trunk, anogenital	Yes	Yes	Yes (3 + 7)	No

junctivitis and AD respectively.

In the present study, 54.2% of the patients had at least one first degree family member with atopy. This was similar to the previous report of childhood AD in which a family history of atopic disease was found in between 58% and 68% of cases.[25]

In our study, patients with adult-onset AD had a number of positive minor criteria of Hanifin and Rajka ranging from 3 to 9 (mean 5.7). Patients with 4 or lower minor criteria had mainly mild disease. The most frequent major criterion was typical morphology and distribution and the most frequent minor criterion was course influenced by environment or emotion. Ozkaya *et al.* [9] reported that the patients with 6 or fewer minor criteria had mild disease. The most frequent laboratory minor criterion was immediate skin test reactivity and the most frequent minor feature was itching when sweating.

Fourteen of 63 patients (22.2%) with the diagnosis of AD according to the criteria of Hanifin and Rajka could not fulfill the UK Working Party's criteria.[3] Similarly to the study of Ozkaya, [9] 20.3% of our adult-onset AD patients could not be given a diagnosis of adult-onset AD according to the UK Working Party's criteria which is the simplified criteria suitable for epidemiologic study.

Our country has a warm and humid climate. This might explain why many AD cases had no or a mild degree of xerosis. Moreover, many patients born in a humid climate might have subclinical AD or delayed onset of AD.

Concerning contact sensitization, Ingordo et al,[8] reported that nickel sulphate, potassium dichromate, cobalt chloride and mercaptobenzothiazole were the most detected allergens. In their study, the "sole" ADs were more represented in infancy onset ADs while the ADs with contact sensitization were more frequent in adolescence onset ADs. In their 44 adult-onset AD cases, the "sole" ADs were 63.7% and the ADs with contact sensitization were 36.3%. However, clinically non-relevant sensitizations were observed in 68.7% of cases. In our study, after careful history taking, patch testing was performed in only 10 patients to rule out possible contact factors. Positive results were obtained in 9 cases, so our AD with contact sensitization were 15.3% (9 of 59 cases). However, the current dermatitis could not be related to the contact allergens in any patients. The common positive allergens were fragrance and nickel.

Even though the delayed type hypersensitivity was impaired [26], AD patients can be sensitized by contact allergens.[27] The capability of contact sensitization in AD may be inversely related to the severity of the disease.[27, 28] It has been proposed that chronic impairment of barrier function and prolonged exposure to irritants predisposed AD patients to contact sensitization.[29]

In our study, serum total IgE levels were elevated in 6 of 10 patients measured (60%). An elevated serum IgE is found in 45% to 82% of atopic patients depending on the study.[25]

Skin prick testing showed positive results (mostly to multiple allergens) in 25 of 29 patients (86.2%) in this study. Bannister *et al.*[6] reported multiple positive reactions in 76% of their adult-onset AD patients tested. These agreed with previous reports which found a higher incidence of positive skin prick tests in atopics versus nonatopics.[25, 30-32]

Most of the clinical features of adult-onset AD found in this Asian study were similar to the previous reports in non-Asian population. The discrepancy were as follows: 1) the more female predominant; 2) the trunk as the most common site of nonflexural involvement; 3) the moderate severity in majority of patients; 4) the cut point of four or less minor features for mild disease; 5) the most common minor criteria of atopic dermatitis as "the course influenced by environment or emotion" and less common of xerosis, probably due to the warm and humid climate in our country.

There were some limitations in this study. First, patients may have problems in recalling past history of atopic dermatitis since the onset, also in the family history of atopy. Second, the skin lesions on the examining day might not represent the whole clinical pictures of morphology and distribution of rashes. Third, there were only a small number of subjects for skin prick test, patch test and serum total

IgE due to the number of visits required, financial constraint, transportation and needle fear.

In summary, we agree with other authors that adult-onset AD is not a rare but under-recognized eczematous condition. Apart from the typical flexural localization and typical eczematous pattern, patients may also have a nonflexural distribution and other nontypical morphologic variants.

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