

ORIGINAL ARTICLE

Clinical analyses of atopic dermatitis in the aged

Ryoji TANEI,¹ Kensei KATSUOKA²¹Department of Dermatology, Tokyo Metropolitan Geriatric Hospital, Tokyo, and ²Department of Dermatology, Kitasato University School of Medicine, Sagami-hara, Kanagawa, Japan**ABSTRACT**

The aim of the present study was to analyze the characteristics of atopic dermatitis (AD) in the senile phase. Subjects were comprised of 16 patients investigated for clinical features, serum immunoglobulin (Ig)E levels and skin manifestations. Mean age was 76.9 ± 6.2 years (range, 68–87), with a man : woman ratio of 3:1. Mean age at onset was 67.7 ± 15.7 years. Eight patients (50%) had personal histories of chronic eczema until the young adult phase and three patients (18.8%) showed the classic course of child AD. Eczematous erythroderma in 10 patients (62.5%) and unclassified chronic eczema in five patients (31.3%) were the predominant clinical presentations. Mean total IgE level in sera of the 16 patients was $8810 \pm 13\,511$ IU/mL (range, 5–53 605). Fourteen patients showed positive results for antigen-specific IgE antibodies, and the mean total IgE level for these patients was $10\,056 \pm 14\,044$ IU/mL. Specific IgE to the main antigen, *Dermatophagoides farinae*, was observed in 12 patients (85.7%), representing the principal antibody in eight patients (57.1%). Eczematous dermatitis manifested predominantly in the face and neck, trunk and extensor and flexure sites of extremities, and less commonly in the antecubital and popliteal areas. Other stigmata of AD were observed as follows: red face in 10 patients (62.5%); Hertoghe's sign in six (37.5%); goose-skin in four (25%); facial pallor in three (18.8%); and dirty neck in one (6.3%). These results indicate that senile-type AD represents a characteristic subgroup of AD that appears in the last stage of life in AD patients.

Key words: atopic dermatitis, clinical feature, immunoglobulin E, senile phase, the aged.

INTRODUCTION

Atopic dermatitis (AD) is a chronic relapsing skin disorder manifesting as dry skin, itching and various forms of eczematous inflammation. In typical cases, the first signs of AD appear in the infantile phase (up to 2 years) or childhood phase (up to 12 years) and healing of AD occurs with increasing age until the adolescent/young adult phase (between 12 years and young adult). Improvement and/or clearance of AD in most cases is observed until after the adolescent/young adult phase. However, AD cases in which clinical manifestations persist or first appear during the adolescent/young adult phase and the subsequent late adult phase have increased in Japan, as so-called adult-type AD.¹

Characteristic symptoms of AD differ according to the period of life. In the infantile phase, erythematous and papulovesicular eruptions frequently developing to oozing and crusted lesions are often observed on the face. In the childhood phase, atopic dry skin and lichenified flexural eczema of the extremities become more prominent. In the adolescent and adult phases, atopic red face and chronic lichenified eczema on the trunk predominate.^{2,3}

Characteristics of AD in the senile phase remain unclear, but elderly patients with AD have gradually been increasing in Japan in recent years.⁴ Clinical features of AD in the senile phase have been considered to broadly resemble those in the adolescent and adult phases, as AD in the elderly has been

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uncommon. The present report therefore analyzed the features of AD in the aged.

METHODS

Patients and criteria of AD

We performed a preliminary investigation of 66 possible cases of AD in aged patients (47 men, 19 women; ≥ 65 years old) who had been admitted to Tokyo Metropolitan Geriatric Hospital with pruritic and persistent (>6 months) chronic unlocalized eczematous dermatitis between April 1998 and March 2007. The criteria of Hanifin and Rajka⁵ and the Japanese Dermatological Association⁶ were used for the diagnosis of AD in these cases. A definitive diagnosis of AD was made for patients who satisfied both AD criteria in this study. In the same period, we diagnosed and treated 4100 cases of hospital attendances by the aged for various types of eczema and dermatitis.

Clinical features of AD

Clinical findings and AD-associated manifestations were investigated in the definitive cases of AD as follows: age and sex; onset of eczema; personal histories of chronic eczema until the young adult phase; personal and family histories of allergic disease; clinical presentation; and severity of presentations. Severity of AD was scored using the grading of AD by Rajka and Langeland.⁷

Serum immunoglobulin E antibody levels

All patients were examined for serum levels of total immunoglobulin (Ig)E and antigen-specific IgE antibodies. Total IgE levels were determined by enzyme immunoassay (EIA). Antigen-specific IgE levels for 26 antigens were detected using a multiple antigen simultaneous test⁸ (MAST 26; SRL, Tokyo, Japan), as summarized in Table 2.

Skin manifestations of AD

Cutaneous signs and symptoms of AD were investigated in definitive cases of AD as follows: degree and distribution of eczematous dermatitis, including marked lichenifications and prurigo-form eruptions, and other characteristic stigma of AD such as red face, facial pallor, Hertoghe's sign, dirty neck and goose-skin.^{3,5,6}

Histopathology of AD skin lesions

To support the clinical diagnosis of AD, skin biopsy specimens were obtained from the skin lesions of chronic eczema or lichenification in several patients. Hematoxylin–eosin staining and Giemsa staining were performed on sections for the evaluation of routine histopathological findings and mast cell infiltration, respectively. Mast cell numbers were counted by microscopic examination at $\times 400$ magnification in three areas of cell-rich infiltration in the upper-middle dermis, and averaged counts were compared. As controls, skin specimens from three aged patients with non-atopic chronic eczema (so-called eczema vulgare) were also examined. Statistical significance was examined using a two-sample Student's *t*-test with Welch's correction.

RESULTS

Diagnosis of AD

A definitive diagnosis of AD was made for 16 of the 66 patients (24.2%). The rate of AD to eczema and dermatitis in cases of the aged was 16/4100 (0.39%) in the study period. For the diagnosis of AD in this study, flexural lichenification according to the criteria of Hanifin and Rajka⁵ was the most important hallmark (Fig. 1). Personal or family history of atopy (asthma, allergic rhinitis, AD)⁵ greatly influenced the diagnosis (Table 1). Elevated serum levels of total IgE and antigen-specific IgE antibodies could support the diagnosis (Table 2). Presence of chronic eczematous dermatitis on the face and neck (Fig. 2) and lichenifications on the trunk (Fig. 3) were also diagnostic features of AD to rule out other types of eczema and dermatitis, such as asteatotic dermatitis (Table 3).

Clinical features of AD

Mean age of the AD patients was 76.9 ± 6.2 years (range, 68–87 years), with a man : woman ratio of 3:1. Mean age at onset was 67.7 ± 15.7 years. Eight of the 16 patients (50%) had personal histories of chronic eczema until the young adult phase, and three (18.8%) showed appearance of eczema in the infantile or childhood phase and improvement until the adolescent phase, corresponding to the classic course of childhood AD (cases 8, 9 and 13). Histories of bronchial asthma



Figure 1. Case 6. Marked lichenifications are apparent in the flexure (thin arrows) and extensor (thick arrows) surfaces of the left arm. Note that eczematous dermatitis is not obvious in the antecubital area (arrowhead).



Figure 2. Case 6. Marked lichenifications on the forehead and loss of the eyebrows (Hertoghe's sign) are observed on the face with post-inflammatory diffuse pigmentation. Hertoghe's sign is seen not only in the lateral eyebrows, but also in the frontal eyebrows.

and allergic rhinitis were observed in five (31.3%) and four patients (25%), respectively. The predominant clinical presentations were eczematous erythroderma in 10 patients (62.5%) and unclassified chronic eczema in five patients (31.3%). Complications of the prurigo-form eruptions were observed in three of the 10 patients with erythroderma, three of the five patients with chronic eczema and one patient with nummular-type dermatitis. Mean severity for the 16 patients was 7.2 ± 1.7 (Table 1).

Serum IgE antibodies levels

Mean total IgE level in sera of the 16 patients was $8810 \pm 13\,511$ IU/mL (range, 5–53 605), and mean total IgE for the 14 patients who displayed positive results for antigen-specific IgE antibodies (cases



Figure 3. Case 1. Marked lichenifications on the upper back.

Table 1. Clinical features of atopic dermatitis in the aged

Case	Age/sex	Onset (years)	Personal history of chronic eczema until young adult phase	Associated allergic diseases	Family history of allergic diseases	Clinical presentation	Severity [†]
1	70/M	60	Occasional appearances of eczema from 15 years	–	–	Erythroderma, partial prurigo	7.5
2	77/M	19	Eczema from 19 years	Rhinitis	–	Chronic eczema, partial prurigo	8
3	73/M	72	Occasional appearances of eczema from 29 years	–	–	Erythroderma, partial prurigo	8
4	82/M	77	–	–	–	Erythroderma	9
5	68/F	66	Occasional appearances of eczema from 20 years	–	–	Chronic eczema, hand eczema, blepharitis, AsD and urticaria	5
6	87/M	83	Eczema in the adolescent/young adult phase	Asthma in the childhood phase	–	Erythroderma	9
7	81/M	80	–	–	Grandchild with AD	Erythroderma	8
8	84/F	81	Eczema in the childhood phase	Conjunctivitis	–	Erythroderma	8
9	71/M	61	Eczema up to 5 years	Rhinoconjunctivitis	–	Erythroderma	8
10	80/M	66	–	Asthma in the infantile phase	Mother with pruritus	NuD, AsD, chronic prurigo	5
11	77/M	70	–	Urticaria in the childhood phase Pollinosis	–	Chronic eczema, NuD, AuD, blepharitis	5
12	84/F	81	–	Asthma from her 70s Rhinconjunctivitis	Daughter with AD	Erythroderma	8
13	77/M	75	Eczema up to 15 years	Asthma up to 15 years	Older sister with asthma	Erythroderma, partial NuD, nodular prurigo	8.5
14	68/M	67	–	Urticaria from 18 years	–	Chronic eczema, partial prurigo	5
15	70/M	51	–	–	Sister and child with AD	Chronic eczema, partial prurigo	4
16	81/F	74	–	Asthma from her 60s	Mother with asthma	Erythroderma	9

–, absence; AD, atopic dermatitis; AsD, asteatotic dermatitis; AuD, autosensitization dermatitis; NuD, nummular dermatitis; prurigo, prurigo forming papules and/or nodules. [†]Severity scoring of Rajika and Langeland:⁷ 3–4, mild; 4.5–7.5, moderate; 8–9, severe.

Table 2. Serum immunoglobulin (Ig)E antibodies levels in aged patients with atopic dermatitis

Case	Total IgE (IU/mL) (normal ≤ 400)	Antigen-specific IgE (MAST 26)				
		Class 3	Class 2	Class 1	Class 1/0	Class 0
1	53 605	–	4 Ag (So, Sh, Cr, EW)	21 Ag (the others)	1 Ag (Mu)	–
2	19 619	5 Ag (<u>DE</u> , <u>CD</u> , Sh, DE, HD)	4 Ag (Ri, Cr, AF, Mi)	10 Ag (TG, Sa, PN, CC, AT, CA, RM, CH, SVG, Tu)	7 Ag	–
3	15 238	1 Ag (DF)	–	1 Ag (Sh)	5 Ag	19 Ag
4	14 964	4 Ag (<u>DE</u> , HD CC, Mi)	–	1 Ag (TG)	8 Ag	13 Ag
5	11 002	8 Ag (DE, TG, SVG, CA, Ri, HD, RM, JC)	5 Ag (So, CWP, DF, Mu, CD)	12 Ag (Cr, CM, EW, AF, PN, Mi, Be, Sh, SA, Tu, CC, CH)	1 Ag	–
6	8 649	–	–	9 Ag (PN, Sh, DF, EW, CWP, DE, HD, TG, AF)	13 Ag	4 Ag
7	6 378	–	1 Ag (AF)	1 Ag (CA)	2 Ag	22 Ag
8	4 309	1 Ag (<u>DE</u>)	–	3 Ag (SVG, HD, TG)	16 Ag	6 Ag
9	2 413	2 Ag (DF JC)	1 Ag (TG)	1 Ag (SVG)	8 Ag	14 Ag
10	1 161	–	4 Ag (TG, SVG, CC, Mi)	1 Ag (RM)	–	21 Ag
11	1 119	5 Ag (<u>DE</u> , SVG, TG, RM, Ri)	5 Ag (JC, So, Mu, Mi, CWP)	2 Ag (HD, CC)	13 Ag	1 Ag
12	1 045	1 Ag (<u>DE</u>)	1 Ag (Cr)	1 Ag (HD)	4 Ag	19 Ag
13	714	–	1 Ag (DF)	–	2 Ag	23 Ag
14	574	–	6 Ag (AF, DF, JC, HD, EW, CD)	16 Ag (Sh, CWP, Mi, SVG, CC, CM, Tu, RM, PN, CA, CH, AT, Cr, Ri, So, Mu)	3 Ag	1 Ag
15	160	–	–	–	–	26 Ag
16	5	–	–	–	–	26 Ag

MAST 26 (SRL, Tokyo, Japan) antigen (Ag) abbreviations: AF, *Aspergillus fumigatus*; AT, *Alternaria tenuis*; Be, beef; CA, *Candida albicans*; CC, cheddar cheese; CD, cat dander; CH, *Cladosporium herbarum*; CM, chicken meat; Cr, crab; CWP, cultivated wheat pollen; DE, dog epithelium; DF, *Dermatophagoides farinae*; EW, egg white; HD, house dust; JC, Japanese cedar; Mi, milk; Mu, mugwort; PN, *Penicillium notatum*; Ri, rice; RM, ragweed mixture; Sa, salmon; Sh, shrimp; So, soybean; SVG, sweet vernal grass; TG, Timothy grass; Tu, tuna. Assessment: positive, class 3, 2 and 1; borderline, class 1/0; negative, class 0. Class 3 (with underline), ≥99.9; class 3 (without underline), 20.1–99.8; class 2, 11.3–20.0; class 1, 4.41–11.2; class 1/0, 1.01–4.40; class 0, ≥1.00 (Lumi count). Antigens are presented in order of value height from left to right side.

1–14) was $10\,056 \pm 14\,044$ IU/mL. Positive antigens in these 14 patients were as follows: *Dermatophagoides farinae* in 12 patients (85.7%), house dust and Timothy grass in nine patients (64.3%), sweet vernal grass in eight patients (57.1%) and milk and cheddar cheese in seven patients (50%). *D. farinae* was also the principal antigen in eight of the 14 patients (57.1%), and antibody levels to this antigen in five patients exceeded the highest limit (Table 2).

Skin manifestations of AD

Skin manifestations were predominantly observed in the trunk and extensor sites of the extremities in 16 patients (100%), flexure sites of the upper extremities in 15 patients (93.8%), flexure sites of the lower extremities in 14 patients (87.5%), and face and neck in 13 patients (81.3%). Conversely, noticeable skin manifestations were only observed in the antecubital region in four patients (25%) and the popliteal area in six patients (37.5%). In those areas, localized unaffected skin tended to be present, occasionally with some scratch dermatitis (Figs 1,4). Marked lichenifications localized in both areas were seen in one patient (case 12). Prurigo-form eruptions appeared mainly in the extremities. All patients showed more or less of the skin dryness as a manifestation of senile xerosis. Other stigma of AD developed as follows: red face in 10 patients (62.5%); Hertoghe's sign in six patients (37.5%); goose-skin in four patients (25%); facial pallor in three patients (18.8%); and dirty neck in one patient (6.3%) (Table 3).

Histopathology of AD skin lesions

On histopathological analysis, chronic eczematous reaction was observed in all skin specimens from eight examined patients (cases 1, 3, 4, 6, 7, 9, 13 and 16). Compared to control specimens, increased mast cell infiltration in the dermis was demonstrated in five of the seven patients with antigen-specific IgE antibodies (cases 1, 3, 4, 9 and 13), but not in the one patient with normal IgE levels in sera (Tables 2,4).

DISCUSSION

In this study, some characteristics of AD in the senile phase became apparent. In the analyses of



Figure 4. Case 1. Unaffected skin surrounded by flexural eczema and lichenifications is apparent in the antecubital area of the right arm.

clinical features (Table 1), aged patients showed a male dominance of senile AD with a man : woman ratio of 3:1. Three patterns of AD onset were apparent: (i) senile onset (cases 4, 7, 10–12 and 14–16); (ii) senile recurrence with a history of classic child AD (cases 8, 9 and 13); and (iii) senile recurrence and/or continuation of adult AD (cases 1–3, 5 and 6). Eczematous erythroderma and unclassified chronic eczema were the predominant clinical presentations.

The results of serum IgE analyses (Table 2) showed that senile-phase AD patients, as in other generations, could be divided into two groups: (i) patients with seropositive atopic diathesis, showing elevated levels of total IgE and antigen-specific IgE antibodies (cases 1–14); and (ii) patients with seronegative atopic diathesis, with personal and/or

Table 3. Skin manifestations in aged patients with atopic dermatitis (eczematous dermatitis¹ and other stigmas²)

Case	Face and neck	Trunk	Upper extremities				Lower extremities			
			Extensor sites	Flexure sites	Antecubital areas		Extensor sites	Flexure sites	Popliteal areas	
1	±/red face, Hertoghe's sign	++	++ prurigo	++ prurigo	-		++ prurigo	++ prurigo	±	
2	±	++	++ prurigo	+	±		++ prurigo	+	±	
3	±/red face, Hertoghe's sign	++	++	++	+		++ prurigo	++ prurigo	+	
4	±/red face	++	++	++	-		++	++	-	
5	±/facial pallor	+	+	+	-		+	±	-	
6	±/red face, Hertoghe's sign	++	++	++	±		++	++	±	
7	±/red face, Hertoghe's sign	++/goose skin	++	++	-		++	++	±	
8	±/red face, facial pallor	++	++	++	+		++	+	+	
9	±/red face, Hertoghe's sign, dirty neck	++	++	++	±		++	++	++	
10	-	++ prurigo	++ prurigo	++ prurigo	-		++ prurigo	++ prurigo	-	
11	±/red face, Hertoghe's sign	+	+	±	-		+	-	-	
12	+	±/goose-skin	+	+	±		+	+	±	
13	±/red face	++ prurigo/goose-skin	++ prurigo	++ prurigo	+		++ prurigo	++ prurigo	+	
14	-	++	++	++	-		++ prurigo	+	-	
15	±/red face	++ prurigo/goose skin	++	++	-		++ prurigo	++	-	
16	±/facial pallor	++	++	++	-		++	++	±	

t₊, absence; ±, slight; ++, presence; ++, with marked lichenification; prurigo, with prurigo forming papules and/or nodules. ¹Red face (including post-inflammatory brownish diffuse pigmentation), facial pallor, Hertoghe's sign, dirty neck, goose-skin (follicular lichenified papules).

Table 4. Histopathology and mast cell infiltration in the lesional skin of atopic dermatitis in the aged

Case	Histopathology	Mast cells
1	Chronic eczematous reaction	38.3 ± 6.0*
3	Chronic eczematous reaction	55.3 ± 11.4*
4	Chronic eczematous reaction	30.3 ± 6.8*
6	Chronic eczematous reaction	4.7 ± 2.5
7	Chronic eczematous reaction	3.3 ± 0.6
9	Chronic eczematous reaction	60.3 ± 5.5*
13	Chronic eczematous reaction	27.7 ± 2.1*
16	Chronic eczematous reaction	6.7 ± 3.8
Control	Chronic eczematous reaction	10.9 ± 3.6

Values represent mean number of mast cells per field (×400) and standard deviation (SD). *P < 0.001 (increased mean ± SD vs control).

family histories of AD and/or AD-associated allergic diseases (cases 15 and 16). Mean total IgE for 14 seropositive patients was $10\,056 \pm 14\,044$ IU/mL. Interestingly, total IgE levels were higher in patients with histories of adult AD (cases 1–3, 5 and 6) than in patients with histories of classic child AD (cases 8, 9 and 13). In the former patients, IgE production in the mechanisms of atopic allergy may have been continuously irritated by latent, irregular or persistent manifestations of adult AD. The major antigens were *Dermatophagoides* in 12 patients (85.7%), house dust and Timothy grass in nine patients (64.3%), sweet vernal grass in eight patients (57.1%) and milk and cheese in seven patients (50%). Similar to the findings of adult AD,¹ *Dermatophagoides* was also the principal antigen in eight patients (57.1%). Although positive correlations between serum IgE levels and mast cell numbers in skin lesions could not be obtained in every examined patient (Tables 2,4), histopathological analyses showed increased mast cell infiltration in lesional skin from five of the seven patients with seropositive IgE (cases 1, 3, 4, 9 and 13). Atopic IgE-mediated allergy may thus play an important role in the pathogenesis of skin lesions,⁹ even in senile AD.

Skin manifestations were demonstrated predominantly in the face and neck (81.3%), trunk and extensor sites of the extremities (100%), and flexure sites of the upper (93.8%) and lower (87.5%) extremities. Distributions of senile AD resembled those of adult AD,³ but the high morbidities in each body part might be associated with accumulations

of severe cases in the present study caused by the rigidity of the criteria defined by Hanifin and Rajka.⁵ Characteristic stigma of AD were also observed, such as red face (62.5%), Hertoghe's sign (37.5%), facial pallor (18.8%) and dirty neck (6.3%) in the face and neck, and goose-skin (25%) on the trunk (Table 3).

Marked lichenifications localized in the antecubital and popliteal areas, the most typical signs of classic AD, were only observed in one patient. These signs may be uncommon in senile AD.¹⁰ Conversely, localized unaffected skin, which could be surrounded by flexural eczematous dermatitis, was observed in antecubital areas of 12 patients (75%) and popliteal areas of 10 patients (62.5%) (Figs 1,4). These reverse signs might be typical in senile AD, but are also observed in the classic child AD and adult AD as atypical symptoms.¹¹

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