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Clinical characteristics of elderly patients with atopic dermatitis — a retrospective observational study

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Abstract: Atopic dermatitis (AD) is a chronic, recurrent inflammatory dermatosis. The most characteristic symptoms of the disease include itch, eczematous eruptions and excessive dryness of the skin. Elderly patients with AD represent a poorly characterized population because the physiological ageing, possible comorbidity and polypharmacy modify the clinical presentation typically observed in the younger age groups. The aim of the study is to comprehensively assess the clinical characteristics of elderly patients (>60 years old) with AD. Data were collected from 26 AD patients treated in the Department of Dermatology of the University Hospital in Krakow. Late-onset AD with generalized/prurigo lesions was the most predominant phenotype. Skin biopsy was required in 15 (58%) patients in the differential diagnosis process. Allergic rhinitis, a positive family history of atopy and xerosis were associated with a higher number of hospitalizations during the year prior to the last admission ($p = 0.034$, $p = 0.046$ and $p = 0.036$, respectively). Xerosis was more prevalent among subjects with polypharmacy ($p = 0.046$) and higher serum total IgE concentration ($p = 0.048$). AD in elderly patients is a new phenotype of the disease that requires careful differential diagnosis. Aged patients with an individual or family history of atopy, due to the increased incidence of severe exacerbations of AD, may benefit from the introduction of proactive therapy.

Keywords: elderly atopic dermatitis, clinical characteristics of patients, phenotype, atopy, differential diagnosis.

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Introduction

Atopic dermatitis (AD, atopic eczema) is a chronic and recurrent inflammatory dermatosis of a complex, multifactorial pathophysiology. Characteristic symptoms of the disease include itch and excessively dry skin, imposed by deterioration of the epidermal barrier and an abnormal immune response [1]. Currently, more than 230 million people worldwide suffer from AD, and therefore it is considered the most prevalent inflammatory skin disease [2].

The chronic course and exacerbations of AD with numerous visits to physicians of various specialties followed by a wide range of diagnostic as well as therapeutic interventions significantly affect the patient's quality of life [3]. Disorders of the central and peripheral nervous system, including sleep disorders and depression, are substantial comorbidities of AD, which is reflected by the historical names of atopic eczema (*nevrodermite diffuse*; Brocq 1902, *Die Neurodermitis*; Rost and Marchionini 1932) [4, 5].

The course of AD in elderly patients is subject to numerous alterations resulting from physiological senescence, multimorbidity (including the so-called geriatric giants), polypharmacy (possible drug interactions), as well as functional dependence [6]. Therefore, this group of patients (new AD phenotype) poses an exceptional challenge in the scope of diagnosis and treatment [7].

It should be emphasized that until the 1980s AD was not considered to occur in people of age over 50 years [8]. Prevalence in population aged over 60 years is estimated at 1–3% [9].

Despite numerous scientific reports investigating atopic eczema, studies disclosing the clinical characteristics of elderly patients with AD remain scarce. Considering the progressive ageing of the society, it is warranted to explore this research topic more intensively.

The purpose of the study is to assess the clinical characteristics of elderly patients (>60 years old) treated for AD in the Dermatology Department of University Hospital in Krakow, in the years 2012–2022.

Material and Methods

Data were collected from the electronic records of 26 patients admitted due to AD at the Inpatient or Outpatient (IPD or OPD, respectively) Department of Dermatology in the University Hospital in Krakow in the years 2012–2022. The study included patients who were >60 years old at the time of the last hospitalization or visit to OPD. The exclusion criteria were: age <60 years and the coexistence of other inflammatory skin diseases.

The diagnosis of AD in every subject was confirmed by a dermatology-venereology specialist with respect to the Hanifin-Rajka criteria [10]. Xerosis was assessed on the basis of the following clinical indicators described by Augustin *et al.*: visible scaling, roughness of the skin surface, reduced skin elasticity, and the presence of fissures [11]. Extrinsic AD (eAD) was recognized if: (1) serum total immunoglobulin E (tIgE) concentration >100 IU/mL and/or (2) allergen-specific IgE antibodies were identified (serum or prick tests). IgE concentration was assessed by fluorimetry in the UniCAP apparatus (Phadia, Stockholm, Sweden). If none of the above was found, an intrinsic AD phenotype (iAD) was diagnosed [12].

Information regarding basic demographic characteristics, clinical symptoms of the disease, the course of the diagnostic process and the implemented treatment were collected. The assessment of elderly patients included particularly: Charlson Comorbidity Index (CCI), dependence (determined if the patient reported the inability to independently perform more than one activity listed in the Katz scale [13, 14]) and polypharmacy (chronic use of >5 drugs). The number of admissions to OPD, exacerbations of the disease (including erythroderma) and hospitalizations during the year prior to the last admission to Dermatology Department was also recorded.

Clinical AD phenotypes were classified according to the dynamics and the age at which the first symptoms appeared (Table 1) following the classification used by Chello *et al.* [15].

Table 1. Classification of AD in the elderly (>60 years of age) according to the age of onset of symptoms and the dynamics of exacerbations and remissions of the disease [15].

— *Continous type* — first symptoms in childhood, no long-term remission with maintenance of symptoms until adulthood.
— *Late onset* — first symptoms in adulthood.
— *Outgrow-recurrence* — first symptoms in childhood, long-term remission of symptoms, recurrence in adulthood.

All analyzed laboratory tests were performed according to the standard protocol.

The study received a positive opinion of the Bioethics Committee of the Jagiellonian University in Krakow (No. 1072.6120.63.2022). It was conducted with respect to the principles set out in the Declaration of Helsinki.

Statistical Analysis

Interval data were presented as mean ± standard deviation or median and range — if the assessment of data in the Shapiro–Wilk test indicated a distribution other than normal. Quantitative data were presented as number and proportion of cases (*N*, %).

The comparison of nominal variables distributions' was performed with the χ^2 test or the 2-tailed Fischer's exact test (if the expected values for any group were <5).

The groups were compared using the Student's t-test (or Welch's test in the case of heterogeneity of variance in Levene's test) or the Mann–Whitney *U* test (in the absence of a normal distribution of variable in any of the groups).

The Spearman rank correlation (*r*) was used to determine the strength and direction of the relationship between the interval variables.

If data on a given parameter were not available (missing data), cases were not included in the analysis. In all statistical tests the level of significance was decided to be $\alpha = 0.05$. All analyzes were performed using Dell Statistica (Data Analysis Software System), version 13.3.

Results

The study included 26 patients (15 men, 11 women) aged >60 years (mean 72.3 ± 7.0) who met the inclusion criteria. The clinical characteristics of the study participants are presented in Tables 2 and 3. For further analysis, the patients were divided according to the clinical phenotype of AD, into eAD and iAD (n = 19 [73%] and n = 7 [27%], respectively).

Table 2. General characteristics of the study group. Data are presented as mean ± SD, Me [interquartile range Q1–Q3] or as number and percentage of cases N(%) from a given column.

Feature	Total (N = 26)	eAD (N = 19)	iAD (N = 7)
Age (years)	72.3 ± 7.0	72.8 ± 6.6	70.7 ± 8.2
Sex (female/male)	11 (42%) vs 15 (58%)	9 (47%) vs 10 (53%)	2 (29%) vs 5 (71%)
Family history of atopy	6 (23%)	5 (26%)	1 (14%)
Comorbidities — atopic			
Allergic asthma[1)]	9 (35%)	9 (47%)	0 (0%)
Allergic rhinitis	5 (19%)	4 (21%)	1 (14%)
Food allergy	2 (8%)	1 (5%)	1 (14%)
Allergic conjunctivitis	1 (4%)	1 (5%)	0 (0%)
Comorbidities — non-atopic			
Hypertension	11 (42%)	8 (42%)	3 (43%)
Diabetes type 2	5 (19%)	4 (21%)	1 (14%)

Table 2. cont.

Feature	Total (N = 26)	eAD (N = 19)	iAD (N = 7)
Ischaemic cardiac disease	5 (19%)	4 (21%)	1 (14%)
Atrial fibrillation	5 (19%)	4 (21%)	1 (14%)
Polypharmacy	17 (65%)	13 (68%)	4 (57%)
tIgE (IU/mL)[2)]	557 [62–1973]	1105 [450–2660]	42 [19–78]
Eosinophils in peripheral blood count (10^3/μL)	0.23 [0.02–0.63]	0.27 [0.02–0.77]	0.17 [0.01–0.58]

[1)] eAD vs iAD — p = 0.058
[2)] eAD vs iAD — p <0.001
Abbreviations: AD — atopic dermatitis; eAD — extrinsic AD; iAD — intrinsic AD; Me — median; Q — quartile; SD — standard deviation; tIgE — total immunoglobulin E.

Table 3. Clinical characteristics of AD among the study participants. Data are presented as Me [min.–max. range] or as the number and percentage of cases N(%) from a given column.

Characteristic	Total (N = 26)	eAD (N = 19)	iAD (N = 7)
Dynamics of AD course			
Continous type *Late onset* *Outgrow recurrence*	2 (8%) 23 (88%) 1 (4%)	2 (11%) 16 (84%) 1 (5%)	0 (0%) 7 (100%) 0 (0%)
Number of visits in OPD in the last year	3 [0–8]	3 [0–8]	4 [1–8]
Number of hospitalizations in the last year			
0 *1* *2*	16 (62%) 5 (19%) 5 (19%)	12 (63%) 4 (21%) 3 (16%)	4 (57%) 1 (14%) 2 (29%)
An episode of erythroderma within the last year	5 (19%)	5 (26%)	0 (0%)
Xerosis[1)]	16 (62%)	14 (74%)	2 (29%)
Clinical phenotype[2)]			
Generalized/prurigo *Chronic hand eczema* *Face and neck* *Nummular eczema*	21 (81%) 0 (0%) 3 (12%) 2 (8%)	16 (84%) 0 (0%) 3 (16%) 0 (0%)	5 (71%) 0 (0%) 0 (0%) 2 (29%)

Table 3. cont.

Localization of lesions			
Face	17 (65%)	13 (68%)	4 (57%)
Neck	10 (38%)	9 (47%)	1 (14%)
Upper extremities[3)]	24 (92%)	19 (100%)	5 (71%)
Lower extremities	19 (73%)	15 (79%)	4 (57%)
Trunk	20 (77%)	15 (79%)	5 (71%)
The need to perform a biopsy in the process of the differential diagnosis	15 (58%)	12 (63%)	3 (43%)

[1)] eAD vs iAD — p = 0.067
[2)] eAD vs iAD — **p = 0.036**
[3)] eAD vs iAD — p = 0.063
Abbreviations: AD — atopic dermatitis; eAD — extrinsic AD; iAD — intrinsic AD; Me — median; OPD — outpatient department.

Of the atopic comorbidities, allergic asthma was the most common (9 patients, 35%), while from the non-atopic diseases them most frequent was hypertension (11 patients, 42%).

Geriatric evaluation revealed a median CCI of 3.5 (range from 2 to 6). Polypharmacy was present in 17 patients (65%). Dependence was recognized in 2 patients (8%).

In 23 (88%) patients AD symptoms occurred for the first time in adulthood (*late onset* type), and in 16 of them (62%) over 60 years of age. The predominant clinical phenotype was *generalized/prurigo* (n = 21, 81%), and the most common localization of the lesions were the upper extremities (n = 24, 92%) (Table 3).

Most of the patients applicated emollients (n = 26, 100%), topical glucocorticosteroids (TCS; n = 25, 96%) and antihistamines (n = 22, 85%). Only 3 (12%) participants used topical calcineurin inhibitors (TCIs). Cyclosporine (CsA) therapy was initiated in 3 (12%) subjects, while 4 (15%) of them were treated with phototherapy (n = 2 [8%] UVB 311 nm, n = 2 [8%] PUVA) (Fig. 1).

Skin biopsy was performed in 15 (58%) patients during the differential diagnosis of AD.

The median serum tIgE concentration in the patients was 557 IU/mL (Q1 = 62 IU/mL, Q3 = 1793 IU/mL).

Allergic rhinitis (AR), positive family history of atopy and xerosis recognized by a dermatology specialist were associated with a higher frequency of hospitalization in the year preceding the last visit to the Dermatology Department (p = 0.034, p = 0.046 and p = 0.036, respectively) (Table 4). However, no relationship was found between the analyzed variables and the number of visits to OPD during the year preceding the last admission to the Department of Dermatology.

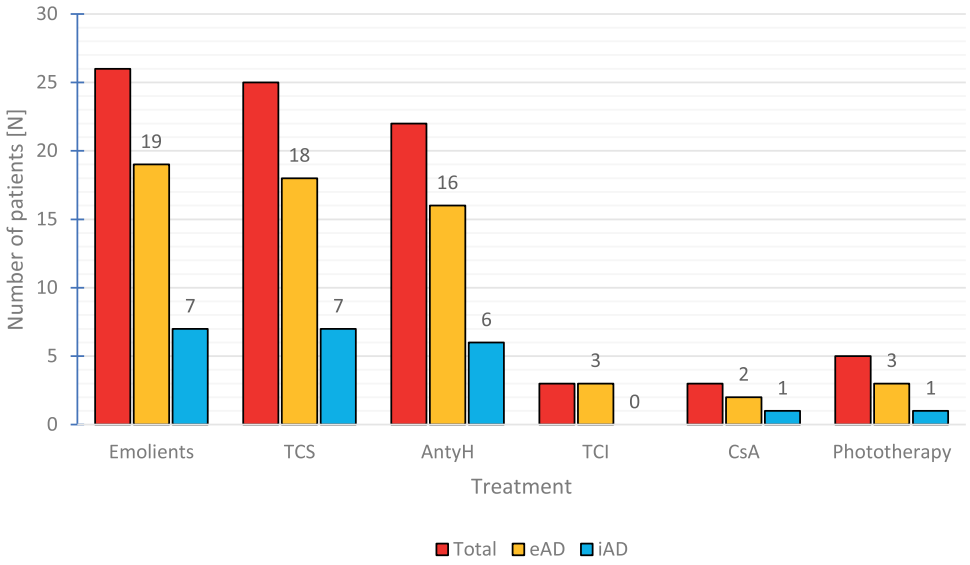

Fig. 1. Treatments used by patients from the studied group. The clinical phenotype was divided into eAD and iAD.

Table 4. Factors related to the number of hospitalizations in the year preceding the last admission to Dermatology Department. In the table, the data are presented as the mean ± SD to more clearly illustrate the differences between the groups, while the Mann–Whitney *U* test was used in the calculations (analyzed relationship between step and dichotomous variables).

Feature	No	Yes	p-Value
Sex (female)	0.5 ± 0.9	0.7 ± 0.7	0.5
Atopic history in family	0.4 ± 0.8	1.2 ± 0.8	**0.046**
Allergic asthma	0.6 ± 0.9	0.6 ± 0.7	0.9
Allergic rhinitis	0.4 ± 0.7	1.4 ± 0.9	**0.034**
Food allergy	0.5 ± 0.8	1.5 ± 0.7	0.2
Hypertension	0.6 ± 0.8	0.5 ± 0.8	0.9
Diabetes type 2	0.6 ± 0.8	0.6 ± 0.9	0.9
Polypharmacy	0.3 ± 0.7	0.7 ± 0.8	0.3
Xerosis	0.1 ± 0.3	0.9 ± 0.9	**0.036**

Abbreviations: SD — standard deviation.

The subjects with xerosis, had higher concentrations of tIgE in the serum compared to the remaining (Me: 1501 [Q1: 614, Q3: 2900] IU/mL vs Me: 201 [Q1: 42, Q3: 616] IU/mL] , p = 0.048). To this, 81% of patients with polypharmacy had xerosis, as opposed to 40% observed in the other subjects (p = 0.046).

Discussion

To the best of our knowledge, this is the first such study on a group of Polish patients from the Lesser Poland region. Furthermore, to our knowledge, we are the first in the literature to address aspects of AD that are relevant in the context of care of elderly patients. Our analysis identified several clinically relevant factors associated with disease exacerbations. The investigated group showed similarities to populations described by other researchers, suggesting that there is an appropriate level of external validity.

Williamson *et al.* suggested that the clinical symptoms of AD manifest in the elderly due to the combination of few triggering factors [16]. Ageing leads to loss of skin elasticity, thinning of the epidermis, a decrease in lipid content and a decrease in the number of tight junction proteins such as, e.g., occludins or claudins [17]. The following defect of the epidermal barrier enables an increased transfer of allergens, bacteria, and irritants [18]. Dysfunction of the skin barrier and a abnormal immune system responses lead to immunization and ultimately the symptoms of AD [1]. Aging is followed by changes in the functionalities of the immune system, such as a decrease in the number of Langerhans cells and a deterioration of the antigen-specific immune response [19]. It was shown that in patients aged >65 (compared to those in the age group 18–64) after exposure to various skin-damaging factors, TEWL (transepidermal water loss) requires significantly longer time to return to baseline values [20].

Moreover, multiple factors related to the ageing process modify the classic (i.e. observed in younger patients) course of AD: the presence of concomitant diseases (geriatric syndromes), (poly)pharmacy, as well as abnormal sweating and the composition of the skin and the gastrointestinal microbiome [16].

In the study by Wang *et al.* on patients over 60 years of age who suffered from AD, the onset of the disease in adulthood was approximately 5-fold more common than in childhood [21]. Similarly, Chello *et al.* identified a late-onset form in over 60% of elderly patients (in this study defined as a group >65 years of age) [15]. Our data are consistent with the above, as we observed that almost 90% of AD cases had onset in adulthood (including ~60% of diagnoses over 60 years of age). Before the establishment of a final diagnosis, up to 58% of patients required skin biopsy to complete the differential diagnosis. This emphasizes the significance of histopathological evaluation in differentiating AD from other chronic skin conditions (especially cutaneous lymphoma) in elderly patients [22].

In our study, the male to female ratio was 1.5:1, similar to that described by Wang *et al.* (2.25:1) and Tanei *et al.* (2.16:1) [21, 23]. Only Chello *et al.* investigated a group in which the proportion of women was higher (1.53:1) [15]. Analyzes of national registries from Great Britain and Finland indicate that AD in the elderly is more prevalent among men than women [24, 25]. The explanation for this observation is not definitively established. Presumably, estrogens involved in the regulation of the immune system function, as well as androgens affecting the secretion of sebum, both play a role. Estrogens exhibit antioxidant properties, protect against photoaging modulate telomerase activity, and are hypothesized to slow down ageing by preserving telomere length [26]. The decline in testosterone concentration in men is associated with augmented synthesis of T_H2 cytokines, such as IL-4, IL-5 and IL-13 [27]. In older men, this may predispose to development of eAD subtype. In our study, the majority of patients suffered from eAD (73%, a proportion similar to observed in younger age groups). In another study conducted in the Polish population, eAD was also more common [28].

The dominant clinical phenotype in our study was generalized/prurigo (81% of patients), also observed most frequently by Chello *et al.* (55% of patients) [15]. Similarly, in another study in the Polish population, generalized skin lesions prevailed [28]. In their research, Wang *et al.* noted the less frequent involvement of the face, neck, elbow, and popliteal fossae, as well as the flexor surfaces of the upper limbs and the dorsal surface of the hands, compared to the younger group of patients. Opposingly, lesions in the area of the trunk, lower limbs and extensor surfaces of the upper limbs prevailed [21]. In our study, the most common location of the lesions was the upper limbs (92%), and relatively less often they occurred in the area of the face and neck. Tanei described similar observations (dominant generalized lesions, involvement of the upper limbs in 95% of cases) [23].

The coexistence of other atopic diseases was found in 54% of our subjects and similar incidents were reported by other researchers (Chello *et al.*: 65%, Bozek *et al.*: 60% and Tanei *et al.*: 50%) [15, 23, 28]. Concomitant atopic diseases are known to increase the risk of worse control of AD symptoms, although this relationship was not previously assessed in elderly patients [12, 29, 30]. Our analysis indicate that such patients particularly frequently suffer from severe AD exacerbations.

Patients were treated with respect to the proper recommendations for the adult population. Therefore, the crucial principles of management were avoiding contact with allergens and regular application of emollients. TCS were used by the majority of patients, while only three subjects used TCI. The less frequent use of TCIs, compared to TCSs, might be the consequence of low awareness of the advantages of their use (including proactive therapy). Most of the patients took antihistamines. The use of these drugs is currently not recommended by the Polish Society of Dermatology (PTD) and the European EuroGuiDerm guidelines [31, 32]. Nevertheless, the PTD

guidelines indicate that some patients may benefit from using antihistamines — especially if other treatments were not effective in controlling pruritus or in case of coexisting AR.

Only three subjects were treated systemically with CsA. This may have been due to the presence of objective contraindications or concerns about the side effects of systemic treatment, including in particular the impact on blood pressure and kidney function.

The frequency of hospitalization because of AD exacerbation was significantly higher in the group of patients with a positive family history of atopy, diagnosed AR, as well as xerosis recognized by a dermatologist. So far, such an analysis has not been described in the literature. Patients with AR were hospitalized twice as frequently as patients without this comorbidity. It could be hypothesized that stronger sensitization leads to aggravated symptoms after exposure to the allergen in patients with two or more atopic diseases. We also found that a family history of atopy is associated with an increased rate of hospitalization. This may indicate a genetic predisposition to a more severe course of AD.

Xerosis was more common in patients with polypharmacy (81% vs 40% in the remaining group). This ailment in elderly patients may stem from difficulties in the correct application of emollients and was also associated with an increased frequency of hospitalization due to AD exacerbations. Lesser self-reliance of some elderly patients may tamper systematic medicines taking with consequent exacerbations of the disease. Xerosis also significantly contributes to the aggravation of pruritus [33]. In addition, patients with severe xerosis had significantly higher serum tIgE concentrations compared to the other subjects. The group assessed by Tanei was characterized by high serum tIgE concentrations, while Wang *et al.* observed significantly lower tIgE concentrations in elderly patients [9, 21]. It should be taken into account that high concentrations of tIgE are common finding among elderly AD patients, which reflects the dominance of T_H2-dependent inflammatory processes [34].

The median CCI was 3.5 (range 2 to 6), and polypharmacy was used in 17 patients (65%). Elderly people, due to the common multimorbidity, often take multiple medicines, which significantly increases the risk of interactions and side effects. It is worth emphasizing that the treatment of AD alone contributes to an increased burden of polypharmacotherapy (the classic WHO definition includes also topical drugs).

Study limitations

This is a single-center retrospective study in a relatively small population. Therefore, it is possible that the analyzed relationships between the variables are an inaccurate estimate of the real relationships. They also do not constitute the basis for inferring cause and effect relationships.

Conclusions

Elderly people are an unique population of AD patients, which is distinguished by a different clinical picture, challenging diagnostic process, as well as uncommon modifiers to the course of the disease.

In the studied population the dominant pattern of the dynamics and clinical phenotype of AD was late onset, generalized/prurigo. The most common location of lesions were the upper limbs.

The study showed that elderly patients with a family or personal history of atopy are at particular risk of severe AD exacerbations with an increased frequency of hospitalization. Therefore, proactive therapy might be particularly beneficial for these patients.

In the treatment of elderly patients, special attention should be paid to the characteristics of this population, such as multimorbidity and polypharmacy. Taking into account other comorbidities in the elderly, such as renal failure, hypertension, or dementia, awareness should be raised when using drugs such as methotrexate or cyclosporine.

Conflict of interest

None declared.

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