Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
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ORIGINAL RESEARCH

OPEN ACCESS

Immunological differences between atopic dermatitis, psoriasis, and their combination in adult patients

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Received 7 December 2021; Accepted 6 May 2022
Available online 1 July 2022

KEYWORDS
Atopic Dermatitis;
Cytokine;
Immunoglobulin E;
Lymphocytes;
Psoriasis

Abstract
Objectives: The simultaneous occurrence of psoriasis (PS) dominated by Th1 lymphocytes and atopic dermatitis (AD) driven by Th2 cells is rare. This study analyzed a group of adult patients with concomitant PS and AD (ADPS) and compared the cytokine profiles of these patients with those of subjects with homogenous PS or AD and healthy controls.
Materials and methods: All patients underwent dermatological examinations, including assessment of Scoring Atopic dermatitis (SCORAD) index and Psoriasis Area Severity Index (PASI) scores, TNF-α, IFN-γ, Il-2, Il-4, Il-5, Il-6, Il-8, Il-12, I-17A, Il-18, Il-22, Il-33, and T. There were 39 patients with a diagnosis of ADPS, 45 patients with PS, 47 patients with AD, and 42 healthy controls.
Results: Patients with ADPS were mainly men with a proportional distribution of skin lesion areas. Significant differences were observed in the concentration of Il-17A between patients with ADPS and those with AD or PS and controls, which were as follows: 16.1 ± 5.4, 5.8 ± 2.1, 5.0 ± 3.1, and 3.3 ± 1.8 pg/mL, respectively. In conclusion, AD and PS might coexist as a combination disease. The role of T helper 17 cells may be more essential than previously thought.

Introduction

Psoriasis (PS) and atopic dermatitis (AD) are clinically different. Moreover, AD and PS are heterogeneous, and their pathomechanisms are complex and have not been defined in detail. AD is an early childhood disease that continues into adulthood in some patients. Briefly, the disease is driven by the overproduction of Il-4, Il-13, and immunoglobulin E (IgE) by Th2 cells. However, low IgE values and high Th1 activity are observed.[1,2] PS occurs mainly in adult patients and is driven by Th-17 and Il-17 lymphocytes. The activation of Th-22 and Th1 pathways with increased Il-22 and IFN gamma production are observed in both conditions. AD and PS constitute a significant health problem due

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https://doi.org/10.15586/aei.v50i4.557

to their high prevalence and treatment difficulties.[1-3] The coexistence of AD controlled by Th2 cells and PS driven by Th17 cells is uncommon, and it affects adults and children. The order in which these diseases appear may vary, and the final diagnosis may be made only after a longer period of observation.[4,5]

The aim of this study was to compare the clinical characteristics and cytokine profiles of adult patients with concomitant AD and PS (ADPS) with those of patients with AD or PS alone and healthy controls.

Materials and Methods

This prospective study evaluated 39 patients with concomitant ADPS and compared their profiles with 45 patients with AD, 47 patients with PS, and 42 healthy controls.

Patients were eligible if they were diagnosed with AD and/or PS, were between 18 and 65 years of age, of Caucasian race, and had mild-to-severe AD symptoms according to the objective SCORing Atopic Dermatitis (SCORAD) Index and/or mild-to-severe PS according to the objective PASI (Psoriasis Area Severity Index). Patients were observed for 12 months or more.

The AD diagnosis was based on the patient's clinical characteristics according to Hanifin and Rajka criteria.[6]

PS was confirmed based on typical morphology (well-demarcated psoriatic plaques, guttate disease, acral fingertip eruptions, or napkin or pustular psoriasis) and history.[7,8]

Patients with a diagnosis of both AD and concomitant PS were observed for a minimum of 12 months to confirm the diagnosis. The exclusion criteria were as follows: (1) presence of other active skin diseases, including non-specified eczema and erythroderma, (2) those undergoing immunosuppressant treatment including oral corticosteroids, (3) presence of other chronic diseases, and (4) lack of a written consent.

All the studied patients were treated with basic local treatment, including topical steroids. Antihistamines and emollients were used in patients with AD. Patients on systemic steroids, UV therapy, or biological and other immunosuppressive therapies were excluded from the study.

Study protocol

All patients underwent complete dermatological examination, including the assessment of SCORAD and PASI scores, and blood samples were obtained for cytokine analysis. TNF- α, IFN-γ, Il-2, Il-4, Il-5, Il-6, Il-8, Il-12, Il-17A, Il-18, Il-22, and Il-24 were measured using ELISA (Thermo Fisher Scientific, US). The minimum detectable concentration of analyzed cytokines is $<$10 pg/mL in blood serum according to the manufacturer's expected detection level of IFN-γ (IU/mL), which was 0.3 IU/mL.[9]

Statistical analysis

Statistical analysis was carried out using Statistica 8.2 (SaftPOl, Krakow, Poland). The Wilcoxon test or Student's t-test was performed to compare relevant variables. $P<0.05$ was considered significant.

Results

The characteristics of the groups, including family history and area of the affected skin, are presented in Table 1. There was a preponderance of males in the ADPS group compared to the rest of the groups. In the ADPS group, the distribution of the infected skin area was similar to that in the PS group, and the trunk area was less frequently affected in the ADPS group than in the AD group. The diagnosis of arthritis was relatively rare in ADPS patients and comparable to that in AD patients. In patients with ADPS, well-demarcated psoriatic plaques were most common among all forms of this disease. Severe disease was observed in 18 (46%) patients with ADPS as well as in 17 (39%) patients with AD and 19 patients with PS (40%).

The cytokine profile in the blood serum of studied patients in comparison to that in the blood serum of controls was presented in Table 2.

Discussion

Adult patients with ADPS analyzed in this study seem to be the largest group analyzed in the literature to date. Most of the patients diagnosed with ADPS had symptoms of AD or PS in childhood, and they had both diseases before the age of 18 (Due to the lack of detailed documentation, the data was not published.). The order of appearance of these diseases was different but similar to those described by other authors previously. Most of them experienced these diseases at different life stages, such as development of AD in childhood, years of remission, and the development of PS later in adulthood. The concurrence or flare-up of both diseases at the same time or coincidence in the same period of life (e.g., when one flares up, the other subsides or vice versa) was relatively rare. This is consistent with the earlier observations by other authors on adults and children.[1,4,10]

In contrast to children with coexisting AD and PS, the form characterized by well-delimited plaque was dominant in adults, and other forms of psoriasis were less frequent. However, the small sample sizes make the comparison difficult. As in other observations, there was a preponderance of males in the ADPS group, but it is difficult to explain this relationship.[4,11] A potential explanation is that a different immune and hormonal profile determine the emergence of such a disease.

The obtained cytokine profiles showed many similarities between the groups. This phenomenon shows the systemic nature of these diseases, which is especially important compared to the control group. This data is consistent with other observations.[3,12]

However, significant differences were also noticed among the concentrations of the tested cytokines. The significantly higher concentration of IL-17A, which distinguished the ADPS group from the rest of the groups, underscores the importance of the stimulation of Th17 lymphocytes in this disease and possibly their crucial role. T helper 17 cells produce cytokines, which affect keratinocyte proliferation and stimulate inflammation.[13,14] This role of T helper 17 cells may be crucial especially in AD concomitant with PS. Similar observations were made previously in

Table 1 Characteristics of the studied population.

	ADPS (n=39)	AD (n=45)	PS (n=47)	Controls (n=42)
Mean age (years)	45.5±11.3	39.6±14.5	43±9.1	40.9±10.2
Female (%)	12 (31)*	28 (62)	30 (64)	30 (71)
Other atopic diseases	4 (10)	15 (33)**	2(4)	-
BA (%)	11 (28)	33 (73)**	5 (11)	1 (2)
AR (%)				
Family history				
ADEA (%)	8 (21)	32 (71)***	9 (19)	7 (17)
PS (%)	10 (26)	9(20)	4 (25)	7 (17)
Area of affected skin:				-
head	13 (33)	16 (36)	16 (34)	
arms	17 (44)	19 (42)	18 (38)	
legs	14 (36)	16 (35)	17 (36)	
trunk	20 (51)	8 (18)****	23 (49)	
nails	9 (23)	10 (22)	14 (30)	
SCORAD	41±13	58±24	-	-
PASI	27±9	-	34±9	-
BMI>23	11 (28)	10 (22)	9 (19)	11 (26)
Confirmed arthritis	4 (10)	1 (2)	15 (32)*****	

AD: Atopic dermatitis; AR: Allergic rhinitis; ADEA: Atopic diseases; ADPS: AD concomitant with PS; BA: Allergic bronchial asthma; BMI: Body mass index; PASI: Psoriasis Area and Severity Index; PS: Psoriasis; SCORAD: Scoring atopic dermatitis scale. *Significant domination of male in the ADPS group compared to AD and PS groups ($P<0.05$); **More frequent BA and AR in the AD group compared to ADPS and PS groups ($P<0.05$); ***More frequent family history of ADEA in patients with AD than in patients with PS or AD ($P<0.05$); ****The skin of the trunk was more frequently affected in patients with AD ($P=0.05$); *****Arthritis was more frequent in the PS group than in the other groups ($P<0.05$).

Table 2 The cytokine profile in the blood serum of studied patients (values are the mean±SD) in comparison to that in the blood serum of controls.

Cytokines	ADPS (n=39)	AD (n=45)	PS (n=47)	Controls (n=34)
TNF-α (pg/mL)	18.9±10.2	21.5±11.3	29±9.2	10.5±6.3*
IFN-γ (IU/mL)	0.41±0.13	0.38±0.11	0.56±0.29	0.32±0.12
Il-2 (pg/mL)	40.2±8.1	34.9±5.8	147.9±90**	145±102**
Il-4 (pg/mL)	351±196***	298±113***	60.8±11.3	54±11
Il-5 (pg/mL)	1384±658	1080±780	1156±890	4.3±19*
Il-6 (pg/mL)	20.9±7.2	49.9±24.2	20.9±3.3	19.5±16
Il-8 (pg/mL)	28.8±10.3	22.8±11.6	25.2±8.4	
Il-12 (pg/mL)	30.1±12.7	29±10.3	27.8±12	19±11
Il-17A (pg/mL)	16.1±5.4****	5.8±2.1	5.0±3.1	3.3±1.8
Il-18 (pg/mL)	89.4±22.7*****	220±115	189±85	32±19*****
Il-22 (pg/mL)	13.7±5.8	15.9±8.1	54±10.4	3.1±2.1*
Il-24 (pg/mL)	130.6±87.9	121±75	450±129	32±7.5*

AD: Atopic dermatitis; ADPS: AD concomitant with PS; PS: Psoriasis.
*Significantly lower mean serum concentration in the control group than in the other groups ($P<0.05$); **Significantly higher mean serum concentration in the control and PS groups than in ADPS and AD groups ($P<0.05$); ***Significantly higher mean serum concentration in the ADPS and AD groups than in the PS and control groups ($P<0.05$); ****Significantly higher mean serum concentration in the ADPS group than in other groups ($P<0.05$); *****Significantly lower mean serum concentration in ADPS and control groups than in AD and PS groups ($P<0.05$).

children, which showed the relatively long-term effect of this Th-17 mechanism.[5] In addition, the presence of a high concentration of Il-4, as in AD, emphasizes the undeniable importance of the Th2 lymphocyte stimulation mechanism, indicating an essential interaction of these two mechanisms of inflammation. This is consistent with the data in the literature.[15,16] However, the relatively low values of Il-17A in PS patients compared to those observed in other studies may indicate ambiguity regarding the importance of Il-17A in this disease.[17,18]

On the other hand, in a small group of patients, the possible presence of Il-17A in the skin and not in the blood serum may indicate the unreliability of this result, making it a limitation of work. The analysis of the infiltration of subpopulations of Th1, Th17, and Th2 lymphocytes in the skin could more accurately explain the complex immune mechanism involved in ADPS. Because such attempts were made only in individual patients, it was difficult to make general conclusions.[1,16,17] The lack of determination of other types of Il-17, which may also play an essential role in the mechanism of the analyzed diseases, and the relatively small groups of patients and doubts regarding the final classification of skin lesions despite the performance of skin biopsy were some of the other limitations of this study.

It is worth emphasizing that in a dozen or so cases, biopsies of skin lesions were performed on the examined patients, and in many cases, there was no final decision on their type (data not published). Patients with suspicious skin lesions were, however, excluded from the study.

Conclusion

AD and PS might coexist, resulting in overlapping of disease characteristics. T helper 17 cells seem to be crucial in the underlying mechanism.

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