

## Pityriasis Alba, a New Clinical Clue for Extrinsic Atopic Dermatitis

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### Abstract:

**Background:** *No clinical clues to differentiate between extrinsic atopic dermatitis (eAD) and intrinsic atopic dermatitis (iAD).*

**Aim:** *To compare presence of Pityriasis Alba (PA) in patients with extrinsic and intrinsic type of AD.*

**Subjects & Methods:** *IL-4 and Ig-E were measured in 85 Patients' serum with enzyme linked immune sorbent assay (ELISA). Forty three patients with (eAD) (group I) (n=43) and forty two patients with (iAD) (group II) completed the study (n=42).*

**Results:** *There was statistically significant correlation between PA and (eAD).*

**Conclusion:** *Pityriasis Alba could be used as a pathogenic clue in differentiating extrinsic AD from intrinsic AD.*

**Keywords:** *extrinsic atopic dermatitis; intrinsic atopic dermatitis; Immunoglobulin-E; Interleukin-4; Pityriasis alba.*

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### 1. INTRODUCTION

The most common hypopigmentary disorder was Pityriasis Alba (24.7%) [1]. PA is a skin disorder that presents with asymptomatic, ill-defined, slightly scaling patches with variable hypopigmentation [2]. Although its etiology is not well established, several factors are implicated including infection (Pityrosporum, Streptococcus, Aspergillus and Staphylococcus), nutritional deficiencies, atopy and dry skin, environmental factors (such as variations in temperature and air humidity, altitude and excessive exposure to sun) but none has been confirmed [3].

AD is categorized into two groups according to the laboratory findings and associated diseases. Non-allergic AD, nonatopic eczema, atopiform dermatitis or nonatopic AD [4] are used interchangeably with intrinsic atopic dermatitis (iAD), which has normal serum IgE levels and it is found in a relevant proportion of all AD patients [5]. The extrinsic atopic dermatitis (eAD) is called IgE-associated dermatitis and is frequently related to allergic bronchial asthma or allergic rhinoconjunctivitis [6-8].

Interleukin-4 (IL-4) has a role in differentiation of naive helper T cells (Th0 cells) to Th2 cells. Afterwards, Th2 cells produce more IL-4 when activated by IL-4 which in turn leads to autocrine stimulation that prolongs Th2 responses. A prominent activity of IL-4 is the stimulation of class switching of the immunoglobulin genes of B cells [9]. Aggregation of antigens and binding of Ig-E to the FcεRI on mast cells ends in releasing mediators from the cells like histamine, leukotrienes, and certain interleukins [10]. These chemicals cause many of the symptoms associated with allergy, such as local inflammation in eczema, airway constriction in asthma, increased vascular permeability, and increased mucus secretion in allergic rhinitis. These chemicals are presumed, to permit other immune cells to enter tissues, and lead to a potentially fatal drop in blood pressure as in anaphylaxis [9-10].

There aren't clinical diagnostic tools for distinguishing iAD from eAD (5). However, there is no report to compare the skin conditions between iAD and eAD patients. The purpose of this study was to compare the presence of PA in patients with extrinsic and intrinsic type of AD and if it could a clue for distinguishing them.

## 2. SUBJECTS AND METHODS

### Subjects

This descriptive comparative study was carried out in Dermatology outpatient clinic, Suez Canal University Hospital for a period of 6 months in accordance with the guidelines of the Helsinki Declaration, and was performed after obtaining the informed consent from all parents of the children.

By interviewing with 233 children; 148 were excluded because either receiving medical treatment, having other skin diseases, having other systemic diseases or those who refused to participate. So, only 85 patients with atopic dermatitis enrolled. Patients were assigned in two groups: 43 patients with (eAD) and 42 patients with (iAD) according to Tokura classification [11] by assessing them serologically (IgE), clinically, Immunologically (IL-4). IgE was considered to be normal if <20 Iu/ml, Borderline 20-100 Iu/ml, and high if >100 Iu/ml (cut-off value for an elevated IgE level was set at 100 IU/ml) [12-13]. IL-4 cut off point  $\geq 0.02$  pg/ml [14]

### Methods

All of the studied patients were subjected to the following:

Full history-taking, general and systemic examination with special emphasis on presence or absence of PA. Serum levels of Ig-E and IL-4 were measured in all subjects by ELISA (a polystyrene microtiter plate) (ELISA kits from BD, USA) according to the manufacturer's protocol.

## 3. STATISTICAL ANALYSIS

Statistical analysis was performed using the program SPSS version 15 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean  $\pm$  SD while qualitative data were expressed as numbers and percentages (%). Student's t-test was used to test the significance of difference for quantitative variables that follow normal distribution and chi-square was used to test the significance of difference for qualitative variables. A probability value (P value) < 0.05 was considered statistically significant.

## 4. RESULTS

In 85 patients, there were 50 females (59.5%) and 34 males (40.5%) with a mean age of  $9.7 \pm 8.4$  years, ranging from 3 to 18 years. Serum level Ig-E and IL-4 were statistically significantly higher in eAD group versus iAD group. Mean  $\pm$  SD of serum level of Ig-E and IL-4 were ( $230.26 \pm 277.14$  and  $69.53 \pm 19.72$ ) in eAD group versus ( $72.76 \pm 125.13$  and  $30.13 \pm 21.92$ ) in iAD group respectively [Table (1)]. Family history of PA and AD was positive in 90.5 % and 100% respectively in eAD group, which was significantly higher than iAD group [Table (2)]. There was a significant positive correlation between PA and eAD ( $r = 0.810$  and P value < 0.001) [Table (3)]

**Table1.** Demographic data of the Extrinsic AD and Intrinsic AD

Variable			Extrinsic AD		Intrinsic AD		t-test	P-value
			No.	%	No.	%		
Ig-E Iu/ml	Normal	<20	0	0	39	92.8	2.6	0.005*
	Borderline	20-100	0	0	3	7.1	2.7	0.008*
	High	>100	43	100%	0	0	2.3	0.009*
	Mean $\pm$ SD		$230.26 \pm 277.14$		$72.76 \pm 125.13$		2.71	0.008*
IL-4 Pg/ml	High		41	95.3	4	9.5	1.1	0.008*
	Normal		2	4.7	38	90.5	1.2	0.009*
	Mean $\pm$ SD		$69.53 \pm 19.72$		$30.13 \pm 21.92$		1.20	0.009*

\*Statistically significant difference

**Table2.** Comparison between level of IgE and IL-4 in Extrinsic AD and Intrinsic AD with and without family history of P. Alba

		Extrinsic AD		Intrinsic AD		U	P-value
		No.	%	No.	%		
Family history of P. Alba	+ ve	39	90.7	2	4.8	41.00	0.049*
	- ve	4	9.3	40	95.2	34.00	0.008*
Family history of AD	+ ve	43	100	5	11.9	55.00	0.04*
	- ve	0	0	37	88.1	33.50	0.007*

\*Statistically significant difference

NS: no statistically significant difference

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**Table3.** Relation between Pityriasis Alba and Extrinsic AD and Intrinsic AD

		Extrinsic AD		Intrinsic AD		t-test	P-value
		No.	%	No.	%		
P. alba	+ve	42	97.7	2	4.8	0.810**	< 0.001
	-ve	1	2.3	40	95.2	0.823**	< 0.001

\*\* Correlation is significant at the 0.01 level (2-tailed).

### 5. DISCUSSION

PA is more prevalent in cold weather; this can be explained on the basis of increased skin dryness in winter. It is considered as one of the minor manifestations of atopy, although atopic symptoms are often not evident by the time PA appears. However, it is expected that those patients with PA will have AD later in their life [15].

Our study showed, significant elevation of serum level Ig-E and IL-4 in eAD versus iAD group. The results of this study agreed with Bardana 2004 and Ott et al (2009) [16, 17], serum IgE and IL-4 levels were found to be associated with allergen-specific IgE status. Serum IgE is considered to be a significant parameter for differentiation between eAD and iAD. Extrinsic AD is associated with high serum IgE and IL-4 levels and exhibits allergen-specific IgE to allergens and foods [16]. In contrast, intrinsic AD, with normal IgE levels (below 150-200 kU/L) [18, 19], low IL-4, and they do not have allergen-specific IgE to allergens and foods [16].

In 2008, Brenninkmeijer and colleagues found that iAD more in female, with high frequency of the Dennie-Morgan infra-orbital folds, late onset of the disease and milder disease severity [20]. However, Tokura Y suggested that the dermatological manifestations of eAD and iAD were indistinguishable [21]. Our study's results revealed a positive correlation of Pityriasis alba with eAD versus iAD. Thus, we could use Pityriasis alba as a significant clinical clue for differentiation between eAD and iAD. This also agreed with Al-mesari et al [22] as they found statistically significant higher IgE and IL-4 levels in patients with P. alba versus normal volunteers.

Skin barrier function is usually assessed by transepidermal water loss and skin surface hydration. The skin barrier function was preserved in iAD but impaired in eAD [23], probably because of filaggrin gene mutation [21, 23]. Filaggrin mutations were statistically significantly correlated with high serum IgE and PA [24, 25]. By disturbing skin barrier, environmental allergens enter into the skin and increases density of Langerhans cells in the epidermis. After binding of environmental allergens to the IgE receptors on Langerhans cells, Th2 immune response and atopic inflammation triggered [26, 27].

In this study family history of AD and PA were significantly correlated with extrinsic AD. This can be explained by enhanced Th2 cell producing more IL-4 that may be related to genetic background and heredity. Also, Brenninkmeijer and colleagues found a less frequent association of intrinsic form with a family history of atopy and PA [20]

Finally, the PA was significantly correlated with extrinsic AD; we can consider it a pathognomonic clue in differentiating it from intrinsic type.

### 6. CONCLUSION

Pityriasis Alba could be used as a pathognomonic clue in differentiating extrinsic AD from intrinsic AD.

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