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Title: Real-world evaluation of "Eczema in psoriatico": bridging the gap between dermatology and dermatopathology

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Real-world evaluation of "Eczema in psoriatico": bridging the gap between dermatology and dermatopathology

Abstract

Background: The diagnosis of psoriasis is mainly made by clinical examination but on some occasions according to the localization or duration of the lesions when spongiosis is more prominent, it can be challenging and may be considered as overlapping eczema.

Objectives: To evaluate the patients for ‘eczema in psoriatico’ and to present the differences between psoriasis.

Method: Biopsy outcomes of thirty-one patients who were histologically diagnosed with psoriasis and psoriasiform dermatitis because of the erythematous and scaly plaque lesions located on hands and feet, between 2013 and 2015 years, were evaluated retrospectively. Histopathologic findings compatible with psoriasis and accompanied by spongiosis and spongiotic vesicles were evaluated as eczema in psoriatico and compared with psoriasis.

Results: In this study thirty-one patients, including 18 patients with eczema in psoriatico and 13 patients with psoriasis of hands and/or feet were included. Of the 31 patients, 15 (48,4 %) were women and 16 (51,6 %) were men, in 61,3 % of cases, biopsies were taken from hands (61.1 % of ‘eczema in psoriatico’, 61,5 % of psoriasis) and 38.7% from feet (38,9 % of ‘eczema in psoriatico’, 38,5 % of psoriasis). There was a statistically significant difference between two groups in terms of parakeratosis severity and distribution, the presence of neutrophil and plasma in stratum corneum, the presence of granular layer loss and suprapapillar plate thinning, the shape of retes, the presence of lymphocytic exocytosis, spongiosis and spongiotic vesicles, the intensity of infiltrates in the papillar dermis and the presence of dermal edema ($p<0,05$).

Conclusion: Histology supports a continuum between psoriasis and eczema that share histological similarities and at the same time should be considered a separate entity, eczema in psoriatico

Keywords: Eczema in psoriatico; eczematous psoriasis; eczema; psoriasis

Introduction

The differential diagnosis of scaling erythematous plaques on hands and feet is often difficult, and not always possible, especially in isolated involvements, due to overlapping clinical and histological findings. Psoriasis is a chronic, systemic inflammatory disease affecting 0.5–11.4% of the population which is associated with several cutaneous and noncutaneous comorbidities. (1-5) In literature, the co-existence of eczema and psoriasis was evaluated also during biologic therapies capable to elicit inflammatory reactions such as the eczematous eruptions during IL-17 inhibitors therapy. Thus, the eczema occurrence/co-occurrence in psoriatic patients started to be understood and also accepted, furthermore during biologics switching eczematous manifestations are common. (6-8) In our observations, there is also a large group of patients with erythrosquamous plaques on hands and feet that present with clinical and histological features of both psoriasis and eczema (especially chronic hyperkeratotic –raghadiform form). Kolesnik M. reported that “eczema in psoriatico” was psoriasiform dermatitis with neutrophils and plasma exudation in parakeratosis, lymphocytic exocytosis in the epidermis, full-thickness spongiosis or formations of spongiotic vesicles and had overlapping features with both psoriasis and contact dermatitis. (9) In this study, we aimed to evaluate the histopathologic findings of psoriasis and “eczema in psoriatico” on hands and feet to find out whether “eczema in psoriatico” was a new entity or just a combination of psoriasis and eczema.

Material and methods: In this study, 4 mm the punch biopsies were obtained from patients seen at the Department of Dermatology and Venereology outpatient clinic, with a primary

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clinical diagnosis of psoriasis or eczema on their hands and feet, from January 2013 and to December 2015 years, were examined. Thirty-one patients who have histologically diagnosed with psoriasis and psoriasiform dermatitis for 2-12 months were finally selected for the study. Patients diagnosed with eczema who are <18 years of age were excluded due to the ethical committee approval. Examination of hematoxylin-eosin (H&E) sections was done by a dermatopathologist (EZ) blind to clinical diagnosis. The histological parameters were chosen according to the features that were considered helpful in the diagnosis of psoriasis and eczema. Biopsies were evaluated in terms of the intensity of parakeratosis (mild; up to 33 %, moderate; between 33 and 66%, strong; more than %66 of stratum corneum) and distribution of parakeratosis (multiple foci, confluent, parakeratosis and orthokeratosis vertically distributed), the presence of neutrophils and/or plasma mounds in the keratotic layer, acanthosis type (regular, irregular and mixed pattern) and grade (mild, moderate and strong), the presence of the granular layer loss and thinning of the suprapapiller plate, the shape of the rete ridges (club-shaped, V-shaped or mixed), the presence of lymphocytic exocytosis, the presence of spongiosis and spongiotic vesicles, perivascular infiltration of lymphocytes in the papillary dermis (mild, moderate and strong) and the existence of papillar dermal edema. Cases with histopathologic findings compatible with psoriasis and accompanied by spongiosis and spongiotic vesicles were evaluated as eczema in psoriatico and histopathological features of these two groups were compared.

Results

Thirty-one patients, including 18 patients with eczema in psoriatico and 13 patients with psoriasis of hands and/or feet were included in the study. Of the 31 patients, 15 (48,4 %) were women and 16 (51,6 %) were men, with a mean age of 46 years (range 21-70 years). In 61,3 % of cases, biopsies were taken from hands (61.1 % of ‘eczema in psoriatico’, 61,5 % of

psoriasis) and 38.7% from feet (38,9 % of ‘eczema in psoriatico’, 38,5 % of psoriasis).

Clinical manifestations in other localization (scalp, knee, elbow) were observed in 19,4% of cases (16,7 % of ‘eczema in psoriatico’, 23,1 % of psoriasis patients. There were no statistical differences between the two groups in terms of age, gender, localization of lesions, localization of biopsy, and the presence of stigmata of psoriasis (Table 1).

The histologic features of both groups were shown in Table 2. Whereas granular layer loss and thinning of suprapapillar plate were detected in all psoriasis patients (100%), granular layer loss was partial in 14 (77,8%) of eczema in psoriatico patients and the total loss was seen only in 4 (22,2%) of them. Also thinning of suprapapillar plate was observed in half of the eczema in psoriatico patients. While mild parakeratosis was a common feature in eczema in psoriatico (61,1 %), moderate parakeratosis was found as a more common feature in psoriasis patients (84,6%). Vertically distributed parakeratosis and orthokeratosis were more often found in eczema in psoriatico (94,4%) than in psoriasis (% 61,5). Neutrophils were seen in the keratotic layer in nine of psoriasis patients (69,2%) and the other four of them (30,8%) had neutrophils and plasma mounds contemporary. Of eczema in psoriatico patients 15 (83,3%) had both neutrophils and plasma mounds in the keratotic layer, only in three (16,7%) of them neutrophils were detected solely. None of the patients had only plasma mounds.

While mixed pattern combining club-shaped and V-shaped rete ridges were more common in eczema in psoriatico patients (88,9%), isolated club-shaped rete ridges were noted more frequently in psoriasis patients (76,9 %).

Regular acanthosis was found more frequent in psoriasis (76,9 %) followed by a mixed pattern (23,1%). In contrast, mixed type acanthosis was more common in eczema in psoriatico patients (72,2 %).

While lymphocytic exocytosis was observed in all eczema in psoriatico patients, it was present only in one psoriasis patient (7,6%). Edema of the papillary dermis was present in %

92,3 of patients with psoriasis, whereas it was a less common feature in patients with eczema in psoriatico (27,8 %). Spongiosis was noted in all cases of eczema in psoriatico. Spongiotic vesicles were seen in more than half of eczema in psoriatico patients (66,7%). Neither spongiosis nor spongiotic vesicles were found in psoriasis patients. Clinical and histopathologic features of eczema in psoriatico patients were shown in Figures 1 and 2. There were statistically significant differences between the two groups in terms of parakeratosis severity and distribution, the presence of neutrophil and plasma mounds in the keratotic layer, the presence of granular layer loss and suprapapillar plate thinning, the shape of rete's, the presence of lymphocytic exocytosis, spongiosis and spongiotic vesicles, the intensity of infiltrates in the papillar dermis and the presence of dermal edema (Table 2) ($p<0,05$). Only a grade of acanthosis was seen in both groups at the same rate.

Discussion

Psoriasis is a complex, chronic, multifactorial, relapsing inflammatory skin disorder characterized by abnormal keratinocyte hyperproliferation ending up thickening of the epidermis and stratum corneum (10-14). Psoriasis is an immune-mediated inflammatory systemic disease, that results from the complex interaction of the individual (genetic/epigenetic components) and the environmental exposure (such as infectious agents, diet) role as a proinflammatory modulation. (15)

The main histologic features of psoriasis include; mounds of parakeratosis, mostly with neutrophils at their summits or confluent parakeratosis, decrease or loss of the granular layer of the epidermis, psoriasiform epidermal hyperplasia with some thin rete ridges of equal length, thinned suprapapillary plate, spongiform pustule at the upper parts of the epidermis, dilated tortuous capillaries and edema of the papillary dermis (11,16). However, it is not always possible to determine the characteristic histologic features of psoriasis in skin biopsies because of the changes in disease activity and concomitant conditions. The most useful

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histologic features in the differential diagnosis are collections of neutrophils within the parakeratosis (Munro's microabscesses), neutrophils within the spinous layer (spongiform pustules of Kogoj), and dilatation of papillary dermal capillaries with overlying thinning of the suprapapillary plate (17). Histologic features like psoriasiform epidermal hyperplasia, parakeratosis, and mild spongiosis can also be seen in chronic eczematous dermatitis such as irritant/allergic contact dermatitis, atopic dermatitis, and nummular dermatitis (18). But the presence of mostly intact granular layer, spongiosis sometimes evolving to vesiculation and irregular epidermal hyperplasia were reported as the useful histologic features to distinguish eczematous dermatitis from psoriasis (19).

There have been some studies in the literature that focused on the differentiation of psoriasis from eczema clinically and histopathologically. However, the results vary from study to study and despite all these clues, in some patients, histopathologic findings pass so intertwined that it is impossible to separate these two entities from each other at especially in some sites (20-23).

Therefore, a new naming need appears in these patients showing clinical and histological features of both psoriasis and eczema.

Ebstein et al. classified the primary and secondary eczematous psoriasis firstly in 1991. They reported the primary eczematous psoriasis as an endogenous process typical for regions like the groin and axilla. Exogenous factors such as irritants and allergens were accused of causing the secondary eczematous psoriasis (24). According to them, the presence of stigmata of psoriasis required for the diagnosis of eczematous psoriasis.

Kapila et al. evaluated pediatric patients with psoriasis or eczema, or both and they classified children with features of both psoriasis and eczema as psoriasis-dermatitis overlap (25).

Kolesnik M. called "eczema in psoriatico" to close the gap between palmoplantar psoriasis and palmoplantar chronic contact dermatitis (9). Moderate to strong parakeratosis, regular

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acanthosis, loss or thinning (also partially) of the granular layer, thinning of suprapapillary plates,

edema of papillary dermis and presence of Munro microabscesses were reported as the histologic features overlapping with psoriasis and neutrophils and plasma exudation in parakeratosis, lymphocytic exocytosis in the epidermis, full-thickness spongiosis or formations of spongiotic vesicles were reported as the features overlapping with contact dermatitis (9).

Abramovits *et al.* found that 20% of psoriasis had “intermediate features” which were characteristics of both psoriasis and eczema, or a personal history of both. The authors suggested that the name of this new category was “PsEma”: A condition that was characterized by showing the overlap of both psoriasis and eczema as clinically, histologically, molecular, biologic, and therapeutically responses (16). In this study, we compared this new entity named differently by different researchers such as eczema in psoriatico, eczematous psoriasis, PsEma, and psoriasis-dermatitis overlap with psoriasis to show whether this entity was just a combination of psoriasis and eczema or a distinct entity (9,23-25). For sure the histopathological findings of the lesions may differ according to the developmental stages, different parts of the skin, and different factors such as medication and trauma for eczema or psoriasis but in this study, we found that these two entities had different characteristics in terms of the intensity, distribution, and mounds of parakeratosis, acanthosis type, the presence of the granular layer loss and thinned suprapapiller plate, the shape of the rete ridges, density of lymphocytic infiltrate in the papillary dermis and the existence of papillar dermal edema outside the presence of lymphocytic exocytosis, spongiosis, and spongiotic vesicles. It was not only limited to the palmoplantar region but also detected on the other sites of palms and soles and flexural regions also.

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As a result, we consider that this new entity named “eczema in psoriatico”, before is a distinct entity from psoriasis. There is a new entity that needs to fill the gap between psoriasis and eczema and to compose a common language between dermatologists and pathologists. It may be named eczema in psoriatico, eczematous psoriasis, or something else. The identification of such a new entity is very important to resolve the confusion in this regard. To put out this new entity's properties, further studies are required.

Statement of Ethics

We conducted our research according to the World Medical Association Declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest to disclose and there were no funding sources supporting the work.

Limitation

The limited sample number is the main restriction of this research.

Data Availability Statement

Data are openly available in a public repository that issues datasets with DOIs.

Author Contributions

Tugba Kevser Uzuncakmak, Filiz Topaloglu Demir, Ebru Itr Zemheri, Ayse Serap Karadag involved in conception and design of the study; Filiz Topaloglu Demir, Ebru Itr Zemheri, Tugba Kevser Uzuncakmak involved in the acquisition of data; and Tugba Kevser Uzuncakmak, Filiz Topaloglu Demir, Ebru Itr Zemheri involved in analysis and/or interpretation of data.

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Table 1: The demographical and clinical characteristics of the patients

Table 2: Comparison of histologic features of eczema in psoriatico and psoriasis

Figure Legends

Figure 1: (a) Hyperkeratotic plaques with fissures localized to the plantar region of eczema in psoriatico patient. A *positive patch test to nickel* was observed at 96 hours (b) Erythematous plaque with scaling and yellowish-brown macules

Figure 2: Different eczema in psoriatico patterns: (a) Mild parakeratosis with neutrophils, regular acanthosis, loss of granular layer, lymphocytic exocytosis with spongiosis, club-shaped rete ridges lymphocytic infiltration in the upper dermis, (b) Strong

para/orthokeratosis with neutrophils & plasma, irregular acanthosis, partial loss of granular layer, spongiotic vesicles, V-shaped rete ridges, lymphocytic infiltration in the upper dermis, (c) Strong para/orthokeratosis with neutrophils & plasma, mixed acanthosis, loss of granular layer, spongiotic vesicles, mixed -shaped rete ridges, lymphocytic infiltration in the upper dermis, (d) Strong confluent parakeratosis with neutrophils, regular acanthosis, loss of granular layer, lymphocytic exocytosis with spongiosis, club-shaped rete ridges lymphocytic infiltration in the upper dermis

Table 1: The demographical and clinical characteristics of the patients

		Eczema in psoriatico		Psoriasis		
		n	%	n	%	p
Age (Year)		47,8±13,2*	24-70**	45,2±12,0*	21-67**	0,590
Sex	Female	11	61,1	4	30,8	0,095
	Male	7	38,9	9	69,2	
Location of lesions	Hand	5	27,8	7	53,8	0,308
	Foot	4	22,2	3	23,1	
	Both	9	50,0	3	23,1	
Location of biopsy	Hand	11	61,1	8	61,5	0,981
	Foot	7	38,9	5	38,5	
Stigmata of psoriasis	No	15	83,3	9	69,2	0,413
	Yes	3	16,7	4	30,8	

*the mean age

**minumum-maximum age

Table 2: Comparison of histologic features of eczema in psoriatico and psoriasis

		Eczema in psoriatico		Psoriasis		
Histologic features		n	%	n	%	p
Parakeratosis	mild	11	61,1	1	7,7	0,005
	moderate	7	38,9	11	84,6	
	strong	0	0,0	1	7,7	
Parakeratosis	multiple foci	0	0,0	2	15,4	0,042
	confluent	1	5,6	3	23,1	
	para- /orthokeratosis	17	94,4	8	61,5	
Parakeratosis	with neutrophils	3	16,7	9	69,2	0,003
	neutrophils & plasma	15	83,3	4	30,8	
Acanthosis	moderate	8	44,4	5	38,5	0,739
	strong	10	55,6	8	61,5	
Acanthosis	regular	4	22,2	10	76,9	0,006
	irregular	1	5,6	0	0,0	
	mixed	13	72,2	3	23,1	
Loss/thinning of granular layer	yes	4	22,2	13	100,0	<0,001
	partially	14	77,8	0	0,0	
Thinning of the suprapapillary plate	no	9	50,0	0	0,0	0,002
	yes	9	50,0	13	100,0	
Rete ridges	club-shaped	0	0,0	10	76,9	<0,001
	V-shaped	2	11,1	2	15,4	
	mixed	16	88,9	1	7,7	
Lymphocytic exocytosis in epidermis	no	0	0,0	12	92,3	<0,001
	yes	18	100,0	1	7,7	
Spongiosis	no	0	0,0	13	100,0	<0,001
	yes	18	100,0	0	0,0	
Spongiotic vesicles	no	6	33,3	13	100,0	<0,001
	yes	12	66,7	0	0,0	
Infiltrate in upper dermis	mild	4	22,2	11	84,6	0,001
	moderate	11	61,1	1	7,7	
	strong	3	16,7	1	7,7	
Oedema of the papillary dermis	no	5	27,8	12	92,3	<0,001
	yes	13	72,2	1	7,7	











