Received: 10 August 2022 | Accepted: 20 December 2022

DOI: 10.1111/ddg.14991

REVIEW

Eczematized psoriasis – a frequent but often neglected variant of plaque psoriasis

Felix Lauffer[1] | **Kilian Eyerich**[2,3]

[1]Department of Dermatology and Allergy, Technical University of Munich, Munich, Germany

[2]Division of Dermatology and Venereology, Department of Medicine Solna, and Center for Molecular Medicine, Karolinska Institutet, Stockholm, Sweden

[3]Department of Dermatology and Venereology, Medical Center, University of Freiburg, Freiburg, Germany

Correspondence
Felix Lauffer, MD, PhD, Department of Dermatology and Allergy, Technical University of Munich, Biedersteinerstrasse 29, 80802 München, Germany.
Email: felix.lauffer@mri.tum.de

Summary

Psoriasis is a common chronic inflammatory skin disease that causes systemic inflammation and severely impacts the patient's quality of life. Several highly effective therapeutics for psoriasis have been approved in recent years. However, in real life, a high proportion of patients either do not experience the clinical improvement observed in clinical trials or develop a secondary loss of efficacy. This may be a result of unrecognized endotypes of psoriasis that need to be characterized in greater depth to enable selection of an appropriate therapy. Eczematized psoriasis, which occurs in approximately 5–10% of patients with psoriasis, is an often-neglected variant of psoriasis. The term "eczematized psoriasis" refers to patients developing psoriasis with similarities to eczema. These patients typically present with severe itching, and skin biopsies often reveal eosinophil granulocytes, serum crusts, or spongiosis, which are frequently observed in eczema. From an immunological perspective, additional signaling pathways that are responsible for eczema reactions might be activated in eczematized psoriasis compared to classical plaque psoriasis. This review summarizes the key clinical, histological, and immunological features of eczematized psoriasis, proposes diagnostic criteria, and evaluates the therapeutic options for eczematized psoriasis.

ESTIMATED PREVALENCE OF ECZEMATIZED PSORIASIS

The incidence and prevalence of plaque-type psoriasis have been well-investigated by multiple epidemiological studies. Depending on the underlying method and geographical region, the incidence of psoriasis varies from 30 to 320 per 100,000 person-years, and the prevalence in Australasia, Europe, and North America is approximately 2%.[1,2]

In contrast to this, the prevalence of eczematized psoriasis is unknown. Three studies investigated consecutive skin biopsies with the diagnosis of psoriasis for overlapping phenotypes with eczema or vice versa. The most recent study enrolled 20 patients with a clinical diagnosis of psoriasis. Of these 20 patients, 15% were diagnosed with eczematous dermatitis rather than psoriasis (clear misdiagnosis by the clinician) and 35% had a psoriasis phenotype with eczematous changes, a phenotype that the authors defined as eczematized psoriasis.[3] The second interesting study reported that 77 of 135 skin biopsies obtained from the palm, with a differential diagnosis of either psoriasis or eczema, had a mixed phenotype of these diseases.[4] The third study also investigated skin biopsies from palms of 30 patients with a suspected diagnosis of hand eczema. Only eight of 30 patients had clear hand eczema, nine had psoriasis, and 13 had a mixed phenotype. Notably, the differential diagnosis of psoriasis and eczema is particularly difficult in the palms, feet, and scalp.

All three studies were biased towards a higher prevalence of eczematized psoriasis because they investigated routine skin histology. However, an experienced dermatologist would only perform a skin biopsy if the phenotypes were clinically overlapping. Although the exact prevalence of eczematized psoriasis is unknown, these studies show that cases with clinical and histological overlap of psoriasis and eczema are challenging in clinical practice.

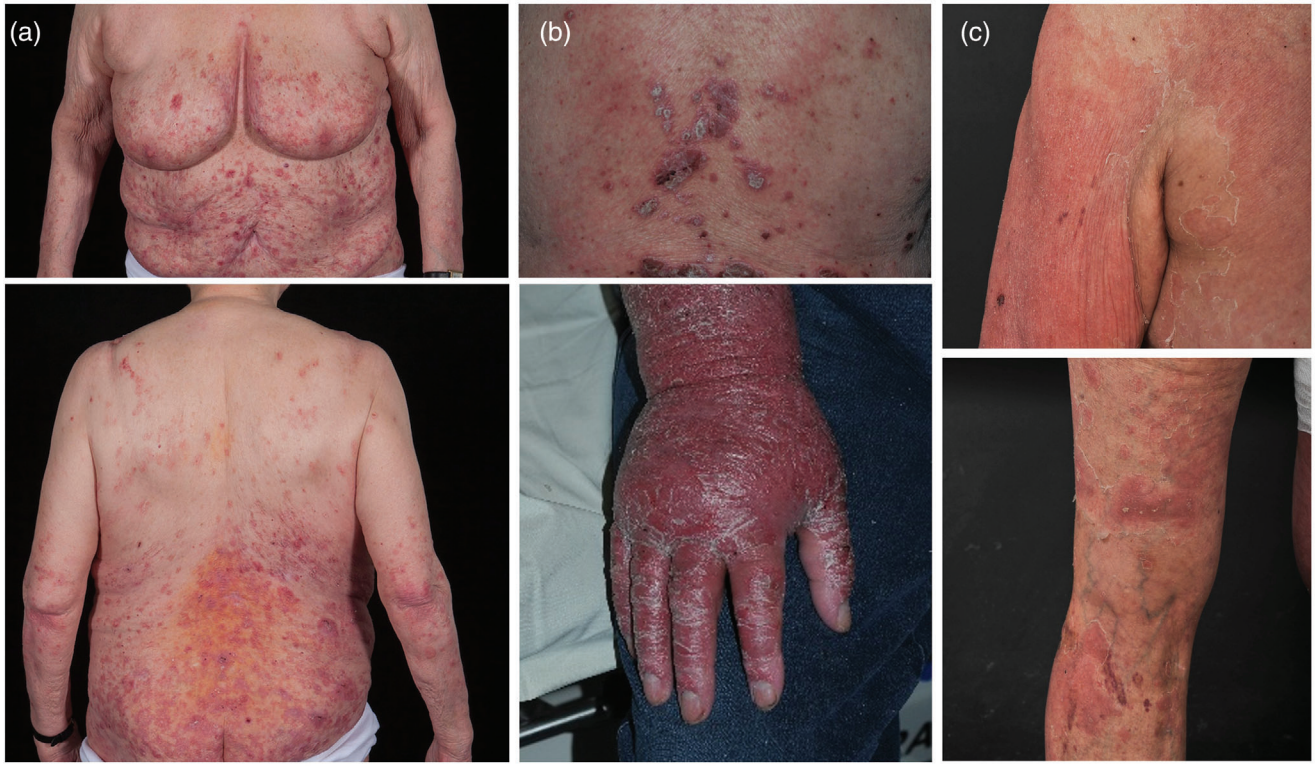

FIGURE 1 Representative clinical pictures of eczematized psoriasis. (a) A 75-year-old woman with a previous diagnosis of plaque psoriasis for the past 15 years, now presenting with severe pruritus. (b) An 82-year-old man with a history of plaque psoriasis for the past 35 years. He received UV therapy, systemic corticosteroids, acitretin, and cyclosporine without sufficient disease control. (c) A 62-year-old woman with a history of plaque psoriasis for more than 20 years, alcohol abuse, and renal insufficiency. She has severe pruritus despite extensive topical treatment with high-potency corticosteroids.

CLINICAL PICTURE

Plaque psoriasis is estimated to be the most common clinical phenotype, accounting for approximately 90% of cases. Dermatologists can easily identify plaque psoriasis because of its characteristic morphological appearance. However, eczematized psoriasis has a more heterogeneous clinical presentation. Based on our clinical experience, patients with eczematized psoriasis are older than those with classical plaque psoriasis and have a mixed phenotype with overlapping features from psoriasis and eczema. Erythematous plaques, a preferential appearance at predilection sites, and a positive family history are shared features between plaque psoriasis and eczema. Eczematized psoriasis is typically not as sharply demarcated as plaque psoriasis, has a variable amount of scaling, and often shows excoriations and hemorrhagic crusts due to extensive scratching (Figure 1). However, in plaque psoriasis, almost all patients with eczematized psoriasis experience itching. In contrast to classical plaque psoriasis, diagnosis of eczematized psoriasis cannot be based solely on skin morphology; additional diagnostic tools are necessary to rule out differential diagnoses, such as contact dermatitis, scabies, fungal infection, (late-onset) atopic dermatitis (AD), nummular eczema, parapsoriasis, or cutaneous T-cell lymphoma.

HISTOLOGICAL PICTURE

Plaque psoriasis has a unique histological architecture that includes acanthosis, hypogranulosis, thinned suprapapillary epidermis, hyperparakeratosis, and Munro's microabscess.

In contrast, the histology of eczematized psoriasis is not well understood. The most common findings in our experience are additional spongiosis, eosinophils and serum crusts (Figure 2).

PATHOGENESIS

Differential pathogenesis of psoriasis and AD

Interestingly, the co-occurrence of psoriasis and AD is very rare, indicating that the diseases are mutually exclusive.[5] The complex pathogenesis of psoriasis and AD is based on the interaction between skin-infiltrating lymphocytes and keratinocytes. However, AD is mediated by type 2 immune cells, whereas psoriasis is dominated by type 3 (Th17) immunity.[6] Hallmarks of type 2 immune cells include *(1)* impairment of the epidermal barrier, *(2)* inhibition of the cutaneous innate immune defense, *(3)* recruitment and/or

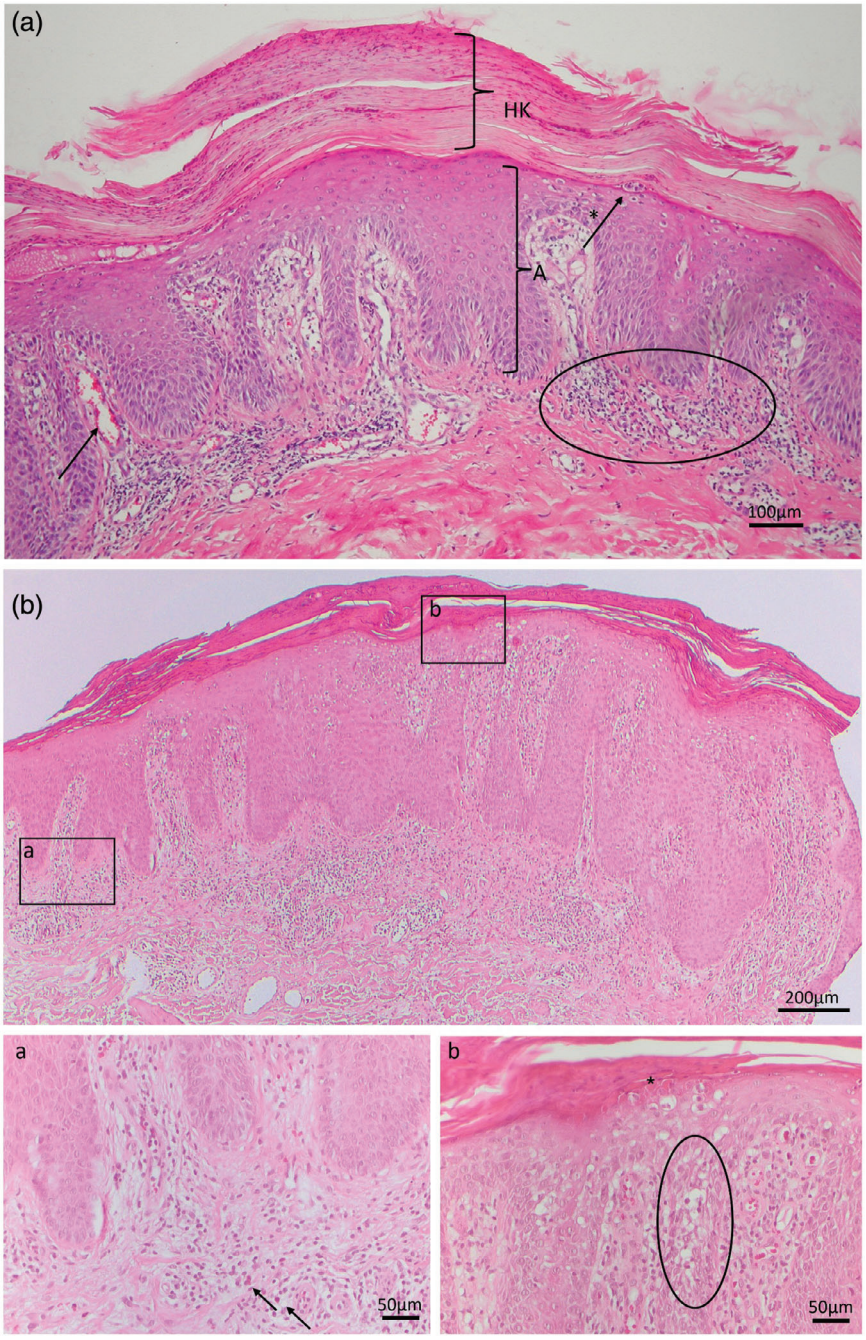

FIGURE 2 (a) Typical histological picture of plaque psoriasis with hyperparakeratosis (HK), regular acanthosis, dilated capillary loops (arrow), neutrophil abscess (arrow with asterisk), and inflammatory infiltrate (circle). (b) Typical histological picture of eczematized psoriasis. Apart from hallmarks of plaque psoriasis, there are serum inclusions in the stratum corneum (asterisk), infiltrating eosinophils (arrow), and spongiosis (circle).

activation of eosinophil and basophil granulocytes as well as mast cells, *(4)* steering humoral immunity, and *(5)* inducing itch via neuro-immune interactions.[7–9] These effects are mediated by type 2 cytokines such as IL-4, IL-5, and IL-13. However, type 3 immune cells *(1)* stimulate innate immunity/antimicrobial peptides in the skin, *(2)* recruit neutrophil granulocytes, and *(3)* induce metabolic activity in the skin, leading to insulin resistance, development of new capillaries, and de-differentiated proliferating keratinocytes.[10,11] These effects are mostly attributable to the cytokines of the IL-17 family,[12] IL-21, IL-22, and IL-26. In the IL-17 family, most evidence exists for IL-17A and IL-17F, both T cell-derived cytokines.[12] Recent evidence suggests that other members of the IL-17 family, such as IL-17C and IL-17E, are critically involved in psoriasis pathogenesis (Figure 3).[13]

The epidemiological antagonism between psoriasis and AD is reflected by the mutual inhibition of type 2 and type 3 immunity. Type 2 cytokines, such as IL-4 or IL-13, inhibit the IL-17A mediated upregulation of antimicrobial peptides in the skin.[14] They also inhibit migration and activation of neutrophil granulocytes in the skin.[15,16] In fact, recombinant IL-4 has been suggested as a therapeutic for psoriasis, although approval has never been achieved.[17] Vice-versa, there are case reports on new-onset psoriasis during anti-IL4/IL-13 receptor therapy.[18,19] Apart from differently polarized T-cell immune responses, there

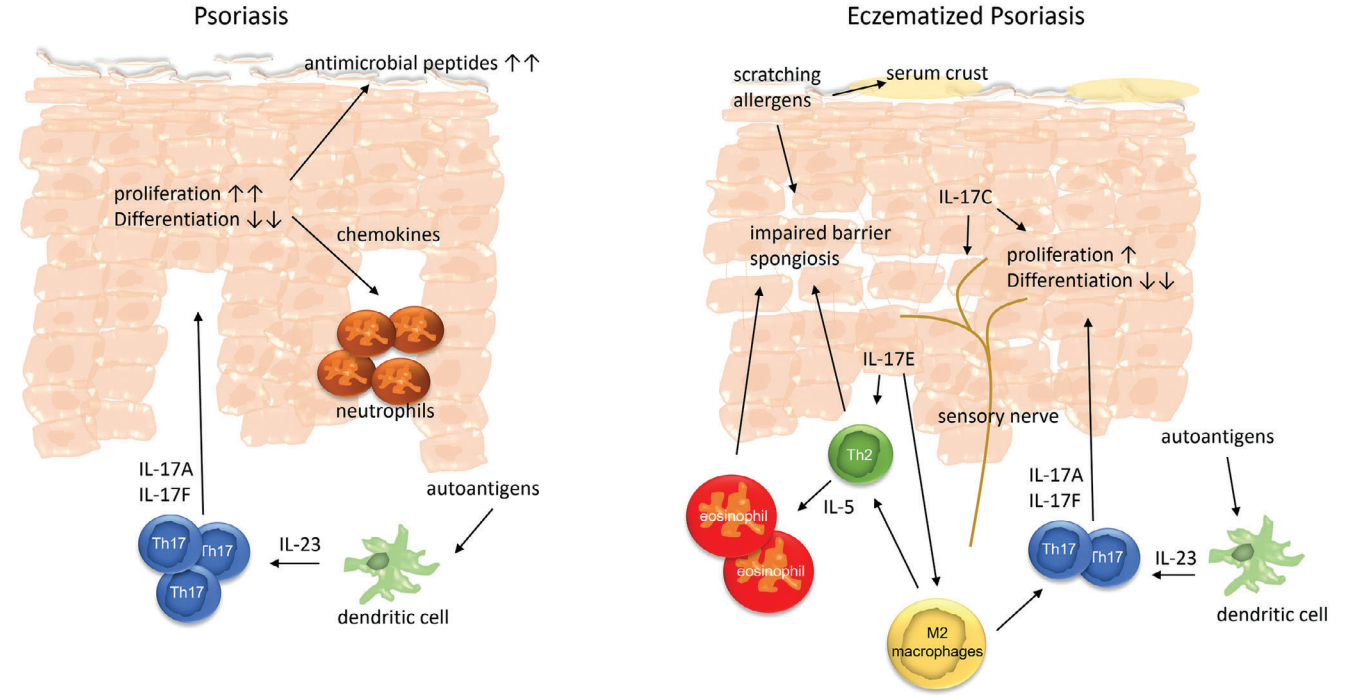

FIGURE 3 Schematic diagram comparing the pathogenesis of plaque type psoriasis and eczematized psoriasis. Mechanic injury, cell stress, and autoantigens initiate a Th17-dominant immune response in plaque psoriasis. Keratinocyte turnover time and differentiation are critically reduced when exposed to IL-17A and IL-17F. Furthermore, keratinocytes release antimicrobial peptides and neutrophil-attracting chemokines. Similar mechanisms might be activated in eczematized psoriasis, but additional pathways lead to clinical and histological features of eczematous skin diseases. IL-17C increases the responsiveness of keratinocytes to proinflammatory triggers, such as TNF-α. Furthermore, IL-17C might be involved in triggering sensory nerve growth and the enhanced perception of itch. As IL-17E is also involved in type 2 inflammation, it might induce additional Th2 polarization leading to spongiosis and eosinophil attraction.

are also other mediators, such as IL-17C or IL-17E and keratinocyte-derived cytokines, which have been described in the context of both type 2 and type 3 inflammatory skin diseases.

Role of IL-17C in the context of psoriasis and AD

Unlike T cell-derived IL-17, IL-17C is exclusively produced by epithelial cells such as keratinocytes. IL-17C is induced by TNF-α, IL-1β, and pathogen-associated molecular patterns. IL-17C, similar to IL-17A, acts synergistically with TNF-α, IL-22 and IL-1β.[20,21] The IL-17C receptor is expressed on epithelial cells, Th17 cells, and sensory nerve cells but not on other hematopoietic immune cells.[22–24] Thus, IL-17C creates three functional loops: *(1)* an autocrine feedback loop on epithelial cells, *(2)* a proinflammatory link between the epithelium and Th17 cells, and *(3)* a stimulation of sensory nerve growth by keratinocytes. In mice, overexpression of IL-17C in keratinocytes (IL-17C$^+$ mice) leads to acute dermatitis, which resembles key features of psoriasis.[25] Using a neutralizing antibody against IL-17C (MOR106), Vandeghinste et al. reported that IL-17C depletion critically reduced ear thickness, expression of inflammatory genes, and immune cell infiltration in a murine skin model of psoriasis (IL-23 injection model).[26] Interestingly, neutralizing IL-17C is highly effective in mouse models of AD.[26] We showed that IL-17C is highly expressed in various inflammatory and autoimmune skin diseases such as AD, psoriasis, lichen planus, pyoderma gangrenosum, and vasculitis.[13] IL-17C amplifies the expression of neutrophil-attracting chemokines (CXCL8), CCL5, CXCL10, and VEGF. Blocking IL-17C signaling in skin biopsies of human psoriasis and AD significantly downregulated the expression of HBD2, IL-36γ, and LCE3A.[13] Thus, IL-17C cannot be attributed to a specific skin disease or type of immune response, but is an independent epidermal amplifier of inflammation in various human skin diseases.

Role of IL-17E (IL-25) in the context of psoriasis and AD

Various cells can produce IL-17E: epithelial cells, endothelial cells, T cells, dendritic cells, macrophages, and type 2 innate lymphoid cells.[27] Overexpression of IL-17E in lung epithelial cells results in increased recruitment of eosinophils and macrophages.[28] Blocking IL-25 signaling ameliorates inflammation in murine allergen-induced asthma models.[29] Therefore, IL-25 has long been associated with Th2-dominant immune reactions. However, in allergic contact dermatitis, IL-17E mediates the release of IL-1β by dendritic cells, which is essential for the activation of

TABLE 1 Suggested biomarkers to diagnose eczematized psoriasis versus psoriasis-like eczema (modified from[33]).

Molecular biomarkers to differentiate psoriasis and eczema				
Marker	**Aim**	**Performance (Correlation coefficient)**	**Independent validation?**	**Reference**
NOS2/ CCL27	Differentiates psoriasis incl. subtypes from eczema incl. subtypes	Sensitivity and specificity > 97%	Yes [34–36]	[6,37,38,39]
IL-36α	Differentiates psoriasis from eczema	0.6	No	[40]
IL-36γ	Differentiates psoriasis from other inflammatory skin diseases	Not reported (n = 150 patients)	No	[41,42]
CCL26	Differentiates psoriasis from atopic dermatitis in Han Chinese patients	Not reported (n = 33 patients)	No	[35]
CXCL9	Differentiates lichen planus from psoriasis or eczema	19/20 lichen patients identified correctly	No	[43]

hapten-specific Th17 cells.[30] Single nucleotide polymorphisms of the IL17E gene are associated with a severe form of psoriasis and the presence of psoriatic arthritis.[31] IL-17E is highly expressed in the epidermis of human psoriasis plaques and in the murine imiquimod model of psoriasis.[32] Injection of IL-17E into healthy mouse skin results in psoriasis-like dermatitis, whereas IL-17E KO significantly reduced skin inflammation in mice after imiquimod application.[32] Thus, IL-17E appears to be involved in both type 2 and type 17 dominant immune reactions, suggesting a potential role in the pathogenesis of eczematized psoriasis.

CURRENT DIAGNOSTIC PROCEDURE

As discussed above, both the clinical and histological pictures differ in eczematized psoriasis from classical psoriasis, with some overlap with the group of eczematous diseases.

Using clinical examination and histology, dermatologists can easily differentiate eczematized psoriasis from either classic plaque-type psoriasis or classic AD. In our experience, the true challenge is to differentiate eczematized psoriasis from eczema with psoriasis-like features, often called "psoriasiform eczema". This is particularly evident in special body areas, such as the palms or soles and scalp, or inverse areas, such as the inguinal regions.

A case series from the University Dermatology Department Magdeburg illustrates the difficulty of distinguishing eczematized psoriasis from eczema variants; of the 132 patients biopsied for the suspected diagnosis of an inflammatory skin disease on the palms, twelve had typical psoriasis, 43 had typical AD, and 77 had a mixed phenotype even after two certified dermatopathologists evaluated the cases.[4] In line with the description above, histological criteria used to differentiate eczematized psoriasis from typical psoriasis or typical AD were parakeratosis, hypogranulosis, dilated capillaries, spongiosis, and lymphocyte exocytosis. Mixed phenotypes, called "eczema in psoriatico" by the authors, showed hallmarks of both psoriasis and AD. Thus, additional tools are necessary to clearly distinguish between AD and psoriasis variants, such as eczematized psoriasis.

Molecular diagnostics of eczematized psoriasis

Several biomarkers have been proposed to differentiate eczematized psoriasis from psoriasis-like eczema (Table 1). For example, our Italian colleagues have proposed IL-36α as a possible biomarker for hand eczema in the differential diagnosis of psoriasis. They first demonstrated the diagnostic gap in the standard procedures described above by investigating 30 patients with suspected hand eczema. Of the 30 patients, eight were clearly diagnosed using anamnesis, patch tests, and clinical examination. In contrast, psoriasis was suspected in nine patients and idiopathic hand eczema in 13. The group then examined several markers of the IL-1 cytokine family; of these, only IL-36α was suitable for distinguishing psoriasis from hand eczema. However, this small study has not yet been validated.[40] Another marker from the IL-1 family group, IL-36γ, has been proposed by other groups as a possible biomarker to differentiate psoriasis from AD.[44,45] Previous studies have demonstrated that IL-36γ is particularly elevated in psoriasis lesions and may be distinguished from other inflammatory skin diseases using immunohistochemistry.[41] IL-36γ may even be determined from tape-stripped samples and used as a classifier.[42] However, of 21 biopsies, only 15 could be correctly assigned, and this method has not yet been prospectively validated.[42]

The lack of prospective validation applies to other relevant proposed markers. For example, CCL26 was identified in a small population of Han Chinese as a marker for differentiation of psoriasis and AD.[35] Another example is one of the first studies in the field of molecular diagnostics that proposed CXCL9 as a biomarker for lichen ruber versus psoriasis and AD.[43] Although HBD2 is expressed 20-fold higher in psoriasis than in AD,[46] it has not been tested as a classifier.

Our group has developed a classifier that reliably distinguishes psoriasis from AD on the basis of the ratio of two

TABLE 2 Proposed diagnostic criteria of eczematized psoriasis.

Eczematized psoriasis must fulfil at least 2 criteria from each column:	
Psoriasis	**Eczema**
Extensor distribution	Flexural distribution
Inverse distribution	Lichenification
Nail phenomena of psoriasis	Vesicles
Psoriatic arthritis	Crusts
Negative smear test for *Staphylococcus (S.) aureus*	*S. aureus* detection
Positive family history of psoriasis	Positive family history of eczema
Histology: dilated capillaries	Positive specific IgE to common aeroallergens
Histology: micro-abscesses	*Histology:* spongiosis
Histology: parakeratosis	*Histology:* eosinophils
If available	
Molecular classifier	> 60% probability for psoriasis in molecular classifier test

biomarkers, NOS2 and CCL27, in paraffin-embedded tissue samples.[6] These genes were identified in a special group of patients with both psoriasis and AD simultaneously.[47] This classifier clearly identifies the underlying psoriasis signature, even in diagnostically challenging patients, such as eczematized psoriasis or hand eczema versus psoriasis palmaris.[37,38,48] However, this classifier is not currently available for use in clinical practice. Therefore, diagnostic criteria are still based on patient history and clinical and histological features.

PROPOSED DIAGNOSTIC CRITERIA

To better identify patients with eczematized psoriasis, we propose the following diagnostic criteria based on our own clinical experience (Table 2). Patients with at least two hallmarks of psoriasis and at least two hallmarks of AD are likely to be diagnosed with eczematized psoriasis. The clinical and histological criteria alone do not differentiate between eczematized psoriasis and psoriasis-like AD. Thus, wherever molecular tests are available, a probability of > 60% for psoriasis supports the diagnosis of eczematized psoriasis versus chronic AD. Prospective studies are required to confirm the validity of these criteria.

THERAPY

Eczematized psoriasis is difficult to treat as immunological alterations in both psoriasis and AD are present. To date, no clinical trials evaluating treatment efficacy in patients with eczematized psoriasis have been conducted, and as expected, no compound has been approved for the treatment of eczematized psoriasis. Cyclosporine or methotrexate might be a good choice for the initial treatment of eczematized psoriasis, as their broad immunosuppressive action is advantageous in a mixed psoriasis phenotype. However, both are often contraindicated in older patients, leading to a higher rate of viral infections, and their efficacy is lower than that of modern biologic therapies.[49] Biologics approved for psoriasis treatment are directed against TNF-α, IL-17A, IL-17F, IL-17RA, IL-23 p19, or IL-23 p40.[50,51] Their efficacy and safety have been evaluated in several phase III clinical studies.[52] Here, the comparative analysis indicated that ixekizumab and brodalumab achieved the highest rates of PASI 90 during the first 8–12 weeks of therapy,[53,54] whereas targeting IL-23 seems to be at least equally effective in the long run.[55] However, in eczematized psoriasis, concomitant efficacy for the immunological basis of eczematous aspects is desirable. Therefore, indirect inferences towards a beneficial effect can be drawn from studies testing these biologics for the treatment of eczematous skin lesions. Anti-TNF-α or anti-IL-17A studies with patients with AD have failed.[56,57] Furthermore, eczematous skin eruptions have been reported under these treatment regimens.[47,58,59] Risankizumab is currently being evaluated for the treatment of AD in a phase II clinical trial (ClinicalTrials.gov Identifier: NCT03706040). At the same time, the occurrence of eczematous skin lesions was observed in one patient receiving guselkumab.[60] Ustekinumab led to higher SCORAD50 rates than did placebo in adults with AD in a phase II clinical trial, but the primary endpoint was not met.[61] Thus, anti-TNF-α and anti-IL-17A biologics are likely to be unfavorable for the treatment of eczematized psoriasis, while the effects of anti-IL-23 p40 and anti-IL-23 p19 are unclear. In contrast to antibodies that neutralize IL-17A, brodalumab blocks the signaling of IL-17A, IL-17C, IL-17E, and IL-17F. Interestingly, Gambardella et al. reported a patient with psoriasis and AD who had a complete clinical response 8 weeks after starting brodalumab therapy.[62] Furthermore, Kimura et al. reported successful control of eczematous skin eruptions by brodalumab in a patient who had previously received ixekizumab for psoriasis.[63] Thus, additional blocking of IL-17C and IL-17E may be a promising strategy to treat eczematized psoriasis. Janus kinase (JAK) inhibition is an evolving therapeutic strategy that has already been approved for the treatment of AD and rheumatologic diseases, such as psoriatic arthritis. Depending on the selectivity for one or more of the four JAKs, the signaling of both type 2 and type 3 immune responses can be blocked. Although the JAK1/2 inhibitor baricitinib and the pan-JAK inhibitor tofacitinib showed beneficial effects in the treatment of plaque psoriasis, there have not been approvals in this indication as the overall efficacy was lower than that achieved by anti-IL-17 or anti-IL-23 biologic therapies.[64,65] However, the selective JAK1 inhibitors upadacitinib and tofacitinib have been approved for the treatment of psoriatic arthritis, and both upadacitinib and baricitinib are approved for the treatment of AD, indicating that JAK1/2 inhibition might also be beneficial for eczematized psoriasis. Inhibition of the fourth JAK TYK2, which is necessary for

IL-12, IL-23, and type 1 interferon signaling, is a potential new treatment for plaque psoriasis that is expected to be approved at the beginning of 2023.[66] However, based on the mechanism of action, the TYK2 inhibitor deucravacitinib is unlikely to also interrupt the pathways activated in eczematous skin reactions, and the clinical trial did not include studies on AD. Finally, apremilast, a phosphodiesterase 4 inhibitor approved for the treatment of plaque psoriasis and psoriatic arthritis, has also been investigated in AD. Simpson et al. reported a 30% improvement in eczema area and severity index score with administration of 40 mg apremilast twice daily, which was significantly higher than that in the placebo group (11% improvement). However, six cases of cellulitis occurred in this treatment arm, which is why the clinical development of apremilast in AD was discontinued.[67] Nevertheless, as the safety profile of 30 mg twice daily was in line with the reported safety profile in other indications, apremilast may be a therapeutic option for eczematized psoriasis, especially in older patients with comorbidities. In summary, there are several psoriasis drugs, which, based on their mechanism of action, simultaneously target type 2 immune pathways, such as the unspecific immunosuppressants methotrexate and cyclosporine, the IL-17 receptor antibody brodalumab, JAK inhibitors, and apremilast. Future studies on eczematized psoriasis are desirable to elucidate the clinical efficacy and safety of these drugs in a controlled manner.

CONCLUSIONS

Disease definition in dermatology has long been based on the description of the clinical phenotype and histological architecture. As common inflammatory skin diseases such as psoriasis or AD show substantial clinical heterogeneity that partially overlaps, the existence of patients with mixed phenotypes was long observed but was not regarded as clinically meaningful. However, the immunological basis of psoriasis as a Th17-dominated disease is in contrast with the Th2-mediated AD, and multiple therapeutic options have become available to treat either condition in a highly specific manner. Thus, mixed phenotypes must be defined more carefully. A prototype example of such an overlapping phenotype is eczematized psoriasis, which we define as psoriasis with clinical, histological, and immunological overlap with AD. We need to refine our diagnostic tools to obtain a better overview of the epidemiology, pathogenesis, and most importantly, therapeutic options for eczematized psoriasis. Molecular diagnostics may be highly beneficial in the future. Finally, once the diagnosis of eczematized psoriasis is clear, personalized treatment options can be selected.

ACKNOWLEDGEMENTS

Open access funding enabled and organized by Projekt DEAL.

CONFLICT OF INTEREST

F.L. received speaker and/or consulting fees from Janssen-Cilag Pharma, Amgen, UCB Pharma, Boehringer-Ingelheim, Bristol-Myers-Squibb, Union Therapeutics, Abbvie, Novartis Pharma, LEO Pharma, Lilly, Roche, Sanofi, Almirall, and Pfizer. K.E. received speaker and/or consulting fees from Abbvie, Almirall, BMS, Boehringer-Ingelheim, Janssen, Leo, Lilly, Novartis, Pfizer, Sanofi, and UCB.

REFERENCES

1. Parisi R, Iskandar IYK, Kontopantelis E, et al. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. *BMJ*. 2020;369:m1590.
2. Hansen I, Augustin M, Schafer I, Mohr N. Epidemiology of skin diseases in Germany: systematic review of the current state of research - part 2: non-infectious skin diseases. *J Dtsch Dermatol Ges*. 2022;20:445-455.
3. Noorily AR, Criscito MC, Cohen JM, Brinster NK. Psoriasis with eczematous features: a retrospective clinicopathologic study. *Am J Dermatopathol*. 2021;43:112-118.
4. Kolesnik M, Franke I, Lux A, Quist SR, et al. Eczema in psoriatico: An important differential diagnosis between chronic allergic contact dermatitis and psoriasis in palmoplantar localization. *Acta Derm Venereol*. 2018;98:50-58.
5. Henseler T, Christophers E. Disease concomitance in psoriasis. *J Am Acad Dermatol*. 1995;32:982-986.
6. Quaranta M, Knapp B, Garzorz N, Mattii M, et al. Intra-individual genome expression analysis reveals a specific molecular signature of psoriasis and eczema. *Sci Transl Med*. 2014;6(244):244ra90.
7. Weidinger S, Beck LA, Bieber T, Kabashima K, et al. Atopic dermatitis. *Nat Rev Dis Primers*. 2018;4:1.
8. Eyerich K, Eyerich S, Biedermann T. The multi-modal immune pathogenesis of atopic eczema. *Trends Immunol*. 2015;36:788-801.
9. Elias PM, Wakefield JS. Could cellular and signaling abnormalities converge to provoke atopic dermatitis? *J Dtsch Dermatol Ges*. 2020;18:1215-1223.
10. Boehncke WH, Schon MP. Psoriasis. *Lancet*. 2015;386:983-994.
11. Schon MP, Manzke V, Erpenbeck L. Animal models of psoriasis-highlights and drawbacks. *J Allergy Clin Immunol*. 2021;147:439-455.
12. Lauffer F, Eyerich K, Boehncke WH, et al. Cytokines of the IL-17 family in psoriasis. *J Dtsch Dermatol Ges*. 2020;18:675-681.
13. Lauffer F, Jargosch M, Baghin V, et al. IL-17C amplifies epithelial inflammation in human psoriasis and atopic eczema. *J Eur Acad Dermatol Venereol*. 2020;34:800-809.
14. Eyerich K, Pennino D, Scarponi C, et al. IL-17 in atopic eczema: linking allergen-specific adaptive and microbial-triggered innate immune response. *J Allergy Clin Immunol*. 2009;123:59-66e4.
15. Impellizzieri D, Ridder F, Raeber ME, et al. IL-4 receptor engagement in human neutrophils impairs their migration and extracellular trap formation. *J Allergy Clin Immunol*. 2019;144:267-79 e4.
16. Woytschak J, Keller N, Krieg C, et al. Type 2 interleukin-4 receptor signaling in neutrophils antagonizes their expansion and migration during infection and inflammation. *Immunity*. 2016;45:172-184.
17. Ghoreschi K, Thomas P, Breit S, et al. Interleukin-4 therapy of psoriasis induces Th2 responses and improves human autoimmune disease. *Nat Med*. 2003;9:40-46.
18. Flanagan KE, Pupo Wiss IM, Pathoulas JT, et al. Dupilumab-induced psoriasis in a patient with atopic dermatitis and alopecia totalis: A case report and literature review. *Dermatol Ther*. 2022;35:e15255.
19. Park JW, Park SJ, Koh YG, et al. Dupilumab-induced palmoplantar psoriasis: Is it true psoriasis? *Dermatitis*. 2022;33:e33-e35.
20. Eyerich S, Wagener J, Wenzel V, et al. IL-22 and TNF-alpha represent a key cytokine combination for epidermal integrity during infection with Candida albicans. *Eur J Immunol*. 2011;41:1894-1901.
21. Kao CY, Chen Y, Thai P, et al. IL-17 markedly up-regulates beta-defensin-2 expression in human airway epithelium via JAK and NF-kappaB signaling pathways. *J Immunol*. 2004;173:3482-3491.

22. Krohn S, Nies JF, Kapffer S, et al. IL-17C/IL-17 Receptor E signaling in CD4(+) t cells promotes TH17 cell-driven glomerular inflammation. *J Am Soc Nephrol*. 2018;29:1210-1222.
23. Chang SH, Reynolds JM, Pappu BP, et al. Interleukin-17C promotes Th17 cell responses and autoimmune disease via interleukin-17 receptor E. *Immunity*. 2011;35:611-621.
24. Peng T, Chanthaphavong RS, Sun S, et al. Keratinocytes produce IL-17c to protect peripheral nervous systems during human HSV-2 reactivation. *J Exp Med*. 2017;214:2315-2329.
25. Johnston A, Fritz Y, Dawes SM, et al. Keratinocyte overexpression of IL-17C promotes psoriasiform skin inflammation. *J Immunol*. 2013;190:2252-2262.
26. Vandeghinste N, Klattig J, Jagerschmidt C, et al. Neutralization of IL-17C reduces skin inflammation in mouse models of psoriasis and atopic dermatitis. *J Invest Dermatol*. 2018;138:1555-1563.
27. Brembilla NC, Senra L, Boehncke WH. The IL-17 family of cytokines in psoriasis: IL-17A and beyond. *Front Immunol*. 2018;9:1682.
28. Angkasekwinai P, Park H, Wang YH, et al. Interleukin 25 promotes the initiation of proallergic type 2 responses. *J Exp Med*. 2007;204:1509-1517.
29. Ballantyne SJ, Barlow JL, Jolin HE, et al. Blocking IL-25 prevents airway hyperresponsiveness in allergic asthma. *J Allergy Clin Immunol*. 2007;120:1324-1331.
30. Suto H, Nambu A, Morita H, et al. IL-25 enhances TH17 cell-mediated contact dermatitis by promoting IL-1beta production by dermal dendritic cells. *J Allergy Clin Immunol*. 2018;142:1500-09 e10.
31. Batalla A, Coto E, Gonzalez-Lara L, et al. Association between single nucleotide polymorphisms IL17RA rs4819554 and IL17E rs79877597 and psoriasis in a Spanish cohort. *J Dermatol Sci*. 2015;80:111-115.
32. Xu M, Lu H, Lee YH, et al. An interleukin-25-mediated autoregulatory circuit in keratinocytes plays a pivotal role in psoriatic skin inflammation. *Immunity*. 2018;48:787-98 e4.
33. Garzorz-Stark N, Eyerich K. [Molecular diagnostics of hand eczema]. *Hautarzt*. 2019;70:760-765.
34. Brunner PM, Israel A, Leonard A, et al. Distinct transcriptomic profiles of early-onset atopic dermatitis in blood and skin of pediatric patients. *Ann Allergy Asthma Immunol*. 2019;122:318-30 e3.
35. Chan TC, Sanyal RD, Pavel AB, et al. Atopic dermatitis in Chinese patients shows TH2/TH17 skewing with psoriasiform features. *J Allergy Clin Immunol*. 2018;142:1013-1017.
36. Stoffel E, Maier H, Riedl E, et al. Analysis of anti-tumour necrosis factor-induced skin lesions reveals strong T helper 1 activation with some distinct immunological characteristics. *Br J Dermatol*. 2018;178:1151-1162.
37. Garzorz-Stark N, Krause L, Lauffer F, et al. A novel molecular disease classifier for psoriasis and eczema. *Exp Dermatol*. 2016;25:767-774.
38. Garzorz N, Eyerich K. NOS2 and CCL27: Clinical implications for psoriasis and eczema diagnosis and management. *Expert Rev Clin Immunol*. 2015;11:167-169.
39. Garzorz-Stark N, Eyerich K. [Personalized medicine in the field of inflammatory skin diseases]. *Hautarzt*. 2019;70:15-20.
40. Schiattarella M, Patruno C, Balato N, et al. Chronic hand eczema: is IL-36alpha helpful in diagnosis and classification? *G Ital Dermatol Venereol*. 2017;152:578-585.
41. D'Erme AM, Wilsmann-Theis D, Wagenpfeil J, et al. IL-36gamma (IL-1F9) is a biomarker for psoriasis skin lesions. *J Invest Dermatol*. 2015;135:1025-1032.
42. Berekmeri A, Latzko A, Alase A, et al. Detection of IL-36gamma through noninvasive tape stripping reliably discriminates psoriasis from atopic eczema. *J Allergy Clin Immunol*. 2018;142:988-91.e4.
43. Wenzel J, Peters B, Zahn S, et al. Gene expression profiling of lichen planus reflects CXCL9+-mediated inflammation and distinguishes this disease from atopic dermatitis and psoriasis. *J Invest Dermatol*. 2008;128:67-78.
44. Buhl AL, Wenzel J. Interleukin-36 in Infectious and Inflammatory Skin Diseases. *Front Immunol*. 2019;10:1162.
45. Martin P, Goldstein JD, Mermoud L, et al. IL-1 Family antagonists in mouse and human skin inflammation. *Front Immunol*. 2021;12:652846.
46. de Jongh GJ, Zeeuwen PL, Kucharekova M, et al. High expression levels of keratinocyte antimicrobial proteins in psoriasis compared with atopic dermatitis. *J Invest Dermatol*. 2005;125:1163-1173.
47. Eyerich S, Onken AT, Weidinger S, et al. Mutual antagonism of T cells causing psoriasis and atopic eczema. *N Engl J Med*. 2011;365:231-238.
48. Bentz P, Eyerich K, Weisshaar E. Psoriasis or eczema? One-year results from the DGUV research project FB323 with application of the molecular classifier in occupational dermatoses. *J Dtsch Dermatol Ges*. 2022;20:1233-1234.
49. Buhl T, Beissert S, Gaffal E, et al. COVID-19 and implications for dermatological and allergological diseases. *J Dtsch Dermatol Ges*. 2020;18:815-824.
50. Nast A, Altenburg A, Augustin M, et al. German S3-Guideline on the treatment of Psoriasis vulgaris, adapted from EuroGuiDerm – Part 1: Treatment goals and treatment recommendations. *J Dtsch Dermatol Ges*. 2021;19:934-950.
51. Nast A, Altenburg A, Augustin M, et al. German S3-Guideline on the treatment of Psoriasis vulgaris, adapted from EuroGuiDerm – Part 2: Treatment monitoring and specific clinical or comorbid situations. *J Dtsch Dermatol Ges*. 2021;19:1092-1115.
52. Xu S, Gao X, Deng J, et al. Comparative efficacy and safety of biologics in moderate to severe plaque psoriasis: a multiple-treatments meta-analysis. *J Dtsch Dermatol Ges*. 2021;19:47-56.
53. Warren RB, See K, Burge R, et al. Rapid response of biologic treatments of moderate-to-severe plaque psoriasis: A comprehensive investigation using Bayesian and Frequentist Network meta-analyses. *Dermatol Ther (Heidelb)*. 2020;10:73-86.
54. Warren RB, Gooderham M, Burge R, et al. Comparison of cumulative clinical benefits of biologics for the treatment of psoriasis over 16 weeks: Results from a network meta-analysis. *J Am Acad Dermatol*. 2020;82:1138-1149.
55. Blauvelt A, Leonardi C, Elewski B, et al. A head-to-head comparison of ixekizumab vs. guselkumab in patients with moderate-to-severe plaque psoriasis: 24-week efficacy and safety results from a randomized, double-blinded trial. *Br J Dermatol*. 2021;184(6):1047-1058.
56. Ungar B, Pavel AB, Li R, et al. Phase 2 randomized, double-blind study of IL-17 targeting with secukinumab in atopic dermatitis. *J Allergy Clin Immunol*. 2021;147:394-397.
57. Jacobi A, Antoni C, Manger B, et al. Infliximab in the treatment of moderate to severe atopic dermatitis. *J Am Acad Dermatol*. 2005;52:522-526.
58. Ruiz-Villaverde R, Galan-Gutierrez M. Exacerbation of atopic dermatitis in a patient treated with infliximab. *Actas Dermosifiliogr*. 2012;103:743-746.
59. Burlando M, Cozzani E, Russo R, Parodi A. Atopic-like dermatitis after secukinumab injection: A case report. *Dermatol Ther*. 2019;32:e12751.
60. Reyn B, Hillary T, Gils A. Eczematous eruption after guselkumab treatment for psoriasis. *JAAD Case Rep*. 2019;5:973-975.
61. Khattri S, Brunner PM, Garcet S, et al. Efficacy and safety of ustekinumab treatment in adults with moderate-to-severe atopic dermatitis. *Exp Dermatol*. 2017;26:28-35.
62. Gambardella A, Licata G, De Rosa A, et al. Concurrent atopic dermatitis and psoriasis successfully treated with brodalumab. *Dermatitis*. 2021;32(1S):e86-e88.
63. Kimura R, Sugita K, Yamamoto O. Successful switching to brodalumab in a patient with severe psoriasis developing ixekizumab-induced eczema. *Eur J Dermatol*. 2020;30:732-734.
64. Papp KA, Menter MA, Raman M, et al. A randomized phase 2b trial of baricitinib, an oral Janus kinase (JAK) 1/JAK2 inhibitor, in patients with moderate-to-severe psoriasis. *Br J Dermatol*. 2016;174:1266-1276.
65. Tian F, Chen Z, Xu T. Efficacy and safety of tofacitinib for the treatment of chronic plaque psoriasis: a systematic review and meta-analysis. *J Int Med Res*. 2019;47:2342-2350.

66. Armstrong AW, Gooderham M, Warren RB, et al. Deucravacitinib versus placebo and apremilast in moderate to severe plaque psoriasis: efficacy and safety results from the 52-week, randomized, double-blinded, placebo-controlled phase 3 POETYK PSO-1 trial. *J Am Acad Dermatol*. 2023;88(1):29-39.
67. Simpson EL, Imafuku S, Poulin Y, et al. A phase 2 randomized trial of apremilast in patients with atopic dermatitis. *J Invest Dermatol*. 2019;139:1063-1072.

How to cite this article: Lauffer F, Eyerich K. Eczematized psoriasis – a frequent but often neglected variant of plaque psoriasis. *JDDG: Journal der Deutschen Dermatologischen Gesellschaft*. 2023;21:445–453.
https://doi.org/10.1111/ddg.14991