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A rare case with prominent features of both discoid lupus erythematosus and pemphigus foliaceus

Dear Editor,

The actual concurrence of lupus erythematosus (LE) and pemphigus is a rare phenomenon, that is different from pemphigus erythematosus (PE), which is a variant of pemphigus foliaceus (PF) with LE-like features.[1,2] Here, we present a case that has both discoid lupus erythematosus (DLE) and PF.

A 54-year-old man was admitted to our clinic for wounds on his face and scalp that has been present for 5 years. For the last 5 months, new lesions have developed on his chest and back. Dermatological examination revealed well-demarcated, erythemato-squamous plaques, some with atrophic centre or with cicatricial alopecia, on the scalp, nose, malar area and lips. In addition, the new lesions on the trunk and back consisted of bullae and erosions with scale-crusts (Fig. 1). Histopathology and direct immunofluorescence microscopy (DIF) from malar area revealed findings that were compatible with DLE and PF. Serologic tests (ANA and ENA) for systemic lupus erythematosus were negative. ELISA showed positive results for antidesmoglein 1 (Dsg1, 138 U/mL) antibody. Paraffin sections of a lesional biopsy were sent to Centre of Blistering Diseases at the University of Groningen to identify whether Dsg1 ectodomain is present in the epidermal basement membrane zone (BMZ). DIF showed clustered IgG depositions on the epithelial cell surface (ECS) as well as clustering of Dsg1 by double staining, which is typical for PF. However, we did not find evidence of IgG along the BMZ nor of Dsg1 ectodomain depositions along the BMZ. Although clusters of Dsg1 were present at the basal sides of keratinocytes, these contained the complete Dsg1 molecule as they were positive for both the endodomain and the ectodomain (Fig. 2).

In conclusion, with clinical manifestations and absent of IgG and Dsg1 ectodomain depositions along the BMZ region, we diagnosed this patient as coexistence of DLE and truncal PF. The lesions cleared with topical corticosteroid and oral hydroxychloroquine. For the time being, the diseases have maintained in remission for 4 years.

Pemphigus foliaceus and LE are both autoimmune diseases but with different autoantibodies, that is, anti-Dsg1 and ANA, respectively.[3,4] A dual autoimmune response with one organ-specific response for pemphigus and another response that manifests as a different phenotype, such as cutaneous LE, was suggested as underlying cause of this coexistence.[5] So, the dual response mechanism could be the underlying mechanism in our patient.

PE was first described in 1926 by Senear and Usher [6] as a condition with a lupus-like butterfly rash or severe seborrhoeic dermatitis, which they suggested was a combination of PV and LE. When insights into the differences between PV and PF crystallized, PE was not classified with PV but considered an early or a non-generalized form of PF.[7] PE is considered an early localized

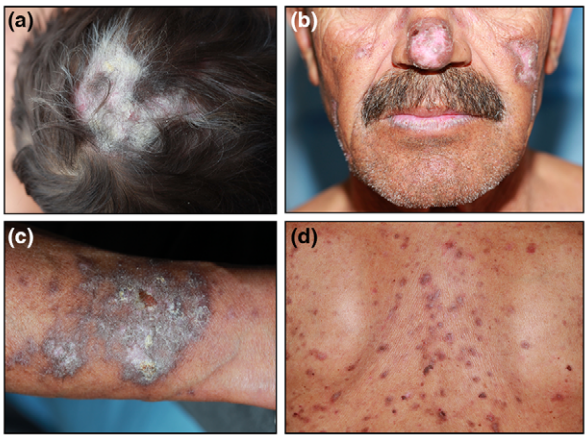

Figure 1 (a) An erythematous, scaly plaque on the scalp, (b) Plaques with central depigmented atrophy on the nose, malar area and lower lips, (c) An erosive erythematous, scaly plaque on the right forearm, (d) Vesicles on erythematous base and haemorrhagic crusts on back.

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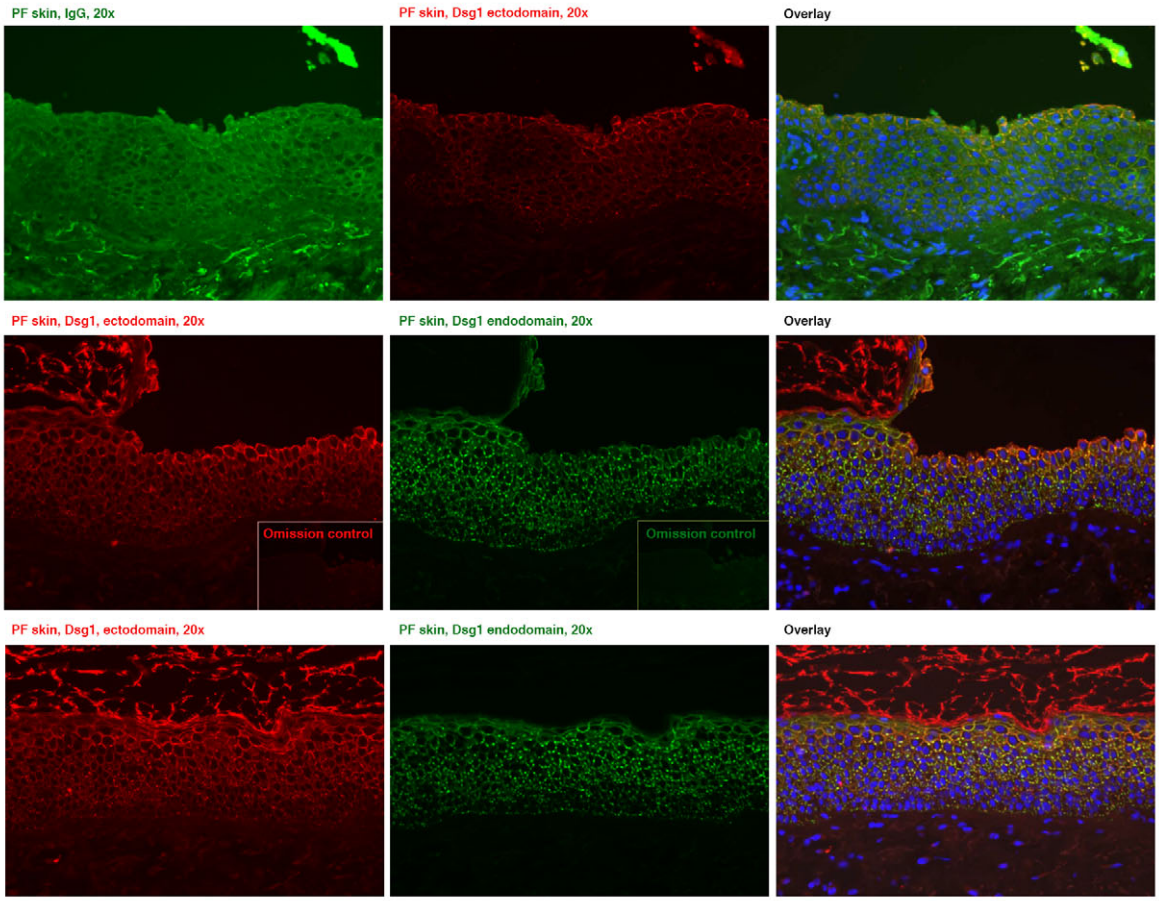

Figure 2 DIF of Dsg1 and IgG from malar lesional skin biopsy in PF patient. Top row: In vivo IgG depositions at the epithelial cell surface, but not along the BMZ. Bottom row: Dsg1 ectodomain depositions are less clustered than Dsg1 endodomain. Dsg1 endodomain depositions at the BMZ, but not of Dsg1 ectodomain.

form of PF not related to LE and usually has concomitant BMZ deposition of immunoglobulin and complement in lesional skin in addition to ECS staining in the epidermis, whereas PF is a generalized process that lacks BMZ staining.[8]

Few patients have been reported to actually have the two diseases concurrently.[9] Our case had typical atrophic DLE lesions on scalp and face, and positive lupus band test, in addition generalized superficial bullae and erosions and immunopathology compatible with PF. In addition, we did not find IgG and Dsg1 ectodomain depositions along the BMZ region that is typical for PE.[10] We therefore think this patient first had cutaneous DLE and then later developed classic PF without the PE subtype.

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Biologic switching between interleukin 17A antagonists secukinumab and ixekizumab: a 12-week, multicenter, retrospective study

Dear Editor,

A recent review by Hu *et al.*[1] highlights the use of biologic switching in clinical practice to maximize skin clearance and improve clinical outcomes. However, efficacy and safety outcomes of ixekizumab therapy in patients who did not respond to, lost response, or were intolerant to secukinumab was not mentioned in their review and is lacking. As such, dermatologists may be hesitant to switch between interleukin (IL) 17A antagonists, electing to try an alternative biologic with a different mechanism of action. We recently published a series of 17 patients switching between IL-17A antagonists, suggesting ixekizumab is a promising treatment option with good clinical outcome and few adverse events (AE) for plaque psoriasis patients with prior exposure to secukinumab.[2] Due to the importance of this topic and lack of available evidence, we present here an additional 14 patients. In the current study, we aimed to further investigate whether plaque psoriasis patients with prior exposure to secukinumab will (i) achieve efficacious outcomes with ixekizumab, (ii) experience the same safety outcomes as they did with secukinumab and (iii) allow us to predict ixekizumab efficacy outcomes based on duration of exposure and reason for discontinuation of secukinumab.

Inclusion criteria for this multicenter retrospective chart review included all consecutive patients 18 years of age or older with moderate to severe plaque psoriasis and treated with ixekizumab therapy following discontinuation of secukinumab. The clinically significant endpoint for efficacy was 75% or more improvement from baseline in PASI (PASI 75) following 12 weeks of ixekizumab treatment. In instances where PASI was not documented, physician global assessment (PGA) of 0 (clear) or 1 (almost clear) was used. Safety endpoints were quantified by reported AEs.

A total of 31 patients met inclusion criteria and were included in the present work (Table 1). Of the 31 patients, 22 (71.0%) achieved PASI 75 or PGA of 0/1 after 12 weeks of ixekizumab therapy (Table 2). These results are less than the 87.3–89.7% seen with IL-17A naive patients treated with ixekizumab in randomized controlled trials (RCTs).[3,4] Of note, all patients in the present work previously failed one or more biologic therapies (mean: 3.6 ± 1.3) compared to the 15.1–40% of patients in RCTs. As such, it is unclear whether the decrease in PASI 75 response rate within our cohort is due to prior exposure to an IL-17A agent or the complexity of our patient population who have numerous comorbid disorders and have failed on average 3.6 ± 1.3 biologics prior to ixekizumab. Furthermore, it is important to recognize that PGA 0/1 is more challenging to achieve than PASI 75. Therefore, the use of PGA as a primary endpoint within our study may be contributory to our lower efficacy rates.

Interestingly, proportionally more patients with ≥53 weeks of secukinumab exposure achieved PASI 75 at week 12 (100%, n = 7/7) compared to those who discontinued treatment between 4–26 (50.0%, n = 4/8) and 27–52 weeks (68.8%, n = 11/16). Although those who were treated with secukinumab for longer than 52 weeks appear to be more likely to respond

Table 1 Summary of patient characteristics prior to starting ixekizumab therapy

Variable	Value N = 31
Sex – no. (%)	
Male	20 (64.5)
Female	11 (35.5)
Mean age – y ± SD	49.1 ± 11.0
Mean weight – kg ± SD	97.3 ± 29.3
Comorbidities – no. (%)	
Psoriatic arthritis	22 (71.0)
Hypertension	14 (45.2)
Dyslipidemia	10 (32.2)
Diabetes	7 (22.6)
Psychiatric disorders	3 (9.7)
Malignancy	2 (6.4)
Renal disease	2 (6.4)
mean ± SD	2.0 ± 1.5
Number of previously failed therapies – mean ± SD	
Systemic	5.8 ± 1.8
Biologic	3.6 ± 1.3
Number of weeks treated with secukinumab	
mean ± SD	41.1 ± 23.4
Minimum/Maximum	4/85

n, number of subjects meeting criteria; SD, standard deviation; y, years.

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