Erythrodermic presentation of psoriasis in a patient treated with dupilumab

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Dupilumab is an interleukin (IL)-4 receptor α (IL-4Rα) antagonist that inhibits IL-4 and IL-13 signaling, key mediators of T-helper (Th) 2-mediated inflammation.[1] Whereas an immune shift toward Th2 drives atopic dermatitis and thus a blockade in the Th2 inflammatory cascade is an effective treatment, the opposing shift toward Th1 and Th17 cells is implicated in the pathogenesis of psoriasis.[2] We present an erythrodermic presentation of psoriasis in a patient treated with dupilumab for a dermatitis that was clinically diagnosed as atopic dermatitis.

Abbreviations used:

IL: interleukin
Th: T-helper

REPORT OF A CASE

A woman in her 50s with a history of asthma and atopic dermatitis presented to the Emergency Department with erythroderma. A clinical diagnosis of atopic dermatitis was made by a local dermatologist many years ago, which had been treated with intermittent courses of prednisone. Four months before her presentation to our department, however, new plaques developed that were unlike her usual flares. They involved previously unaffected areas including the midback and anterior legs, were more painful with thicker scale, and did not resolve with a course of prednisone. Two months after the onset of the new eruption, after an initial course of oral steroids did not resolve her rash, her dermatologist initiated dupilumab. Her rash continued to progress over the next 2 months to involve most of her skin. She took no chronic medications and did not have any other new drug exposures.

Upon evaluation, she was tachycardic but afebrile. Skin examination found erythematous plaques involving the trunk and bilateral upper and lower extremities with thick white scale (Fig 1). On dermoscopic examination, few pinpoint pustules were appreciable on the legs and abdomen. Scalp examination found oval pink plaques with thick, adherent scale. The face was relatively spared.

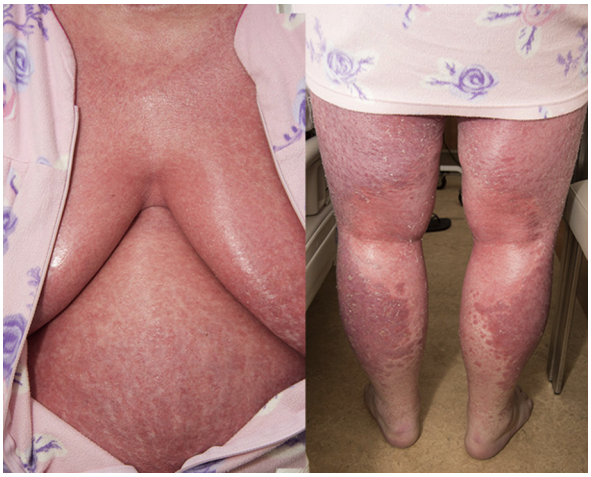

Fig 1. Clinical presentation. Diffuse erythema involving the chest and well-demarcated pink plaques with thick scale on the posterior legs.

Our clinical differential diagnosis included drug-induced psoriasis versus new-onset erythrodermic psoriasis; less likely were acute generalized exanthematous pustulosis or any other cause of erythroderma, including cutaneous T-cell lymphoma.

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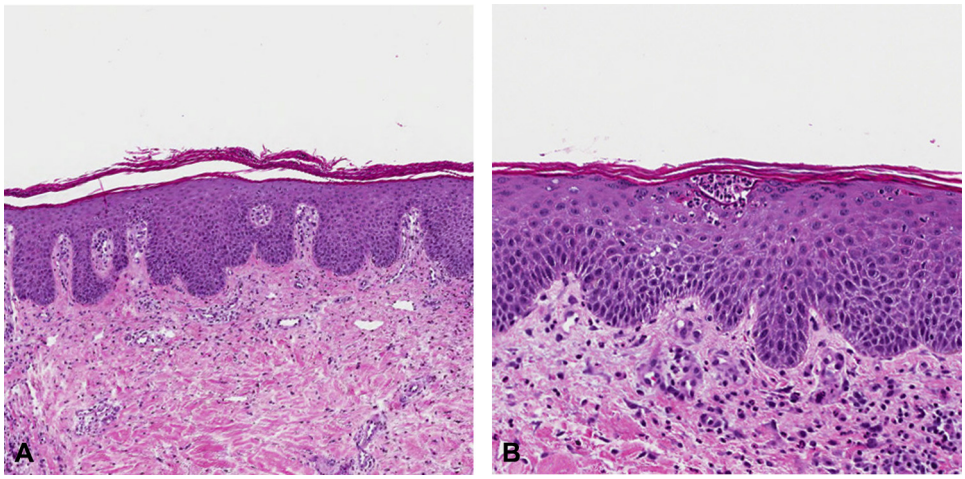

Fig 2. Histopathologic findings. **A**, Punch biopsy from the arm. Histologic examination shows psoriasiform hyperplasia with diminished granular layer and parakeratotic scale. **B**, Punch biopsy from the abdomen. Histologic examination shows acanthosis, mild spongiosis, and intraepidermal neutrophils forming subcorneal pustules.

Laboratory evaluation was significant for leukocytosis (13,960/μL) with neutrophilia (10,760/μL) and elevated C-reactive protein (12.3 mg/dL) and erythrocyte sedimentation rate (31 mm/h). Eosinophils (370/μL, 2.7%) and serum calcium (8.7 mg/dL) were normal. The pustules were not cultured as they were minute.

Two punch biopsies were performed. The biopsy from the arm found psoriasiform hyperplasia with a diminished granular layer and focal collections of neutrophils within parakeratotic scale. There was a brisk perivascular and diffuse dermal infiltrate of neutrophils with admixed histiocytes and occasional eosinophils (Fig 2, *A*). The biopsy from the abdomen found irregular acanthosis, mild spongiosis, and intraepidermal neutrophils forming subcorneal pustules. The granular layer was maintained with focal parakeratosis (Fig 2, *B*). Periodic acid—Schiff stain of both specimens was negative. The findings were more consistent with drug-induced psoriasis than acute generalized exanthematous pustulosis. Findings of cutaneous T-cell lymphoma, such as a lichenoid infiltrate of atypical lymphocytes with exocytosis, were not seen.

Based on the clinical, laboratory, and histologic findings, erythrodermic psoriasis was diagnosed. Dupilumab was discontinued, and the patient was started on methotrexate and topical steroids with marked improvement. After several months, she tapered off of methotrexate, and her skin returned to baseline.

DISCUSSION

Psoriasis and atopic dermatitis are both T-cell—mediated inflammatory diseases in which T-cell—derived cytokines signal keratinocytes to alter growth and differentiation. Although recent research implicates Th17 cells and associated IL-17, IL-23, and IL-12 as the key inflammatory mediators in psoriasis, the immune imbalance in these 2 diseases is classically thought to exist at opposing ends of a spectrum, with a Th1 shift driving psoriasis and a Th2 shift driving atopic dermatitis.[3]

Our patient's history suggests new-onset psoriasis that was initially misdiagnosed as worsening atopic dermatitis. With this error of diagnostic inertia, coupled with a powerful immunomodulatory medication, the disease progressed to an erythrodermic presentation. Although progression of disease may have occurred independently from treatment with dupilumab, we hypothesize that blockade of Th2-mediated inflammation with dupilumab, and a resultant shift toward Th1, was a pathogenic factor in our patient's development of erythrodermic psoriasis. Alternative explanations for the patient's history include that her skin disease was actually psoriasis from the outset or that atopic dermatitis was in fact the correct diagnosis and initiation of dupilumab therapy preceded the onset of psoriasis.

To our knowledge, new presentation of psoriasis or exacerbation of psoriasis has not been reported in the setting of dupilumab therapy, suggesting that the proposed immune shift mechanism, if true, may only be clinically relevant in predisposed individuals. The postmarketing experience with dupilumab is limited. Entry into clinical trials of dupilumab are very closely controlled, with inclusion criteria mandating diagnostic rigor, specific disease severity scores and areas of body surface involvement, and inadequate response to prior treatments.[4] Based on

her history, our patient would not have been eligible to participate in a clinical trial for dupilumab. As with any new medication that enters the market, additional adverse events are revealed as a result of postmarketing surveillance.

A corollary exists in the literature for other immunomodulatory medications used frequently by dermatologists: eczema has been reported as an adverse effect of anti–tumor necrosis factor-α therapy for psoriasis and other inflammatory diseases.[5] This counterintuitive response is also postulated to be a consequence of altering the Th1/Th2 balance, lending support to our hypothesized mechanism behind the exacerbation of psoriasis as an adverse effect of treatment with dupilumab.

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