Non–Drug-Induced Pemphigus Foliaceus in a Patient With Rheumatoid Arthritis

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PRACTICE **POINTS**

- Physicians should consider pemphigus foliaceus in the differential diagnosis in patients with rheumatoid arthritis and blistering eruptions.
- Appropriate analyses should be performed, including skin biopsy for histologic and immunohistochemical examination as well as search for circulating antibodies.

To the Editor:

The term *pemphigus* describes a group of autoimmune blistering diseases that are histologically characterized by intraepidermal blisters caused by acantholysis. There are several types of pemphigus foliaceus, such as classic and endemic pemphigus foliaceus, pemphigus erythematosus, pemphigus herpetiformis, and drug-induced pemphigus foliaceus.[1]

Drug-induced pemphigus foliaceus in patients treated with penicillamine for rheumatoid arthritis (RA) is well documented in the literature.[2] An association between pemphigus foliaceus and RA without penicillamine therapy is rare. We present a case of a patient with a history of RA who developed this bullous disease.

A 67-year-old woman with a 15-year history of seropositive RA presented with widespread skin lesions of 4 weeks' duration. Confluent scaly crusted erosions on an erythematous base were present on the back (Figure 1), chest, and abdomen. There was no alteration of the mucous membranes. Medical treatment consisted of methotrexate (10 mg weekly), folic acid (5 mg twice weekly), prednisolone (5 mg daily), and ketoprofen (50 mg daily). Routine blood analysis was unremarkable, except for a positive rheumatoid factor. Histologic examination showed a subcorneal

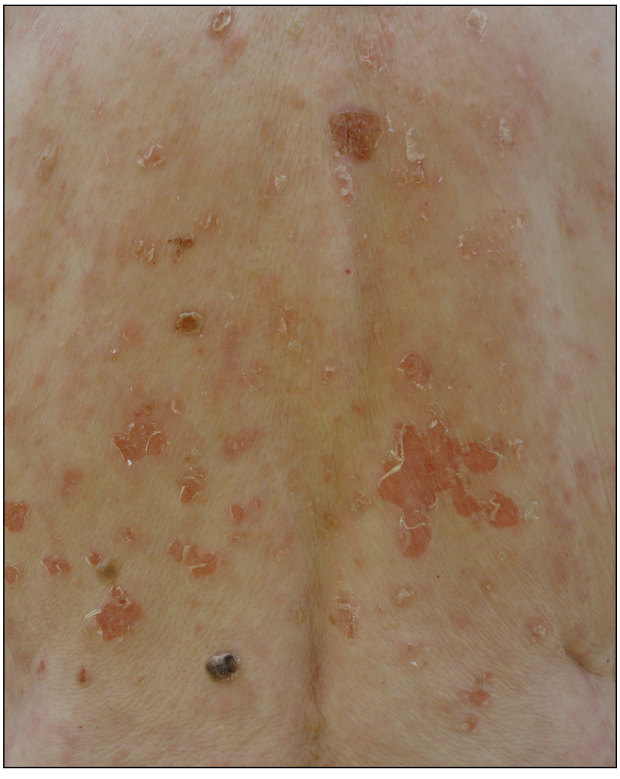

Figure 1. Multiple erosions and crusted lesions were present on the back.

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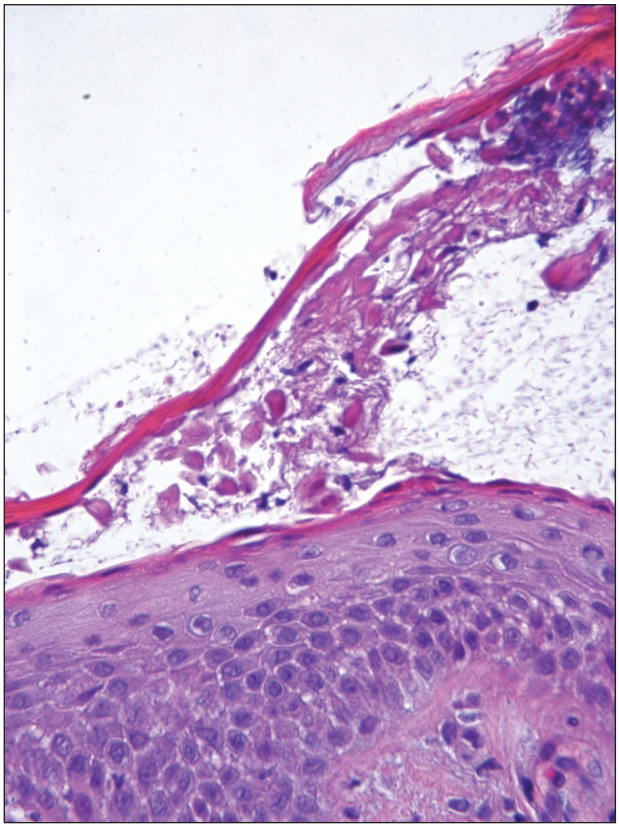

Figure 2. Subcorneal bulla containing acantholytic keratinocytes and neutrophils (H&E, original magnification ×100).

bulla containing acantholytic keratinocytes and neutrophils. There was a mild lymphocytic and eosinophilic infiltrate in the papillary dermis (Figure 2).

Determination of anti-desmoglein 1 and 3 antibodies was performed by a commercial enzyme-linked immunosorbent assay. Desmoglein 1 antibodies were positive with titers of 30 U/mL (positive, ≥20 U/mL), whereas desmoglein 3 antibody was negative. Thus, a diagnosis of pemphigus foliaceus was established. The polymerase chain reaction ligation-based typing method and the nucleotide sequence was used to examine the protein drought-repressed 4 gene complex, *DR4*, which tested positive.

Based on a diagnosis of pemphigus foliaceus, the patient's corticosteroid treatment was changed from 5 mg daily of prednisolone to 40 mg daily of methylprednisolone, leading to marked improvement of the cutaneous lesions. After tapering the steroid dosage over a period of 3 months, no relapse occurred.

Pemphigus foliaceus is a rare autoimmune blistering disease. It can be induced by drugs, such as penicillamine and captopril.[2,3] Captopril, an angiotensin-converting enzyme inhibitor, is closely related to penicillamine structurally. Both drugs have highly active thiol groups capable of reducing disulfide bonds and inducing acantholysis.[4] The drugs taken by our patient typically are not known to induce pemphigus foliaceus.

The association of pemphigus foliaceus with RA in the absence of penicillamine therapy was first described by Wilkinson et al.[4] Since then, additional cases have been published.[5,6] Pemphigus foliaceus also has been described with other autoimmune conditions such as autoimmune thyroid disease.[7]

Rheumatoid arthritis has been genetically linked to the HLA-DR4 gene complex, which also was found in our patient. Patients with pemphigus foliaceus and RA have an increased frequency of the class II major histocompatibility complex, serologically defined HLA-DR4, and HLA-DRw6 haplotypes.[4] Therefore, we believe that the association of pemphigus foliaceus and RA in our patient might not be fortuitous.

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