Multiple granulomatous dermatitides in a patient with rheumatoid arthritis

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INTRODUCTION

Granulomatous dermatitides often arise as a cutaneous reaction pattern to an underlying systemic inflammatory process, such as autoimmune disease. Here we present a case of multiple types of granulomatous dermatitides in a patient with rheumatoid arthritis.

CASE REPORT

A woman in her 70s was referred for a 20-year history of progressive skin disease consisting of annular plaques on her trunk and extremities, atrophic plaques on her legs, and painful subcutaneous nodules on her hands and feet (Fig 1). She complained of mild shortness of breath, polyarthralgias, and numbness and tingling of the lower extremities consistent with a sensory peripheral neuropathy. She had 2 episodes of ocular necrotizing scleritis that resolved with high-dose prednisone.

Physical examination found extensive pink scaly annular plaques on her upper back, arms, and legs; nodules on the dorsal hands and fingers overlying joints; and atrophic, orange-brown and hyperpigmented plaques on the lower shins as well as a symmetric polyarthritis. She also had transient red-brown subcutaneous nodules on the lower legs.

Laboratory blood analysis found a leukocyte count of 18.5 thousand/μL (normal, 3.8−10.8 thousand/μL) with a serum eosinophilia count of 4736 cells per microliter (normal, 15−500 cells per microliter) and high-sensitivity C-reactive protein level of 2.8 mg/L (normal, <1 mg/L). Negative examinations included antineutrophil cytoplasmic antibodies, urinalysis, antinuclear antibody, rheumatoid factor, anticitrullinated protein antibodies, erythrocyte sedimentation rate, angiotensin-converting enzyme, and chest radiograph. Pulmonary function tests found mild restrictive and obstructive lung disease. Hand radiograph found erosions involving the distal fifth metacarpals bilaterally.

Histologic examination of the annular plaques and nodules on the dorsal hands and upper back found palisading granulomatous inflammation with mucinous degeneration of collagen consistent with granuloma annulare, whereas biopsy findings of the nodules on the right lower leg were consistent with erythema nodosum (Fig 2, *A* and *B*). Histologic evaluation of the papules overlying the joint spaces found palisaded histiocytes around eosinophilic material consistent with rheumatoid nodules (Fig 2, *C*). Histologic examination of the atrophic, hyperpigmented plaque on the shin found interstitial granulomatous infiltrate involving the superficial and deep dermis with layering of inflammatory infiltrate and dense hyalinized collagen consistent with necrobiosis lipoidica (not shown).

Considering the clinical and pathologic findings, a diagnosis of seronegative rheumatoid arthritis was rendered, with cutaneous manifestations of rheumatoid nodules (RN), granuloma annulare (GA), erythema nodosum (EN), and necrobiosis lipoidica (NL). She was treated with methotrexate, 22.5 mg

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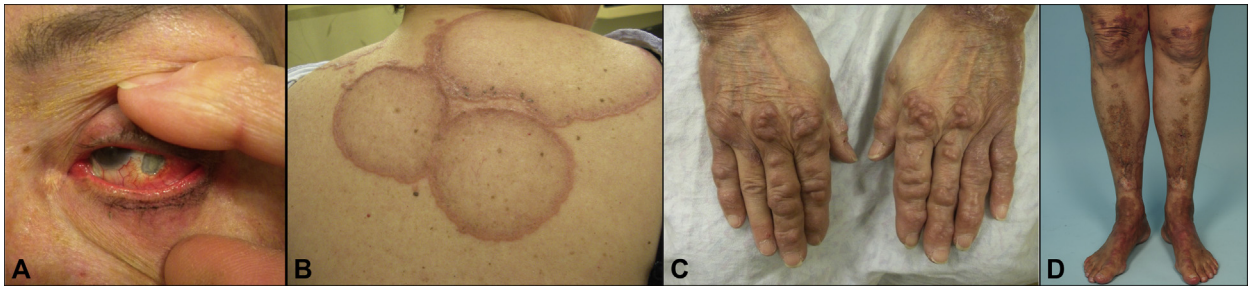

Fig 1. Clinical findings, pretreatment. **A**, Necrotizing scleritis of the left eye. **B**, Pink, scaly annular plaques on the upper back. **C**, Firm nodules on the dorsal hands. **D**, Atrophic, hyperpigmented plaques on the bilateral anterior legs.

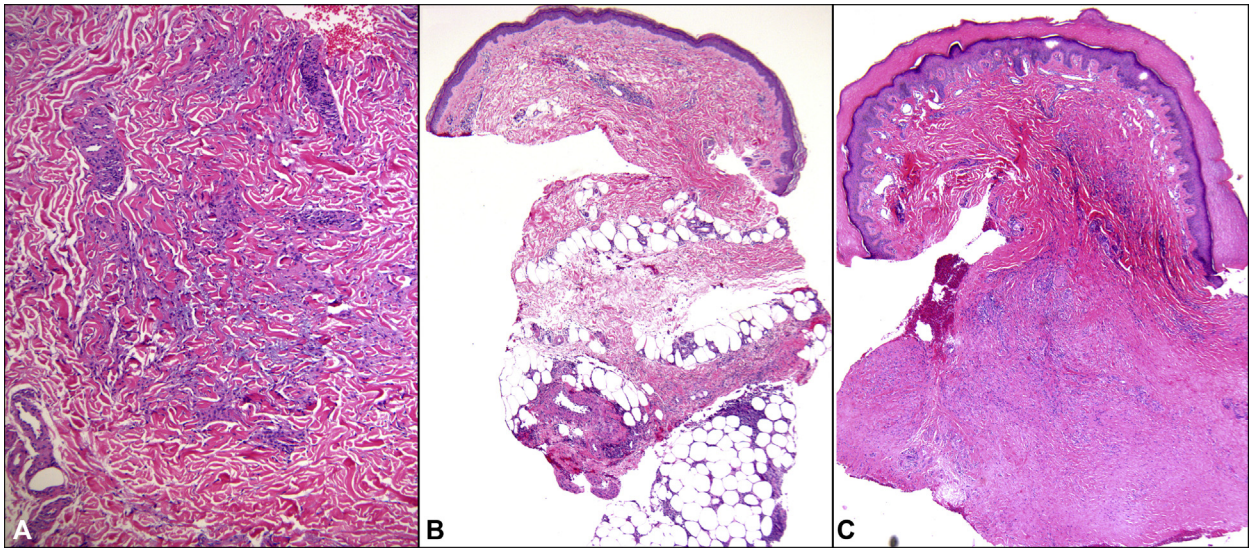

Fig 2. Histopathologic features. **A**, Histologic examination of the annular plaques on the upper back shows a palisaded histiocytic granuloma surrounding a focus of mucinous necrobiosis within the superficial to mid dermis (original magnification ×10). **B**, Biopsy of a nodule on the right lower leg shows a septal panniculitis (original magnification ×5). **C,** Histologic analysis of the nodules on the dorsal hands shows homogenous eosinophilic material with a palisade of histiocytes (original magnification ×5). (**A**–**C**, Hematoxylin-eosin stain; original magnifications: **A**, ×10; **B** and **C**, ×5.)

weekly, pentoxifylline, 400 mg twice daily, and triamcinolone acetonide ointment with significant improvement in her cutaneous disease and other symptoms (Fig 3).

DISCUSSION

Our patient's constellation of symptoms of an erosive, symmetrical polyarthritis, necrotizing scleritis, mild restrictive and obstructive lung disease, hypereosinophilia, and peripheral neuropathy, are most consistent with rheumatoid arthritis (RA); atypical eosinophilic granulomatosis with polyangiitis was also strongly considered. We argue that our patient's multiple reactive granulomatous dermatitides erupted as a result of this underlying inflammatory process.

RA is a systemic inflammatory disorder characterized by articular and extra-articular manifestations. More specifically there is some combination of morning stiffness, symmetric polyarthritis, radiographic changes of erosions and bone decalcifications, positive rheumatoid factor, and rheumatoid nodules. Our patient has many uncommon extra-articular manifestations of RA. Necrotizing scleritis, characterized by severe eye pain and pain with eye movement, is one of the ocular inflammatory diseases associated with severe rheumatoid arthritis, affecting 0.2% to 6.3% of RA patients.[1] Hypereosinophilia, although not common in

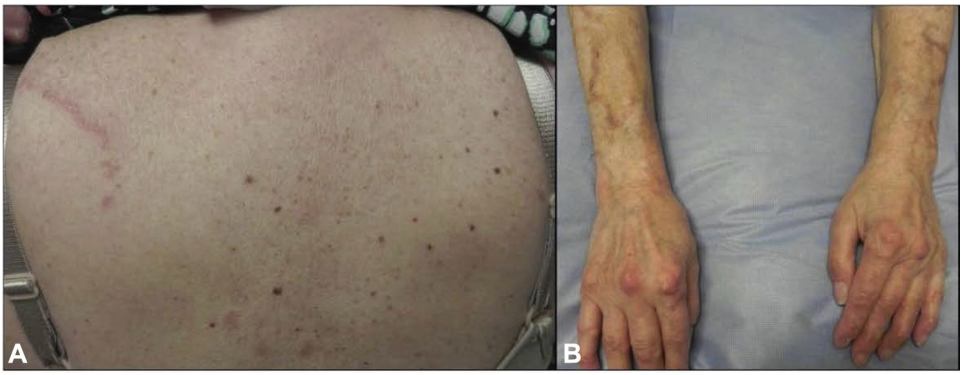

Fig 3. Clinical findings, posttreatment. **A**, Upper back, significant improvement of granuloma annulare. **B**, Bilateral dorsal forearms and hands, significant improvement of granuloma annulare and rheumatoid nodules.

connective tissue disease, is seen in about 7.6% of patients with RA.[2] A distal symmetric sensory neuropathy characterized by paresthesias, numbness, and pain, thought to be caused by vasculitis, is seen in RA.[3] Finally, in this clinical milieu, the mild restrictive and obstructive lung disease is most consistent with airway disease in RA, which represents either bronchiolitis or bronchiectasis, which has variable prognosis.[4] The classic cutaneous manifestation of RA is the rheumatoid nodule, as seen in our patient. Less common cutaneous manifestations of RA include cutaneous rheumatoid vasculitis, cutaneous ulcers in Felty syndrome, rheumatoid neutrophilic dermatosis, and intravascular or intralymphatic histiocytosis of the skin.[5]

It has been argued that granulomatous dermatitides can present as a reaction to underlying systemic inflammation such as autoimmune or metabolic disease, medications, or malignancy. In fact, the umbrella term, *reactive granulomatous dermatitis*, which encompasses palisaded neutrophilic and granulomatous dermatitis, interstitial granulomatous dermatitis, and interstitial granulomatous drug reaction, has been created to highlight not only the similar histopathology of these diseases but also the reactive nature of their proposed etiopathology.[6] Reactive granulomatous dermatitides are associated with connective tissue disease (EN), inflammatory arthritides (EN, RN), hematologic disorders (GA), infections such as HIV (GA), streptococcal infection (EN), tuberculosis (EN), systemic fungal infections (EN), inflammatory bowel disease (EN), diabetes mellitus (NL), solid organ malignancies (GA), and medications (EN, GA).

Given that rheumatoid arthritis is an autoimmune disease characterized by granulomatous inflammation, it is, therefore, not surprising that RA could be associated with an increased risk of multiple granulomatous dermatitides. This case of RN, EN, GA, and NL presenting in a patient with RA highlights the importance of maintaining a high index of suspicion for underlying systemic disease because of the reactive nature of granulomatous dermatitis, while further demonstrating that cutaneous granulomatous dermatitis may represent a nonspecific reaction pattern wherein there may be substantial overlap among various entities.

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