Palisaded neutrophilic granulomatous dermatitis: Spectrum of histologic findings in a single patient

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INTRODUCTION

Palisaded neutrophilic granulomatous dermatitis (PNGD) is a typically associated with underlying disease states, including autoimmune connective tissue disease, lymphoproliferative disorders, and infections.[1-3] Although most common in patients with rheumatoid arthritis (RA), PNGD can also be seen in patients with systemic lupus erythematosus and systemic vasculitides.[3,4] Clinically, PNGD presents with tender, erythematous-to-violaceous papules, plaques, or nodules affecting the extensor surfaces. Acral, including palmar, involvement is characteristic, and umbilicated papules overlying bony prominences are also described.[1,2,5] Histologically, early lesions of PNGD present with neutrophilic infiltrates and leukocytoclastic vasculitis; fully developed lesions feature palisaded granulomas with collagen trapping and neutrophil remnants.[1]

Given the wide range of clinical features, histopathologic findings, and underlying systemic diseases, the diagnosis of PNGD can be challenging, requires careful clinicopathologic correlation, and relies on knowledge of the varying histologic findings. Here, PNGD with underlying RA in a single patient with 3 distinct histopathologic patterns is presented.

Abbreviations used:

GA:	granuloma annulare
PNGD:	palisaded neutrophilic granulomatous dermatitis
RA:	rheumatoid arthritis

CASE REPORT

A 71-year-old woman with history of RA presented with painful, erythematous-to-violaceous plaques on the upper and lower extremities, palmo-

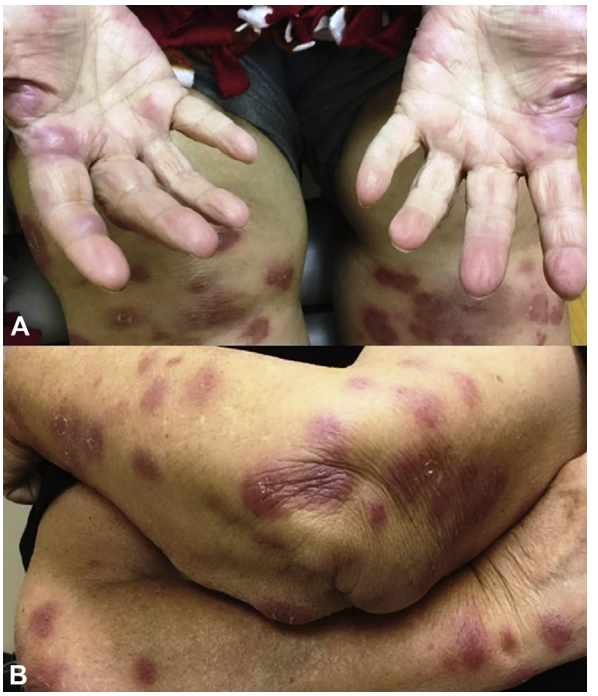

Fig 1. A, Erythematous-to-violaceous plaques and nodules on the palmar surfaces, knees, and shins. **B**, Erythematous plaques on the extensor arms and dorsal hands.

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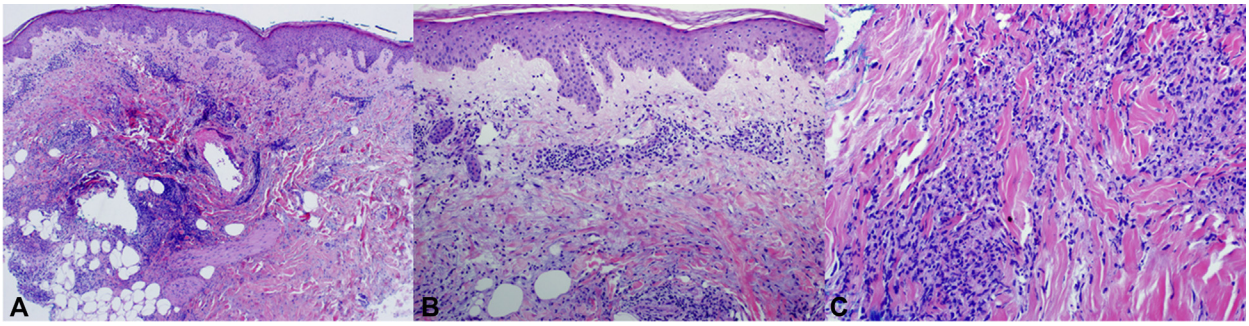

Fig 2. Prominent papillary dermal edema overlying a mixed dermal infiltrate with abundant neutrophils. In isolation, these morphologic findings are strikingly similar to those of neutrophilic dermatoses, such as Sweet syndrome. (Hematoxylin-eosin stain; original magnifications: **A**, ×40; **B**, ×100; **C**, ×200.)

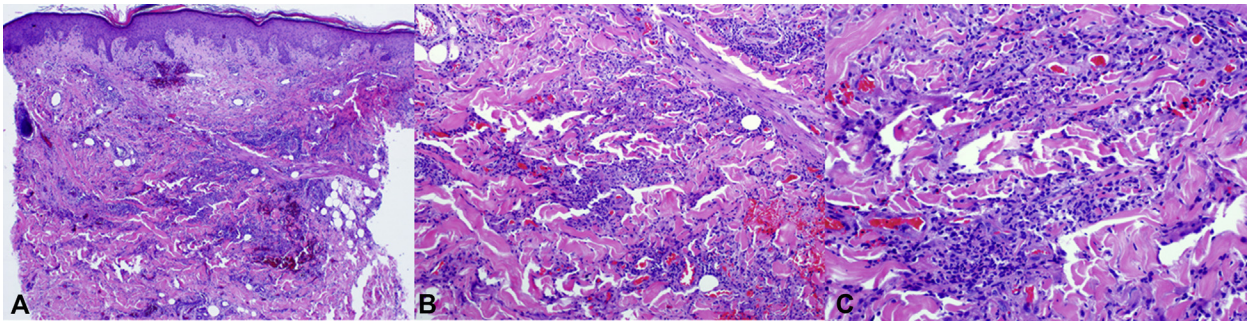

Fig 3. Interstitial and palisading granulomas surround foci of neutrophils with karyorrhectic debris; these features are readily identified as palisaded neutrophilic granulomatous dermatitis. (Hematoxylin-eosin stain; original magnifications: **A**, ×40; **B**, ×100; **C**, ×200.)

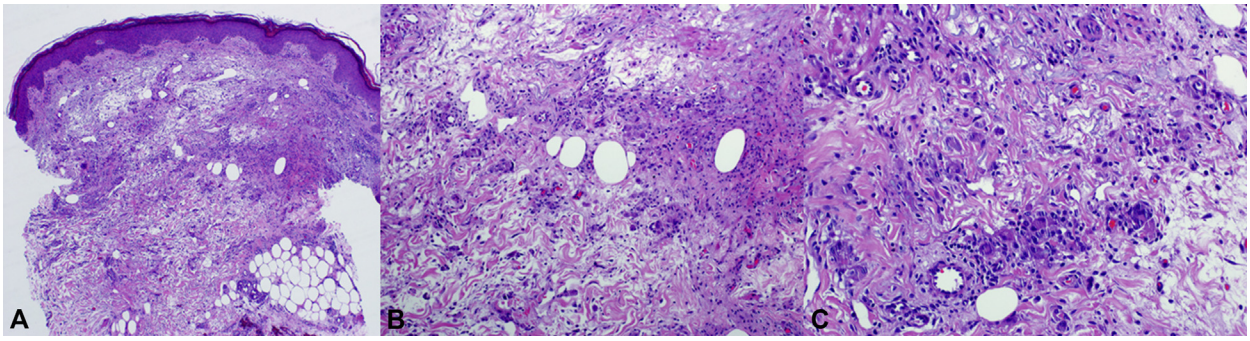

Fig 4. Palisading histiocytes surround degenerating collagen; increased dermal mucin and solar elastosis are also present. These morphologic findings closely resemble GA. (Hematoxylin-eosin stain; original magnifications: **A**, ×40; **B**, ×100; **C**, ×200.)

plantar surfaces, and chest (Fig 1, *A* and *B*). Two days before the onset of the cutaneous findings, the patient noted a flare of her arthritis. Punch biopsy at this time found papillary dermal edema and a diffuse dermal infiltrate with abundant neutrophils, findings analogous to those seen in Sweet syndrome (Fig 2, *A-C*). Two weeks later, 2 additional punch biopsies were performed. The second specimen showed a diffuse interstitial granulomatous dermatitis with focal palisading around foci of neutrophils with leukocytoclasia and nuclear debris (Fig 3, *A-C*). Histopathology findings of the third biopsy showed classic features of granuloma annulare (GA), with palisaded granulomas surrounding degenerated collagen and mucin (Fig 4, *A-C*).

Given the clinical findings, history of RA, and histopathologic features of all 3 specimens, the diagnosis of PNGD was made. Near resolution of

the cutaneous findings and improvement of the arthritic symptoms were observed after a 3-week taper of prednisone (starting at 1 mg/kg/d). The patient was also referred for long-term treatment of RA.

DISCUSSION

Dykman et al[6] first described PNGD in several patients with RA in whom linear bands developed on the truncal surfaces. Histologic findings resembled the palisaded granulomas of rheumatoid nodules.[6] After these early findings, several other terms were used to describe cases with similar histologic findings, including *rheumatoid papules*, *Churg-Strauss granuloma*, *interstitial granulomatous dermatitis*, *superficial rheumatoid necrobiosis*, and *cutaneous necrotizing extravascular granuloma*.[1,3,5] In addition to RA and systemic lupus erythematosus, the myriad underlying diseases includes systemic sclerosis, Sjögren syndrome, autoimmune thyroiditis, hepatitis, inflammatory bowel disease, myelodysplastic syndrome, granulomatosis with polyangiitis (Wegener granulomatosis and Churg-Strauss syndrome), Takayasu arteritis, diabetes, and infections, such as *Streptococcus*, HIV, Epstein-Barr virus, and parvovirus.[7] Chu et al[1] coined the unifying descriptor *PNGD* to encompass these overlapping histologic findings observed in association with varied clinical presentations and systemic diseases. Among 9 patients with PNGD and autoimmune connective tissue disease, 6 patients had systemic lupus erythematosus and 3 had RA.[1]

The histologic continuum of PNGD begins with a cutaneous small-vessel vasculitis (leukocytoclastic vasculitis) with dense neutrophils throughout the dermis. The histologic differential diagnosis of early PNGD includes leukocytoclastic vasculitis, Sweet syndrome, and neutrophilic urticaria.[1,3] Established lesions have palisaded granulomas with trapping of collagen and neutrophilic debris, likely a result of the initial vasculitis. Late findings include fibrosis, prompting consideration of necrobiosis when observed in isolation.[1]

Given that PNGD progresses through a series of histologic stages, an individual biopsy may not find the combination of features (palisaded granulomas with neutrophilic debris) most indicative of this process. The single patient presented here had consistent clinical findings but in association with distinct histologic features in each of 3 biopsies: the acute phase with diffuse neutrophils associated with worsening RA (mimicking Sweet syndrome), palisaded granulomas with neutrophils (most easily identifiable as PNGD), and granulomas surrounding mucin with collagenolysis (simulating GA).

Some investigators considered PNGD to be a clinicopathologic variant of GA, and the findings of the third histologic specimen from our patient support this idea. GA is a chronic and often self-limiting granulomatous dermatitis of unknown etiology.[8] GA presents as erythematous, annular plaques, papules, or patches; disease may be localized or generalized. In palisaded GA, granulomas encircle mucin and degenerated collagen; in interstitial GA, lymphohistiocytic infiltrates dissect between collagen; and in deep GA, subcutaneous granulomas mimic rheumatoid nodulosis.[2] Interstitial granulomatous dermatitis may also be on a spectrum with PNGD and a variant of GA. Clinical features of interstitial granulomatous dermatitis are typified by annular plaques affecting the flexures, whereas the histopathology is characterized by an interstitial infiltrate of histiocytes including giant cells with elastophagocytosis, along with lymphocytes, eosinophils, and plasma cells. Underlying associations include drug reactions (calcium channel blockers, lipid-lowering agents, diuretics, angiotensin-converting enzyme inhibitors) and systemic disease (RA, inflammatory bowel disease, diabetes, hepatitis, Epstein-Barr virus, and HIV).[9]

PNGD encompasses a spectrum of histologic findings, including those simulating GA, which vary based on the stage of the lesion sampled. Dermatologists and dermatopathologists should be aware of these different morphologies to permit successful clinicopathologic correlation and diagnosis, both of which are important given the significant association with underlying systemic disease.

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