Quiz

Multiple cutaneous nodules in a patient with rheumatoid arthritis

A 79-year-old woman presented to the dermatology clinic with multiple papules and nodules on all four limbs which had first developed 6 months previously. Furthermore, she had a 30-year history of seropositive rheumatoid arthritis which was controlled by administering nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs; however, she had no history of tumor necrosis factor-α (TNF-α) inhibitor use. On dermatologic examination, we noted the presence of multiple erythematous to violaceous papules and nodules on her limbs, particularly on the extensor surfaces [Figure 1].

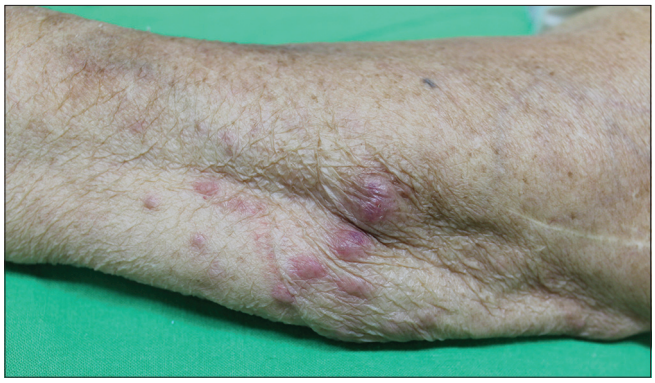

Figure 1: Multiple erythematous to violaceous papules and nodules located on the elbow

Skin biopsy of an erythematous nodule on her elbow was performed. Histopathological examination showed diffuse interstitial and granulomatous infiltration throughout the dermis [Figure 2]. In addition, dense neutrophilic infiltrates, leukocytoclasia, and histiocytes palisading around the degenerated collagen were observed. In addition, granular basophilic debris was noted in the areas of sclerosis [Figure 3].

WHAT IS YOUR DIAGNOSIS?

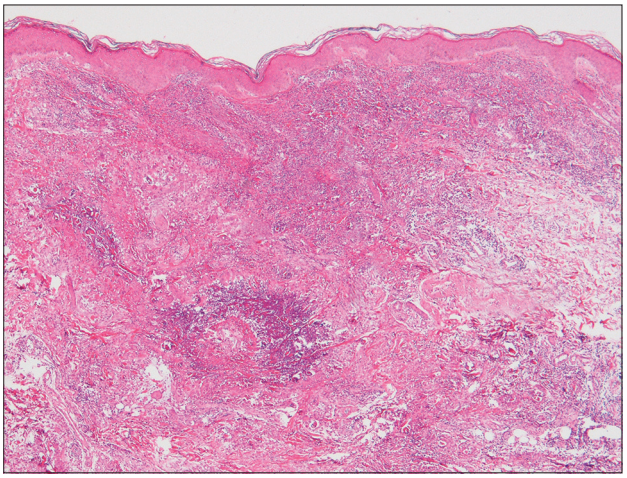

Figure 2: Histopathology showing diffuse interstitial and granulomatous infiltration throughout the dermis with extensive areas of collagen degeneration (H and E, × 20)

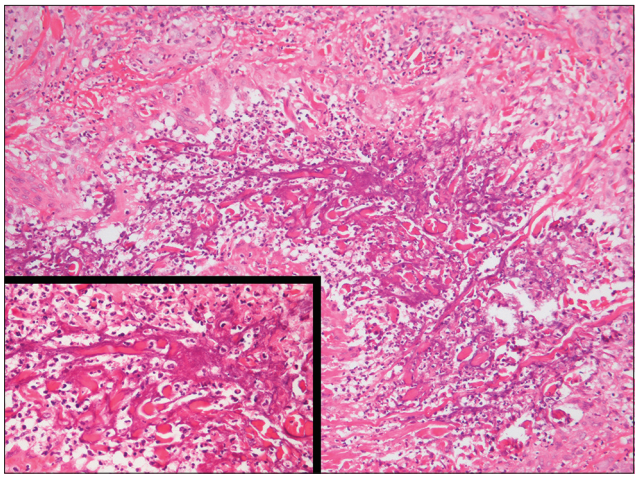

Figure 3: Palisaded histiocytes surrounding the center of the area with basophilic degeneration of collagen, numerous neutrophils, fibrin, and leukocytoclasia (H and E, × 200); inset with higher magnification (H and E, × 400)

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Answer
Palisaded neutrophilic granulomatous dermatitis

DISCUSSION

Palisaded neutrophilic granulomatous dermatitis (PNGD) is a rare condition with a variable clinical and histolopathological presentation. PNGD is associated with several systemic diseases including rheumatoid arthritis, systemic lupus erythematosus, lymphoproliferative disorders, inflammatory bowel disease, and systemic vasculitis.[1,2]

PNGD has been referred to as interstitial granulomatous dermatitis with arthritis, rheumatoid papules, Churg-Strauss granuloma, cutaneous extravascular necrotizing granuloma, and superficial ulcerating rheumatoid necrobiosis.

Most PNGD cases involve patients with rheumatoid arthritis.[1,3] The lesions may be tender or asymptomatic, and are usually distributed on the lateral trunk or symmetrically on the extensor surfaces of the extremities.[1,3] The clinical morphology of early stage PNGD usually manifests as urticarial papules. In late disease, lesions are more indurated and pleomorphic, presenting as linear subcutaneous cords, waxy papules, erythematous nodules, or annular violaceous plaques.[1,3]

The histopathological findings of PNGD are diverse. In 1994, Chu *et al*., suggested that PNGD represents a range of histopathological symptoms on a continuum of disease.[2] In early disease, the main findings are leukocytoclastic vasculitis with dense neutrophilic infiltrates and degenerated collagen. In mature lesions, palisaded granulomas develop around leukocytoclastic debris, fibrin, and altered collagen bundles. In late disease, there is dermal fibrosis and scant neutrophilic debris.[2]

The differential diagnosis of PNGD is complex and depends on the disease stage. Early disease should be differentiated from urticaria and small vessel leukocytoclastic vasculitis. For mature lesions, the main differential diagnosis is interstitial granuloma annulare. Late disease should be distinguished from necrobiosis lipoidica.[2] In patients with a prolonged history of rheumatoid arthritis, rheumatoid nodules should be considered. However, rheumatoid nodules are usually located deeply in the subcutis with large areas of eosinophilic fibrinoid necrobiosis and dense lymphocytic infiltrates. We excluded the diagnosis of rheumatoid nodules in our case due to the presence of basophilic degeneration of collagen with numerous neutrophils.

The exact etiology of PNGD remains elusive but the histopathology is consistent with the evolution of an immune complex-mediated disease.[2] Immune complex deposition in dermal vessels activates complement and neutrophils leading to subsequent collagen damage and granuloma formation.[1,2]

Recent case reports suggest an increased incidence of PNGD in rheumatoid arthritis patients administered TNF-α inhibitors.[4,5] TNF-α inhibitors are reported to be paradoxically associated with symptoms of autoimmunity and flares of vasculitis. Therefore, the altered antigenicity of dermal collagen, immune complex deposition on the vessel wall, and leukocytoclastic vasculitis caused by TNF-α inhibitors are believed to be the initial events in PNGD pathogenesis.[4,5]

PNGD lesions may persist for several months to a few years although most cases are self-limiting. Clinical improvement has been reported in patients administered topical steroids, systemic low-dose steroids, or dapsone.[1,4]

In conclusion, PNGD is a heterogeneous condition with dense neutrophilic infiltration, altered collagen, palisaded granulomas, leukocytoclastic debris, or fibrinoid necrosis. As it has a highly variable clinical and pathologic presentation, a high index of suspicion is required for accurate diagnosis. This condition should be considered in patients with a history of connective tissue disease who present with violaceous papules on the extremities or band-like plaques on the trunk.

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