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Case Presentation

An Erythematous papular eruption in a woman with Crohn disease treated with infliximab

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Abstract

We report the case of a 44-year-old woman with a history of Crohn disease treated with infliximab who presented with erythematous papules and plaques on the upper extremities accompanied by fevers. She was subsequently diagnosed with palisaded neutrophilic and granulomatous dermatitis (PNGD). Whereas immune-complex mediated diseases such as rheumatoid arthritis and systemic lupus erythematosus are most commonly associated, inflammatory bowel disease deserves increased consideration as one of the systemic diseases that can present with PNGD. Additionally, PNGD should remain in the differential diagnosis of cutaneous eruptions that develop in the setting of tumor necrosis factor (TNF) antagonist therapy.

Keywords: palisaded neutrophilic and granulomatous dermatitis (PNGD), interstitial granulomatous dermatitis (IGD), immune-complex mediated diseases, inflammatory bowel disease, tumor necrosis factor-α (TNF-α) antagonists

Case synopsis

A 44-year-old woman presented with a four-day history of a rash accompanied by fevers reaching 39.5°C. The lesions spread and became increasingly pruritic before becoming tender with defervescence. Blood counts and electrolytes were normal. C-reactive protein was 60.2 mg/L. Physical examination revealed 0.5 to 2.0 cm blanching erythematous edematous papules and plaques on the upper extremities, with the extensor surfaces being most involved (Figure 1).

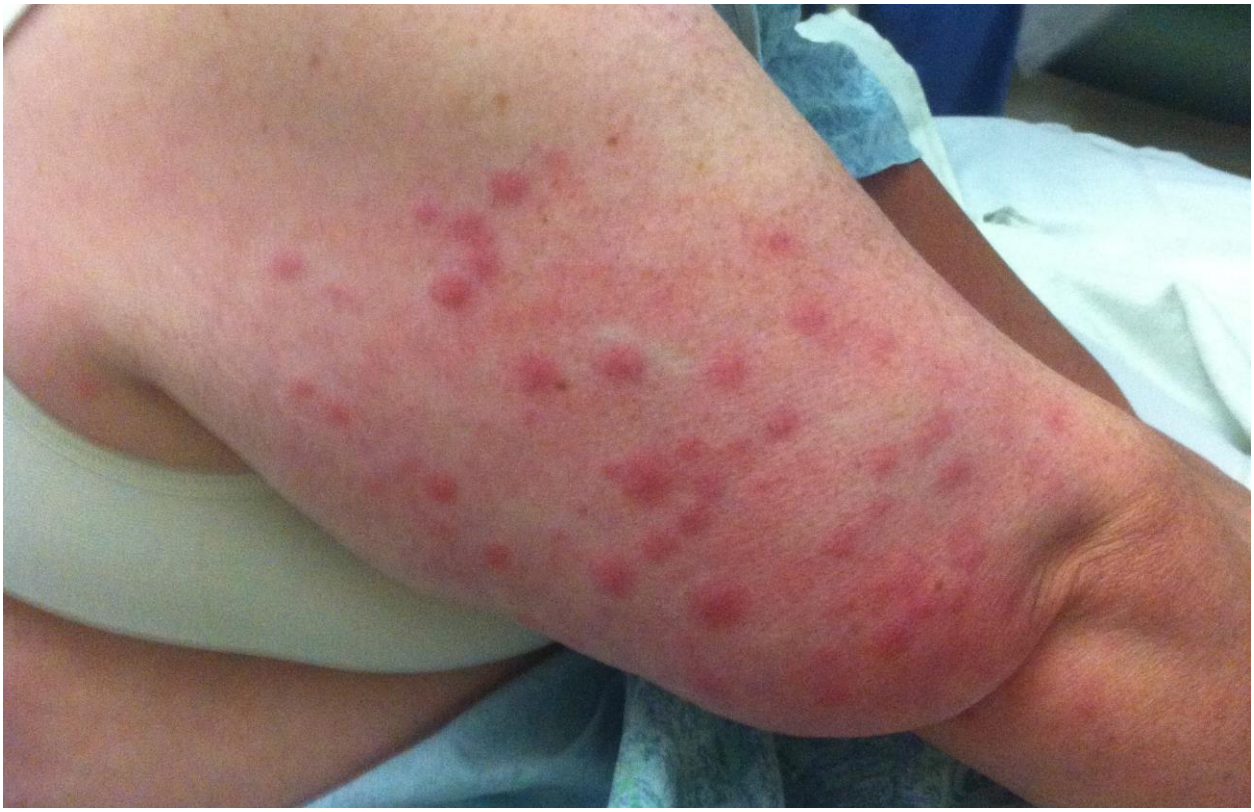

Figure 1. Multiple erythematous papules on the extensor surface of the upper extremity.

The patient had a history of Crohn disease complicated by perirectal abscesses, fistulae, and enteropathic arthritis. Her Crohn disease was treated with infliximab and she was scheduled to receive an infusion four days after the onset of the rash. She had a similar episode of fever and rash six weeks prior, a few days before her scheduled infliximab infusion.

Skin biopsy of the right triceps showed a perivascular and interstitial infiltrate within the dermis that encircled collagen fibers at the deep margin (Figure 2). The epidermis was largely unremarkable. There was no evidence of vasculitis.

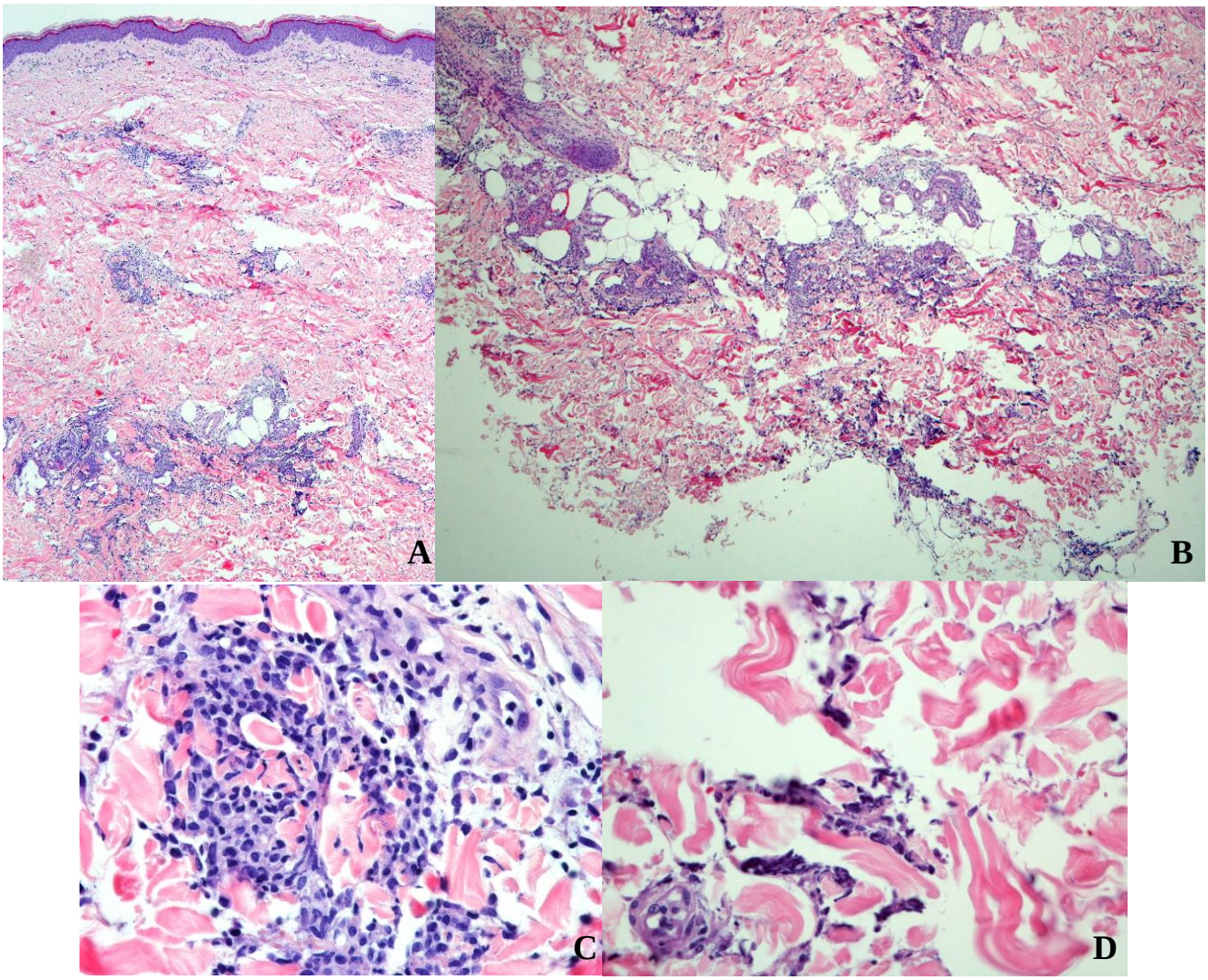

Figure 2. (A, B), There is a perivascular and interstitial infiltrate of lymphocytes, plasma cells, neutrophils, and scattered eosinophils within the dermis. (C, D), At the deep margin, the infiltrate encircles collagen fibers. Haematoxylin and eosin, original magnification (A, B) x 40; (C, D) x 400.

Based on clinical and histological findings, a diagnosis of palisaded neutrophilic and granulomatous dermatitis (PNGD) was made. The patient was treated with a loading dose of methylprednisolone (Solumedrol) 125 mg and then started on oral prednisone 40 mg daily, with great improvement of her skin findings.

Discussion

Palisaded neutrophilic and granulomatous dermatitis is most commonly associated with immune-complex mediated diseases such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic vasculitides, and lymphoproliferative disorders. Wilmoth and Perniciaro noted an immunoreactive state in 21 of 22 patients with PNGD and concluded that PNGD is a cutaneous marker of an underlying autoimmune or immunoreactive systemic illness [1].

The cutaneous findings of PNGD are protean, but are frequently described as symmetrically-distributed erythematous papules and plaques over the extensor surfaces of the extremities [2]. Occasionally, lesions have been described as tender or pruritic and cyclical fevers have been associated. Additionally, presentation often occurs with exacerbation of the underlying systemic disease.

Numerous terms have been used to describe this condition including interstitial granulomatous dermatitis with arthritis, linear granuloma annulare, Churg-Strauss granuloma, rheumatoid granuloma, superficial ulcerating rheumatoid necrobiosis, and cutaneous extravascular necrotizing granuloma [3]. Chu *et al*. proposed the name PNGD to describe this continuum of clinical and histopathological appearances that occurred with evolution of the lesions [4]. More recently, it has been proposed that PNGD and interstitial granulomatous disease (IGD) should be considered as part of the same clinicopathological spectrum, and that IGD should be the preferred term since it better summarizes the essential pathological features [5]. Both conditions have significant clinical, histological, and pathological overlap and frequently develop in patients with an immunoreactive systemic illness. This recent study found that coexistence of the interstitial and palisaded inflammatory patterns occurred in 90% of cases [5].

There are two reports of PNGD in patients with inflammatory bowel disease (IBD) [2, 6]. The first describes a patient with chronic ulcerative colitis (UC) who presented with fever, polyarthritis, and pulmonary infiltrates [2]. The second discusses a patient with quiescent UC who presented with recurrent tender papules and plaques on the hands associated with finger swelling, polyarthralgias, and a low-grade fever [6]. Our patient with Crohn disease further supports IBD as a systemic disease that can be involved in the pathogenesis of PNGD.

Another correlation of note is the potential association between tumor necrosis factor (TNF) antagonists and PNGD. Tumor necrosis factor is involved in the pathogenesis of many of the inflammatory conditions frequently associated with PNGD. Our literature search has revealed a total of ten patients on TNF antagonists (including infliximab) who developed PNGD [3, 7, 8, 9]. Several of these eruptions resolved with discontinuation of the TNF antagonist [3, 7, 8, 9]. By contrast, our patient developed the rash shortly prior to two scheduled infliximab infusions and improved with systemic corticosteroids and the infusion. This suggests that the underlying systemic disease, rather than the TNF antagonist, was responsible for the development of PNGD in this case.

Conclusion

In conclusion, erythematous papules and plaques over the extensor surfaces of the extremities in patients with underlying systemic disease including IBD should raise suspicion for PNGD. If PNGD is diagnosed in a patient without a known systemic disease, further diagnostic workup is warranted. Furthermore, although the association between PNGD and TNF antagonist therapy remains controversial, PNGD should remain in the differential diagnosis of cutaneous manifestations that develop in the setting of diseases treated by TNF antagonist therapy.

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