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Interstitial granulomatous dermatitis successfully treated with etanercept

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Female, 51
Final Diagnosis: Interstitial Granulomatous Dermatitis
Symptoms: Joint pain • pruritic rush
Medication: Etanercept
Clinical Procedure: —
Specialty: Rheumatology

Objective: Rare disease
Background: Interstitial granulomatous disease (IGD) is a rare skin condition that presents with erythematous and violaceous plaques, and may be associated with pruritus and pain. The cause remains unknown, but is often associated with autoimmune disease and drug-related adverse effects. It is diagnosed via biopsy, and the treatment remains unclear.
Case Report: We report a case of biopsy-proven IGD associated with rheumatoid arthritis that was treated successfully with etanercept therapy.
Conclusions: We emphasize that anti-TNF antibodies may be clinically effective for the treatment of IGD.

MeSH Keywords: Etanercept • Rheumatoid Arthritis • Interstitial Granulomatous Dermatitis (IGD)

Full-text PDF: http://www.amjcaserep.com/download/index/idArt/890074

Background

Interstitial granulomatous dermatitis (IGD) is a rare disease that clinically presents with a pruritic and painful rash revealing symmetric, erythematous, and violaceous plaques over the lateral trunk, buttocks, and thighs [1]. Fewer than 70 cases have been documented in the literature [2]. Diagnosed via skin biopsy, it is characterized by the infiltration of the mid-to-deep reticular dermis with palisadic histiocytes with areas of thick collagen bundles. Variable evidence of phagocytosis may be seen. Neutrophils and eosinophils may also be present in the infiltrate [3].

A disease of unknown etiology, IGD is associated with autoimmune diseases, which include connective tissue disease (SLE, RA), vitiligo, thyroiditis, and diabetes [4]. It has been hypothesized that the deposition of immune complexes in the dermal vessels may be the trigger, which is then followed by complement and neutrophil activation. This damages dermal collagen, which in turn gives rise to a granulomatous infiltrate in response to the insult [3,5]. It is more often seen in women, as are autoimmune diseases [6,7]. Various medications, particularly calcium channel blockers, lipid-lowering agents, angiotensin-converting enzyme inhibitors, antihistamines, anticonvulsants, and antidepressants have been associated with IGD. Most recently, anti-TNF agents such as etanercept, infliximab, and adalimumab have been implicated as the cause of drug-induced IGD [8,9].

We report a case of rheumatoid arthritis (RA) associated with IGD in which treatment with etanercept resolved the cutaneous lesions.

Case Report

A 51-year-old woman diagnosed with RA in 2002, not on any medications, presented to our rheumatology clinic for follow-up of her condition. She was initially treated with Methotrexate (7.5–15 mg/week) and non-steroidal anti-inflammatory drugs for 1 year with little improvement, and was thus switched to etanercept (50 mg/week) and celecoxib (200 mg as needed) with marked improvement. However, due to financial reasons, Etanercept was stopped in July 2011. Subsequently, the patient developed worsening joint pains associated with a pruritic rash on her arms and thighs, and at this time presented to our clinic in August, 2012. She reported she had never had skin lesions in the past and it had been present for 6 weeks. The eruption was characterized by red and pink papules and nodules, symmetric in distribution, on the extensor aspects of the arms and inner aspects of the thighs.

Lab data revealed CCP IgG, >250 UI/ml; ESR, 54 mm/hr; and CRP, 4.84 mg/dl. X-rays of involved joints revealed erosive arthritis. Cutaneous biopsy of the involved region showed histiocytes

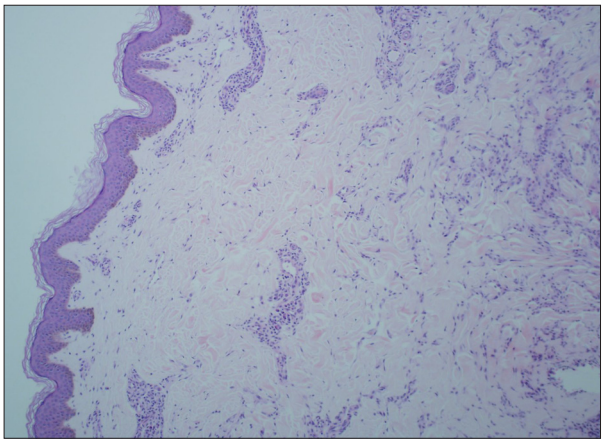

Figure 1. Low magnification (hematoxylin and eosin stain, ×100), showing mixed histiocytic infiltrate involving the mid- to deep reticular dermis.

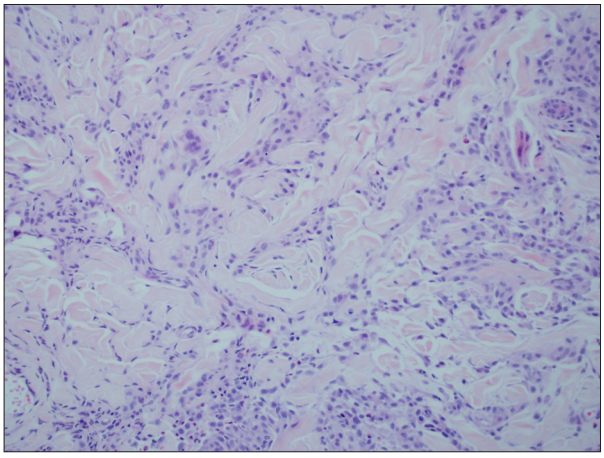

Figure 2. Higher magnification (hematoxylin and eosin stain, ×200), prominent histiocytes with polygonal and cuboidal cytoplasm are seen around collagen bundles, in the characteristic palisaded pattern; scattered eosinophils and plasma cells may also be seen.

with prominent polygonal and cuboidal cytoplasm irregularly insinuated between collagen bundles of the mid- to deep dermis. There was also a mixed infiltrate of eosinophils and plasma cells (Figures 1 and 2).

Treatment with etanercept (50 mg/week) and celecoxib (200 mg as needed) was started. After 2 months, the skin lesions had completely resolved, with significant improvement of her joint pain. There was no re-occurrence of the skin condition at 12-month follow-up.

Discussion

The occurrence of IGD in association with RA is well documented, especially with high titers of RF [5,10–12]. Although the

exact cause remains unknown, the underlying inflammatory process of the dermis and subsequent granulomatous infiltrate seem to be involved in the pathogenesis of the disease [3]. The importance of tumor necrosis factor alpha (TNF-α) along with interferon-γ for proper granuloma formation has been demonstrated by several reports of tuberculosis reactivation occurring in patients treated for RA with TNF-α receptor antibodies. TNF-α is involved in a number of processes that help maintain granulomas, including endothelial cell activation, induction of adhesion molecules, growth of new blood vessels, and regulation of other inflammatory cytokines [13].

Treatment for IGD is not well established. In cases of drug-induced IGD, the withdrawal of the offending agent can resolve the cutaneous lesions [14,15]. The majority of documented IGD cases have been treated with systemic or topical glucocorticoids, either singly or together [6,16,17]. Narrow-band ultraviolet B phototherapy in conjunction with topical steroids has also been used successfully [10]. Alghamdi et al. described treatment with IVIG therapy [18]. Gerbing et al. and Wollina et al. reported treatment with hydroxychloroquine and cyclosporine, respectively [19,20].

In conjunction with the underlying pathogenesis, biological agents have been the topic of recent discussion for the treatment of IGD. Ustekinumab, tocilizumab, and infliximab have all been described in effectively treating IGD [2,21,22]. In our case, etanercept was successful in resolving the cutaneous lesions characteristic of IGD. Zoli et al. reported a similar case in which IGD in RA was responsive to etanercept therapy [23]. Etanercept is a TNF-receptor-IgG fusion protein inhibiting the binding of TNF to its receptors, and thus helps prevent the maintenance of granulomas [24].

Conclusions

We presented a case of IGD associated with RA in which etanercept was successful in treatment. This suggests that anti-TNF antibodies may be clinically effective for the treatment of IGD.

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Statement

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