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Review Article

THERAPEUTIC EFFICACY OF CERTOLIZUMAB PEGOL IN THE TREATMENT OF RHEUMATOID ARTHRITIS ASSOCIATED WITH ERITEMA ELEVATUM DIUTINUM: CASE REPORT AND LITERATURE REVIEW

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ABSTRACT

Erythema Elevatum Diutinum (EED) is a rare and chronic form of vasculitis manifested as skin lesions predominantly. EED has been described in association with hematological malignancies, infections and rheumatological diseases. We report the case of a patient with rheumatoid arthritis (RA) who presents with skin manifestation in hand and elbows. Skin biopsy confirmed the diagnosis of EED and treatment with Certolizumab Pegol (Cimzia ®) resulted in improvement of skin lesions. Since EED is rarely reported in association with RA as neither exists literature describing the use of anti-TNF monotherapy for EED, we present the therapeutic efficacy of Certolixumab Pegol (Cimzia ®) in the treatment of EED in a patient with rheumatoid arthritis.

INTRODUCTION

Erythema Elevatum Diutinum (EED) was first described in 1988 by Hutchinson and in 1889 by Radcliff Crocker who described two patients, then in 1984 Williams named the disease EED (1). EED is a rare disorder with dermal compromise and manifests as painless brown papules, plaques or nodules predominantly found in the extensor surfaces areas of limbs. As described above, most of the time these lesions are painless, but some reports described tender lesion with pain characterized as a burning sensation. The etiology of this disorder is unknown, it starts spontaneously in a period of time ranging from 5 to 10 years and it associated with concomitantly infectious disease (2), neoplasia (3) or immunological entities (4) such as rheumatoid arthritis which relates to de occurrence of EDD (9). Few cases have been reported neither its association with rheumatoid arthritis, we described the association of EED and rheumatoid arthritis as well as the first description of response to anti TNF treatment.

Case Presentation

A 49-year-old male with past medical history of rheumatoid arthritis, diagnosed in 2011 and who initially was treated with methotrexate and leflunomide, presented to the Rheumatology Clinic at a tertiary university Hospital in Bogota with elevated transaminases, persistent inflammation (DAS 28 VSG: 2.18), articular compromise described as morning stiffness, arthralgia and new papular type lesion on the surface of elbows and hand dorsum (figure 1), considering therapeutic failure and drug toxicity. Switch to anti TNF monotherapy with Certolizumab Pegol (400 mg) was made with previous biopsy specimen taken before initiation of treatment. Biopsy demonstrated neutrophilic infiltrate of the dermis with collagen degeneration and in some areas deposits of fibrinous material. Perivascular lymphocyte infiltrate was observed as well as fibrin thrombi in vascular structures. During follow up, it was noted control of symptoms and remission of skin lesions (suspension of Certolizumab Pegol led to reactivation of skin lesions) and with the biopsy results a diagnosis of erythema EED was established.

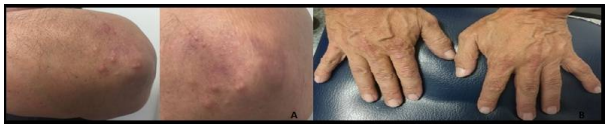

Figure 1

DISCUSSION

The most frequent skin manifestation in EED are red - brown eruptions, yellow papules, plaques or nodules as shown in the present report. Early lesions are usually more erythematous

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with soft texture while older lesion are hard and fibrous in appearance[1]. Frequently anatomical sites are extension surfaces of the elbows, knee, ankles, hands and fingers, other places include with a less common presentation: face, retro auricular area, trunk, glutes and genitals. Nodular lesions that progress to larger masses appear to be more common in patients with human immunodeficiency virus (HIV) infections, so acquired immunosuppression must be ruled out. Cutaneous manifestations of EED are usually asymptomatic or associated with burning sensation or pruritus, and among the extra-cutaneous manifestations described in the literature are arthralgia, fever, keratitis, scleritis and pan-uveitis [1].

Although EED is a rare entity, it has been associated with different clinical scenarios including infectious diseases such as HIV, beta hemolytic streptococci infection, hepatitis C virus, tuberculosis secondary to deposition of immunocomplexes in blood vessels. Hematological or autoimmune disorders which include IgA monoclonal gammopathies, myelodysplastic syndromes, proliferative myelopathies (B cell lymphoma and hairy cell leukemia) 2, inflammatory bowel disease, celiac disease, recurrent polychondritis, systemic lupus erythematosus, dermatomyositis and rheumatoid arthritis 2. In this report with a very rare association and just a few reports in the literature as written by Nakajima *et al.* In 1999, describing a 53-year-old female patient with a diagnosis of rheumatoid arthritis and development of EED twelve years later after diagnosis of RA was made3.

The histopathological features of EED vary over time; early presentation include peri-vascular neutrophil infiltrate in the upper and middle dermis that progress to fibrin deposits around the walls of small vessels 4.

Its diagnosis relies on the clinical and histological findings. Since there are no serological studies to stablish the diagnosis, the clinical evaluation should include skin biopsy as well as rule out infectious, hematological or rheumatoid entities (HIV ELISA, hepatitis B virus HVB, hepatitis C HBC, antinuclear antibodies ANAS, anti-DNA antibodies, anti-neutrophil cytoplasm antibodies, chest x-ray and urine analysis) 1. Therapy is based on establishing the underlying disorder and initiating specific treatment, first line agent of treatment is Dapsone which has been shown to decrease size of skin lesions in the series reported1, 5, 3 other alternatives described in the literature include Tetracycline, Colchicine, Methotrexate, Chloroquine, and Cyclosporine 5. Topical treatment as an option include Dapsone or short cycles of corticosteroid 6, 7.

Overall prognosis is good and there is usually no progression to systemic vasculitis, post-therapy relapses have been reported even up to 10 years. Description of response to the use of Anti TNF monotherapy (Certolizumab Pegol) has not been described in the literature. The present case supports the possibility of integrating this new therapeutically approach among patients with rheumatoid arthritis and EED.

CONCLUSION

EED is a rare entity, although with a good prognosis and response to treatment it is always necessary to establish association with infectious, hematological, or autoimmune diseases in order to initiate specific treatments. Although there are no randomized studies in autoimmune pathology that demonstrate the association of this disease with immunological activity, its improvement once therapy is started (in this case anti-TNF therapy for rheumatoid arthritis), could provide some ideas about its physiopathology and the degree of autoimmune activity related to skin findings.

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