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Case report

Efficacy of Tocilizumab in the treatment of Eosinophilic fasciitis: Report of one case

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ABSTRACT

A 43-year-old man was diagnosed with an Eosinophilic fasciitis with cutaneous and articular involvement. The patient experienced an early response with high-dose corticosteroids achieving a global remission of disease. Nevertheless, during the steroids tapering phase, he presented a new flare and subsequently developed a corticosteroid refractory disease. The addition of Methotrexate in monotherapy then associated with an anti-tumor necrosis factor agent did not show any additional benefit. Therefore Tocilizumab, a humanized monoclonal antibody against the interleukin-6 receptor, was initiated achieving an immediate response that persists after 36 months of follow-up. The use of this biological agent allows prednisone withdrawal at 3 months and remission of both articular and cutaneous manifestations at 6 months. This report describes for the first time the efficacy of an anti interleukin-6 agent in Eosinophilic fasciitis treatment.

1. Introduction

Eosinophilic fasciitis (EF) is a rare connective-tissue disease described by Shulman in 1974 [1]. The diagnosis relies on skin or subcutaneous abnormalities associated to an involvement of muscular fascia confirmed by an inflammatory infiltration of lymphocytes and eosinophils in a skin/muscle/fascia biopsy-specimen. A peripheral eosinophilia is common, but is not required for the diagnosis. The classical symptom of EF is the progressive skin thickness that includes the typical groove sign. Articular symptoms with painful joints and arthritis can be associated and could represent the predominant symptom in some patients. EF could be related to solid or hematologic neoplasms or it could be the result of dietary products or toxic oil [2]. Corticosteroids are currently the cornerstone of treatment [3]. To date, some options have been reported in the setting of corticosteroids dependence or corticosteroids refractory disease with variable outcomes.

2. Case report

A 43-year-old man presented with sub acute arthralgias and myalgias associated with progressive skin stiffness in his upper limbs. A depressed vein aspect (groove sign) located on the dorsal aspect of the right wrist was found. An asymmetric oligoarthritis of one wrist, both knees and one ankle were present. No medical condition was known before. No Raynaud, sclerodactyly, deep morphea, tendon friction rubs, capillaroscopy abnormalities or autoantibodies positivity were found. No history of dietary substances was noted. Laboratory showed an increased C-reactive protein (CRP) 124 mg/l, erythrocyte sedimentation rate (ESR) 109 mm/h and a mild hypereosinophilia 820/mm^3 at the onset. Blood count and chemistry were normal. Parasitic serologies were negatives. Body computed tomography scan reported no elements on account of solid or hematologic neoplasia.

Due to myalgia, a magnetic resonance imaging (MRI) of both legs has been performed showing high signal intensity within the fascia and marked fascia enhancement after gadolinium administration (Fig. 1). Then, a target skin/muscle/fascia biopsy was performed showing a fasciitis with perivascular lymphocytes and eosinophils infiltration compatible with an EF (Fig. 2).

A steroid-based treatment was initiated by three pulses of 500 milligrams of methylprednisolone followed by oral prednisone at 1 mg/kg/day. After 4 weeks, an improvement in both articular and skin involvement was observed as a decrease in inflammatory markers. Three months later, while the prednisone was at 0.5 mg/kg/day, the patient presented a relapse of disease with oligoarthritis and high titers of inflammatory markers (CRP 84 mg/l and ESR 96 mm/h). Methotrexate was then introduced at 20 mg per week during 12 weeks, without any additional benefit. Subsequently, an anti-tumor necrosis factor agent (anti-TNF), Etanercept,

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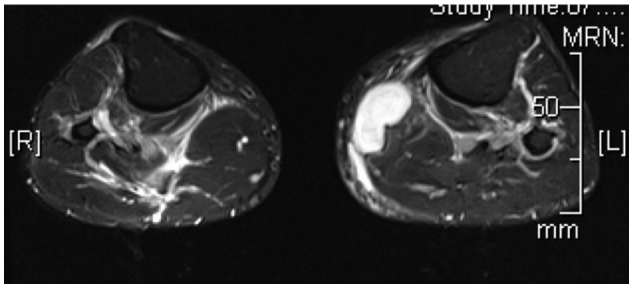

Fig. 1. Thigh muscle magnetic resonance imaging (MRI): the T2-sequence shows increased signal intensity within deep fascial layer predominantly in the right thigh.

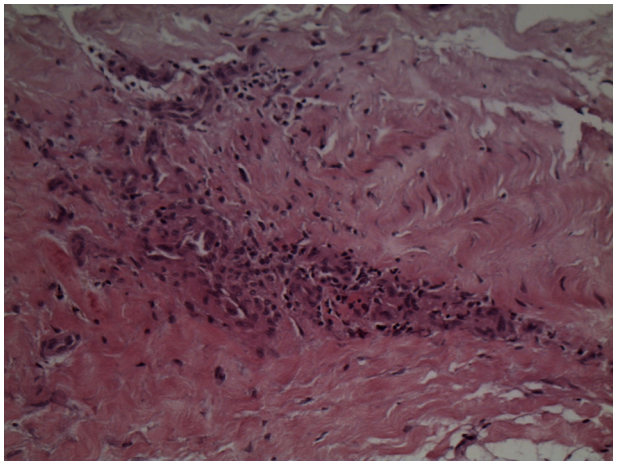

Fig. 2. Fascia and muscular thigh biopsy: the haematoxylin-eosin staining shows intense, perivascular inflammatory infiltrates within the fascia, composed mainly of neutrophils.

was added at 50 mg per week. The patient did not experience any changes within 3 months of follow-up. The maintenance of corticosteroid up to 1 mg/kg did not allow symptoms control therefore a corticosteroid refractory disease became evident.

After discontinuing Methotrexate and Etanercept, an inhibitor of IL-6 receptor, Tocilizumab (TCZ), was initiated. This treatment was introduced at 8 mg/kg monthly achieving a significant improvement. After 1 month we observed only a wrist synovitis and at 6 months the absence of arthritis was noted. Progressive regression of groove sign was noted in following months. After 3 months, the inflammatory markers were normalized (CRP 2 mg/l and ESR 14 mm). Corticosteroids were discontinued at 3 months of TCZ introduction. Patient did not experience any adverse effects and currently EF is in remission within 36 months of starting TCZ.

3. Discussion

In this case we report for the first time, to our knowledge, the efficiency of a therapy targeting IL-6 cytokine in a case of EF refractory to steroids and other immunosuppressive drugs.

The introduction of an immunosuppressive drug is limited to those patients who develop a steroid resistant disease. The choice is not based in clinical guidelines and the more common agent is Methotrexate [4]. Other drug-regimens described in small cases series with variables results are: anti-TNF including Etanercept [5,6], azathioprine or cyclosporine. Our patient evolved with a corticosteroid refractory disease characterized by a predominantly articular involvement associated to major inflammatory response. The introduction of a biologic drug blocking IL-6 and approved for the treatment of rheumatoid arthritis seemed an efficient approach. A long-term response was achieved with positive outcomes in articular, cutaneous and biological levels.

Several case reports exhibits positive effects of TCZ on non-RA connective tissues diseases, large-vessel vasculitis and others heterogeneous inflammatory conditions like Still's disease, amyloidosis and Castleman's disease [7]. At the moment, we cannot provide an explanation of tocilizumab effect in our patient but previously, Viallard et al. reported an increased production of the leukemia inhibitory factor (an IL-6 class cytokine), in peripheral blood mononuclear cells from EF patients [8]. Besides, the skin involvement of EF is close to those related of scleroderma as morphea and recently, two patients with systemic scleroderma (SSc) treated with TCZ at 8 mg/kg during 6 months showed softening of the skin with a significant reduction in one score of skin hardness [9]. An observational study including 15 SSc patients with refractory articular involvement treated by TCZ showed that 2/3 reached EULAR good response criteria at 5 months [10].

Further reports are needed to determine the role of TCZ in the treatment of EF. However, on the basis of our experience and within the context of a corticosteroid dependence or failure, we believe that clinicians should consider TCZ in EF especially for those patients who presented with an articular involvement.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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