Successful treatment of refractory eosinophilic fasciitis with reslizumab

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INTRODUCTION

Eosinophilic fasciitis is a rare inflammatory condition with abrupt onset of cutaneous edema that progresses to induration of the extremities and can mimic scleroderma.1 However, patients lack the classic features of scleroderma, including extracutaneous organ involvement, sclerodactyly, Raynaud disease, and nail-fold capillary changes. Clinical presentation of eosinophilic fasciitis consists of nonpitting edema, indurated skin, and pathognomonic venous furrowing, known as “groove sign”; some reports suggest that symptoms tend to start abruptly after physical exertion. The classic histologic diagnosis of eosinophilic fasciitis requires a full-thickness skin biopsy, including the underlying muscle and fascia; findings consist of hypertrophied fascia with inflammatory cell infiltration (lymphocytes and plasma cells). However, owing to partial treatment and delay in biopsy, histologic findings can be variable. Eosinophilic infiltration of the fascia is observed in approximately 50% of cases and more likely to be found in early stages of the disease.2 It can occur with or without the presence of peripheral eosinophilia.2 Systemic corticosteroids remain the first-line treatment for eosinophilic fasciitis and methotrexate is the most commonly used steroid-sparing agent.3,4 There are no approved medications for refractory cases. The exact etiology of the disease is unknown, but in recent years, an elevated level of interleukin (IL) 5, an eosinophil cationic protein, has been proposed as contributing to the genesis of the disease.5

CASE PRESENTATION

The patient was an athletic 65-year-old white woman, a retired nurse, who ran several times a week and was an avid golfer. She had a history of mild intermittent untreated asthma and essential hypertension, which was well controlled with hydrochlorothiazide. In 2016, she had sudden onset of redness, swelling, and burning of the skin covering the anterior aspect of both shins and forearms. She was treated in the emergency department, screened for deep vein thrombosis, and treated for cellulitis, but when the symptoms continued for 5 months, she was referred to rheumatology for evaluation. She did not report Raynaud disease, trouble swallowing, cutaneous telangiectasia, calcinosis, or photosensitive rashes. She had no family history of autoimmune disease.

On physical examination, she had skin induration on the forearms (wrists to elbows) and mild elbow flexion contracture with decreased range of motion in elbow extension. The patient’s legs exhibited mild bilateral edema, erythema, and induration of the skin, as well as calf tenderness and mild flexion contraction of the knees, leading to reduced range of motion (Fig 1). Results of blood testing were negative for antinuclear antibody and SCL-70 antibody, negative for myositis antibody panel, and normal for antibody levels, including IgG subtypes. However, she was found to have elevated eosinophil levels according to a complete blood cell count (30%, or 2900 absolute eosinophils). An en bloc skin biopsy was performed and included the subdermal fascia.
The biopsy revealed thickened and mildly fibrotic subcutaneous septa and mild dermal and superficial subcutaneous perivascular and interstitial lymphocytic infiltrates (Fig 2), findings compatible with eosinophilic fasciitis in this clinical context.

The patient initially began receiving 60 mg of prednisone, which was slowly tapered to 10 mg daily, and started to improve quickly with physical therapy. Hydroxychloroquine 200 mg twice a day was added as a steroid-sparing agent, but she developed recurrence of skin inflammation and skin tightening when the steroids were tapered below 10 mg. We added methotrexate to her regimen, which was titrated up to 25 mg weekly, but once again when her steroid dosing was tapered, she experienced worsening symptoms. She then began receiving mycophenolate 1000 mg twice a day, added to the previous medications, but experienced gastrointestinal adverse effects, and also her liver enzyme levels became elevated, necessitating discontinuation of this medication. She had ongoing symptoms of skin tightness. Given the presence of peripheral eosinophilia, we were able to prescribe reslizumab, an infusion-based humanized monoclonal antibody with anti–IL-5 activity. The addition of this medication at 3 mg/kg intravenously every 4 weeks led to the stabilization of her symptoms, and her prednisone was tapered to discontinuation. The tightness in her skin improved and the edema and erythema resolved. We were able to taper her dose of methotrexate to 15 mg weekly, and she has not received prednisone for the past 2 years. The addition of reslizumab as a maintenance therapy to her regimen has had a major positive effect on her quality of life: she has regained full range of motion in her joints and is able to golf again.

DISCUSSION

Eosinophilic fasciitis is rare and at first glance may be difficult to differentiate from local scleroderma (morphea). Therefore, clinical suspicion is needed to ensure that the diagnosis is not missed. Early diagnosis and treatment are important in the prognosis of this disease and response to treatment. There is a tendency to rely on methotrexate and corticosteroids, but when the disease is refractory, there are no clinical guidelines or approved therapies for this potentially devastating condition. Previous case reports have been published for successful treatment with cyclosporine, rituximab, and tofacitinib. We chose an anti–IL-5 agent as an additional treatment because IL-5 is the major cytokine responsible for the growth, differentiation, recruitment, activation, and survival of eosinophils. Furthermore, anti–IL-5 agents generally have more benign adverse-effect profiles than the previously tested agents. Three anti–IL-5 agents have been approved by the Food and Drug Administration thus far: mepolizumab, benralizumab, and reslizumab. We chose the latter because of its weight-based dosing and intravenous mode of delivery, but theoretically any inhibitory anti–IL-5 agent could have efficacy in treatment of eosinophilic fasciitis. Prospective studies should be conducted, including clinical trials and evidence-based guidelines.

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