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Rituximab as a therapeutic consideration for refractory eosinophilic fasciitis

Eosinophilic fasciitis (EF), also known as Shulman syndrome, is a rare disease considered to be part of the severe end of the morphea spectrum. Most typically, EF presents as acute or subacute development of pitting edema and erythema of the extremities excluding the hands and feet, with possible involvement of the neck and trunk in a symmetric distribution. With disease progression, tissue sclerosis deepens causing skin tightening and restrictive mobility. Clinical signs of disease may be observed, including peau d'orange appearance of the skin and the groove sign, which manifests as skin furrowing along the course of veins most pronounced with limb elevation.

The current treatment recommendation for EF is combination therapy using high-dose systemic corticosteroids plus immunosuppressive therapy, with preference for inclusion of low-dose methotrexate as part of maintenance therapy.[1] Therapies which have shown efficacy in managing EF include high-dose pulsed intravenous (IV) methotrexate,[1] infliximab,[2] azathioprine,[3] sulfasalazine,[4] sirolimus,[5] mycophenolate mofetil,[6,7] cyclophosphamide,[8,9] eculizumab,[10] cyclosporine,[4] tocilizumab,[11] PUVA,[12] immunoglobulins,[13] and bone marrow transplantation,[14] among others.

Isolated reports exist on the use of rituximab in treatment-refractory EF. As a chimeric monoclonal antibody, rituximab targets the CD-20 antigen present on the cell surface of mature B-lymphocytes.[15,16] Using rituximab, successful outcomes have been observed in a patient with EF and hypergammaglobulinemia[16] and in a patient with EF associated with aplastic anemia.[17] In the patient with EF and hypergammaglobulinemia, skin lesions resolved, peripheral eosinophilia normalized, and immunoglobulin G (IgG) levels decreased with a 375 mg/m^2 IV rituximab infusion delivered for four consecutive weeks or two doses of 1g of IV rituximab given 2 weeks apart. In this report, rituximab was used to treat the aforementioned patient with EF and hypergammaglobulinemia as well as a patient with hypergammaglobulinemic purpura of Waldenstrom, with one patient receiving the 375 mg/m^2 IV rituximab infusion for four consecutive weeks and the other receiving two doses of 1 g of IV rituximab given 2 weeks apart; however, it was not stated which infusion schedule was received by which patient.[16]

In the patient who had EF in association with aplastic anemia, IV rituximab was delivered at a dose of 375 mg/m^2 per week for 4 weeks and resulted in subsequent cytopenic regression, followed by relapse of disease. A second course of four rituximab infusions delivered at the same dose and infusion schedule in this patient resulted in another cytopenic regression as well as complete resolution of skin abnormalities.[17] Rituximab failure has been reported in a patient who received two 1 g IV infusions of rituximab for treatment-refractory EF. Following rituximab therapy, this patient showed no improvement after 4 months of observation but did later demonstrate improvement in EF with tocilizumab.[11]

Recently, we observed clinical improvement following use of combination therapy with oral corticosteroids, methotrexate, and rituximab in a 67-year-old male diagnosed with EF. This patient, who had a history of sarcoidosis, latent tuberculosis, and testicular seminoma treated with radiotherapy and orchiectomy, presented with reports of a 3-month history of "pebbly skin changes," diffuse myalgias, and tense abdominal and limb swelling. Physical examination revealed erythematous-to-hyperpigmented, firm, indurated abdominal and lower back plaques with a bound-down appearance. All extremities exhibited firmness to palpation with rippled skin texture changes, and a positive groove sign was observed at the medial aspect of both arms (Fig. 1). Evaluation was remarkable for peripheral eosinophilia, and excisional biopsy revealed eosinophilic inflammatory fasciitis, dermal collagen thickening, and normal muscle. Magnetic resonance imaging showed diffuse superficial and deep fascial thickening. Findings were consistent with EF. Previously

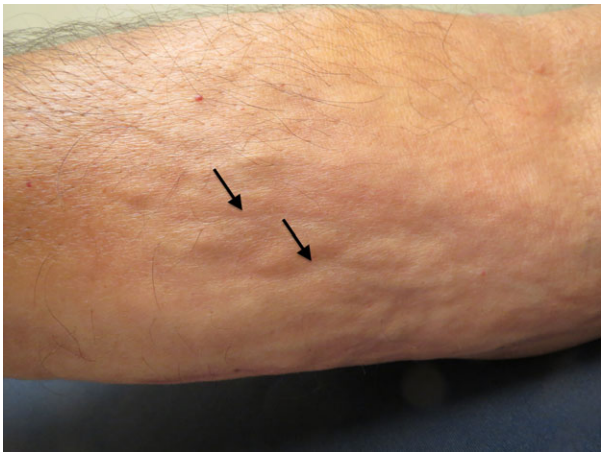

Figure 1 The groove sign is observed on the right medial arm. Note skin furrowing along the course of veins which occurs secondary to fascial sclerosus and is accentuated by limb elevation.

attempted treatments included 14 cycles of photopheresis, mycophenolate mofetil, oral prednisone, pulsed methylprednisolone, IV immunoglobulin, hydroxychloroquine, cyclophosphamide, and 126 treatments of ultraviolet A1 phototherapy. Following combination therapy using oral corticosteroids, methotrexate, and rituximab (1 g delivered IV, 2 weeks apart) with two separate courses given 5 months apart, the patient's disease state improved as demonstrated by reduction in skin tautness, improved range of motion, and normalization of laboratory values including peripheral eosinophilia.

Rapid responses have been observed in almost all of the cases of EF involving treatment with rituximab and an anti-CD20 mechanism may be involved.[16] Our findings further support inclusion of rituximab as part of the armamentarium for treatment-resistant cases of EF. Rituximab can be an effective steroid-sparing agent and provide significant symptomatic relief during flares.

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Treatment optimization with secukinumab 150 mg for moderate-to-severe psoriasis in clinical practice: a single-center open-label 52-week study

Secukinumab, a monoclonal antibody that efficaciously targets IL-17A in moderate-to-severe psoriasis, has one presentation (150 mg) and two authorized dosages: 150 mg for psoriatic arthritis and spondylitis and 300 mg for psoriasis, based on better psoriasis area and severity index (PASI) 90 responses and modified investigator's global assessment scores of 0–1 observed in randomized controlled trials (RCTs).[1] The 150 mg regimen achieved a PASI 75 response of around 80% and 65% at weeks 24 and 52, respectively, in RCTs.[1] Extension studies showed efficacy was maintained over 3 years of continuous treatment, with lower rates of candidiasis and other infections than the 300 mg regimen.[2,3]

Prompted by these efficacy and safety data, we conducted a single-center prospective study including adults with moderate-to-severe psoriasis assigned to a pre-established secukinumab 150 mg protocol and followed up for 52 weeks. The protocol was principally based on an ongoing secukinumab 300 mg dose-optimization trial, OPTIMISE[4] (Fig. 1). Local Ethics Committee approval was obtained, and all patients provided written informed consent.

We included 20 consecutive patients who attended our department between January and August 2016. Patients had no remarkable comorbidities. Table 1 shows the main clinical features and efficacy and safety outcomes. Fifteen (75%) and twelve (60%) patients achieved PASI 75 and 90 responses,