Session #2557
Interesting Cases I – Saturday, March 14, 2020

Case Report #2

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Case Title
Eosinophilic Fasciitis Treated With Reslizumab

Summary
We describe the first ever case of eosinophilic fasciitis (EF) treated with an anti IL5 monoclonal antibody, reslizumab. A 65-year-old woman with woody hard, erythematous skin on her lower extremities associated with peripheral eosinophilia was diagnosed with EF based on biopsy. She failed to respond to a combination of steroids, methotrexate, hydroxychloroquine and mycophenolate; but when she was started on reslizumab, her clinical picture improved dramatically. EF is a rare disease with no approved therapy and this case provides one possible treatment option for patients.

Patient Presentation
N. P. is a 65-year-old white female, who presented in November 2016 with a 5-month history of gradually progressive skin tightness involving first the lower extremities, then the upper extremities, sparing the hands and feet, associated with decreased range of motion in ankles, knees and elbows. These symptoms lead to limitation of daily activities, and her usual exercise program. Review of systems revealed no other pertinent positives and specifically she did not have any shortness of breath, headache, scalp tenderness, jaw claudication, photosensitivity, oral ulcers, or Raynaud's phenomenon. Past medical history was significant for asthma on budesonide inhaler and essential hypertension controlled with hydrochlorothiazide.
She had no previous surgeries.
Family history was significant for esophageal cancer in father and sister, and her mother had breast cancer. She had no family members with autoimmune disease.
Patient is a widow, and works as a registered nurse. She is a life-long non-smoker and denies using drugs. She drinks maximum of 4 glasses of wine in a week. She is post-menopausal and sexually active with a male partner.
She has no known drug or food allergies.
On exam, she had stable vitals. Relevant positive findings included:
- Upper extremities: bilateral skin induration in forearms from wrists up to mid arms, mild elbow flexion contracture with decreased range of motion in elbow extension.
- Lower extremities: mild bilateral leg edema, bilateral skin induration from ankles up to mid thighs, mild calf tenderness, mild flexion contracture of knees with decreased ROM in knee extension.

The rest of her physical exam was normal.

Diagnosis

On first look, her presentation looked like bilateral cellulitis. However, given the five-month progressive nature, this was an unlikely diagnosis. Other differentials included cutaneous T-cell lymphoma and a paraneoplastic rash, vasculitis, cutaneous lupus, dermatomyositis, an allergic reaction to one of her medications or a nutritional deficiency. However, given the hard, indurated nature of the skin, the closest mimic was scleroderma. In order to clarify her diagnosis, we ordered an array of labs and also sent her for a skin tissue biopsy.

Testing

Perhaps the most revealing diagnostic test was her complete blood count with differential, which revealed peripheral eosinophilia (absolute 2900 or 30% eos). The remainder of her CBC, chemistry, creatinine kinase, and thyroid function were normal. Infectious workup was negative. She had a negative ANA, ruling out lupus and a negative SCL-70 and other scleroderma-related antibodies. She had a normal sedimentation rate, but her C-reactive protein was elevated at 12.6 mg/dl. She had normal immunoglobulin levels. Her serum protein electrophoresis showed IgG gammopathy, but this was polyclonal in nature. She had a normal B12 level.

Finally, a skin biopsy was done and showed thickened subcutaneous fibrous septa and perivascular interstitial lymphocytic infiltrate, favoring the diagnosis of eosinophilic fasciitis.

Treatment

Eosinophilic fasciitis is a very rare condition, with no approved therapy. However, given the eosinophilic and inflammatory nature of the condition, we started treatment with steroid monotherapy. Her eosinophil count dropped and she felt less pain. However given that she continued to have tight skin and discomfort, she was started on hydroxychloroquine 200 mg twice daily, and then on methotrexate 20 mg weekly with folic acid 1 mg daily. She only partially responded to this regimen and continued to be quite symptomatic. We sent her to Mass General Hospital in Boston for a second opinion, because they have seen about 25 patients with this condition. The patient was put on a combination of methotrexate and mycophenolate, and remained on steroids. She felt unwell on the combination of the two medications and her liver enzymes started to rise as a side effect of the drugs. She continued to have tight, thickened skin with a lot of discomfort. She had a difficult time tapering off steroids. She discontinued mycophenolate.

Targeting the peripheral and tissue eosinophilia in this condition, we sought approval for an anti-IL5 monoclonal antibody. There are no trial of these drugs in eosinophilic fasciitis and no previous cases reported. After discussion with the patient, we were able to get insurance approval for reslizumab, and she was started on infusions based on asthma dosing. About a month after starting this medication, she was able to discontinue oral steroids. She has been able to cut down her dose of methotrexate in half.

Patient Outcomes

Our patient has experienced a remarkable improvement in her condition. Her skin color has returned to her normal tone and she no longer has pain. Her skin is dramatically softer than the initial presentation, though there is some persistent “woodiness” to the overall texture. She continues to slowly taper off methotrexate with plans to discontinue this medication, followed by hopefully discontinuing her hydroxychloroquine as well.

Lessons Learned

Eosinophilic fasciitis is a rare scleroderma mimic-disorder first described by Shulman et al in 1975. There are less than 300 reported cases in literature. The disease is usually well-responsive to corticosteroids; however refractory disease has been seen.

A 2003 study by French et al described for the first time that the increased IL-5 production may be responsible for the eosinophilia and eosinophil-mediated tissue injuries. Our patient showed significant improvement following reslizumab infusion. This is in support of using IL-5 inhibitors for refractory cases of EF, as IL-5 inhibitors suppress eosinophil activity by inhibiting the maturation, recruitment and activation of eosinophils. However further clinical trials are required to evaluate the accuracy of the above hypothesis.