CLINICAL VIGNETTE

Large Granular Lymphocytosis with Eosinophilic fasciitis

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A 46-year-old female presented with 1-2 weeks of bilateral painful leg swelling, mainly in the calf region, which worsened with walking. The swelling developed acutely and other parts of body were spared. Venous Dopplers were negative for both legs.

Her past history was significant for mild anemia, sinusitis and tachycardia with negative cardiac workup. Chest x-ray and sinus CT were normal. She was treated empirically with doxycycline for lyme disease two years previously. There was no other significant past history and no history of prior leg swelling.

On exam temperature was 99.0 F. She was anxious and tachycardic with regular rhythm. There was bilateral tender swelling of the calves with minimal swelling of the ankles. The overlying skin was tense and mildly erythematous. The remainder of the exam was benign. Laboratory evaluation included WBC 5.3 thousand /mm3 with 95.2 % lymphocyte with significantly low neutrophils. Lymphocytes had large granular appearance but there were no blasts seen. She was anemic with normal indices, hemoglobin 9.2.g/dl, hematocrit 28.0% and platelets of 445,000. No schistocytes were seen. ESR was elevated at 86. D Dimer and fibrinogen were increased. LDH, CK & Aldolase were normal. Globulin was increased at 4.0 but polyclonal. Liver function tests were normal. Lupus anticoagulant and ANA were negative. Iron saturation was low with normal ferritin. Rheumatoid Factor high at 503 (N<14), C3 high 239 (90-180) and CRP was elevated. Hepatitis, HIV and cryoglobulin were negative. An IgM western blot was positive for lyme disease. Blood cultures were negative. Clonal T cell gene rearrangement confirmed T-LGL (gamma delta type) CD3+ CD57+CD56-ve. MRI showed symmetric bilateral gastrocnemius inflammation with possible myositis with diffuse dermal and subcutaneous changes. Abdominal CT scan revealed a borderline enlarged spleen, without adenopathy or evidence of cancer. Skin & Muscle Biopsy revealed septal & lobular panniculitis. Review of her biopsy at UCLA revealed Eosinophilic fasciitis with perimysial and endomysial infiltration.

She was treated with prednisone and cyclosporine along with PCP prophylaxis. Her leg pain and swelling improved as well as her ESR, RF titer and neutropenia.

Large Granular Lymphocyte Syndrome is Lymphocyte proliferative disease of clonal origin with PCR amplification of TCR gamma gene (CD3+, CD57+, CD 56-) or natural killer cells (CD3-, CD 56+)[1-4]. It has been reported in association with Rheumatoid Arthritis and ANA positivity[5].

This patient had a positive Rheumatoid Factor but had no arthritis symptoms. Presentation can overlap with Felty syndrome[6,7].

Anemia and thrombocytopenia are frequently present. Myeloid hypoplasia is often seen and several mechanisms have been attributed as causes, both through local production of cytokines in bone marrow through Fas ligand, and antibody mediated[6,8-11]. Nonclonal LGL expression has been seen associated with viral infections, myelodysplasia, dasatinib therapy as well as in atomic bomb survivors[12].

Splenomegaly (which was border line in this patient) is seen both with LGL and felty syndrome, infiltration of other organs have been described occasionally[9].

Eosinophilic fasciitis is an uncommon disorder with unclear pathogenesis. It presents with erythema and edema of limbs or trunk. Peripheral blood frequently shows eosinophilia in early phase which was not documented in this case[13,14].

Subsequent collagenous thickening of dermis & subcutaneous fascia can give "peau de orange" appearance. Unlike scleroderma, digits, hands and feet are usually spared and organs are not involved.

Perimyostis may occur causing muscle pain and weakness. Endocrine and neurologic findings have been reported. About 10% patients had hematological disorders.

MRI is helpful in suspected eosinophilic fasciitis and biopsy confirmed the final diagnosis. The etiology of eosinophilic fasciitis is not clear, and occasionally is associated with strenuous exercise or initialization of hemodialysis and association of infection with B Burgdorferi has been reported. This patient has IgM positivity for B Burgdoreferi and was empirically treated with 2 weeks of doxycycline. She had no clinical symptoms suggesting infection and the lab results were possibly false positive with polyclonal gammopathy[7,13].

The patient was treated with Prednisone and cyclosporine for LGL with neutropenia as well as eosinophilic fasciitis. Other patients have been treated for LGL with methotrexate, cyclophosphamide and Alemtuzumab if the T cell LGL have CD52 expression[15].

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