Isolated chronic severe neutropenia in eosinophilic fasciitis. Failure of response to granulocyte colony-stimulating factor

Sirs,

Since the first report by Shulman in 1974 (1), eosinophilic fasciitis has been readily described. Characteristic of this syndrome are cutaneous changes resembling scleroderma with “peau d’orange” appearance, eosinophilia, hypergammaglobulinemia, thickening and infiltration of the deep fascia, and lack of visceral involvement or serologic features of systemic sclerosis (2). It has generally a benign course; systemic corticosteroids and hydroxychloroquine are good therapeutic alternatives (3). Several hemopathies, both malignant and non-malignant, have been associated with this syndrome (4, 5). We call attention upon a case of eosinophilic fasciitis associated chronic neutropenia resistant to recombinant granulocyte, and granulocyte/monocyte stimulator cytokines.

A 43-year-old woman was admitted with a 6-month history of muscle tenderness, intense fatigue, and bilateral legs edema, and later of her arms, wrists, and hands. Rheumatoid arthritis was considered but no improvement was noticed after a trial of DMARDs and NSAIDs. Initial laboratory disclosed a total leukocyte count of 14.3 x 10^9/L, eosinophils 5.8 x 10^9/L, and non-corrected ESR of 24 mm/h. Parasitic factors, viral and parvovirus antibodies, or bacterial cultures, were all normal or negative. A 4-week trial with cytosporine was initiated, and in the next few days, neutrophils 0.1 x 10^9/L, eosinophils 1.1 x 10^9/L, antinuclear antibodies, rheumatoid factor, C3 and C4, immunoglobulins, as well as anti-cytomegalovirus, Ebstein-Barr virus, and parvovirus antibodies, or bacterial cultures, were all normal or negative. A biopsy encompassing skin through muscular fascia was consistent with eosinophilic fascitis (Fig. 1). Bone marrow showed 15% of mature plasmatic cells and granulocyte maturation arrest. Oral prednisone, 60 mg/day was initiated, and in the next few days, general symptoms, edema, skin thickening, and eosinophils improved, but neutopenia remained with no other blood abnormalities. During the next eight weeks unresponsive to several courses of granulocyte, and granulocyte-macrophage colony-stimulating factors. Finally, after a 4-week trial with cyclosporine (5 mg/kg/day) a increase to 1.8 x 10^9/L granulocytes was observed. White cell counts remain normal after 12 months of follow-up with cyclosporine.

Associations between Shulman’s syndrome, pernicious and hemolytic anemia, immune mediated thrombocytopenia, as well as megakaryocytic aplasia, pure red-cell aplasia, and aplastic anemia have been described (2, 3, 5). Isolated neutropenia has not been reported in this regard, as it is described (4). Neutropenia might be found in other systemic autoimmune diseases. The mechanism of chronic neutropenia in such conditions involves auto-antibodies production against granulocyte antigens which induce early granulocyte apoptosis. The so-called non-immune chronic idiopathic neutropenia is found in patients with intense macrophage activity and subsequently, high levels of pro-inflammatory cytokines; such a pattern also described in eosinophilic fasciitis might be the underlying mechanism in this case (6). Albendazol has been described in eosinophilic fasciitis. Failure of response to granulocyte colony-stimulating factor requires further evaluation; cyclosporine might be considered as the best option for glucocorticoid-resistant patients.

Fig. 1. Inflammatory infiltrate composed by eosinophils in the muscular fascia (P. Pasquel, 40X, HE)

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References