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CASE REPORT

Long-term remission by cyclosporine in a patient with eosinophilic fasciitis associated with primary biliary cirrhosis

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Abstract A 70-year-old man was admitted to the hospital in June 1994 because of cutaneous induration of the extremities. Eosinophilic fasciitis was diagnosed on the basis of the course and distribution of the cutaneous lesions. Cyclosporine (100 mg/day) was given. After 4 weeks of treatment, cutaneous induration and limited joint mobility improved. Liver dysfunction had been diagnosed 5 years before the onset of eosinophilic fasciitis. Primary biliary cirrhosis (PBC) was diagnosed on the basis of the elevated serum biliary-enzyme levels, strongly positive antimitochondrial antibody titer, and histologic features of the liver-biopsy specimens showed stage-3 PBC. These findings suggested that eosinophilic fasciitis developed in association with PBC. PBC is often accompanied by autoimmune diseases, such as Sjögren's syndrome and Hashimoto's disease. To our knowledge, eosinophilic fasciitis associated with PBC has not been reported previously. We believe this is the first time a case of eosinophilic fasciitis occurring in a patient with PBC is documented.

Keywords Cyclosporine · Eosinophilic fasciitis · Long-term remission · Primary biliary cirrhosis (PBC)

Introduction

Eosinophilic fasciitis, first described by Shulman in 1974, is characterized by symmetrical woody induration of the skin, primarily affecting the extremities, and rapid progression 2 weeks to 2 months after disease onset [1]. Induration leads to limited joint mobility and flexion contracture. Other characteristics include the absence of induration of the fingers and toes, and a history of vigorous exercise or physical stress before the onset of illness. Eosinophilic fasciitis can be distinguished from scleroderma by the absence of Raynaud's phenomenon, sclerodactyly, and visceral involvement. Pathological examination reveals thickening of the fascia and inflammatory-cell infiltration. However, the muscularis, dermis, and epidermis are normal. Eosinophilic fasciitis usually responds to treatment with steroids [2], but is often accompanied by blood diseases such as aplastic anemia, which affect the prognosis [3]. We describe our experience with a patient who had primary biliary cirrhosis (PBC) accompanied by eosinophilic fasciitis. Steroids were not given. The patient had a remission after short-term treatment with cyclosporine and was followed for 12 years without recurrence of eosinophilic fasciitis or blood disease.

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Case report

A 70-year-old man was admitted to the hospital in June 1994 because of cutaneous induration of the extremities. In 1993, painful reddening and swelling developed in both lower legs after farm work, pursued as a hobby. In January 1994, cutaneous induration of both lower legs and forearms progressed rapidly, leading to limited mobility of the knees, elbows, and wrists. In 1989, liver dysfunction was diagnosed, but he was observed without the use of medication. He did not drink alcohol and had never taken L-tryptophan.

The results of a physical examination of the chest were normal. The liver and spleen were not palpable. The patient

had cutaneous induration of both forearms and lower legs. Flexion and extension of the knees, elbows, and wrists were limited. Mild induration affected the dorsum of the hands and feet, but not the fingers or toes. No arthralgia or Raynaud's phenomenon was present.

The peripheral white-cell count was 5,500/μl (eosinophils, 500/μl); the red-cell count, 338×10^4/μl; the hemoglobin level, 10.8 g/dl; the platelet count, 220×10^3/μl; the erythrocyte sedimentation rate, 66 mm/h; and the C-reactive protein level, 0.8 mg/dl. The patient had elevated serum biliary-enzyme levels: GOT was 36 U/l; GPT 20 U/l; LDH 378 U/l; ALP 438 U/l; γ-GTP 230 U/l; and LAP 147 U/l. The immunoglobulin levels were high: IgG, 3,550 mg/dl; and IgM, 568 mg/dl. The serum complement level was normal. Serologic tests for autoantibodies, including antinuclear antibody, anti-DNA antibody, anti-RNP antibody, anti-SSA antibody, anti-Scl-70 antibody, and anti-smooth-muscle antibody, were negative. The antimitochondrial antibody titer was high (1:1,280). Liver biopsy revealed fibrocellular expansion of the para-portal areas, disappearance of the bile ducts, and lymphocyte-predominant inflammatory cell infiltration. Stage 3 PBC was diagnosed on the basis of the elevated serum biliary-enzyme levels, strongly positive antimitochondrial antibody titer, and histologic features of the liver-biopsy specimens. Biopsy of the affected skin revealed thickening of the fascia and inflammatory changes. Eosinophilic fasciitis was diagnosed on the basis of the course and distribution of the cutaneous lesions.

Cyclosporine (100 mg/day) was given. After 4 weeks of treatment, cutaneous induration and limited joint mobility improved. After 6 months of treatment, the patient had hypertension and an elevated serum creatinine level, considered adverse effects of cyclosporine. Treatment with cyclosporine was therefore discontinued. Subsequently, cutaneous induration gradually improved despite the withdrawal of cyclosporine. Induration of the forearms resolved. Only mild induration at the anterior surface of the tibia remained. The patient was followed for 12 years without recurrence of eosinophilic fasciitis or blood disease.

Discussion

This patient had characteristic clinical signs of eosinophilic fasciitis, such as induration of the extremities, excluding the fingers and toes, orange peel appearance, and bowing of the legs. There was no Raynaud's phenomenon or visceral involvement. Biopsy of the affected skin showed marked thickening of the fascia and inflammatory-cell infiltration. Eosinophilic fasciitis was thus diagnosed. Simultaneously, elevated serum biliary-enzyme levels and a high antimitochondrial antibody titer were present. A liver biopsy confirmed the diagnosis of PBC. Liver dysfunction had been diagnosed 5 years before the onset of eosinophilic fasciitis. Histologic examination of a liver specimen showed stage 3 PBC. These findings suggested that eosinophilic fasciitis developed in association with PBC. PBC is often accompanied by autoimmune diseases such as Sjögren's syndrome and Hashimoto's disease. To our knowledge, eosinophilic fasciitis associated with PBC has not been reported previously. We believe this is the first time a case of eosinophilic fasciitis occurring in a patient with PBC is documented.

Steroids can improve the histologic changes of the liver only in the early stage of PBC [4]. However, steroids are not used because they act synergistically with PBC and decrease bone mineral density [5]. In general, ursodesoxycholic acid and colchicine are prescribed. As for immunosuppressive therapy, double-blind studies have confirmed that methotrexate and cyclosporine are safe and effective. Cyclosporine improves the results of biochemical tests and inhibits the progression of histologic changes of the liver [6]. As compared with other diseases, PBC has been associated with higher incidences of adverse reactions such as hypertension and renal dysfunction in patients receiving low-dose cyclosporine [7]. This higher risk of adverse reactions is attributed to the fact that cyclosporine is metabolized in the liver and undergoes enterohepatic circulation [8].

Steroids are used as first-line drugs for the treatment of eosinophilic fasciitis. Initial treatment with moderate doses of steroids generally leads to remission. Our patient had eosinophilic fasciitis and PBC, both of which were active and required treatment. We considered whether we should disregard the risk of osteoporosis and give the patient steroids, established to be effective for eosinophilic fasciitis, or give the patient cyclosporine, likely to be effective for both eosinophilic fasciitis and PBC. We selected the latter alternative. In week 4 of treatment with cyclosporine, limited joint mobility improved, confirming that cyclosporine was effective. After 6 months of treatment with low-dose cyclosporine, hypertension and renal dysfunction developed, as reported previously. Cyclosporine was thus withdrawn, but eosinophilic fasciitis has remained in remission. The cutaneous lesions and limited joint mobility of the forearms have improved substantially, indicating an excellent response. Steroids are considered the treatment of choice for eosinophilic fasciitis and are most effective. Given that eosinophilic fasciitis is often associated with blood diseases indicated for cyclosporine treatment. Cyclosporine may be an important option for the initial management of eosinophilic fasciitis.

Disclosures None.

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