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CASE REPORT

Cetirizine: An Effective Agent in Kimura's Disease

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Introduction

Kimura's disease is a chronic inflammatory condition of unknown etiology usually found in young Asian men (1). It is characterized by tumor-like lesions in the soft tissue and lymph nodes of the head and neck or in the parotid gland. It may also involve the upper limbs. Histopathologic investigation of such lesions reveals abnormal proliferation of small vessels, associated with a prominent infiltration of eosinophils together with plasma cells and scattered lymphoid follicles. The lesions in Kimura's disease are always benign, although they may be easily mistaken for a malignant tumor. Usually there are no systemic visceral manifestations except for an association with nephrotic syndrome and eosinophilia (2,3).

In the past, the treatment of choice for the subcutaneous lesions was surgical resection (4). However, several case reports have described the beneficial effect of treatment with corticosteroids and other immunosuppressive agents or radiotherapy (5). In the present report, we describe the beneficial effect of cetirizine—a selective H1 receptor blocker—in a patient with Kimura's disease.

Case report

A 42-year-old woman of North African origin visited the orthopedic clinic reporting the sudden appearance of subcutaneous lesions in her left arm and in the right side of her neck. At first, the lesions were ~0.5–0.7 cm and there was associated pruritus. Two months later, both lesions had slowly grown to ~2.0 cm in diameter. Due to the clinical suspicion of malignancy, a magnetic resonance image of the arm was obtained and a diagnosis of a possible hemangioma was suggested. Because the lesions grew rapidly, the treating physician decided to excise both of them surgically. The lesion on the arm was situated in the subcutaneous fat, was partially encapsulated, and appeared to be a lymph node. The lesion in the neck was intramuscular. On histologic examination of both specimens, numerous lymphoid follicles were seen with prominent reactive germinal centers (Figure 1). These were separated by expanded interfollicular areas rich in eosinophils with numerous high endothelial venules. The lining endothelium of the venules was not prominent. In both biopsy samples, the lymphoid component overshadowed the vascular component. No infectious agents or atypical lymphoid cells were seen. The morphologic picture was typical of Kimura's disease. Three months later, the patient noticed a new lesion on her right arm. Again the lesion was resected and the histopathology of the specimen was similar to the previous samples, confirming the diagnosis of Kimura's disease. Four months later, due to recurrence of the lesions in her left arm, she was referred to our rheumatology clinic. On physical examination the patient looked well. The only positive finding was a nontender subcutaneous lesion of ~2 cm on her left forearm.

Laboratory tests disclosed a normal erythrocyte sedimentation rate and C-reactive protein level, and the serologic test results for rheumatoid factor and fluorescent antinuclear antibodies were negative. Complete blood count revealed normal levels of white blood cells (9,100/mm^3), hemoglobin, and platelets with eosinophilia of 13.1% (1,180/mm^3). The serum level of IgE was 110 units/ml (normal $<$ 100). Urinalysis and kidney function test results were normal.

Based on the scant published literature regarding treatment of Kimura's disease, we decided to treat the patient with prednisone 30 mg daily with slow tapering. Each time she decreased the dosage below 10 mg/day, she experienced a flare of the disease with the appearance of new subcutaneous lesions and an elevated eosinophil count ($>$1,000/mm^3) in the blood. Therefore we had to increase the steroid dosage and add azathioprine. Following 2 years of steroid treatment (with azathioprine, omeprasole, and calcium and vitamin D supplements), the patient felt better and the skin lesions and the eosinophilia disappeared. Nevertheless, she developed cushingoid symptoms and unacceptable hirsutism all over her body. We decided to discontinue steroid treatment and try cetirizine, an antiallergic H1 receptor antagonist with antiinflammatory activity. Following cetirizine treatment (10 mg/day), the patient became asymptomatic, with no skin lesions and with a normal blood eosinophil count. All corticosteroid side effects promptly resolved. She has been in complete remission for the past 6 months.

The patient described herein had only subcutaneous

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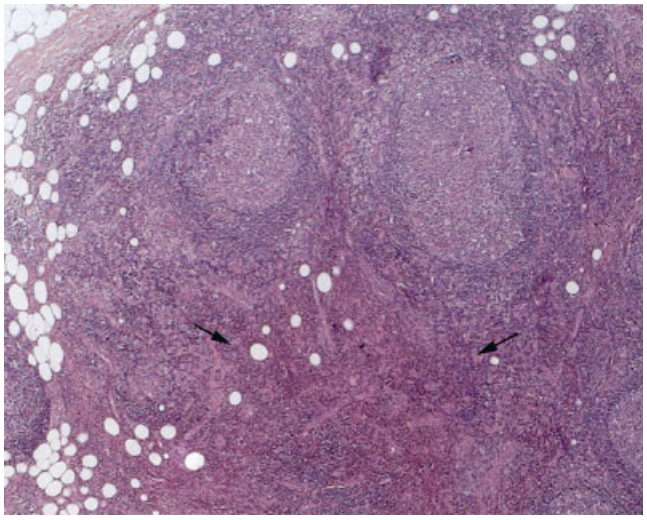

Figure 1. Histologic picture of the subcutaneous mass: in the upper half of the picture there are two 2 lymphoid follicles with prominent germinal centers. In the interfollicular region (between the **arrows**), high endothelial venules and numerous eosinophils are seen. Hematoxylin and eosin stain, original magnification × 5.

and intramuscular lesions and eosinophilia, with no renal involvement. Nevertheless, she required steroid therapy due to the recurrence of the subcutaneous lesions and due to the failure of repeated surgical resections to cure the disease. Corticosteroid treatment was beneficial in diminishing the lesions and lowering the count of blood eosinophils. However, the side effects, especially the prominent moon face with severe hirsutism, posed a serious difficulty in continuing this treatment. Therefore, we looked for an alternative.

In 1998, Tsukagoshi et al described a case of Kimura's disease with atopic bronchial asthma, eosinophilia, and hyperimmunoglobulinemia E. The patient was treated with an antiallergic drug (suplatast tosilat) with good response (6). In our case, the patient was not atopic and did not have bronchial asthma or other allergic diseases. Nevertheless, the manifestations of itching, eosinophilia, and tissue eosinophil infiltration are characteristic features of an ongoing allergic inflammatory reaction. We thus hypothesized that an antiallergic agent, such as cetirizine, might be beneficial in our patient.

Cetirizine is a selective histamine H1 receptor blocker widely used for the treatment of allergic rhinitis and chronic urticaria. In addition to its known antihistaminic properties, cetirizine has well documented antiinflammatory effects both in vitro and in vivo. It inhibits eosinophil chemotaxis and adhesion to endothelial cells. It also suppresses the generation of various proinflammatory cytokines and decreases intercellular adhesion molecule 1 expression (7,8). Moreover, cetirizine reduces allergen-induced eosinophil influx and accumulation in the human skin, nose, and airways (9).

In the present patient, cetirizine induced a complete remission of the clinical signs and symptoms within 2 months of treatment, and corticosteroids were gradually discontinued. This dramatic response may indicate that eosinophils rather than other cell types play a pivotal role in the pathogenesis of Kimura's disease. Thus, inhibition of eosinophil recruitment and activity may be an important part of the treatment of Kimura's syndrome.

We suggest that a therapeutic trial with antiallergic antiinflammatory agents, such as cetirizine, be tried prior to corticosteroids or for sparing the effect of corticosteroids in this rare disorder.

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