Case report

Two Japanese cases with MAGIC syndrome (Mouth and Genital Ulcers with Inflamed Cartilage)

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ABSTRACT

We describe two cases, a 28-year-old woman and a 46–year-old man, with mouth and genital ulcers with inflamed cartilage (chondritis of the nose and ears) (MAGIC syndrome). The conditions of both patients were resolved by treatment with corticosteroid and colchicine. We also review the English literature related to this rare syndrome.

Introduction

In 1985, Firestein *et al*. described five patients with features of both relapsing polychondritis and Behçet's disease. They proposed "MAGIC syndrome" (mouth and genital ulcers with inflamed cartilage) (1). Since then, only four cases have been reported in the English literature. Here we describe two additional cases, reviewing the English literature.

Case 1

A 28-year-old woman was admitted to our hospital with arthralgia of the right knee and painful of swelling of the ear lobes in March 2003. She occasionally developed painful oral ulcers. Five months before admission, she experienced redness of the eye and was diagnosed with conjunctivitis by an ophthalmologist. Since then, the patient developed intermittent arthralgia of the knees, costal cartilage, ear lobes, and oral ulcers. On admission, the ear auricles were red and swollen. Arthritis of both the right knee and costal cartilage were noted. Laboratory data was as follows: ESR 77.5 mm/h, WBC 9900/μL (neutrophils 74.9%, lymphocytes 16.8%, monocytes 5.8%, eosinophils 1.9%, basophils 0.6%), Hb 11.8 g/dl, PLT 26.5 x 10^4/μL, and C-reactive protein (CRP) 1.6 mg/dl. Urinalysis did not demonstrate protein on dipstick. Renal and liver functions were normal. Immunological tests demonstrated immunoglobulin (Ig) D 14.1 mg/dl, CH_{50} 48.8 U/ml, both antinuclear antibody and RAPA were negative. Serologic HLA analysis demonstrated A24, A11, B52, B54, CW, DR15, DQ1 DQ3. Radiographs of knees and costal cartilage were within normal limits. Biopsy of the cartilage portion of an ear lobe demonstrated infiltration of lymphoid cells. The patient was diagnosed with relapsing polychondritis (2, 3), and treated with oral prednisolone (50 mg/day). With improved symptoms, she was discharged taking oral prednisolone (35 mg/day). The patient was followed at our outpatient clinic with prednisolone being tapered. When she was taking 12 mg of prednisolone, both oral and genital ulcers appeared. Isogladine maleate (4mg/day), a drug used for the treatment of gastritis and peptic ulcer, reinforces gap junctional intracellular communication and resolved the symptoms in this case. Finally, the patient was diagnosed with relapsing polychondritis associated with mouth and genital ulcer, *i.e.*, MAGIC syndrome. She is currently taking 5 mg of oral prednisolone and remains in good condition as of June 2006.

Case 2

A 51-year-old man consulted our outpatient clinic in February 1992 because of erythema nodosum on the legs. For three years, he had experienced oral ulcers, genital ulcers and erythema nodosum. Laboratory data at the first visit showed ESR 4.2 mm/h, WBC 5400/μL (neutrophils 63%, lymphocytes 30%, monocytes 6% and basophils 1%), Hb 15.3 g/dl, plt 18.3 x 10^4/μL, and CRP 0.2 mg/dL. Urinalysis did not demonstrate protein on dipstick. Renal and

liver functions were normal. On immunological test, IgG, IgA and IgM were 1358, 228 and 319 mg/dl, respectively. Antinuclear antibody was 160 ×, RAPA was negative. Serologic HLA analysis demonstrated A2, A24, B51, B52, DR15, DR6, DQ1. The patient was diagnosed with Behçet's disease (4, 5), treated with corticosteroid (5 mg/day) and cholchicine. Since May 1996, the ear auricles have sometimes become swollen without pain. In November 1997, his right ear became swollen and painful. The patient was diagnosed with chondritis at an otolaryngologic clinic because of tenderness of the cartilage portion of the ear lobes. Finally, the patient was diagnosed with MAGIC syndrome. The symptoms were resolved with 10 mg/day of prednisolone.

Discussion

Our cases fulfilled Firestein's criteria for MAGIC syndrome (1). Case 1 was diagnosed with relapsing polychon dritis and genital ulcers developed thereafter. The patient also demonstrated recurrent painful oral ulcers. As Papadimitraki *et al.* pointed out, aphthous ulcers of Behçet's disease often appear prior to other manifestations of Behçet's disease (6). She was finally diagnosed with MAGIC syndrome. Case 2 was first diagnosed with Behçet's disease. Four years later, the feature of relapsing polychondritis developed. The combination of Behçet's disease and relapsing polychondritis is very rare. Since Firestein proposed MAGIC syndrome in 1985, only four additional cases have been reported in the English literature.

The clinical features of eleven previously reported cases (1, 7-10), five men and six women, are as follows. Age at disease onset ranged from ten years old to fifty-nine years old. Eight cases were diagnosed with Behçet's disease and during the follow-up period, the clinical features of relapsing polychondritis appeared. However, two cases were diagnosed with relapsing polychondritis, then the feature of Behçet's disease developed. As for treatment for MAGIC syndrome, colchicine, corticosteroid or dapsone have been reported to be effective. Our cases also showed a good response to oral prednisolone and colchicine.

The pathogenesis of both Behçet's disease and relapsing polychondritis remains unclear, although similarities between the clinical manifestations of these two diseases imply a similar pathogenic mechanism. In Behçet's disease, vasculitis may play a role in the pathogenesis (11, 12). However, several authors reported that antibodies to type II collagen can be found in patients with relapsing polychondritis (13, 14). Ebringer *et al.* detected antibodies to fetal cartilage by an indirect immunofluorecence method in two thirds of patients with relapsing polychondritis (15). However, type II collagen and antibodies to fetal cartilage were neither sensitive nor specific for relapsing polychondritis. Urinary type II collagen neoepitope (UTIINE) seem to parallel the severity of the relapsing polychondritis (6, 16). UTIINE has been shown to reflect an enhanced TH1 immune-response, which is associated uncontrolled disease. As Firestein pointed out, autoimmunity to components of cartilage such as proteoglycan or elastic tissue may be involved in the mechanism of disease onset (1).

In summary, we report two Japanese cases of MAGIC syndrome. Since Firestin first reported five cases of MAGIC syndrome in 1985, only four cases have been reported in the English literature. To clarify the pathogenesis of MAGIC syndrome, additional cases and further research is needed.

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