A Case of Polychondritis in a Patient with Behçet’s Disease

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Polychondritis is an inflammatory disorder that affects various cartilaginous structures, and the clinical features include auricular, nasal and respiratory tract chondritis. It also involves the eyes, audiovestibular apparatus, joints and vascular structures. Polychondritis can be associated with several rheumatologic diseases such as systemic lupus erythematosus, rheumatoid arthritis and systemic vasculitis. However, polychondritis is a rare complication of Behçet’s disease (BD) and only ten cases with combined BD and polychondritis have been reported on around the world. In this report, we describe a 40-year-old Korean man with BD who suffered from polychondritis that manifested as bilateral auricular chondritis, conjunctivitis and arthritis.

Key Words : Polychondritis, Behçet’s disease

INTRODUCTION

Behçet’s disease (BD) is a chronic inflammatory disease that is characterized by recurrent oral and genital ulceration and uveitis, the other clinical manifestations include skin lesions, arthritis, thrombosis, neurologic symptoms and intestinal ulceration. Polychondritis is known as a rare complication of BD and no case of BD combined with polychondritis had been reported on until Firestein et al. reported on five patients with both BD and relapsing polychondritis (RP) in 1985. Only five more cases have been reported since then. We recently experienced a case of a 40-year-old male patient with both BD and polychondritis, and we report herein on this unusual case along with a review of the literature.

CASE REPORT

A 40-year-old man was referred to our hospital for further evaluation of his fever, oral ulcers and skin rashes that had lasted for 10 days. He had previously suffered from intermittent oral ulceration and uveitis that had been treated with oral prednisolone and intraocular injections of triamcinolone at another hospital 1 year prior to this admission.

On the physical examination, his blood pressure was 130/80 mmHg, the pulse rate was 80 per minute and the body temperature was 38.4°C. He had conjunctival injections in both eyes and several aphthous ulcers on the tongue (Figure 1A) and buccal mucosa. A small round ulcer with tenderness was found on the penile root (Figure 1B). Several round erythematous skin lesions were present on the chest and thigh (Figure 2A). His left knee joint was swollen (Figure 2B). His left knee joint was swollen (Figure 2B) and tender, and needle aspiration revealed turbid inflammatory synovial fluid.

The laboratory findings were as follows: hemoglobin 14.8 g/dL, white blood cell count 10,400/μL, platelet count 291,000/μL, erythrocyte sedimentation rate 104 mm/hr and C-reactive protein 205 mg/L (normal range, 0~3.4 mg/L). The renal and liver function tests were normal and the tests for rheumatoid factor and antinuclear antibody were negative. The urinalysis was normal and no microorganisms were grown on both the blood and urine cultures. His chest radiography showed no
abnormal findings and mild splenomegaly was observed on abdominal sonography. Gastroduodenoscopy revealed a gastric ulcer and no ileocecal lesion was found on colonoscopy examination. Skin biopsy was performed and the histologic examination showed perivascular mononuclear cell infiltrations, extravasation of the red blood cells and fibrinoid necrosis of the blood vessel walls; all of these findings were compatible with cutaneous vasculitis combined with BD (Figure 3).

On the 5th day of admission, both ear auricles became swollen, red and tender (Figure 4). He remembered having a similar auricular inflammation 2 years ago that had improved after taking non-steroidal anti-inflammatory drugs. After he was administered with colchicine 1.2 mg/day and prednisolone 30 mg/day, his clinical symptoms improved and he was discharged on the tenth day of admission.
DISCUSSION

Polychondritis is an inflammation of the various cartilaginous structures such as the auricle, nose and trachea, and it has also been known to involve the eye and the joints. When polychondritis is relapsing, it is called relapsing polychondritis (RP). In RP, various cutaneous manifestations are also seen, including palpable purura, erythema nodosum, panniculitis, livedo reticularis and urticaria.

There have been case reports on polychondritis combined with other rheumatologic diseases such as systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and systemic vasculitis. However, there have been no reports of polychondritis combined with BD until Firestein et al. first reported on five patients who had the features characteristic of both BD and RP, and those authors termed this as mouth and genital ulcers with inflamed cartilage (MAGIC) syndrome. Polychondritis is still known as a rare complication of BD and only five more cases of BD combined with polychondritis have been reported on since Firestein’s report.

In our patient, BD was diagnosed based upon the recurrent oral and genital ulcers, the skin vasculitis, the arthritis and the past history of uveitis. The chondritis developed at the bilateral auricles, eye and the joints during the acute exacerbation period of BD, and this resolved with the improvement of the symptoms of BD. This suggests that the development of polychondritis may have been associated with BD in our case. As for treatment for the combined cases of BD and RP, colchicine, steroid and dapsone have been reported to be effective. Our patient also showed a good response to colchicine and oral prednisolone.

Skin involvement in BD includes various lesions such as erythema nodosum, pustules, papules, pseudofolliculitis, acneiform folliculitis, Sweet’s syndrome, or pyoderma gangrenosum. The histopathology of the papulopustular lesions usually shows vasculopathy that is characterized by the perivascular infiltration of mononuclear cells, and this infiltrate is mainly composed of lymphocytes. The lesions are sometimes accompanied by luminal thrombosis, necrosis or mural fibrin deposition. Neutrophilic vascular reaction has also been reported. The erythema nodosum-like lesion is known to be characterized by extravascular neutrophilic infiltration and panniculitis, and this can be followed by lymphocyte infiltration during the evolution of the skin lesions. In our case, the main histopathologic finding of the skin lesions was perivascular mononuclear cell infiltration and fibrinoid necrosis of the vessel walls, which are the characteristic findings of vasculopathy.

Although cases of BD combined with polychondritis have rarely been reported, BD and polychondritis do not seem to be separate entities. There are some overlapping manifestations for BD and RP. Firestein et al. compared the frequency of the various clinical features in BD and RP (Table 1), and they showed that some of the manifestations that are considered unique for one disease could be found in the other disease. These similarities between the clinical manifestations of BD and RP imply that there seems to be something in common for the pathogenesis of BD and polychondritis. The pathogenesis of both BD and RP is associated with autoimmunity. In patients with RP, the antibodies to collagen type II, IX and XI are elevated in the sera and the frequency of human leukocyte antigen (HLA)-DR4 is increased. Additionally, RP has been associated with other autoimmune diseases such as RA and SLE. In patients with BD, autoantibodies such as antiendothelial cell antibody and antibody to α-tropomyosin have been reported.
been found\textsuperscript{18-20} and it has been postulated that cross-reactivity and molecular mimicry between the peptides from the streptococcal proteins or the viral heat shock proteins (HSPs), which are homologues of human HSPs, and the mucosal antigens result in the selection of autoreactive T cells\textsuperscript{21}). Firestein et al. have proposed that autoimmunity to components of the cartilage other than type II collagen, such as proteoglycans or elastic tissue, could be the common mechanism of BD and RP\textsuperscript{22}. In particular, elastic tissue is ubiquitous in the human mucosa that is mainly involved in BD, and in the cartilage too, which is the major target of RP. However, because of the rarity of the combined cases, there have not yet been any investigations about the common pathogenesis of the two diseases, and so additional research is clearly needed. Although there have been only a few reports about polychondritis combined with BD, we think this combination of diseases might have been overlooked so far and closer scrutiny would reveal more cases.

**REFERENCES**

1) International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's Disease. Lancet 335:1078-1080, 1990
2) Firestein GS, Gruber HE, Weisman MH, Zvaifler NJ, Barber J, O'Duffy JD. Mouth and genital ulcers with inflamed cartilage: MAGIC syndrome. Am J Med 79:65-72, 1985
3) Orme RL, Nordlund JJ, Barich L, Brown T. The MAGIC syndrome (mouth and genital ulcers with inflamed cartilage). Arch Dermatol 126:940-944, 1990
4) Le Thi Huong D, Wechsler B, Piette JC, Papo T, Jaccard A, Jault F, Gandjbakhch I, Godeau P. Aortic insufficiency and recurrent valve prosthesis dehiscence in MAGIC syndrome. J Rheumatol 20:397-398, 1993
5) Imai H, Motegi M, Mizuki N, Ohtani H, Komatsuda A, Hamai K, Miura AB. Mouth and genital ulcers with inflamed cartilage (MAGIC syndrome): a case report and literature review. Am J Med Sci 314:330-332, 1997
6) Fernandez-Morras F, Fornos C, Argimon J, Pujadas R. Aneurysmatic aortitis in the MAGIC syndrome. Med Clin 109:694-695, 1997
7) Gamboa F, Rivera JM, Mayoral L, Grillo A. Behçet's disease and relapsing polychondritis (MAGIC syndrome) associated with antiphospholipid syndrome. Med Clin 110:678-679, 1998
8) Hochberg MC. Relapsing polychondritis. In: Ruddy S, Harris ED, Sledge CB, Budd RC, Sergeant JS, eds. Kelley's textbook of rheumatology. 6th ed. pp. 1463-1467. Philadelphia, W.B. Saunders, 2001
9) Franssen MJ, Boerbooms AM, van de Putte LB. Polychondritis and rheumatoid arthritis: case report and review of the literature. Clin Rheumatol 6:453-457, 1987
10) Hairisdragul V, Johnson WW. Association between relapsing polychondritis and systemic lupus erythematosus. South Med J 87:753-757, 1994
11) Michel CJ. Vasculitis and relapsing polychondritis. Rheum Dis Clin North Am 16:441-444, 1990
12) Calamia KT. Behçet's disease. In: Kippel JH, Crofford LJ, Stone JH, Weyand CM, eds. Primer on the rheumatic diseases. 12th ed. pp. 415-418. Atlanta, Arthritis Foundation, 2001
13) Magro CM, Crowson AN. Cutaneous manifestations of Behçet's disease. Int J Dermatol 34:159-165, 1995
14) Chun Si, Su WP, Lee S, Rogers RS 3rd. Erythema nodosum-like lesions in Behçet's syndrome: a histopathologic study of 30 cases. J Cutan Pathol 16:259-265, 1989
15) Foidart JM, Abe S, Martin GR, Zizic TM, Barnett EV, Lawley TJ, Katz SI. Antibodies to type II collagen in relapsing polychondritis. N Engl J Med 299:1203-1207, 1978
16) Akselholm S, Mollenhuauer J, Scheuplein F, Stoss H, Kalden JR, Burkhartt B, Burmester GR. Preferential cellular and humoral immune reactivities to native and denatured collagen types IX and XI in a patient with fatal relapsing polychondritis. J Rheumatol 20:1419-1424, 1993
17) Lang B, Rothenfusser A, Lanchbury JS, Rauh G, Breedveld FC, Urlacher A, Albert ED, Peter HH, Melchers I. Susceptibility to relapsing polychondritis is associated with HLA-DR4. Arthritis Rheum 36:660-664, 1993
18) Direskeneli H, Keser G, D'Cruz D, Khamashta MA, Akoglu T, Yazici H, Yurdakul S, Hamuryudan V, Ozgun S, Goral AJ. Anti-endothelial cell antibodies, endothelial proliferation and von Willebrand factor antigen in Behçet's disease. Clin Rheumatol 14:55-61, 1995
19) Mor F, Weinberger A, Cohen IR. Identification of alpha-tropomyosin as a target self-antigen in Behçet's syndrome. Eur J Immunol 32:356-365, 2002
20) Lee KH, Chung HS, Kim HS, Oh SH, Ha MK, Baik JH, Lee S, Bang D. Human alpha-enolase from endothelial cells as a target antigen of anti-endothelial cell antibody in Behçet's disease. Arthritis Rheum 48:2025-2025, 2003
21) Lehner T. The role of heat shock protein, microbial and autoimmune agents in the aetiology of Behçet's disease. Int Rev Immunol 14:21-32, 1997