**CASE REPORT**

**Tonsillectomy to Effectively Treat a Patient with Behçet’s Disease**

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**Abstract**

Behçet’s disease (BD) is a polysymptomatic and recurrent systemic vasculitis with a chronic course and unknown cause. We herein report a 27-year-old woman who had suffered from a recurrent fever and tonsillitis for nearly ten years with BD for whom tonsillectomy was effective.

**Key words:** Behçet’s, tonsillectomy, tonsillitis

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**Introduction**

Behçet’s disease (BD) is a polysymptomatic and recurrent systemic vasculitis with a chronic course and unknown cause (1, 2). We herein report a BD patient who had suffered from a recurrent fever and tonsillitis for nearly ten years. After tonsillectomy, her disease activity notably decreased. Thus, tonsillectomy may be effective for BD patients if the disease is complicated by severe and recurrent tonsillitis. To the best of our knowledge, this is the first case report to demonstrate that tonsillectomy is effective for BD in the English literature.

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**Case Report**

A 27-year-old woman was referred to our outpatient clinic due to oral ulcers in October 2009. She had a history of recurrent oral aphthae for the last ten years and recurrent tonsillitis for the previous year. In September 2009, she developed a genital ulcer and was treated at a gynecology clinic, and, nearly simultaneously, acne developed on her back and chest. On an ophthalmologic examination, she had no iritis or uveitis. Furthermore, she did not exhibit acne or erythema nodosum. Before visiting our outpatient clinic, she suffered from a fever and severe tonsillitis in October 2008 and June 2009, respectively. The patient was diagnosed with BD (incomplete type) because of the recurrent oral ulcers, genital ulcer, and acne according to the Behçet’s Disease Research Committee Criteria in Japan and International BD Study Group Criteria in October 2009 at our outpatient clinic. Oral prednisolone (5 mg/day) was started. Thereafter, tonsillitis and oral ulcers appeared intermittently. On admission, the laboratory data were as follows: erythrocyte sedimentation rate (ESR): 16 mm/h, WBC: 3,900/µL (neutrophils: 53.1%, lymphocytes: 35.2%, monocytes: 6.5%), Hb: 12.5 g/dL, platelets (PLT): 24.8×10⁴/µL, and C-reactive protein (CRP): 0.15 mg/dL. A urinalysis did not demonstrate any protein on a dipstick test and the renal and liver functions were normal. Immunological tests demonstrated that immunoglobulin (Ig) G, IgA, and IgM were 1,377, 328, and 133 mg/dL, respectively. IgD was <1 mg/dL. Antinuclear antibody was 80x and rheumatoid arthritis particle agglutination (RAPA) were negative. A serologic human leukocyte antigen (HLA) analysis showed A02, A26, B15, and B46. The pathergy reaction was negative. Chest radiography and an electrocardiogram (ECG) both revealed findings within the normal limits. A gastrointestinal evaluation was normal. Soon thereafter, in December, she had multiple oral ulcers, a high fever, tonsillitis, and the soft palate was swollen. The laboratory data on this admission were as follows: ESR: 74 mm/h, WBC: 6,200/µL (neutrophils 80.0%, lymphocytes: 14.0%, monocytes: 4.5%) Hb: 12.1 g/dL, PLT: 19.0×10⁴/µL, CRP: 9.36 mg/dL, ASLO: 20 IU/mL, and ASK: <80. A swab culture showed normal bacterial flora. After loxoprofen sodium hydrate and amoxicillin therapy were initiated,
her clinical condition improved. Although she had been taking methylprednisolone (4 mg/day) at the outpatient clinic, she had experienced recurrent episodes of a fever and tonsillitis approximately once a month. At that time, she was being treated with prednisolone (10-20 mg). She was finally referred to the otolaryngology department and underwent elective tonsillectomy (Figure). After tonsillectomy, the patient’s symptoms and signs improved. She is currently in a favorable condition, taking methylprednisolone at 3 mg per day. At the latest outpatient visit, the patient has not suffered from any oral or genital ulcers since undergoing tonsillectomy. Her other clinical manifestations of Behçet’s disease are currently well controlled.

Discussion

This patient fulfilled the Behçet’s Disease Research Committee Criteria and International Study Group Criteria for the diagnosis of BD. She had demonstrated a recurrent fever and tonsillitis for nearly ten years. After tonsillectomy, the symptoms and signs improved. Thus, tonsillectomy was effective for her tonsillitis.

The incidence of tonsillitis has been reported to be more frequent in BD patients (3, 4). A focal infection, such as tonsillitis, may be related to the etiology of BD. In some reports, BD patients were often exposed to agricultural chemicals before the onset of the disease (3, 5). In a comparison of 30 BD patients and 60 controls, an increased risk of BD was associated with tonsillectomy; this finding is consistent with a triggering of the disease by infection during childhood.

There have only been a few case reports of BD flares and/or other clinical manifestations developing after tonsillectomy. Abadi et al. (6) reported a case of BD associated with myositis of the calf that was temporally associated with tonsillectomy. Wagner et al. (7) described a patient with BD who presented with a persistent fever and neck soft-tissue swelling, despite broad antibiotic treatment, two weeks after acute tonsillitis and tonsillectomy. They suggested that both tonsillitis and tonsillectomy triggered small-vessel vasculitis in the surrounding neck soft-tissue in their patient (8).

Jalessi et al. (9) investigated the association between tonsillectomy and/or adenoidectomy and the subsequent development of BD in a prospective case control study involving 128 BD patients and 139 non-BD controls. In their study, tonsillectomy was neither causally related to the development of BD nor to the manifestation of the disease.

Morales-Angulo et al. (10) reviewed the medical records of 33 BD patients to identify orthonolaryngological manifestations in such patients. Most of these patients presented with oral ulcers (97%), eight patients presented with oropharyngeal ulcers, five patients experienced audio-vestibular symptoms, and one patient had vestibular neuritis. In four patients (12%), the presence of odynophagia was identified secondary to the presence of oropharyngeal lesions, which was initially interpreted as acute or recurrent tonsillitis. Oh et al. (11) evaluated the epidemiological and clinical features of 149 patients with only aphthous ulcers and 294 BD patients. BD patients had a more common history of tonsillitis and dental caries. In addition, BD patients with persistently high antistreptolysin O titers more frequently had a history of tonsillitis.

Since there were significantly higher incidences of tonsillitis, dental caries, and periodontitis in BD patients than healthy controls, oral bacteria, especially Streptococcus sanguinis, have been suggested to be involved in the disease’s etiology. Isogai et al. (12) reported that the flora of BD patients showed a greater proportion of S. sanguinis. In addition, they reported that an uncommon type of S. sanguinis was found in all BD cases. The uncommon type has been reported to cause a much greater stimulation of neutrophilic activity and platelet clotting, as well as show greater cross-antigenicity with human tissue than the common type of S. sanguinis. BD patients also demonstrated significantly higher agglutinating antibody titers against the uncommon strain. Tsuchida et al. (13) reported that the uncommon type of S. sanguinis has been proposed as a highly likely pathogen in BD. The interaction of HLA-B51 or other precipitation factors and the uncommon type of S. sanguinis may act as a potent environmental co-factor that can repeatedly enter the body through oral disease. In this patient, reexposure to Streptococcus antigen was suggested to be the cause of tonsillitis.

BD patients display elevated lymphocytic activity and de-

Figure. a, b: Hematoxylin and Eosin staining of the tonsils. a: Reactive hyperplasia due to chronic inflammation is noted. Many lymphoid follicles are present (original magnification 20×). b: b is a square area of a. Many inflammatory cells are observed (original magnification 400×).
layed dermal sensitivity to Streptococcus antigen. Moreover, they show an increase in Streptococcus-derived antigens. Because BD patients show a higher incidence of chronic tonsillitis, these chronic foci may contribute to sensitizing BD patients and may result in intense hypersensitivity to streptococcal strains. Kaneko et al. (14) demonstrated that the production of proinflammatory cytokines by peripheral blood mononuclear cells (PBMCs) in BD patients was enhanced when stimulated with streptococcal antigens in a culture system. Thus, the intense hypersensitivity to streptococcal antigens acquired after streptococcal infection is thought to play an important role in the appearance of symptoms in BD patients. We speculate that in our case, after tonsillectomy, localized exposure to antigens, such as Streptococcus, was reduced and the clinical symptoms of BD were improved.

Kobayashi et al. (15) reported the clinical manifestation of reactive arthritis (ReA) induced by tonsillitis. Thirteen of 21 (62%) patients were demonstrated to be positive for ASO and ASK. Group A Streptococcus was demonstrated in 57.1% of the patients. HLA-B39 and B40 (B61) were significantly present. Eight of the 21 patients underwent tonsillectomy. Sterile inflammatory arthritis induced by tonsillitis was cured by resection of microabscesses in the tonsils. Thus, they reported that ReA induced by tonsillitis is one form of “focal infection.”

Pustulosis palmaris et plantaris (PPP) is known to be related to focal infection of the tonsils. Some reports demonstrated that after tonsillectomy, not only skin lesions but also pustulotic arthro-osteitis markedly and continually improved (16). It has been reported that the expression of inducible co-stimulator (ICOS), a co-stimulatory receptor on activated T cells, was significantly higher in tonsil tissues from PPP patients. Thus, the activation of T cells via ICOS stimulation in focal infections likely triggers skin and skeletal inflammation associated with PPP, resulting in tissue damage. The mechanism for the efficacy of tonsillectomy has not yet been clarified. However, we speculate that specific genetic factors and the activation of T cells may play important roles.

In summary, we herein presented a woman with BD who had suffered from a recurrent fever and tonsillitis for nearly ten years for whom tonsillectomy was effective. We speculate that specific genetic factors and the activation of T cells may play a role in the effectiveness of tonsillectomy in BD patients.

More cases are needed to clarify the mechanism of the efficacy of tonsillectomy. After tonsillectomy, the present patient’s symptoms and signs improved. Therefore, tonsillectomy may be a treatment option for recurrent and resistant tonsillitis with BD.

The authors state that they have no Conflict of Interest (COI).

References