Clinical Case Reports

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CASE REPORT

Oral infection control to assist infliximab therapy in a Behçet's disease patient with severe eye inflammation in response to dental treatment: a case report

Chieko Kudo[1], Hiroshi Wakabayashi[2], Masayuki Shimoe[3], Hiroya Kobayashi[1,a], Takashi Ito[1], Toshinori Ohkawa[3,b], Arisa Isoshima-Nakamura[3], Junji Mineshiba[1,c], Norie Yoshioka[4], Kumiko Nawachi[5], Hiroshi Maeda[3], Toshihiko Matsuo[6], Hirofumi Makino[7] & Shogo Takashiba[3]

[1]Department of Periodontics and Endodontics, Okayama University Hospital, Okayama, Japan
[2]Department of Pathology and Experimental Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[3]Department of Pathophysiology – Periodontal Science, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[4]Department of Oral and Maxillofacial Surgery, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[5]Department of Oral Rehabilitation and Regenerative Medicine, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[6]Department of Ophthalmology, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan
[7]Department of Medicine and Clinical Science, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Correspondence
Shogo Takashiba, Department of Pathophysiology – Periodontal Science, Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, 2-5-1 Shikata-cho, Kita-ku, Okayama 700-8525, Japan. Tel: +81-86-235-6675; Fax: +81-86-235-6679; E-mail: stakashi@okayama-u.ac.jp

[a]Present address: Clinical Research Center for Diabetes, Tokushima University Hospital, Tokushima, Japan

[b]Present address: Department of Oral Care and Clinical Education, Tokushima University Hospital, Tokushima, Japan

[c]Present address: Hanamizuki Dental Clinic, Okayama, Japan

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Key Clinical Message

We report a case of Behçet's disease which was aggravated by psychological stress and oral infection. The control of oral infection under medical and dental collaboration is important for providing Behçet's disease patients with the optimal medical care and for facilitating the relief of the primary disease.

Keywords

Behçet's disease, infliximab, oral infection.

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Introduction

Behçet's disease is a systemic inflammatory disorder which is both refractory and chronic. Recently, it has been reported that recurrences of Behçet's disease have been observed in vulnerable patients following dental treatment, and that there is an association between oral infection and Behçet's disease [1, 2]. At our institution, a patient suffering from Behçet's disease was affected by the disease in the ocular region following dental procedures. Herein, we report a case of this patient whose oral infection was able to be removed without the worsening of Behçet's disease under collaborative medical and dental care prior to the initiation of infliximab therapy.

Case Report

In January 2012, a 32-year-old man was referred to the Department of Periodontics and Endodontics from the Department of Rheumatology of Okayama University Hospital in Okayama, Japan. The aim of referral from the department was to determine the cause of the gingival swelling or existence of other oral infection.

The subject was diagnosed with Behçet's disease in 2003 suffering predominantly from refractory retinochoroiditis and erythema nodosum. He had initially been treated with oral prednisolone (PSL) and cyclosporine A (CYA), and colchicine was added to the treatment regime in 2010. Nonetheless, the patient had suffered repeated uveitis attacks in the meantime. Though it was planned to treat the subject with infliximab for uveitis attacks, the therapy was postponed due to oral hygiene failure. The patient had been referred to our department for removal of oral inflammation prior to undergoing infliximab therapy. However, he had refused the dental consultation the reason being that the subject had suffered chronically from reduced visual acuity following each dental treatment from 2002. He continued to refuse dental consultation for 4 years. In January 2012, he revisited our department, because he was suffering from a combination of swelling on the left side of his face with pyrexia (38.3°C).

On being referred to the Department of Periodontics and Endodontics from the Department of Rheumatology (baseline Fig. 1), it was found that the patient's visual acuity had declined to such an extent that his walking required assistance. He had acneiform eruptions on his face. Additionally, the subject had glaucoma as aconsequence of refractory uveitis. Laboratory data revealed white blood count (WBC) of 9.9×10^3 μL and C-reactive protein (CRP) of 2.1 mg/dL.

At baseline, the patient was suffering severe halitosis. Clinical oral examination revealed voluminous dental plaques and calculus, and redness and swelling of the gingiva. Multiple dental caries and tooth stumps were present (Fig. 1A). The swelling on the left side of the subject's face had already subsided. Radiographic examination revealed radiolucencies in dentine, periapical radiolucencies, moderate horizontal alveolar bone loss, and localizes areas of severe vertical alveolar bone loss (Fig. 1B).

Periodontal infection in the patient's mouth was detected as follows. Subgingival plaque samples were collected from three sites in the patient's mouth using paper points, and total bacteria, *Aggregatibacter actinomycetemcomitans* (*A. actinomycetemcomitans*), *Porphyromonas gingivalis* (*P. gingivalis*), and *Prevotella intermedia* (*P. intermedia*) were quantified using real-time quantitative polymerase chain reaction (PCR) [3]. The total bacterial number in the subgingival plaque of the left maxillary central incisor (21) was at a high level (1.99×10^4 cells). Similarly, the number of *P. gingivalis* cells in the subgingival plaque of the right mandibular first premolar (44) was also at a high level (1.47×10^4 cells) (Fig. 3A). The total bacterial number and the number of *P. gingivalis* cells in other sites were of normal range. Also, the number of *A. actinomycetemcomitans* and *P. intermedia* cells in three sites were of normal range (data not shown). The humoral immune responses to 13 periodontal bacteria were assayed by enzyme-linked immunosorbent assay (ELISA) as described previously [4]. The serum IgG antibody titers against *Porphyromonas gingivalis* (*P. gingivalis*) FDC381 and *P. gingivalis* SU63 were elevated over the mean of healthy subjects' +2 standard deviations (Fig. 3A). Other serum IgG antibody titers were within normal ranges (data not shown).

The subject was diagnosed with chronic periodontitis and multiple dental caries. The oral problems precluding infliximab therapy were poor plaque control and multiple evident oral infections. The purpose of infliximab therapy for patients with Behçet's disease is to reduce intraocular inflammation (uveoretinitis) [5]. It has been reported that chronic infection might cause sepsis or pneumonia in a patient treated with infliximab [6, 7]. Therefore, for this patient, oral infections such as chronic periodontitis and multiple caries precluded infliximab therapy, and the removal of oral infection was an urgent need.

However, the subject felt anxiety toward dental treatment owing to a history of reduced visual acuity following previous dental treatment. In fact, even after the removal of a small amount of calculus on first oral examination at our department, the patient reported to us that a high fever (38.0°C), joint pain, and ocular inflammation had continued for 5 days after the treatment. Also, due to reduced visual acuity, the patient was unable to attend as an outpatient unless accompanied by a member of his family. In view of the distance necessary in traveling

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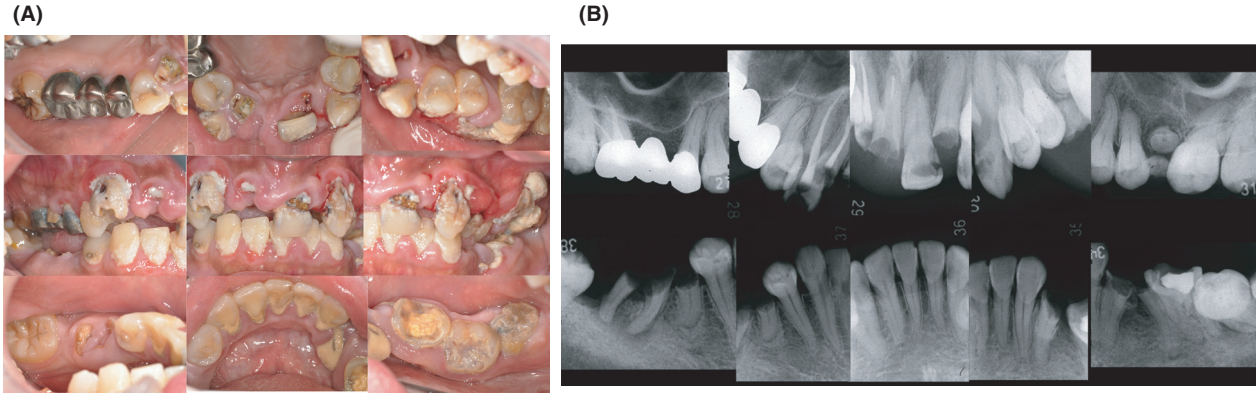

Figure 1. Intraoral view (A) and radiographs (B) at baseline. (A) Inflamed gingiva (redness and swelling) and decayed teeth with cavities due to dental biofilm are visible. (B) Alveolar bone resorption (radiolucencies around teeth) and decayed teeth (radiolucencies in teeth) suggest the existence of infectious focus.

between his home and the hospital and his family's schedule, one outpatient visit per month was considered the maximum possible. In order to solve these problems, the removal of oral infection by dental treatment was performed in cooperation with the Department of Rheumatology during the patient's hospitalization.

At first, instruction on correct brushing of the teeth was given to the subject in outpatient care for 3 months prior to the desired hospitalization date. Also, trabeculectomies in both eyes were performed in the Department of Ophthalmology. The patient's intraocular pressure (IOP) decreased to 5.4 mmHg from 21.8 mmHg in the right eye and to 6.4 mmHg from 23.9 mmHg in the left eye. Accordingly, CRP decreased to normal range before dental treatment. Subsequently, the dental treatment (scaling and root planing, tooth extraction, root canal treatment, and caries treatment) was performed under general management with medication administered by the Department of Rheumatology during the patient′s 2-week hospitalization. The patient underwent a period of dental treatment at the Department of Periodontics and Endodontics and Department of Oral and Maxillofacial Surgery. Simultaneously, the Department of Rheumatology was responsible for increasing the dose of PSL to 30 mg/day, and a dose of antibiotics (amoxicillin [750 mg/day], trimethoprim-sulfamethoxazole [2.5 mg/day]) was initiated. Furthermore, in the Department of Ophthalmology, levofloxacin hydrate and betamethasone sodium phosphate for ophthalmic administration were administered. After patient discharge, prosthetic treatment was performed in the outpatient department.

During this period of dental treatment, no abnormalities occurred in the patient's systemic condition. 10.7×10^3–12.5×10^3 μL of WBC and CRP of normal range were maintained. In addition, serum immunoglobulin A (IgA), IgG, and IgM (which were followed up during a period of the dental treatment) and both IOPs were also maintained within normal ranges (Fig. 3B). His halitosis and the redness and swelling of the gingiva improved remarkably (Fig. 2A). Radiographic examination revealed obvious lamina dura in the alveolar bone and loss of periapical radiolucencies (Fig. 2B). The total bacterial number in subgingival plaque of maxillary left central incisor and the number of *P. gingivalis* cells in subgingival plaque of mandibular right first premolar, decreased to normal level after brushing of the teeth for 3 months, and have continued to maintain normal range during and after this period of dental treatment. The serum IgG antibody titer against *P. gingivalis* FDC381 decreased to near normal ranges after brushing of the teeth for 3 months, fluctuated during this period of dental treatment, and has continued to maintain near normal range after dental treatment. The serum IgG antibody titer against *P. gingivalis* SU63 has been maintained over the mean of healthy subjects' +2 standard deviations from baseline to post dental treatment (Fig. 3A and B).

In October 2012, the patient began to receive intravenous administration of 5 mg/kg infliximab. His systemic condition has remained stable with no experience of serious infections, such as odontogenic fever, since the commencement of the infliximab therapy. In addition, the patient has been able to continue his own oral hygiene during this supportive periodontal therapy (SPT). The Behcet's Syndrome Activity Score (BSAS) was rated depending on the patient's own perception of disease activity and evaluated for the patient before and after dental treatment at the medical clinic [8]. Though one to three stomatitises appeared in the patient's mouth before dental treatment, they disappeared after the treatment. The number of skin rashes was constant at 6 or more

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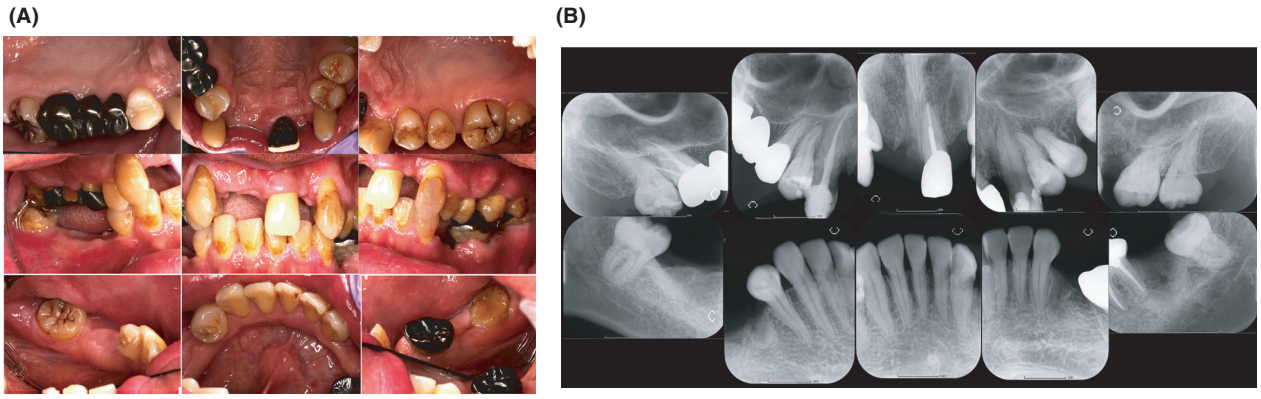

Figure 2. Intraoral view (A) and radiographs (B) before supportive periodontal therapy. (A) The gingival inflammation (redness and swelling) and tooth decay disappeared by removing the infection in the mouth. (B) The disappearance of radiolucencies around teeth at baseline by removing the infection in the mouth suggests the absence of infectious focus.

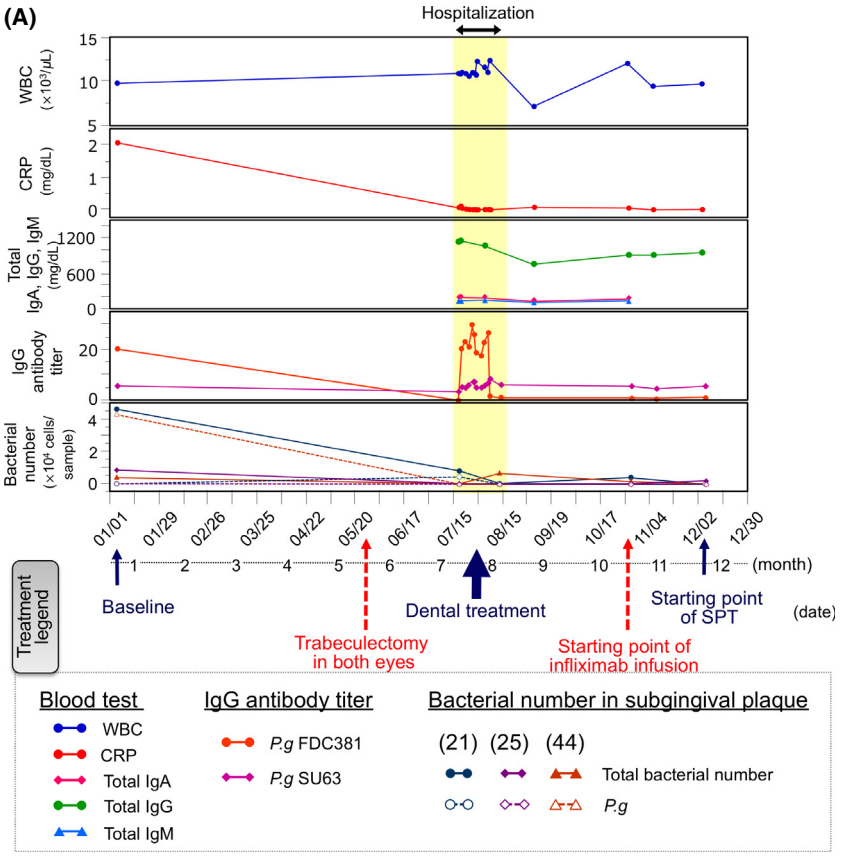

Figure 3. Changes in blood and periodontal bacterial examination results: (A) before and after dental treatment; (B) during dental treatment. SPT, supportive periodontal therapy; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; IgG antibody titer, IgG antibody titer to periodontal bacteria; bacterial number, Bacterial number in subgingival plaque; *P.g*, *Porphyromonas gingivalis*; *B.f*, *Bacteroides forsythus*; 21, left maxillary central incisor; 25, left maxillary second premolar; 44, right mandibular first premolar. CT, cavity treatment; RCT, root canal treatment; SRP, scaling and root planing; PSL, prednisolone, CYA, cyclosporin; Amoxil, amoxicillin; TMP-SMZ, rimethoprim-sulfamethoxazole; AMPH, amphotericin B syrup; Norvasc, amlodipine besilate; INN, benzbromarone; Alfa-D, alfacalcido.

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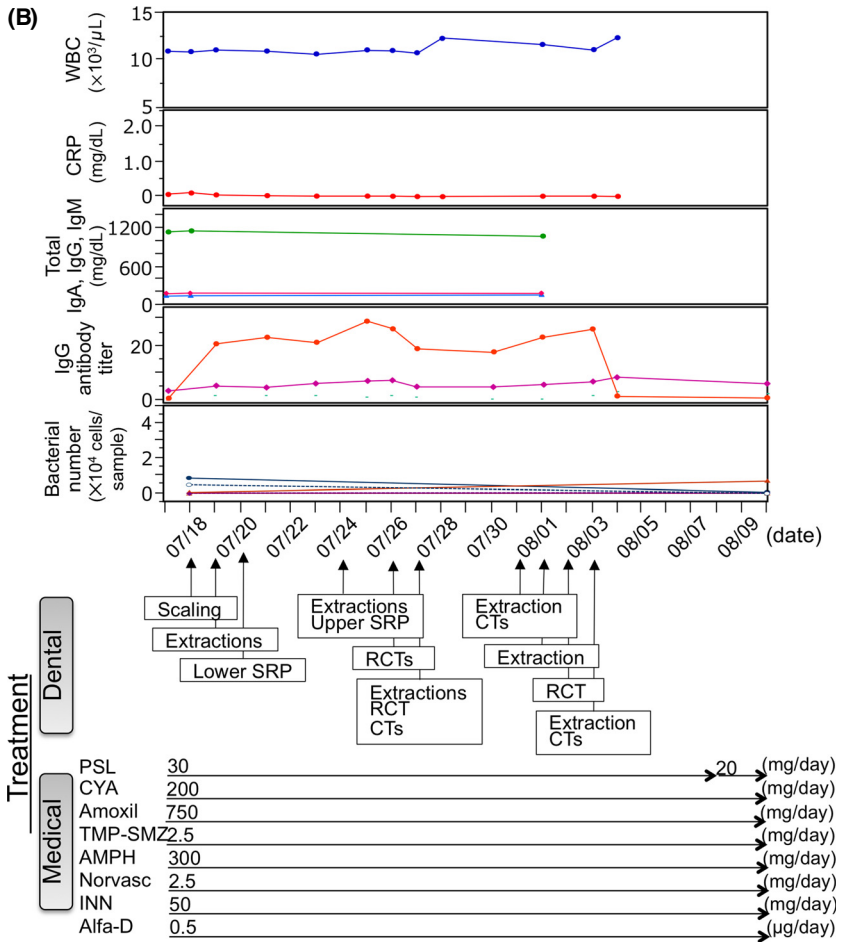

before and after dental treatment. Though the patient's overall perception scales were constant at 0/10 scales until post dental treatment, after starting infliximab therapy they were sustained at 2/10 scales.

Discussion

This is a case of a patient whose oral infection was removed before the subject underwent infliximab therapy under collaborative medical and dental care for Behçet's disease. On several occasions he had experienced acute exacerbations of ocular involvement following dental treatment. This concurs with previous reports of such symptoms of Behçet's disease occurring immediately after dental treatment [2]. It has been reported that the recurrent incidence of Behçet's disease is related to stress factors [9]. It is considered that oral infection and the psychological stress caused by dental treatment might have become the precipitating factor in this Behçet's disease patient.

In Behçet's disease patients, a rise in tumor necrosis factor alpha (TNF-α) production is associated with clinical deterioration [10]. Infliximab is anti-TNF-α monoclonal antibody which works by binding to the TNF-α, and could have a role for inducing remission in Behçet's disease [11]. However, patients undergoing treatment with anti-TNF-α therapy are open to falling subject to opportunistic infection for immunosuppression [12]. Also, a case has been reported in which a rheumatoid arthritis patient with oral infection, who was undergoing immunosuppression using immunosuppressive medications, fell subject to sepsis [13]. Therefore, good oral hygiene is essential in a patient scheduled for infliximab infusion.

However, this patient showed a negative attitude to dental treatment, owing to a fear of it aggravating his primary disease. It was explained repeatedly to the patient by both the medical doctor and the dentist, that there was a danger that infliximab therapy with oral infection might be fatal. In addition, the patient was informed that dental treatment would be performed under hospitalization by medical doctors. Consequently, the patient consented to dental treatment. At first, oral

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hygiene instruction was given to the patient in outpatient care on a monthly basis for 3 months. Accordingly, gingival inflammation and halitosis decreased remarkably with no high fever, joint pain, or ocular inflammation. As the result, the patient's anxiety toward dental treatment reduced and his attitude to it became more positive. The dental treatment, including teeth extraction, could be performed without systematic inflammation by general control using immunosuppressive agents, antibiotics, antifungal agent, antihypertensive agent, and uric acid-lowering agents at the medical clinic.

The patient's periodontal infection level was monitored by utilizing the bacterial number in the subgingival plaque and the serum IgG antibody titer against periodontal pathogen. Both the bacterial number in subgingival plaque of *P. gingivalis* cells and the IgG titer against *P. gingivalis* FDC381 (which were at a high level at baseline.) decreased under periodontal treatment corresponding to an improvement in periodontal condition. It has been reported that periodontal patients with *P. gingivalis* show a higher number of total bacteria compared to those without *P. gingivalis* [14]. Hence, it is shown that the patient had a large amount of bacteria in his mouth at baseline (Fig. 3A). Also, the serum IgG antibody titers against periodontal pathogens indicate infection levels of the pathogens. *P. gingivalis* is considered one of the main pathogens involved in periodontitis [15]. The IgG titer against *P. gingivalis* is associated with periodontal severity and is useful to screen hitherto chronic periodontitis patients [16]. From the above, it is seen that the patient was highly infected with *P. gingivalis* at baseline. The IgG antibody production against *P. gingivalis* FDC381 was abnormally promoted during this period of dental treatment, even under the administration of immunosuppressive agents and antibiotics. The specific phenomenon may indicate that the patient has a high sensitivity of the immune system. On the other hand, the IgG titer against *P. gingivalis* SU63 was maintained over normal range after dental treatment. The IgG titer against *Bacteroides forsythus,* in the IgG titers which were within normal ranges at baseline, was maintained over normal range during and after dental treatment (data not shown). There are reports describing that periodontal status is worse in Behçet's disease patients and is associated with disease severity [1, 17]. The periodic follow-up of the IgG titer against *P. gingivalis* SU63 during SPT is necessary to prevent recurrence of periodontal disease in the patient. Since periodontal disease is also called a "silent disease" with no subjective symptoms, it is difficult for the medical doctor to estimate the presence of oral infection in Behçet's disease patients [18]. Consequently, a blood IgG antibody titer test may be useful for estimating oral infection in Behçet's disease patients.

In this case, according to changes in the BSAS, the stomatitis disappeared under dental treatment. Additionally, infliximab therapy was performed on the patient without side effects. Consequently, the removal of oral infection in a patient with Behçet's disease is a significant factor in Behçet's disease treatment.

In conclusion, it is considered that the early control of oral infection in Behçet's disease patients contributes to the effectiveness of anti-TNF-α therapy and the relief of the primary disease. Additionally, medical and dental collaboration is important for providing Behçet's disease patients the optimal medical care and in supporting the self-management of the patient.

Conflict of Interest

None declared.

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