

8-28-2018

Role of Dentists in the Management of Behcet's Disease: A Case Report

Nurfianti Ahmad Patoni

Oral Medicine Residency Program, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia

Mohaideen AM. Sitheeque

Division of Oral Medicine, Faculty of Dental Sciences, University of Peradeniya, Sri Lanka

Afi Savitri Sarsito

Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia

Anandina Irmagita Soegyanto

Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia

Yuniardini Septorini Wimardhani

Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia

Follow this and additional works at: <https://scholarhub.ui.ac.id/jdi>

Recommended Citation

Patoni, N. A., Sitheeque, M. A., Sarsito, A. S., Soegyanto, A. I., & Wimardhani, Y. S. Role of Dentists in the Management of Behcet's Disease: A Case Report. *J Dent Indones.* 2018;25(2): 125-129

This Case Report is brought to you for free and open access by the Faculty of Dentistry at UI Scholars Hub. It has been accepted for inclusion in Journal of Dentistry Indonesia by an authorized editor of UI Scholars Hub.

CASE REPORT

Role of Dentists in the Management of Behcet's Disease: A Case Report

Nurfianti Ahmad Patoni¹, Mohaideen AM. Sitheeque², Afi Savitri Sarsito³, Anandina Irmagita Soegyanto³, Yuniardini Septorini Wimardhani³

¹*Oral Medicine Residency Program, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia*

²*Division of Oral Medicine, Faculty of Dental Sciences, University of Peradeniya, Sri Lanka*

³*Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia*
Corresponding e-mail to: yuniardini@ui.ac.id

ABSTRACT

Behcet's disease (BD) is a multi-system recurrent inflammatory disorder occurring in the form of vasculitis of an unknown etiology. It most frequently affects oral and genital mucosa, skin, eyes, joints, and blood vessels. The definitive diagnosis of BD is based on major symptoms such as recurrent oral and genital ulcers and recurrent skin and ocular lesions, accompanied by symptoms related to various systems. However, early BD manifestations are very similar to recurrent aphthous stomatitis (RAS). Several years from its first appearance are often required for a definitive diagnosis. **Objective:** To describe a dentist's role in BD management in a patient with a history of highly recurrent RAS. **Case Report:** We evaluated a 38-year-old man with a 10-year history of recurrent oral ulcers, accompanied by skin and eyes lesions. His intraoral examination revealed multi-sized ulcers with a yellowish-white base and regular edges, surrounded by an erythematous halo. Ulcers were located on the tongue, floor of the mouth, and gingival mucosa. Although BD diagnosis was not histopathologically confirmed, the patient's lesions met the International Criteria for Behcet's disease with a score of 5. Oral ulcers were managed with chlorhexidine mouthwash 2 times/day and supportive measures. A multidisciplinary approach was used for this patient to provide comprehensive treatment. **Conclusion:** Dentists can be the first clinicians to detect the possible development of BD in patients with symptoms similar to RAS, but additionally having skin and eye lesions.

Key words: Behcet's disease, oral ulceration, recurrent aphthous stomatitis

How to cite the article: Nurfianti Ahmad Patoni, Mohaideen AM Sitheeque, Afi Savitri Sarsito, Anandina Irmagita Soegyanto, Yuniardini Septorini Wimardhani. Role of dentists in the management of Behcet's disease: a case report. *J Dent Indones.* 2018;25(2):125-9.

INTRODUCTION

Behcet's disease (BD) is a multi-system recurrent inflammatory disorder characterized by the development of vasculitis of an unknown etiology.¹⁻³ BD affects almost all systems, including the vascular, central nervous, gastrointestinal, pulmonary, and urologic systems and the joints. The disease is characterized by four major symptoms: oral aphthous ulcers, genital ulcers, skin lesions, and ocular lesions. Additionally, one or more minor symptoms can be observed, including arthritis, gastrointestinal ulceration, epididymitis, vascular lesions, and symptoms involving the central nervous system.³⁻⁵

In 1937, Hûlusi Behcet, a Turkish dermatologist, was the first to comprehensively describe a triad of symptoms including recurrent oral ulcers, genital

ulcers, and uveitis, which were subsequently labeled as Behcet's syndrome.^{3,4} BD prevalence is related to an ancient trade route known as the "Silk Road." BD occurs worldwide with marked regional differences. Its highest incidence has been observed in the Mediterranean regions, Middle East, and Far East (Table 1).^{3,6-8}

The age at onset ranges between 20 and 40. BD more frequently and severely affects males. The male-to-female ratio differs among countries. Specifically, females are more commonly affected in Japan and Korea, whereas males are more commonly affected in the Middle East region. Severe manifestations such as uveitis and neurological and vascular involvement are predominantly observed in males.^{2,7,8} Behcet's disease is a recurrent multisystem vasculitis that can affect any organ or system, but was originally described as orogenital ulcerations and uveitis. Specific criteria have been proposed for diagnosis and identification

Table 1. Worldwide Prevalence of Behcet's Disease

Country	Prevalence Per 100,000
Turkey	20–421
Saudi Arabia	19.5
Iraq	17
Iran	16.7–80
Japan	14.6
Egypt	7.6
Hong Kong	2.6
Taiwan	1
The United States	0.33
European countries	0.27–7.5

of affected organs by different national authorities. Behcet's disease is proposed to be due to an antigen/antibody reaction. The antigen can be external (microbial or other

Recurrent aphthous stomatitis (RAS) is a disorder characterized by recurrent ulcers confined to the oral mucosa in patients otherwise asymptomatic.⁹ Because recurring oral ulcers are found in BD and RAS, the latter is considered during BD's differential diagnosis. Histopathological examination is necessary for a clinical distinction.^{4,5,10} RAS is the most frequent chronic disease of the oral cavity, affecting 5%–25% of the population. It more frequently affects females and individuals of higher socioeconomic levels.¹¹ The age at onset ranges between 10 and 40 years. BD's definitive diagnosis relies on the presence of major symptoms, occasionally accompanied by minor symptoms.^{4,5,11}

We report the case of patient with a 10-year history of RAS who then developed skin lesions and eyes symptoms, changing the diagnosis to BD.

CASE REPORT

A 38-year-old male was referred from the Internal Medicine Department for an oral biopsy to identify vasculitis for potential BD diagnosis. He had a 10-year history of RAS (feverless) and later developed skin and eye lesions. These ulcers were painful and self-healed in 3–4 weeks. Ulcer-free intervals lasted about 2 weeks. As per a dentist's prescription, the patient took triamcinolon acetonide and nystatin oral suspension. In the previous 2 years, the patient suffered from pullulent and painful vesicles of both the thighs. No genital ulcers were reported, whereas itchiness and soreness were present.

A recent complaint of red eyes and blurred vision was diagnosed as uveitis. As a differential diagnosis, an internist requested screening for human immunodeficiency virus (HIV), venereal disease research laboratory (VDRL), Treponema pallidum hemagglutination assay (TPHA), toxoplasma, rubella, cytomegalovirus,

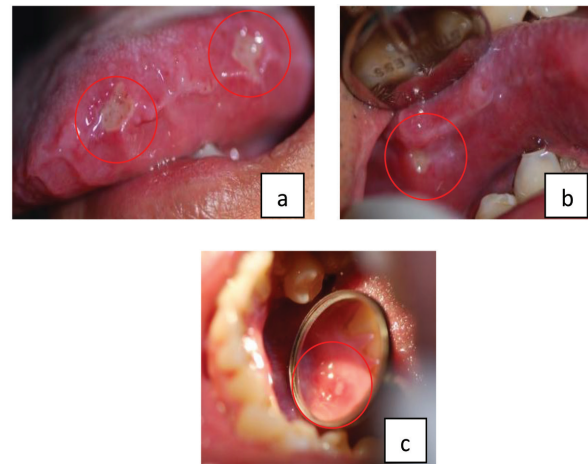


Figure 1. Regular ulcer on the left lateral of tongue region 34 and 37 (a), on the right lateral of tongue region 47(b), on the border gingival lingual and floor of the mouth region 32 (c).

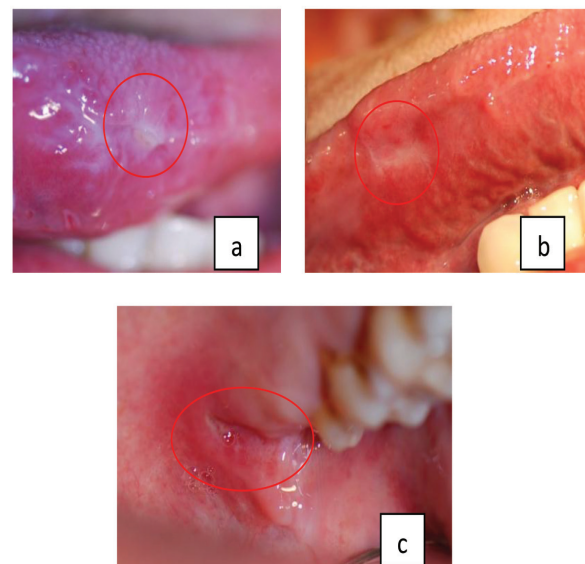


Figure 2. Second visit 2 weeks later, healing of ulcer on the right lateral of tongue (a), on the left lateral of a

and herpes simplex virus (TORCH), and anti-nuclear antibody (ANA). Blood tests showed a low count of leukocytes, basophils, lymphocytes, and neutrophils, with a high erythrocyte sedimentation rate. HIV, VDRL, and TPHA screenings were non-reactive. TORCH examination revealed reactive anti-toxoplasma IgG, anti-cytomegalovirus IgG, and anti-HSV II IgG. ANA examination results were positive, with speckled pattern and a titer of 1/100. A pathergy test was negative, and mycological examination showed absence of fungal infections.

An intraoral examination revealed fair oral hygiene; subgingival and supragingival calculus; and ulcers 2–5 mm in diameter, surrounded by an erythematous halo and yellowish-white base, located at the border between

Table 2. International Study Group criteria for the Diagnosis of Behcet's Disease

Recurrent oral ulceration	Minor/major aphthous or herpetiform ulcer that recurred at least 3 times in a 12-month period observed by the physician or patient
Plus two of the following:	
Recurrent genital ulceration	Aphthous ulcer or scarring observed by the physician or patient
Eye lesions	Anterior/posterior uveitis, cells in the vitreous on slit-lamp examination or retinal vasculitis observed by an ophthalmologist
Cutaneous lesions	Erythema nodosum observed by physician or patient, pseudofolliculitis or papulopustular lesions, or acneiform nodules observed by physician in postadolescent patients not receiving corticosteroids
Positive pathergy test	Interpreted by the physician at 24–48 h

the gingival and floor of the mouth in the region 32 and in the lateral tongue in the regions 47, 37, and 34 (Figure 1). History and clinical examination provided a working diagnosis of oral manifestations of BD and chronic gingivitis. A biopsy of an ulcer on the left lateral tongue was performed. Oral ulcers were treated with mouthwash containing 0.2% chlorhexidine 2 times/day.

The biopsy revealed chronic ulcers, without any evidence of malignancy and vasculitis, thus not confirming BD's diagnosis. Oral examination revealed healing ulcers, with traumatic laceration on the left palate in the region 28 following oral treatment during biopsy (Figure 2). The medications included prednisolone, azathioprine, omeprazole, folic acid, and prednisolone eye drops (for 1 week). The oral diagnosis was based on BD's oral manifestations, traumatic ulcers, and chronic gingivitis. Oral ulcers were treated using moistened gauze compresses with 0.2% chlorhexidine 3 times/day and supportive multivitamins containing vitamin B complex, vitamin C, vitamin E, folic acid and zinc, once a day.

DISCUSSION

BD manifestations are variable, depending on ethnic, geographic, and individual differences. Manifestations range from mucocutaneous and eye symptoms to systemic involvement with serious complications. The criteria for BD diagnosis were outlined by the International Study Group in 1990 (Table 2).^{4,8,12}

However, application of these criteria in daily practice is very difficult. Moreover, because organs are not involved, it is less sensitive. Meanwhile, several studies

Table 3. Criteria for The Diagnosis of Behcet's Disease.

Sign/symptom	Points
Ocular lesions	2
Genital aphthosis	2
Oral aphthosis	2
Skin lesions	1
Neurological manifestations	1
Vascular manifestations	1
Positive pathergy test	1

International Criteria for Behcet's Disease: scoring ≥ 4 indicates Behcet's disease

have reported that use of a positive pathergy test has decreased since the mid-1980s. The International Team for the Revision of the International Criteria for Behcet's Disease (ICBD) has recently proposed a new set of criteria, including neurological, vascular, mucocutaneous, and ocular manifestations, where a pathergy test is included, but not in the primary scoring criteria. A 2014 draft revision also included minor symptoms (i.e., neurological and vascular manifestations), whereas the pathergy test and HLA-B51 were considered as supportive examinations (Table 3).^{8,13}

BD pathogenesis showed a prominent role of T lymphocytes, hyperactive neutrophils, and elevated levels of pro-inflammatory cytokines IL-8, IL-17, and TNF- α . These factors stimulate adhesion of molecules on vascular endothelial cells including CD54 (intercellular adhesion molecule-1 [ICAM-1]), vascular adhesion molecule 1 (VCAM-1), and E-selectin by human dermal microvascular endothelial cells. Neutrophil infiltration in the perivascular causes vasculitis.^{9,14} HSV infection was suggested as a possible etiologic or triggering factor in BD. In a study by Lee et al., HSV type 1 was detected using PCR in the saliva, intestinal ulcers, and genital ulcers of BD patients (absent in healthy controls), and HSV induced the production of various cell adhesion molecules.¹⁵

A Japanese study on 412 patients showed that oral aphthae were the most frequent initial symptom, appearing in average 7.2 ± 10.2 years before BD diagnosis. Genital ulcers and skin and eye lesions appeared as the initial symptoms in approximately 25% patients. Conversely, gastrointestinal, neurological, and vascular complications developed post-diagnosis.⁸ Oral aphthous as initial BD symptoms was found in 96.4% of patients in Iran, 98.2% in Japan, 100% in Turkey, 97.5% in Korea, 100% in Morocco, and 100% in UK. Oral ulcers are usually located on the tongue (79.6%), lips (79.1%), buccal cavity (73.7%), gingiva (59.5%), and, occasionally, tonsils (29.5%), palate (27.5%), pharynx (25.3%), larynx, and esophagus. Interval between recurrences varies from several days to several months.^{14,16}

Table 4. Classification of Recurrent Aphthous Stomatitis (Roy S. Rogers)

Simple Aphthosis	Complex Aphthosis
Common	Uncommon
Episodic	Episodic or continuous
Short-lived lesion	Persistent
Few lesions	Few to many lesions
3–6 episodes/year	Frequent or continuous ulceration
Prompt healing	Slow healing
Minimal pain	Marked pain
Limited to oral cavity	May have genital lesions

Recurrent oral ulcers in BD are critical for diagnosis; however a distinction from RAS is difficult. Roy S. Rogers classified oral aphthous into simple and complex aphthosis (Table 4). BD patients usually have complex aphthosis. Simple aphthosis is the most common with episodic and short-lived lesions, typically occurring in younger individuals (20%–50%). Complex aphthosis is rare, persistent, and associated with chronic systemic diseases.¹⁷ Major ulcers (diameter >10 mm) are linked to the highest risk of BD, whereas minor ulcers (diameter <10 mm) to the lowest risk. Compared with RAS patients, BD patients develop oral ulcers at ≥ 2 locations. RAS patients with complex aphthosis require monitoring using BD clinical criteria due to the possibility of developing BD. The mortality and morbidity rates in BD are based on the involvement of the gastrointestinal tract and vascular or central nervous systems. Such conditions may cause life-threatening complications including bowel perforation, arterial occlusion, and outbreak aneurisma.^{3,4}

In this report, oral ulcers were characterized by similar features among each other. Specifically, they were minor aphthous, with a yellowish-white base and surrounded by an erythematous halo and well-circumscribed and round ulcers. These ulcers self-healed and spread to different sites of the oral cavity. Tursen found that histopathological examination of oral ulcers in BD showed nonspecific pathological findings, with lymphocytic vasculitis identified in severe ulcerations.¹⁸ In the present study, BD diagnosis was not confirmed by histopathological examination possibly due to the ulcers' healing process. However, the patient's lesions (oral, eye, and skin lesions) met the ICBD guidelines with a score of 5.

Till date, there is no specific diagnostic laboratory test or histopathological finding for BD. A definitive diagnosis relies on clinical features that requires several years. Patients with exclusively recurrent oral ulcers may not obtain a definitive diagnosis for BD; therefore, these patients require in-depth examination and accurate follow-up, particularly in countries with a high BD prevalence.¹⁶

CONCLUSION

Dentists' role is important in establishing BD diagnosis; they could be the first to detect the disease. Recurrent oral ulcers are a common initial symptom of BD, accompanied by skin and eye lesions. A multidisciplinary approach is required to diagnose and treat the disease.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the publication of this case report.

ACKNOWLEDGMENTS

We thank the Departments of Ophthalmology, Dermato-Venereology, Internal Medicine, Oral Surgery, and Pathology of The Cipto Mangunkusumo Hospital, Jakarta. We Specially thank Dr. Harum Sasanti for the support during the patient treatment.

REFERENCES

- Shang H, Ye JJ, Ji M, Wang FF, Zhu YY, Qi XM. Anticoagulant and fibrinolytic disorders in patients with Behcet's disease and recurrent aphthous ulcer. *Chin J Physiol.* 2011;54(4):235–40.
- Klissurski M, Milanov I, Stamenova P, Troyanova P, Vassileva E. Mesencephalic form of meningoencephalitis in a patient with HLA-B51 Behcet's disease : case report. *Acta Clin Croat.* 2011;50(2):435–41.
- Cho SB, Cho S, Bang D. New insights in the clinical understanding of Behcet's disease. *Yonsei Med J.* 2012;53(1):35–42.
- Kokturk A. Clinical and pathological manifestations with differential diagnosis in Behcet's disease. *Patholog Res Int.* 2012;2012:1–9.
- Arulrajamurgan PS, Rajendran CP, Ravichandra R, Parthiban M, Rajeswari S, Rukmangatharajan S. Clinical profile of patients with Behcet's disease. *J Indian Rheumatol Assoc.* 2005;13:135–7.
- Hatemi G, Yazici H. Behcet's syndrome and micro-organisms. *Best Pract Res Clin Rheumatol.* 2011;25(3):389–406.
- Al-Mutawa SA, Hegab SM. Behcet's disease. *Clin Exp Med.* 2004;4(3):103–31.
- Ishigatsubo Y, Genetics F. Behcet's Disease. Ishigatsubo Y, editor. Tokyo: Springer Japan; 2015. 1–15 p.
- Woo SB, Greenberg MS. *Burket's Oral Medicine.* 12th ed. Glick M, editor. Connecticut: People's Medical Publishing House, USA; 2015. 173–182 p.

10. Rhee S, Kim Y, Lee E. Comparison of Behcet' s disease and recurrent aphthous ulcer according to characteristics of gastrointestinal symptoms. *J Korean Med Sci.* 2005;20:971–6.
11. Belenguer-Guallar I, Jiménez-Soriano Y, Claramunt-Lozano A. Treatment of recurrent aphthous stomatitis. A literature review. *J Clin Exp Dent.* 2014;6(2):e168–74.
12. Butendieck R. Behcet's disease in the United States. *Duval Cty Med Soc.* 2014;65(2):27–37.
13. Davatchi F. Diagnosis/classification criteria for Behcet's disease. *Patholog Res Int.* 2012;2012:1–5.
14. Lee S., Bang D., Lee E. SS. Behcet's Disease. 1st Editio. Berlin: Springer; 2001. 11–25 p.
15. Kim D, Cho S, Choi M. Immunopathogenic role of herpes simplex virus in Behcet's disease. *Genet Res Int.* 2013;2013:1–6.
16. Zierhut M. OS. Immunology of Behcet's Disease. 1st Edition. Netherlands: Swets and Zeitlinger; 2003. 21–36.
17. Zouboulis C. Adamantiades-Behcet's Disease. New York: Kluwer Academic Publishers; 2004. 311–322.
18. Tursen U. Behcet' s Syndrome From Pathogenesis to Treatment. L E, editor. Milan: Springer; 2014. 68–69.

(Received May 5, 2018, Accepted August 1, 2018)