



General Manifestations of Behçet's Syndrome and the Success of CO₂-Laser as Treatment for Oral Lesions: A Review of the Literature and Case Presentation

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Abstract

This article reviews the oral manifestations of Behçet's Syndrome that have been discussed in the literature and presents the success of the use of CO₂-laser for recurrent aphthous stomatitis (RAS). Behçet's Syndrome is a multisystem inflammatory disease that has the capacity to affect nearly every human system. It is characterized by a wide range of clinical features. In particular, the defining symptom in most cases is recurrent aphthous stomatitis present in the oral cavity. RAS is the most common inflammatory ulcerative condition to affect the oral cavity and is characterized by localized, painful ulcers that may be a manifestation of more complicated diseases, such as Behçet's Syndrome. There is no effective treatment for RAS. In most cases, RAS is managed by anesthetic topical treatments, topical or systemic steroids, or antibiotics. More recently, though, there has been evidence of possible benefit from treatment of aphthous lesions with CO₂-lasers. Our experience treating a patient who suffered from Behçet's Syndrome and RAS showed transient pain relief with the use of CO₂ ablative laser as a monotherapy.

RAS lesions are localized, painful, shallow ulcers that afflict the soft mucosa of the oral cavity.¹ According to the literature, anywhere from 5 to 25 percent of the population is affected by RAS ulcerations.² The precise etiology and pathophysiology of RAS are unknown. However, many predisposing circumstances are known, such as genetic factors, immunological problems, hypersensitivity to food and drugs, hormonal changes, trauma, and environmental and psychological stresses.² Recurrent aphthous lesions may also be the manifestation of more complicated diseases such as Behçet's Syndrome. While the most common clinical feature of Behçet's Syndrome is RAS in the oral cavity, the clinical manifestations may extend to the skin, genital area, and eyes; in severe cases, Behçet's Syndrome may also include vascular and neurological involvement (see Table 1).

There is no cure for RAS, so the majority of treatments focus on relief of localized symptoms. Remedies for aphthous ulcerations include topical corticosteroids, mouthrinses, antibiotics, or local anesthetic gels.² More recently, CO₂-lasers have been used to treat the localized symptoms of RAS. Zand et al. proved in a randomized control study of 15 patients where all of the patients treated with a nonablative, nonthermal CO₂-laser reported a significantly lower level of pain in comparison to placebo ulcerations and following treatment, and 100 percent of patients required no postoperative medication.² A similar study completed by Colvard and Kuo used an ablative CO₂-laser requiring anesthesia and was able to eradicate pain in 88.8 percent of the cases.³ Much of the literature indicates that CO₂-laser treatment could be considered as an alternative relief for RAS.

In this article, we will review the existing literature and present a case in which CO₂-laser ablation was used to treat aphthous ulcerations on a patient diagnosed with Behçet's Syn-



Figure 1. Ulcerative lesions on the right floor of the mouth.



Figure 2. Ulcerative lesions on the right lateral pharyngeal wall.

drome. Furthermore, clinical and laboratory diagnosis of Behçet's Syndrome will be presented, and the more common manifestations of the disease will be discussed.

Case Report

A 53-year-old male patient presented to the department of oral and maxillofacial surgery at Tufts University School of Dental Medicine. The patient's oral condition had been consistently problematic since 1981. His clinical symptoms included persistent oral and oropharyngeal ulcerations (major apthae), which impeded daily functions, including swallowing, drinking fluids, eating, talking, and sleeping. He also suffered from ocular and genital lesions, which were clinically consistent with Behçet's Syndrome.

The patient had a medical history of hypercholesterolemia and depression. The patient also suffered from dilated cardiomyopathy due to the involvement of the myocardium by the disease; severe pain in the legs and feet as a result of joint lesions; burning sensation in the eyes due to ocular lesions; and increased peripheral neuropathy and tinnitus consistent with Behçet's Syndrome. The patient had a 35-year history of recurrent major aphthous stomatitis with high frequency, severity, and duration. Many unsuccessful treatments had been attempted, including administration of steroids and thalidomide. The only marginally successful treatment for the lesions has been a high dosage of corticosteroids, which have had significant side effects.

The patient was referred to our service for laser ablation of prodromal lesions. On clinical examination, four regions were dominated by ulcerative lesions: the right floor of the mouth (see Figure 1), the right lateral pharyngeal wall (see Figure 2), the right lateral tongue, and the alveolar mucosa buccal to tooth #6 (see Figure 3). The significant pain and discomfort of the patient, in combination with the failure of the current treatments, led to the decision to use the CO₂-laser as a treatment for the RAS.

The patient was treated in the outpatient setting under local anesthesia (see Figure 4). All appropriate laser safety measures were observed. The involved areas were infiltrated with a minimal amount of lidocaine 2% with 1:100,000 epinephrine. A CO₂-laser set at low-power

Table 1. Manifestations of Behçet's Syndrome

Article	Authors	Journal	Manifestations Presented in Article
Adamantiades-Behçet Disease: An Enigmatic Process with Oral Manifestations ⁴	Eguia A, et al.	Med Oral Patol Oral Cir Bucal	Recurrent oral ulcers, genital lesions, ocular lesions, joint lesions, neurological lesions, vascular lesions, gastrointestinal lesions, and other complications (cardiac, renal, pulmonary, and pleurae)
Recurrent Aphthous Stomatitis in the Diagnosis of Behçet's Disease ¹	Rogers RS 3rd	Yonsei Med J	Oral recurrent aphthous stomatitis, genital ulcers, and ocular inflammation
Diagnostic Criteria of Behçet's Disease: Problems and Suggestions ⁶	Lee S	Yonsei Med J	Oral, ocular, and genital lesions, arthritis, gastrointestinal lesions, epididymitis, vascular lesions, and central nervous system symptoms
Behçet's Disease ⁵	Kontogiannis V, Powell R	Postgrad Med J	Oral ulcers, genital ulcers, skin lesions, arthritis, fatigue, widespread vasculitis, arterial aneurysms, and neurological, gastrointestinal, brain, and audiovestibular symptoms



Figure 3. Lesions on the alveolar mucosa.



Figure 4. CO₂-laser set at low-power (2W) superpulse mode with a 0.4 mm ceramic tip was used to lightly char the surface.



Figure 5. Ulcerative lesions immediately following CO₂-laser ablation.



Figure 6. Lesions at one-week follow-up, at which time the patient reported considerable relief of symptoms.

(2W) superpulse mode with a 0.4 mm ceramic tip was used, after calibration, in a defocused way to lightly char the surface of the ulcers (see Figures 4 and 5). The patient tolerated the procedure well. On subsequent follow-up, one week after the procedure, the patient reported considerable relief of symptoms on most of the treated ulcers (see Figure 6). The oropharyngeal ulcer displayed only moderate response, but the patient reported an overall improvement of his quality of life. On long-term observation, two months after the procedure, most ulcers had disappeared and the oropharyngeal area, although clinically improved, remained mildly symptomatic. Six months after his original treatment, the patient developed more intraoral aphthous ulcers.

Overall, the CO₂-laser helped to decrease the sensitivity and control the pain for a short period of time. No healing of the ulcerative lesions was appreciated. In our experience, CO₂ ablative lasers can be used for pain control in Behçet's Syndrome patients with some transient benefits.

Discussion

Behçet's Syndrome is a multisystem inflammatory reaction that has the capacity to affect any human organ or system. The disease is characterized by recurrent cycles of remission and relapse, as well as a wide range of clinical features. At one time, the Pathergy Test was used as a diagnostic tool for the disease; however, in many cases it can give a false negative result.^{4,5} To date, there is no conclusive diagnostic test for Behçet's Syndrome, so diagnosis relies solely on the wide range of clinical features. Oral and genital aphthous ulcerations are the most common manifestation of Behçet's Syndrome. However, alone they are not evidence enough for diagnosis of Behçet's Syndrome.

According to Eguia et al., the International Study Group for Behçet's Syndrome established a classification in 1990 that would provide evidence for the disease based on at least three episodes of oral ulcers within a 12-month period and the presence of at least two of the following manifestations: repeated geni-

tal ulcers, ocular lesions, cutaneous lesions, or a positive pathergy test.⁴ Despite the fact that numerous other classification schemes have been developed over the years, no consistent model exists today.^{4,6} Therefore, it is essential to develop a comprehensive clinical history of the patient in order to establish differential diagnosis along with the potential diagnosis of Behçet's Syndrome.

According to Kondogiannis and Powell, oral ulcers are the defining feature in 97 to 100 percent of the cases and the initial symptom in most cases.⁵ Clinically, the oral lesions of Behçet's Syndrome are indistinguishable from RAS.⁴ Therefore, the clinician must be cognizant of defining characteristics of associated RAS systemic disorders.¹ The oral ulcers found in Behçet's Syndrome are typically limited to the nonmasticatory oral mucosa.¹ Eguia et al. classified the oral ulcers of Behçet's Syndrome into three main categories: minor ulcers (less than 1 cm), major ulcers (larger than 1 cm), and herpetiform (1–3 mm).⁴ In many cases, oral ulcers may appear one to three years before any other symptoms.

Less common manifestations of Behçet's Syndrome include genital, cutaneous, ocular, joint, neurological, and vascular lesions. According to Eguia et al., genital lesions occur in 60 to 80 percent of patients, cutaneous lesions occur in 80 percent, ocular lesions occur in 20 to 50 percent, joint lesions occur in 40 to 50 percent, and neurological lesions occur in 5 to 20 percent.⁴ Genital lesions are extremely painful and can result in difficulty with walking. Ocular lesions may result in conjunctivitis, vasculitis, or retina atrophy or loosening. According to Kondogiannis and Powell, ocular involvement can result in vision loss for 25 percent of patients who experience ocular manifestations.⁵

In general, Behçet's Syndrome is characterized by a widespread vasculitis, which can result in a tendency toward thrombosis in many patients. While neurological involvement is less common, it can result in brain and spinal cord damage or emotional and sensory changes.^{4,5} Arterial aneurysms can result from vasculitis and can be potentially lethal. Gastrointestinal lesions are rare and may result in a variety of symptoms, including abdominal pain, dysphagia, and diarrhea.

Table 2. Previous CO₂-laser Studies Completed

Article	Authors	Journal	Study Completed	Number of Patients	Success Rate
Relieving Pain in Minor Aphthous Stomatitis by a Single Session of Non-thermal Carbon Dioxide Laser Irradiation ²	Zand N, et al.	Lasers Med Sci	Single-session non-thermal CO ₂ -laser on relieving pain in minor recurrent ulcers	15	100%
Managing Aphthous Ulcers: Laser Treatment Applied ³	Colvard M, Kuo P	JADA	Ablative CO ₂ -laser on relieving pain in recurrent ulcers	18	88.8%
CO ₂ -laser Treatment of Ulcerative Lesions ⁷	Sharon-Buller A, et al.	Oral Surg Oral Med Oral Path Oral Radiol Endod	CO ₂ -laser therapy for relieving pain in large lesions in the oral cavity	2	100%

The distinct difference between the ulcers of RAS and Behçet's Syndrome remains unclear. RAS is the most common inflammatory ulcerative condition of the oral mucosa.¹ RAS lesions are typically shallow, painless, round-to-oval ulcers.¹ Rogers states that the presence of RAS lesions is critical in the diagnosis of Behçet's Syndrome.¹ However, Eguia et al. indicate the disparity between RAS and Behçet's Syndrome ulcers, explaining that Behçet's Syndrome ulcers tend to appear in unusual places and in higher numbers.⁴ Nevertheless, both forms of ulcers appear to be aphthous in nature and are managed with similar techniques.

In the past, oral aphthous lesions have been treated with anesthetic pastes and mouthwashes, topical or systemic steroids, and antibiotics.⁷ Topical and systemic treatments help to reduce the symptoms and duration of the ulcers, but are not effective in preventing recurrences.⁴ Immunosuppressive drugs, such as thalidomide, are effective in decreasing the number of lesions and the length and severity of ulcers, as well as in increasing the latency period.⁴ However, these drugs can have severe side effects.

Most of these remedies only help to provide temporary pain relief to localized symptoms and do not help to prevent future occurrences. Recently, CO₂-lasers have been considered in order to relieve the symptoms of aphthous lesions. Studies have proven that CO₂-laser therapy has been effective in relieving pain from aphthous lesions.^{2,3,7} The precise mechanism

by which CO₂-lasers are able to effectively reduce pain is unknown. However, Zand et al. provide some of the explanations: the blockage of action potential and conduction of nociceptive signals in afferent neurons; a decrease in the release of chemical mediators; and an increase in the amount of natural analgesics.¹

Conclusion

In the three studies considered, the reduction in pain was significantly greater immediately following laser treatment of aphthous lesions (see Table 2). However, the studies did not indicate whether the decrease in pain was long lasting. In a randomized, controlled study of 15 patients, Zand et al. proved a significant decrease in pain among the treated lesions in comparison to the placebo lesions; however, pain measurements were only taken up to 96 hours after treatment.² In a separate study by Colvard and Kuo, pain measurements were only taken immediately after resolution of anesthesia; however, it was reported that all lesions had healed within 7 to 10 days.³

All three studies indicate evidence that lesions are less likely to occur at the treated site.^{2,3,7} In addition, the studies excluded patients who had any systemic disease, including Behçet's Syndrome, that may have predisposed them to RAS. Although there is significant evidence that recurrent aphthous ulcerations respond positively to CO₂-laser treatment, more research must be completed in regard to aphthous lesions in Behçet's Syn-

drome before any recommendation can be made for the use of CO₂-lasers on Behçet's Syndrome ulcerations. Our experience follows existing literature (see Table 1) and shows that CO₂-lasers can offer a transient relief of symptoms when used as monotherapy for treatment of RAS. ■

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