Case Report: Treatment of Major Aphthous Lesions of Behçet's Disease with Immunomodulatory Effects of Low-Dose Antibiotic Treatment

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ABSTRACT

Aim Behçet's disease (BD) is a multisystemic inflammatory disease. The most common symptoms are recurrent major aphthous lesions in mouth. It is the initial symptom in most (about 80%) of the cases. It is very crucial to treat oral symptoms in order to minimize oral discomfort caused by inflammatory lesions in BD patients. The aim of this case report is to ameliorate the oral symptoms of BD by using the immunomodulatory effects of antibiotics.
Case Report We present treatment of BD's oral symptoms by using the immunomodulatory effects of antibiotics. A 30-year-old patient presented to our clinic with 2 major aphthae and discomfort in eating. The patient was treated with low-dose azithromycin for 3 weeks.
Discussion The low-dose antibiotic therapy is a proven treatment modality for relieving oral symptoms of BD. Low-dose azithromycin was successful in relieving the oral symptoms of BD within 3 weeks. In the treatment of advanced aphthous lesions, the completion of the healing in 3 weeks of treatment and the absence of recurrence of aphthous lesions in 2 months proves the success of the treatment.
Conclusion One week after starting the treatment, improvement was observed in the lesions. After 3 weeks of treatment, the aphthous lesions were completely healed. It was observed that oral symptoms did not return at the end of the 2-month treatment follow-up. Although azithromycin is used in the treatment of aphthous lesions caused by BD, more research is needed in this area.

Keywords Antibiotic, Azithromycin, Behçet's disease, Low-dose antibiotic treatment, Surgery

Introduction

In 1937, a Turkish dermatologist by the name of Hulusi Behcet formally described two patients with the 'triple symptom complex' of recurrent oral ulcerations, genital ulcers and hypopyon (1). It is a multisystemic inflammatory disease. The most common symptoms are recurrent major aphthous lesions in mouth. It is the initial symptom in most (about 80%) of the cases (2). Behçet's disease (BD) is more prevalent in the World in the region of so-called "Silk Road", including Turkey, Iran, Korea, China, Saudi Arabia, and Japan (3) and more common among men aged 20 to 40 years (3). The disease is characterized by a chronic course of relapses that include oral aphthous ulcers, genital ulcers, arthritis, cutaneous, gastrointestinal, and neurologic lesions (4). The most common symptoms of BD are genital and oral ulcers, which are usually the initial manifestations (5).

The management of a patient with BD is complex and oftentimes requires a multidisciplinary approach. While the care of any patient should be individualized, implementation of, and adherence to general guidelines should be considered (6). As the clinical expression of BD is quite heterogeneous, pharmacological therapy is variable and depends largely on the severity of the disease and organ involvement (6). Targets of BD treatment are remission of the active disease, suppression of exacerbations and permanent disabilities in mucous membranes, skin, eye and joints, and enhancement of life quality (7). Oral corticosteroids, immunosuppressive drugs, colchicine, dapsone, azathiyoprin, cyclosporine, apremilast and thalidomide are the drugs that clinicians use to eradicate oral symptoms. However, these drugs have adverse effects and a safer option is required (8-9).

Azithromycin is a type of medicine that fights against bacterial infections. It belongs to a group of medicines called macrolide antibiotics. These medicines have a special ring structure that can attach to the bacteria's ribosomes and stop them from multiplying. Macrolides are made from natural substances and were discovered a long time ago. Erythromycin was the first one found and it was used when people couldn't take penicillin. Azithromycin is a newer medicine that was designed to work better and have fewer side-effects. It can fight against many kinds of bacteria (10).

Azithromycin is a macrolide antibiotic that demonstrates bacteriostatic activity against many gram-positive and gram-negative bacteria as well as atypical agents. It reduces bacterial virulence by inhibition of biofilm formation, bacterial protein synthesis and release of pathogen-associated molecular patterns from bacteria, and also by enhancement of phagocytosis and intracellular killing of bacteria by monocytes (8). Additionally, azithromycin possesses immunomodulatory properties through inhibition of several pro-inflammatory cytokines and chemokines, attenuating the migration of effector cells to the airways (11). Macrolides, including azithromycin, have been shown to inhibit Akt phosphorylation, indicating their ability to modulate cortico-

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steroid resistance mechanisms (12).

Case Report

A 30-year-old female patient diagnosed with BD applied to the Department of Oral, Dental and Maxillofacial Surgery of Istanbul University Faculty of Dentistry with complaints of pain caused by major aphthae in her mouth and discomfort in eating. In the clinical examination, one major aphthae was detected on the right side of the lower lip near the commissure (Figure 1) and on the left tip of the tongue (Figure 2). For the treatment of major aphthae using the proven immunomodulatory effect of azithromycin, the patient was prescribed 500mg azithromycin once daily on Mondays, Wednesdays and Saturdays of the week. The patient was called for follow-ups at the end of the first week and the third week. In the 1st week follow-up, it was observed that the major aphthae started to heal. (Figure 3) After 3 weeks of treatment patient has showed improvement in both major aphthae. (Figure 4) At the follow-up 2 months later, it was observed that the patient's aphthae were completely healed and no side effects were observed against azithromycin. Although azithromycin is used in the treatment of aphthous lesions caused by BD, more research is needed in this area.

Figure 1: First day examination. Major aphthae on lip.

Figure 2: First day examination. Major aphthae on tongue.

Discussion

The immunomodulatory effects of antibiotics mean that they can be used to treat infections as well as inflammation and other conditions that affect the immune system (13).

The immunomodulatory effects of antibiotics depend on many mechanisms. These include:

1. Killing bacteria: Antibiotics treat the infection directly by killing the infecting bacteria. Killing bacteria can strengthen the immune system by reducing the burden of infection that overloads the immune system (14).
2. Reducing inflammation: Antibiotics modulate the inflammatory response of the immune system by reducing the inflammation of infected tissues. This, in turn, can help treat chronic inflammatory diseases (13).
3. Changing the gut microbiota: By changing the gut microbiota, antibiotics can affect the rate and types of bacterial populations in the gut. This may produce immunomodulatory effects on the intestinal immune system (15-16).
4. Effect of immunoregulatory cells: Antibiotics can regulate the immune system response by increasing or suppressing the activation of immune regulatory cells. For example, T-regulatory cells provide immunomodulation by increasing immune tolerance and

Figure 3: 1-week follow-up. Major aphthae started to heal.

Figure 4: 3-week follow-up. Major aphthae healing almost completed.

reducing autoimmune responses (17).

The immunomodulatory effects of antibiotics still remain the subject of research, and the exact mechanisms of these effects are not fully understood (13).

Azithromycin therapy in BD Research on the use of azithromycin in the treatment of oral symptoms of BD is still limited. However, there is some evidence that azithromycin is effective in improving the oral symptoms of BD. In one study, BD patients were given azithromycin 500 mg/day and followed for 4 weeks. At the end of the study, the number of oral aphthae of the patients decreased and the healing processes were accelerated (18).

The use of azithromycin for the treatment of oral symptoms of BD has fewer side effects than other BD treatments (18). However, long-term use of azithromycin may lead to the development of antibiotic resistance. Therefore, the duration and dose of azithromycin therapy should be determined according to the patient's symptoms and condition. In addition, the side effects of the use of azithromycin should be considered.

It is important to choose an appropriate treatment protocol for the treatment of the oral symptoms of BD. Azithromycin is a safe and effective option for the treatment of oral symptoms of BD. Although the side effects of azithromycin therapy are few, its long-term use can lead to the development of antibiotic resistance. As a result, the duration and dose of azithromycin therapy should be determined according to the patient's symptoms and condition. In our patient, treatment with 500mg azithromycin once a day on Mondays, Wednesdays and Saturdays of the week resulted in complete resolution of major aphthae with oral symptoms of BD in 3 weeks. Further research will help us to understand more clearly the role of azithromycin in the treatment of BD.

Declarations

Author Contributions: *Conception/Design of Study- M.K., A.O.; Data Acquisition- A.O.; Data Analysis/Interpretation- A.O.; Drafting Manuscript- M.K., A.O..; Critical Revision of Manuscript- M.K.; Final Approval and Accountability- M.K.; Material and Technical Support- M.K., A.O.; Supervision- M.K.*

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