

Case Report

COULD IT BE BEHÇET'S DISEASE? PHYSICIANS IN PRIMARY HEALTHCARE ARE THE FIRST TO RESPOND

Snežana Knežević^{1,2}, Jelena Vulović³, Marijana Jandrić-Kočić⁴

¹Health Center, Kraljevo, Serbia

²University of Kragujevac, Faculty of Medical Sciences, Serbia

³General Hospital, Department for Anesthesiology and Reanimation, Paraćin, Serbia

⁴Health Center Krupa na Uni, Republic Srpska, Bosnia and Hercegovina

Abstract. Behçet's disease is a chronic relapsing vasculitis with complex immunopathogenesis that can affect multiple organs, although mucocutaneous lesions are predominantly observed. Diagnosis of Behçet's disease is challenging and relies on clinical manifestations as no specific laboratory test is available. A positive Pathergy test should raise suspicion of Behçet's disease. The authors present a clinical case of a 22-year-old woman who presented with intermittent fever, weight loss, odynophagia, dysphagia, left knee arthritis, and multiple painful oral-genital aphthosis. The patient received treatment with benzydamine hydrochloride mouthwash, lidocaine on ulcers, antibiotics, and non-steroidal anti-inflammatory drugs, but the healing process was slow, and a new disease attack occurred two months later. The Pathergy test was performed and found to be positive, prompting consultation with an immunologist and gynecologist. The patient was administered Colchicine (1.5 mg/day), which resulted in decreased symptoms, albeit with a slow healing process. During the 6-month follow-up period, the disease attack was followed by a period of remission. The evidence base for the treatment of Behçet's disease is limited, and current options include symptomatic, non-biological, and biological immunosuppressive drugs to reduce clinical manifestations. A thorough evaluation and education in primary healthcare settings are crucial to facilitate timely multidisciplinary referrals for effective management of Behçet's disease.

Key words: Ewing's sarcoma; PNET; scapula; children, diagnosis, treatment, bone cancer

INTRODUCTION

Behçet's disease (BD) is a chronic relapsing vasculitis with a diverse range of complex immunopathogenesis. While it can affect any organ, mucocutaneous lesions and ocular involvement are predominant manifestations [1]. It is currently believed to be an autoinflammatory disorder triggered by infection and external factors in genetically susceptible individuals [2]. The most robust genetic risk factor for BD is HLA-B*51 [1]. BD, also known as Silk Road Disease, has a significantly higher prevalence in Mediterranean, Central Asian, and Far Eastern countries compared to other regions [3]. Turkey has the highest prevalence worldwide, ranging from 20 to 420 cases per 100,000 individuals, in contrast to prevalence rates of 7.3 to 30.5 cases per 100,000 in Korea, China, Iran, Saudi Arabia, and Japan [4]. This complex disease is characterized by oral and genital aphthosis, as well as anterior uveitis with hypopyon. Aphthous ulcers, clinically indistinguishable from recurrent aphthous stomatitis are often the earliest signs of BD [5]. While genital ulcers are less common in BD, they represent the genital equivalent of oral ulcers [5]. Additionally, lesions resembling erythema nodosum and superficial thrombophlebitis are frequently observed [5]. Clinical skin manifestations play a crucial role in the diagnosis of Behçet's disease [5]. BD is most commonly diagnosed in individuals between the ages of 20 and 40, with no significant gender predilection [1].

THE AIM

The aim of this study was to present a case of Behçet's disease with critical skin symptoms .

Correspondence to: Snežana Knežević
Health Center Kraljevo, Jug Bogdanova 110, Kraljevo, 36000, Serbia
E-mail: lesta59@yahoo.com
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MATERIALS AND METHODS

The study encompassed a thorough analysis of the patient's data, including laboratory and radiology findings, positive results of the pathology test, specialist consultations, treatment approaches, remission periods, and overall outcomes.

CASE REPORT

The authors report an unusual clinical case of a 22-year-old woman who presented with predominantly mucocutaneous lesions and general complaints that exhibited a relapsing and remitting nature. The patient presented to the Primary care physician with symptoms including intermittent fever, weight loss, odynophagia, dysphagia, arthralgias, abdominal pain, and multiple painful superficial round erosions of the oral mucosa and lips, with a diameter of approximately one centimeter (Figs. 1, 2).



Fig. 1 Mucocutaneous lesions on the inside of the lips' mucosal surface



Fig. 2 Mucocutaneous lesions of the lips

During the examination, the patient's left knee exhibited pain, edema, redness, and restricted active and passive range of motion. Blood tests revealed elevated levels of erythrocyte sedimentation rate (57 mm), C-reactive protein (27 mg/dL), leukocyte count (14,000/ μ L), and platelet count (56,000/ μ L). Blood tests for iron, ferritin, total iron-binding capacity, folate, vitamins B1, B2, B6, B12, zinc, and magnesium were performed and found to be within physiological limits. PA radiograph of the knee did not show any evidence of trauma, effusion, or asymmetry of the medial tibiofemoral compartment joint space. The patient was initially treated with non-steroidal anti-inflammatory drugs, benzydamine hydrochloride for mouthwash, lidocaine for ulcers, and antibiotics. Clarithromycin was also prescribed, but there was no resolution. After the completion of antibiotic therapy, the patient experienced a recurrence of oral aphthosis. The ulcers had a necrotic base of yellowish color, surrounded by erythema.

Two months later, the patient developed oral aphthosis again, along with the appearance of genital and conjunctival ulcerations. Upon physical examination, painful oral and genital ulcers were observed. The pathology test was performed, and 24 hours later, a papule surrounded by erythema formed at the site of the needle puncture. Genital ulcers were evaluated by a gynecologist and were found to be localized on the vulva, vagina, and cervix, with large and deep erosions. On the patient's face, a dome-shaped pustule with an erythematous and edematous base was observed in the region of the forehead (Fig 3). The treatment included benzydamine hydrochloride mouthwash, lidocaine for ulcers, antibiotics, and non-steroidal anti-inflammatory drugs. The lesions persisted for a few weeks, and the patient also complained of paresthesia and pain in the left knee.



Fig. 3 Forehead a dome-shaped pustule with an erythematous and edematous base

An immunologist was consulted for further evaluation. Serological tests, including antinuclear antibodies and antineutrophil cytoplasmic antibodies, were performed, and the results were within the physiological range. Given the patient's predominant mucocutaneous and joint involvement, therapy with Colchicine (1.5 mg/day) was initiated, which resulted in decreased symptoms. However, the healing process was slow, and two months later, a new disease attack occurred. This was followed by a period of remission during the 6-month follow-up period.

DISCUSSION

In this case, the patient presented with recurrent mucocutaneous ulcers involving both the oral and genital regions, which are hallmark clinical features of Behçet's disease and represent the most common manifestation of this condition. The diagnosis of Behçet's disease poses challenges due to its reliance on clinical manifestations, which are not specific and can overlap with other diseases. Common clinical features of Behçet's disease include oral and genital aphthosis, pseudofolliculitis, erythema nodosum, uveitis, and articular, neurological, intestinal, and vascular manifestations, making it difficult to differentiate from other conditions such as Pemphigus, Lichen Planus, and Herpes Simplex. Complicating matters further, Behçet's disease follows a relapsing-remitting course, with different symptoms presenting at each attack. Vascular involvement, although not universally observed in all patients, is a prominent feature of Behçet's disease, affecting vessels ranging from capillaries to large vessels. As such, Behçet's disease is classified as a variable vessel vasculitis according to 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides [6]. In 2014, revised criteria were proposed as a guide for the diagnosis and classification of Behçet's disease [7]. To meet the classification criteria for Behçet's disease, a patient must accumulate 4 points from a list of specified items (Table 1).

Table 1 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides [6]

Criteria	Points
Oral aphthosis	2
Genital aphthosis	2
Ocular manifestations	2
Skin manifestations	1
Vascular manifestations	1
Neurological manifestations	1
Positive pathergy test	1

Behçet's disease is thought to be triggered by infectious agents, with viruses, bacteria, and heat-shock proteins implicated in its development [1]. For example, Herpes simplex virus-1 DNA has been detected in saliva and genital ulcer samples, while *Streptococcus sanguinis* found in high concentrations in the oral flora may contribute to the formation of recurrent aphthous lesions [8]. T-cell-mediated inflammation and an imbalance in Th1/Th2 responses, which are augmented by both innate and adaptive immune responses, are believed to play a pivotal role in the pathogenesis of BD [9]. Recent studies have reported a relationship between the disease and tumor necrosis factor- α , psoriasis susceptibility 1 candidate 1, the Mediterranean fever gene, interleukin-1, coagulation factor V, intercellular adhesion molecule-1 and endothelial nitric oxide synthetase genes in addition to the major histocompatibility complex [10]. The pathogenesis of BD is also influenced by the activation of the innate immune system [1].

The main purpose of the treatment of BD is to control symptoms, decrease inflammation, suppress the immune system, and prevent secondary organ damage. Although the disturbance in the laboratory is not a typical finding in patients, in our case the values of the parameters of inflammation were increased [11]. Fatigue is a bothersome and unpleasant symptom that patients face, which patients in this case report did not experience [12]. The choice of treatment for BD varies depending on various factors such as the organs involved, disease severity, age, gender,

and disease duration [11]. Benzydamine hydrochloride mouthwash can help alleviate pain in oral ulcers, although it does not affect healing. Amlexanox, an anti-inflammatory agent, can reduce ulcer size and pain when used as a 5% oral paste four times a day. Antibiotics and antiseptic agents are employed to reduce microbial load [13]. Apremilast, known for its efficacy and safety, has emerged as an important treatment option for mucocutaneous symptoms [14]. Topical anesthetics (such as lidocaine 2–5%, mepivacaine 1.5%, and tetracaine 0.5–1% gel) and silver nitrate are used to decrease the severity of pain in aphthous lesions. Topical corticosteroids are effective in reducing pain and shortening the recovery time of genital ulcers [15]. Zinc sulfate has also shown effectiveness in treating mucocutaneous lesions without significant side effects. Colchicine (1.0-2.0 mg/day) is commonly used for mucocutaneous involvement, while azathioprine (2.5 mg/kg/day) is often employed for ocular involvement and the treatment of arthritis, mucocutaneous, enteral, and neurological lesions [16].

As per the current recommendations from the European Alliance of Associations for Rheumatology (EULAR), colchicine should be considered as the first-line treatment for the prevention of recurrent mucocutaneous lesions, particularly in cases where the lesions involve genital ulcers and joint involvement, as demonstrated in this case report [17]. Papulopustular or acne-like lesions can be managed with topical or systemic measures similar to those used in acne vulgaris [17]. In patients with Behçet's syndrome who have inflammatory ocular disease in the posterior segment, management may involve the use of azathioprine, cyclosporine-A, interferon-alpha, or monoclonal anti-tumor necrosis factor (TNF) antibodies [17]. Cyclophosphamide is typically reserved for severe vascular and parenchymal neurological involvement. Other treatment options that may be utilized in the management of BD include corticosteroid therapy, thalidomide, lenalidomide, dapsone, pentoxifylline, rebamipide, etanercept, rituximab, and alemtuzumab [17].

CONCLUSION

In this case report, an unusual clinical case of Behçet's disease was presented, highlighting the importance of a multidisciplinary approach in its treatment. While mucocutaneous lesions are the most common initial symptom, ophthalmic, neurological, vascular, and gastrointestinal involvements can significantly contribute to morbidity in Behçet's disease. Given the complexity of this condition, the competence of primary healthcare workers in evaluating patients is crucial. A thorough primary healthcare evaluation and education are necessary to facilitate timely multidisciplinary referrals and optimize patient outcomes. Furthermore, further research is warranted to gain a deeper understanding of the pathogenesis, diagnosis, and management of Behçet's disease.

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