AFMN BIOMEDICINE

CASE REPORT

BEHCET'S DISEASE WITH RECURRENT APHTHOUS STOMATITIS, POLYARTHRALGIA, AND SUPERFICIAL VEINS THROMBOSIS

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Behçet's disease is a systemic, chronic, idiopathic inflammatory illness of unknown etiology with a recurrent course, manifested by a characteristic triad: recurrent aphthous stomatitis, ulcerative changes in the mucous membranes and skin of the genital organs, and inflammatory changes in the eyes. In addition, the musculoskeletal system, nervous system, gastrointestinal tract, vascular system, genitourinary tract, and cardiopulmonary system can be affected, leading to significant morbidity and mortality. A prolonged period typically elapses between the onset of symptoms and the diagnosis of Behçet's disease due to variable and sometimes intermittent symptoms, the need to rule out clinical mimics of disease onset, the absence of a specific blood test or disease marker, and, unfortunately, a general lack of awareness about the condition.

We present a case of a 35-year-old male patient with a clinical diagnosis of Behçet's disease featuring mucous membrane involvement (recurrent aphthous stomatitis), joint involvement (polyarthralgia) of the knees and elbows, and polyneuropathy of the lower extremities manifesting as reduced sensitivity without functional impairment, of moderate severity; subacute phlebothrombosis of the superficial veins of the left lower extremity in the recanalization stage, and chronic venous insufficiency stage I without circulatory impairment.

A low incidence of Behçet's disease, combined with its involvement of various systems and organs, complicates diagnosis and precludes early treatment. The collection, systematization, and detailed analysis of available clinical cases will facilitate the development of improved diagnostic and treatment algorithms.

Keywords: Behçet's disease, recurrent aphthous stomatitis, polyarthralgia, superficial veins thrombosis

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INTRODUCTION

Behçet's disease (Adamantiades-Behçet's disease, Silk Road disease) is a systemic chronic idiopathic inflammatory disease of unknown etiology with a relapsing course, characterized by a distinctive triad: recurrent aphthous stomatitis, ulcerative changes of the mucous membranes and skin of the genital organs, and inflammatory changes of the eyes (1). In addition, the targets of involvement may include the musculoskeletal system, nervous system, gastrointestinal tract, vascular system, urogenital tract, and cardiopulmonary system, leading to significant morbidity and mortality (2). There is typically a prolonged interval between the onset of symptoms and the establishment of a diagnosis of Behçet's disease (BD), caused by variable and sometimes intermittent symptoms, the need to rule out clinical mimics of the disease's onset, the absence of a specific blood test or disease marker, and, unfortunately, a general lack of awareness about this condition. In the absence of pathognomonic laboratory tests, the diagnosis of this disease relies on clinical criteria (3).

Adamantiades-Behçet's disease is recorded worldwide, but its prevalence is particularly high in the Middle East, Far East, and Mediterranean regions. This condition is also referred to as the "Silk Road disease," acknowledging the fact that the highest incidence of this pathology has been recorded in countries located along the Silk Road, stretching from East Asia to the Mediterranean. Turkey has the highest prevalence of BD (approximately 80–370 cases per 100,000 population), followed by Iran, Saudi Arabia, Iraq, Israel, northern China, and Korea (4, 5). In the United Kingdom, the estimated prevalence of BD is 0.64 cases per 100,000 population. The classic age group affected by this condition is individuals aged 20–40 years, although BD is also observed in children and older patients. The incidence is higher among men in regions with high prevalence, such as Turkey and the Middle East, but the gender distribution varies in other countries. The disease typically progresses more severely in young men (6).

BD is predominantly sporadic but can occur in familial clusters. The etiology remains unknown to date, but a combination of genetic factors, particularly a strong correlation with human leukocyte antigens, specifically HLA-B51, and environmental factors may play a role. The genetic marker HLA-B51 is detected in approximately 60% of patients with BD. Genome-wide association studies (GWAS) have identified HLA-B51 and HLA ERAP1 (endoplasmic reticulum aminopeptidase 1, also known as a regulator of tumor necrosis factor receptor type 1 shedding) as genes predisposing to the development of BD. In susceptible individuals, as-yet-unidentified environmental factors play a pathogenic role, potentially including microbial exposure, as well as cellular and humoral immunity. The proinflammatory cytokine cascade, inflammatory responses, relapsing-remitting course, and responses to immunosuppressive treatment in BD suggest that the disease has an autoinflammatory-autoimmune nature. The action of infectious agents, particularly heightened sensitivity to *Streptococcus sanguinis* antigens, indicates their possible pathological influence. Although many other infectious agents, including *Staphylococcus aureus*, *Herpes simplex* virus type 1, and *Prevotella species*, have been identified as potential culprits, their direct link to the development of BD has not been confirmed. The current understanding is that exposure to infectious or external agents somehow triggers an autoinflammatory response in genetically predisposed individuals. Despite numerous studies dedicated to the mechanisms underlying BD, a long road lies ahead to fully comprehend the complexity of this pathology (7).

In BD, a characteristic triad of clinical symptoms is observed, involving lesions of the oral mucosa in the form of aphthae, ulcers of the mucous membranes and skin of the genital organs, and ocular involvement in the form of uveitis or iridocyclitis. The formation of oral ulcers is noted in all patients and is considered one of the early symptoms, often preceding the development of systemic manifestations by months or even years. The disease typically begins with the appearance of aphthae with cloudy contents on the gums, tongue, and mucous membranes of the cheeks and lips, which then transform into ulcers 2–12 mm in diameter, bright pink in color, round in shape, with an erythematous border. The surface of the ulcers may be covered with yellow pseudomembranes. These ulcerative defects tend to merge, and the affected area may become a continuous ulcerated surface. On the mucous membranes of the glans penis, vagina, or scrotum, painful aphthae appear, which develop into ulcers resembling those in the oral cavity but are typically larger, deeper, and irregularly shaped. In approximately 10% of patients, ocular involvement is the first symptom of the disease, usually developing after ulcerative stomatitis. Patients with ocular involvement report a variety of complaints, including blurred vision, eye pain, photophobia, tearing, and periorbital hyperemia.

Skin lesions are also frequently observed in the form of erythema nodosum, papules, folliculitis, and rashes resembling erythema multiforme. Subungual abscesses and ulcers are not uncommon. Musculoskeletal involvement occurs in approximately half of the patients and is characterized predominantly by mono- or oligoarthritis of large joints, with polyarthritis developing rarely. Gastrointestinal involvement manifests as abdominal pain and diarrhea. Intestinal bleeding and perforation may occur. The ileocecal region is most commonly affected, with the esophagus, transverse colon, and ascending colon involved less frequently. Chronic progressive central nervous system involvement is noted in 10–20% of patients and is more common in men who develop the disease at a younger age. In the early stages of the disease, during the acute phase, aseptic meningitis or meningoencephalitis may develop, presenting with headache, fever, and neck stiffness. According to various studies, pulmonary involvement in BD ranges from 1% to 7%. Possible manifestations of lung involvement include pulmonary artery aneurysms, arterial and venous thromboses, pulmonary infarction, recurrent pneumonia, obliterative bronchiolitis, and pleuritis. Renal involvement in BD is significantly less common than in other vasculitis cases and is less severe. Proteinuria, hematuria, and mild renal insufficiency are occasionally observed. Cardiac involvement is rare and may present as pericarditis, myocarditis, coronaritis, endocarditis, mitral valve prolapse, or other conditions. Typical symptoms include superficial and deep vein thromboses (8, 9).

Although BD is a relatively young disease (described in 1937), it already has 16 sets of diagnostic/classification criteria. The first of these was proposed by H. Curth in 1946, less than a decade after the disease was described (10). Currently, the criteria of the International Study Group for Behçet's Disease (ISG, 1990), the International Criteria for Behçet's Disease (ICBD, 2006), and the International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD, 2014) are used. The ISG criteria are less sensitive but more specific than the ITR-ICBD criteria.

The ISG criteria utilize five elements: recurrent oral ulcers—small and/or large aphthae or herpetiform ulcerations recurring at least three times per year, observed by a physician and patient; recurrent genital ulcers—aphthous or scarring ulcerations observed by a physician or patient; ocular lesions—anterior uveitis, posterior uveitis, cells in the vitreous on slit-lamp examination, or retinal vasculitis, observed by an ophthalmologist; skin lesions–erythema nodosum, pseudofolliculitis, papulopustular eruptions, or acneiform nodules observed by a physician in postpubertal patients not receiving corticosteroids; and a positive pathergy test evaluated by a physician within 24–48 hours. In the ISG criteria, the presence of oral aphthae is mandatory. Two additional items from the remaining four are required for a reliable BD diagnosis (11).

For the International Criteria for Behçet's Disease (ICBD), vascular manifestations were added to the five elements defined in the ISG criteria, as they are a characteristic feature of BD and were used in many criteria prior to the ISG. Vascular involvement manifests as superficial phlebitis, deep vein thrombosis, large vein thrombosis, arterial thrombosis, or aneurysms. Thus, the ICBD employs six items: aphthous stomatitis, genital aphthae, skin manifestations in the form of pseudovasculitis and erythema nodosum, ocular involvement in the form of anterior or posterior uveitis and retinal vasculitis, vascular manifestations, and a positive pathergy test. In the ICBD, genital mucosal aphthae and ocular involvement carry greater diagnostic weight than others and are thus assigned two points each. The other four elements (oral mucosal aphthae, skin lesions, vascular manifestations, and pathergy test) are assigned one point each. A patient must score three or more points for a reliable BD diagnosis (7).

The International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD), due to the low sensitivity of the ISG clinical diagnostic criteria, prompted their revision and reassessment. The ITR-ICBD presented data from 27 countries, including results from 2,556 patients with clinically diagnosed BD and 1,163 controls with diseases mimicking BD or exhibiting at least one major BD feature. These criteria include seven elements: ocular lesions, oral mucosal aphthae, and genital mucosal aphthae, each assigned two points, while skin lesions, neurological manifestations, and vascular manifestations are assigned one point each. A positive skin pathergy test is also assigned one point. A patient scoring four or more points is classified as having BD (12).

The primary goal of BD treatment is to suppress inflammation and reduce the frequency and severity of disease relapses. For treatment to be effective, it must be initiated as early as possible. The location and extent of involvement, as well as the severity of the disease, are key factors in determining the choice of medications. The European League Against Rheumatism (EULAR) recommendations for BD management, developed in 2008 and updated in 2018, assist in addressing various

aspects of this pathology. Systemic treatment for BD is considered when topical medications are ineffective and begins with the prescription of colchicine, which effectively manages recurrent oral and genital ulcers and may also reduce joint swelling. For moderate-to-severe forms of the disease, corticosteroids (prednisolone, methylprednisolone) are prescribed to control inflammation caused by BD. The most common side effects of corticosteroids faced by BD patients include weight gain, persistent heartburn, high blood pressure, and bone thinning (osteoporosis). Immunosuppressants (azathioprine, cyclosporine A, cyclophosphamide) are often prescribed in combination with corticosteroids to suppress the immune system (level of evidence III, strength of recommendation C). Medications that modify the immune response, such as interferon alpha-2b, are used to regulate the immune system and the intensity of inflammation. It can be used alone or in combination with other drugs to help control the progression of skin ulcers, joint pain, and ocular inflammation. Medications that block tumor necrosis factor-alpha (TNF-α), such as infliximab and adalimumab, are effective in treating certain manifestations and symptoms of BD, particularly in patients with more severe or refractory symptoms, such as refractory thrombosis, providing there is a low risk of bleeding and pulmonary artery aneurysms are ruled out (level of evidence III, strength of recommendation C) (13–16). The use of anticoagulant therapy for the treatment and prevention of thromboembolic complications in BD remains an open question (17–19). Results from a study by E. Seyahi demonstrated the ineffectiveness of anticoagulant therapy without immunosuppressants in preventing recurrent venous thrombosis, leading researchers to conclude that venous thrombosis should be treated with immunosuppressive agents (20).

This study is a fragment of the research work “Development and implementation of innovative technologies in the treatment and prevention of violations of the integrity and patency of blood vessels in wartime conditions”, state registration number–0123U100204.

CASE REPORT

Patient M., born in 1987, was admitted to the therapeutic department on September 7, 2022, for inpatient treatment. At the time of examination, the patient reported complaints of pain in the knee and elbow joints, which had been bothering him since 2015, the presence of painful ulcers (aphthae) on the mucous membrane of the oral cavity and tongue, and a sensation of numbness in the lower extremities that emerged in 2021.

During the collection of the medical history, it was established that the patient had been repeatedly treated in various specialized medical institutions with a diagnosis of reactive arthritis, but without sustained improvement. On objective examination, the patient’s general condition was satisfactory, with clear consciousness. He was oriented in space and time. The patient had a normosthenic body build. BMI was 26.5 kg/m^2. The skin and visible mucous membranes were of normal flesh color. Peripheral lymph nodes were not enlarged. The spinal axis was intact, with full range of motion and no pain. Respiratory rate was 18 breaths per minute. Body temperature was 36.5°C. The thyroid gland was not enlarged on palpation. The spinal axis was intact, with full range of motion. Percussion over the lungs revealed a clear pulmonary sound, and auscultation indicated vesicular breathing with no wheezing detected. Blood pressure was 120/80 mmHg. Pulse was 74 beats per minute, rhythmic, tense, and symmetrical. Cardiac borders were unchanged. Heart sounds were clear and rhythmic, with no accents or murmurs detected. The tongue was moist, with a canker sore 1 cm in size present at the tip of the tongue and another canker sore 5 mm in size on the right lateral surface of the tongue, both covered with a fibrinous coating and painful. On the mucous membrane of the inner surface of the lower lip, three painful aphthae, each 5 mm in size, covered with a fibrinous coating, were identified (Figure 1).

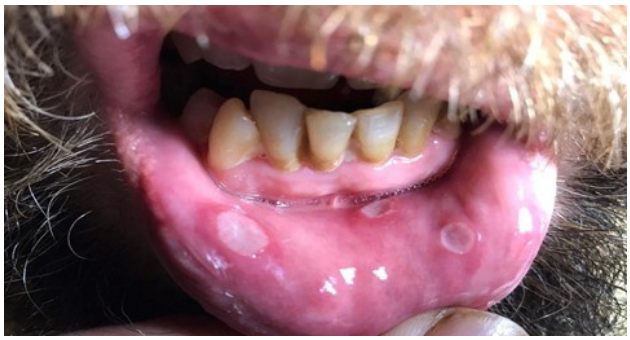

Figure 1. *Canker sore on the mucous membrane of the lower lip*

On objective examination, the following was established: the abdomen was soft and painless on palpation. The liver was not enlarged, palpable along the edge of the right costal arch; the liver edge was soft, elastic, and painless.

The spleen was not palpable. The lumbar thrust symptom was negative on both sides. The kidneys were not palpable. Neurological status: tendon reflexes from the arms and legs were moderately reduced, D=S. Hypesthesia in the lower extremities in a "high socks" pattern. Cranial nerves showed no focal changes. According to otoscopy data, palpation, and percussion of the paranasal sinus projections were unremarkable. The mucous membranes of the upper respiratory tract were pale pink, clean, and nasal breathing is unobstructed. The external auditory canals were clean and patent, the tympanic membranes were gray-pearly, and identifying landmarks were visible. Whispered speech was audible at 6 meters in both ears. Color perception was intact. Visual acuity of the right eye = 1.0, visual acuity of the left eye = 1.0. The ocular adnexa were normal. Normal trichromat. Fundoscopy: optic discs were pale pink with clear borders, A:V ratio = 2:3, maculae showed no changes. Rectal examination: at 3, 7, and 11 o'clock, external and internal nodes up to 0.8 cm in diameter were present without signs of inflammation; sphincter tone was preserved, no blood observed on the glove during palpation, and the coccyx was painless.

Data from laboratory and instrumental examinations: complete blood count: erythrocytes 5.1×10^{12}/L, Hb 156 g/L, leukocytes 6.3×10^{9}/L, platelets 239×10^{9}/L, ESR 3 mm/h; urinalysis–yellow color, complete transparency, specific gravity 1030, acidic pH, glucose and protein not detected, leukocytes 1–3 per field of view, erythrocytes absent, salts absent, flat epithelium 0–1 per field of view, mucus ++++. Biochemical blood analysis: creatinine 86 µmol/L, blood glucose 4.9 mmol/L, ALT 22 U/L, AST 13 U/L, CRP 1.7 mg/L, uric acid 266 µmol/L, rheumatoid factor 9.63 IU/mL, Anti-CCP < 1.5, CIC 172 arbitrary units, antinuclear antibodies IgG 0.97 CP. Blood tests for HIV antibodies–not detected, HBsAg–negative, HCV–negative. Blood analysis for HLA-B51 separated from HLA-B5, EDTA blood– negative, HLA-B52 separated from HLA-B5, EDTA blood–negative.

ECG: sinus rhythm, regular, horizontal position of the heart's electrical axis, heart rate 53 beats per minute. The chest X-ray: the lungs show no visible focal or infiltrative changes. Heart and aorta are within normal limits. The chest X-ray of the knee joints shows no visible bony or traumatic changes. The X-ray of the elbow joints shows no visible bony or traumatic changes.

During the examination, the patient developed complaints of pain in the left lower extremity. An ultrasound examination of the lower extremity vessels was performed, and the patient was examined by a vascular surgeon.

The results of Doppler ultrasonography of the arteries of both lower extremities were as follows. Right: along the course of the common femoral artery (CFA) and superficial femoral artery (SFA), localized single heterogeneous atherosclerotic plaques were identified, predominantly consisting of dense zones, some exhibiting a clear echo-shadow phenomenon. These plaques stenose the lumen of the CFA by up to 20–25% in diameter and the SFA by up to 45–50% in diameter. The intima-media complex (IMC) in the areas accessible for visualization measures 0.9 mm, with normal echogenicity and preserved differentiation into layers. No occlusions were detected. Left: localized single heterogeneous atherosclerotic plaques were observed along the course of the CFA, predominantly consisting of dense zones, some with a clear echo-shadow phenomenon, stenosing the lumen of the CFA by up to 30–35% in diameter. The IMC in the areas accessible for visualization measures 0.9 mm, with normal echogenicity and preserved differentiation into layers. No occlusions were detected. Along the course of the CFA, additional localized single heterogeneous atherosclerotic plaques with predominant dense zones and some exhibiting a clear echo-shadow phenomenon were noted, stenosing the lumen of the CFA by up to 30–35% in diameter.

The results of Doppler ultrasonography of the veins of both lower extremities were as follows. Right: within normal limits. Left: the common femoral vein (CFV), deep femoral vein (DFV), and superficial femoral vein (SFV) were patent, with complete lumen compression and no pathological blood reflux detected. In the area of the ostial valve of the great saphenous vein (GSV), no pathological reflux was detected. The popliteal vein was patent and responsive to compression, with no pathological reflux detected. The posterior tibial veins were patent and responsive to compression. The peroneal veins were patent and responsive to compression. The GSV, at the point of departure from the ostial valve, had a main trunk diameter of 3.3 mm, not dilated, with the lumen decreasing to 2.0 mm without deviating from the main bed. At the level of the upper third of the thigh, the GSV was visualized in the main bed, dilated to 4.8 mm, with the lumen filled up to 80% with isoechoic thrombotic masses (Figure 2A), exhibiting localized parietal blood flow along the posterior wall of the vessel (Figure 2B) and no compression during compression testing. One partially thrombosed perforating vein was identified in the middle third of the thigh (Figure 3). At the level of the knee joint, the GSV lumen measured 2.8 mm and was fully

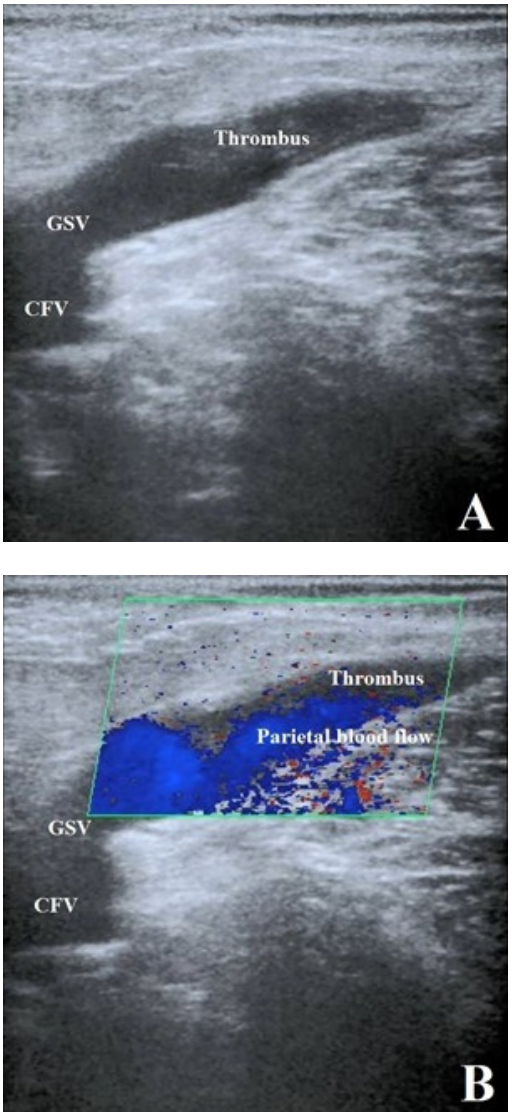

Figure 2. *GSV thrombosis (A) with localized parietal blood flow along the posterior wall (B)*

compressible during compression. On the lower leg, the GSV measured 2.3 mm, not dilated, with a perforating vein in the proximal part from which an enlarged thrombosed branch with up to 20% recanalization was noted. The small saphenous vein (SSV) measured 1.4 mm, not dilated, and was patent; in the middle third of the lower leg, it was dilated to 3.2 mm. In the SSV basin, two dilated insufficient perforating veins were detected in the lower leg. The examination revealed dilated sural veins of the gastrocnemius muscle, as well as the medial and lateral heads of the gastrocnemius muscle, which were patent.

Vascular diagnosis: Consequences of a gunshot through-and-through wound to the right thigh (2015) with damage to the right femoral artery; autovenous prosthetic replacement of the femoral artery using a segment of the great saphenous vein (GSV) from the left lower extremity, manifesting as obliterative atherosclerosis of the lower extremity arteries. Chronic arterial insufficiency stage I of the right lower extremity. Chronic venous insufficiency stage I of the left lower extremity without impairment of circulatory function.

The patient underwent a skin pathergy test, which was negative (Figure 4).

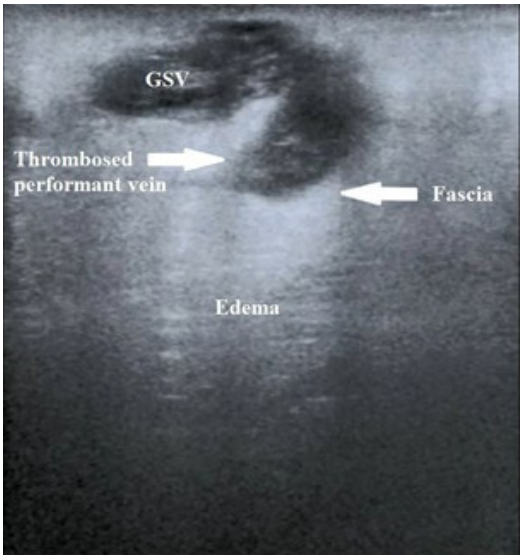

Figure 3. *Partially thrombosed performant vein in the middle third of the thigh*

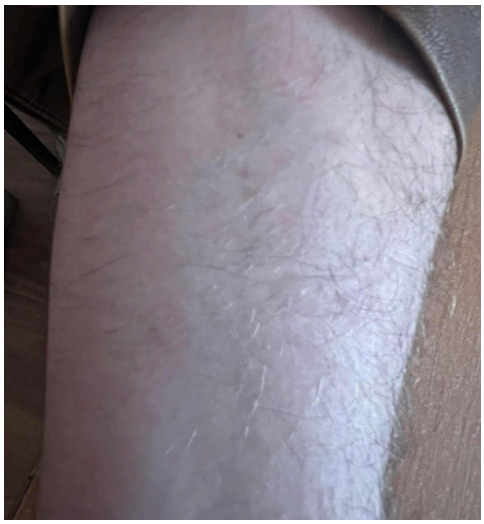

Figure 4. *Skin pathergy test on the inner surface of the left forearm*

According to the criteria of the International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD, 2014), the patient scored four points (two points for oral mucosal aphthae, one point for neurological manifestations, and one point for vascular manifestations).
The following diagnosis was made to the patient–Behçet's disease with involvement of the mucous membranes (recurrent aphthous stomatitis), joint involvement (polyarthralgia) of the knees and elbows, polyneuropathy of the lower extremities manifesting as reduced sensitivity without functional impairment, of moderate severity. Subacute superficial vein phlebothrombosis of the left lower extremity in the recanalization stage, chronic venous insufficiency stage I without circulatory impairment.
Subsequently, the treatment was prescribed to the patient. It included Azathioprine at a dose of 100 mg/day (under monitoring of complete blood count, quantitative CRP, urea, creatinine, and total bilirubin after one month), Methylprednisolone at a dose of 4 mg/day, Colchicine 0.5 mg 1 tablet once daily, Meloxicam 15 mg 1 tablet once daily after meals for 2 weeks, Pantoprazole 40 mg 1 tablet once daily 30 minutes before meals for 6 weeks.
Additionally, a vascular surgeon added a combined Diosmin/Hesperidin preparation at a dose of 900/100 mg/day for 2 months, Acetylsalicylic acid at a dose of 100 mg/day after dinner for 3 months, and Class II compression stockings for the left lower extremity to be worn during the day.
During further observation, upon reducing the dose of Methylprednisolone, the patient experienced a recurrence of canker sores on the mucous membrane of the inner surface of the lower lip, leading to the decision to maintain the dose at 4 mg/day.
Considering the relatively rare occurrence of Behçet's disease and the absence of specific diagnostic tests, establishing a diagnosis can take a prolonged period, as observed in this particular patient.

DISCUSSION

Adamantiades-Behçet's disease is an extremely rare condition, yet it is distributed worldwide. The prevalence of the disease, frequency of clinical manifestations, and genetic predisposition may vary across different regions. The diagnostic process can involve numerous challenges, delaying early diagnosis of the disease, which is critically important for the timely initiation of baseline treatment. The evolution of diagnostic criteria over the past two decades has been made possible only through extensive international collaboration, leading to the development of the International Criteria for Behçet's Disease (ITR-ICBD, 2014), which are currently the most sensitive.
As noted above, BD can affect multiple organs and systems of the body. The most common initial manifestation of this disease is oral cavity involvement, as observed in our patient, while the most frequent manifestation overall is the involvement of the genital mucosa. A similar presentation with initial clinical manifestations was reported in a 29-year-old woman from the Balkan Peninsula in Southern Europe, who experienced recurrent oral and genital ulcers. The mentioned symptoms involving the skin and mucous membranes were characterized by recurrent painful erosions and ulcers. Other dermatological manifestations included erythema nodosum on the skin of the lower extremities (21). Oral aphthae in BD must be differentiated from common aphthae, recurrent aphthous stomatitis, pemphigus vulgaris, herpes simplex, fungal infections, syphilis, and traumatic injuries. Acne-like rashes in BD on the trunk, thighs, or lower extremities typically differ somewhat from classic acne, as they present as sterile pustules, with comedones usually absent (22).
In the literature, a case of BD is described in a 26-year-old man from Poland, who, in addition to painful erosions on the oral mucosa recurring approximately 3 to 7 times per year and on the scrotal skin, exhibited skin involvement of the right thigh in the form of a large erosion. Additionally, acne-like lesions were present on the skin of his face and back (23). In BD, skin ulcers should be distinguished from pyoderma gangrenosum—arguably the most well-known condition associated with the pathergy phenomenon (24).
In contrast to the previous clinical cases, other instances of BD are reported in a 31-year-old dark-skinned man from Tanzania and a 21-year-old man from India, in whom the pathology manifested simultaneously with oral mucosal involvement in the form of painful ulcers recurring at least three or more times per year over several years, recurrent genital aphthae, and posterior uveitis combined with conjunctivitis (25–26). Genital ulcers in BD should be differentiated from syphilis, herpes simplex, chancroid, lymphogranuloma venereum, and genital trauma (27).
Musculoskeletal involvement in BD manifests as painful inflammation of the knee, ankle, elbow, or wrist joints, but without the development of erosive defects. Ocular complications typically appear several years after cutaneous symptoms and can vary, even leading to blindness. BD can also affect the gastrointestinal, cardiovascular, and nervous systems. There may be

erosions of the intestinal mucosa, as well as vomiting and diarrhea. A similar clinical case was reported by scientists from Buenos Aires (the capital of Argentina), who described a 34-year-old patient with an 8-year history of flares of oral and genital mucosal ulcers and intestinal perforation in BD (28). However, such gastrointestinal manifestations were not observed in our patient.

Cardiovascular manifestations in BD may include superficial or deep thrombophlebitis, cardiomyopathy, or pericarditis. Neurological manifestations in this condition arise due to inflammation of the central nervous system, either from localized vascular damage or peripheral polyneuropathy. Neurological symptoms are present in less than 10% of cases and typically develop an average of 5–6 years after the initial non-neurological manifestations. The most common forms result from meningoencephalitis caused not by infection but by inflammation. Neurological deficits are characterized by sensory disturbances, pyramidal syndrome, seizures, cerebellar syndrome, vestibular syndrome, and oculomotor paralysis. Thrombosis of small cerebral vessels or large venous sinuses manifests as intracranial hypertension. Polyneuritis is rare, but when it occurs, it presents with confusion, psychiatric disorders, and dementia (29). A case of BD with neurological manifestations was described by scientists from the University of Malaya in Malaysia (Southeast Asia). In a 47-year-old man, BD manifested with typical clinical features, including oral and genital mucosal ulcers and severe panuveitis. However, two years into the course of the underlying disease, the patient developed complaints of difficulty walking over the past year. Neurological examination revealed pyramidal weakness in both upper and lower extremities, with involvement of cranial nerves IX, X, and XII. The patient also reported blurred vision in both eyes and was examined by an ophthalmologist. Fundoscopy revealed bilateral optic nerve atrophy with attenuated retinal vessels and pigmentary retinal changes. Magnetic resonance imaging of the brain showed small, round, multiple hyperintense foci in both frontal lobes on T2-weighted images. These lesions were absent on T1-weighted images, indicating acute or subacute brain involvement and enabling the diagnosis of “Neuro-Behçet” (30). Neurological manifestations of BD were not observed in our patient.

The pathergy phenomenon in BD patients occurs with varying frequency depending on the patient’s ethnicity. It is typically observed in individuals from regions with high BD prevalence and is estimated to be positive in approximately 70% of cases; however, in our patient, the skin pathergy test was negative (31).

CONCLUSIONS

The main findings of this study can be summarized as follows:

1. Behçet’s disease is a chronic, relapsing systemic vasculitis of unknown etiology, with a prevalence in Europe ranging from approximately 1 case per 15,000 to 500,000 population.
2. Men are more prone to a severe disease course, with the development of pulmonary aneurysms, ocular involvement, thrombophlebitis, and neurological manifestations.
3. The clinical presentation in the typical form of the disease manifests as aphthous stomatitis, uveitis or iridocyclitis, and ulcers of the mucous membranes and skin of the genital organs. Generalization of the pathological process most often presents with involvement of large joints and small-caliber vessels, the central nervous system, lungs, and much less frequently—the heart, gastrointestinal tract, and kidneys.
4. Among narrowly specialized physicians, there is a lack of diagnostic awareness regarding BD, leading them to typically diagnose localized pathology, which in turn may falsely delay the preliminary stage of disease diagnosis.
5. The diagnosis of BD is based on the analysis of the disease’s clinical manifestations, as there are no pathognomonic laboratory tests to verify the diagnosis of BD, while timely establishment of the diagnosis is essential for optimizing the management of such patients and preventing disease progression.

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Statement of Ethics

Complete written informed consent was obtained from the involved patient for the publication of the study and accompanying images.

Competing Interest

The authors declared no relevant conflicts of interest.

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