




## Case report

### A case of Behçet disease with vitiligo, psoriasis and scleritis

Grzegorz Chmielewski<sup>1</sup> , Jakub Kuna<sup>1</sup>, Monika Budkiewicz<sup>2</sup>, Michał Jankowski<sup>2</sup>, Agnieszka Owczarczyk-Saczonek<sup>3</sup>, Magdalena Krajewska-Włodarczyk<sup>1</sup>

<sup>1</sup> Department of Rheumatology, School of Medicine, Collegium Medicum, University of Warmia and Mazury, Olsztyn, Poland

<sup>2</sup> Department of Ophthalmology, Municipal Hospital in Olsztyn, Poland

<sup>3</sup> Department of Dermatology, Sexually Transmitted Diseases and Clinical Immunology, School of Medicine, Collegium Medicum, University of Warmia and Mazury, Olsztyn, Poland

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#### ABSTRACT

**Introduction:** Behçet disease (BD) is a rare systemic vasculitis of unknown aetiology, which can involve different size arteries and veins. The syndrome is characterized by oral aphthous ulcers, genital ulcers, skin and ocular lesions, arthritis, gastrointestinal ulcers, and neurological signs.

**Aim:** The aim of this paper is to discuss comorbidity of BD with other autoimmune diseases referring to a clinical case report.

**Case study:** The study presents a case of BD concurrent with vitiligo, psoriasis and scleritis in a 22-year-old patient.

**Results and discussion:** The aetiology and pathogenesis of BD are unknown. The presented case of BD was accompanied by psoriasis, nodular scleritis, and vitiligo, which is uncommon. In Poland, since the disease is rare and only single cases have been identified, the precise epidemiology is unknown. Currently, more cases are being diagnosed.

**Conclusions:** Due to nonspecific symptoms and rarity in some countries, BD diagnosis can be delayed, which may have a negative effect on a patient's life quality. Further studies exploring the correlation between BD, psoriasis, vitiligo, and nodular scleritis are needed to better understand the pathogenesis and relationship between the diseases.

## 1. INTRODUCTION

Behçet disease (BD) is a systemic, chronic vasculitis characterized by recurrent oral and genital ulceration, along with ocular, gastrointestinal tract, central nervous system and joint lesions. Hippocrates was the first to describe the syndrome. However, the disease was fully described by two other medics. One case was reported in 1931 by Adamantiades, who diagnosed a patient with recurrent iritis, hypopyon, phlebitis, oral and genital ulcers and gonarthrititis.<sup>1</sup> In 1937, after Turkish dermatologist Hulusi Behçet described three patients with oral and genital ulcers, recurrent iritis, the disease is named after him.<sup>2</sup> The disease is also called 'silk route disease,' because it mostly occurs in the countries belonging to former silk route, with prevalence of between 80–370 cases per 100 000 of population.<sup>3</sup>

Recently, more cases have been observed in Europe and North America due to globalization and population migration.<sup>4</sup> In the USA, the prevalence is 8.6 cases per 100 000 population and in Western Europe 0.64–7.20 cases per 100 000 population.<sup>5</sup> In Poland, BD is rare and only single cases have been diagnosed.

BD etiopathogenesis is still unknown and complex. Currently, genetic predisposition (presence of the HLA-B51 antigen) and the influence of environmental factors which trigger inflammatory reaction are taken into consideration. Additionally, infectious factors such as *Streptococcus sanguis*, *Herpes simplex virus*, hepatitis viruses and *Parvovirus B19* are probably involved in the pathogenesis of the disease.<sup>2</sup> Due to the wide spectrum and variability of symptoms, the absence of specific diagnostics and its rarity, diagnoses and treatment are often delayed.<sup>3</sup> Currently, there is a noticeable geographical difference in the disease occurrence between the sexes. BD occurs mostly in men in the Middle East, Central Europe and Turkey. However, in women, the syndrome develops mostly in Northern Europe and the Far East.<sup>6</sup> The commonest age group affected is those aged 30–40 years, although it rarely develops before adolescence or after 50.<sup>7</sup> BD is diagnosed according to International Criteria for Behçet's Disease (ICBD) collected in Table 1.

## 2. AIM

This report documents a case of a 22-year-old woman with BD with concurrent vitiligo, psoriasis and scleritis, which is rare. The aim of this paper is to discuss comorbidity refer-

**Table 1. International Criteria for Behçet Disease – point score system: scoring ≥ 4 indicates BD diagnosis.**

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

ring to a clinical case report. Based on the described case, the authors would like to discuss the comorbidity of BD with other autoimmune diseases. As far as it is known, this is the first report of BD with other autoimmune diseases described in Poland.

## 3. CASE STUDY

A 22-year-old woman was admitted to the Rheumatological Ward of Municipal Hospital in Olsztyn with recurrent, aphthous oral ulcers and genital ulcers, which occurred from November 2019. Additionally, the patient suffered from nodular scleritis from June 2020. Furthermore, the patient had acne-like skin lesions for over a year, which developed after minor injuries and were long-lasting. Before administration to the Rheumatological Ward, the woman was twice examined in another gynaecology out-patient clinic, and no genital ulcers were noted. A physical examination revealed skin hyperkeratosis on the feet and vitiligo in the legs and forearms, a 5 mm subcutaneous nodule on the right thigh, and caries. A laboratory examination revealed leukopenia (with no deviation in bone marrow biopsy), microcytic anaemia, iron deficiency

**Table 2. Laboratory results.**

Parameter	Results	Reference range
White blood cells, 10 <sup>3</sup> /μL	2.43↓	4.0–10.0
Neutrophils, 10 <sup>3</sup> /μL	1.03	1.8–7.7
Lymphocytes, 10 <sup>3</sup> /μL	1.14	1–5
Monocytes, 10 <sup>3</sup> /μL	0.18	0–0.8
Eosinophils, 10 <sup>3</sup> /μL	0.07	0.05–0.7
Basophils, 10 <sup>3</sup> /μL	0.01	0–0.2
Erythrocytes, 10 <sup>6</sup> /μL	4.54	3.9–5.2
Haemoglobin, g/dL	11.4↓	12.0–15.5
Haematocrit, %	35.8↓	37–47
Platelets, 10 <sup>3</sup> /μL	186	150–350
MCV, fL	78.9↓	80–96
MCH, pg	25.1↓	27–34
MCHC, g/dL	78.9↓	32.6–36.6
Iron, μg/dL	33.25↓	37–145
UIBC, μg/dL	210	112–346
Alanine transaminase, U/L	8.3	5–40
Aspartate transaminase, U/L	12.7	5–40
Total protein, g/dL	7.35	6.4–8.7
Creatine kinase, U/L	33↓	35–140
C-reactive protein (CRP), mg/L	3.94	<5
Creatinine mg/dL	0.68	0.4–1.3
Glucose mg/dL	95	70–100
Potassium mmol/L	4.16	3.6–5.2
Sodium, mmol/L	142	135–147
Erythrocyte sedimentation rate (ESR)	19↑	<12

Comments: ↓ decrease concentration; ↑ increased concentration.

and high ESR. The pathergy test was negative. A summary of the laboratory results is presented in Table 2.

Three weeks before hospitalization, the patient was treated with topical antibiotics because of conjunctivitis, with no improvement and worsening during treatment. Ophthalmologic examination revealed distance and near visual acuity. In the left eye, hyperaemia and oedema were observed in the sclera and episclera reaching to the corneal limbus with inflammatory infiltrates around the corneal limbus. No lesions were observed in the right eye. The patient was diagnosed with left eye nodular scleritis.

The patient obtained 5 points in the ICBBD (2 points for the ocular lesions, 2 points for the oral aphthosis, and 1 point for skin lesions). Considering the above information, BD was diagnosed.

Methyloprednisolone (1000 mg i.v. every 24 h for 3 days), prednisone (0.5 mg/kg p.o.), methotrexate (15 mg/week p.o.), and naproxen (200 mg p.o. twice a day) were administered. Additionally, for ocular lesions, topical dexamethasone and diclofenac were prescribed. An improvement was observed after 7 days of treatment.

For the psoriatic skin lesions, betamethasone with salicylic acid and 0.5% hydrocortisone ointment and cooling ointment for the hyperkeratotic and eczematous vitiligo skin were applied.

#### 4. DISCUSSION

The presented case is uncommon because BD was accompanied by psoriasis, nodular scleritis and vitiligo. In Poland, since BD is rare and only single cases have been identified, the precise epidemiology is unknown. However, in the past few years, more cases have been diagnosed, not only in emigrants from Asia but also among the natives.<sup>5</sup>

Vitiligo is an autoimmune disease in which basal epidermal melanocytes are targeted and destroyed by CD8<sup>+</sup> lymphocytes.<sup>8</sup> The symptom can accompany other autoimmune diseases such as chronic autoimmune thyroiditis, diabetes mellitus type 1, and pernicious anemia.<sup>9,10</sup> The coexistence of vitiligo and BD is rare and uncommon, and the studies are contradictory. According to some reports, BD can occur with vitiligo, although there are other studies in which there is no connection between the increased risk of BD occurrence and vitiligo.<sup>11–13</sup> Further studies must be undertaken to resolve the matter.

In addition to vitiligo, psoriatic skin lesions also occurred, which is equally uncommon. Although symptoms of BD and psoriasis differ, there are studies focusing on the similarities in pathogenesis. Immunologic dysfunction leading to cytokine overproduction by Th1 and Th17 lymphocytes has been observed in both diseases.<sup>14</sup> Nevertheless, the correlation and pathogenesis in both diseases remain obscure, and further studies are necessary to clarify the matter. However, according to the latest research, patients diagnosed with BD are more likely to develop psoriasis and psoriatic arthritis. Additionally, the risk is greater in people with high BMI and in men.<sup>15</sup>

BD can show a wide spectrum of symptoms, although the main symptom is oral aphthous ulceration, which occurs in 97% of patients. The ulcerations are painful, can have different shapes and sizes, and can heal with a scar.<sup>3</sup> Ulceration in BD can be similar to those seen in the recurrent aphthous stomatitis, which can be divided into large (more than 10 mm in diameter), small (less 10 mm in diameter), and herpes-like (multifocal, approximately 1 mm).<sup>16</sup> In BD, the most common are small ulcerations in the oral cavity.<sup>17</sup> The aphthous lesions are mostly seen in the gingiva, cheek and tongue mucosa. In other parts of the oral cavity and throat, they are rarely seen.<sup>7</sup> In the presented case, the first symptom of BD was a small painful oral aphthous ulceration, which occurred 4 times over 9 months, which took a long time to heal.

Genital ulcerations are also common in BD. Similar to those in the oral cavity, they can be divided into large, small and herpes-like. The lesions heal with a scar. In women, the labia and vulva (and in men, the scrotum) are mostly affected.<sup>18</sup> In the anamnesis, the patient had a genital ulceration.

In addition to oral and genital ulceration, erythema nodosum, superficial thrombophlebitis, and papulopustular lesions can be seen.<sup>19</sup> The pathergy test (in which papulopustular lesions arise in 24–48 h due to skin damage) is non-specific for BD. The test can also be positive in Sweet syndrome and pyoderma gangrenosum. However, the test is mostly positive in patients from 'silk route countries' than in patients from western countries.<sup>20</sup> In the studied case, the pathergy test during hospitalization was negative, although in the anamnesis there was information about papulopustular lesions located on the hands and face, which appeared after small skin injuries which had healed for a couple of months.

Ocular lesions occur in about 70% of patients and are more severe in males. In 10% of cases, BD starts with ocular symptoms and affects both eyes. Typically there is a severe course of the disease with remission and exacerbation. Retina vasculitis and vascular obstruction are the main causes of the visual impairment.<sup>21</sup>

Frequently, BD patients suffer from non-granulomatous choroiditis and retinitis. Rarely, especially in women, there is isolated inflammation of the anterior eye segment.<sup>22</sup> Episcleritis, scleritis, conjunctivitis, corneitis, periophthalmitis, optic neuritis, ocular paralysis are rarely noted. Although choroiditis occurs mostly in the first 3–5 years after BD diagnosis, in 10%–20% of cases the inflammation can be the first symptom of the disease.<sup>23</sup> Transient hypopyon is the most characteristic lesion, although it occurs only in 10%–30% of cases. In the presented case, nodular scleritis was noted, which is atypical for BD.

Although there are reports focusing on genetic predispositions, BD etiopathogenesis is still unknown. There are reports indicating a correlation between HLA-51 antigen presence and BD.<sup>24–26</sup> Currently, other correlations between tumor necrosis factor (TNF) and major histocompatibility complex I (MHCI, MICA) are also being studied, although further studies are needed to confirm the connection.<sup>20</sup> Human leukocyte antigen A\*26 (HLA-A\*26), interleukin-23

receptor (IL23R), and endoplasmic reticulum aminopeptidase 1 (ERAP1) are the main genes that may play a crucial role in the pathogenesis, and they may also be involved in ankylosing spondylitis and psoriasis.<sup>27</sup>

## 5. CONCLUSIONS

- (1) BD diagnosis is difficult due to a lack of characteristic laboratory test results, and a diagnosis is based on clinical signs and the ICBBD.
- (2) BD can be misdiagnosed unless a holistic approach is employed.
- (3) Due to non-specific symptoms and rarity in some countries, a diagnosis can be delayed, which may have a negative effect on the patient's quality of life.
- (4) The delay in diagnosis may be associated with serious complications, especially when the eyes are affected, which may lead to blindness.
- (5) Since BD may occur more frequently in Poland due to the increased migration of the population, physicians should be aware of the disease and be able to diagnose it.
- (6) Further studies, mostly focusing on the correlation between BD, psoriasis, vitiligo, and nodular scleritis, are needed to better understand the pathogenesis and the correlation between diseases.

## Conflict of interest

None declared.

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