Case Report
Frontiers in Medical Case Reports, ISSN: 2582-8142
DOI: https://dx.doi.org/10.47746/FMCR.2025.6501

Diagnostic Challenges of Behçet Disease – Focus on Neurological Involvement (Neuro- Behçet) A Case Report

Karolina Kulicka[1] | Lucie Pothen[2] | Idil Gunes[3] | Rudy Chapusette[4] | Ides M. Colin[1]*

***Correspondence:** Ides M. Colin
Address: [1]Endocrino-Diabetology Research Unit, Department of Internal Medicine, Centre Hospitalier Régional (CHR) Mons-Hainaut/Groupe Jolimont, Mons Belgium/Groupe Helora, [2]Department of Internal Medicine and Infectious Diseases, Cliniques Universitaires Saint-Luc, Université de Louvain (UCLouvain), [3]Department of Radiology, Cliniques Universitaires Saint-Luc, Université de Louvain (UCLouvain), [4]Department of Radiology, Centre Hospitalier Régional (CHR) Mons-Hainaut/Groupe Jolimont, Mons Belgium/Groupe Helora
E-mail ✉: ides.michel.colin@helora.be
Received: 12 September 2025; **Accepted:** 07 October 2025

ABSTRACT

Behçet's disease (BD) is a rare multisystem inflammatory disorder first described in 1937 by Turkish dermatologist Hulusi Behçet. It is classically defined by a triad of recurrent oral aphthous ulcers, genital ulcers, and uveitis. Multiple studies have shown that BD can affect other organs, including the skin, joints, gastrointestinal tract, central nervous system, and blood vessels, and is therefore classified as a systemic vasculitis. The highest prevalence is found along the ancient Silk Road, covering the Middle East, Mediterranean basin, and Far East. We report the case of a 23-year-old man with BD presenting with recurrent fever, cognitive decline, lower extremity vein thrombosis, uveitis, and urinary retention. Despite those signs, the diagnosis was significantly delayed due to confounding factors, including a maternal Factor II mutation and a context of cannabis use. A comprehensive medical history including targeted questions about recurrent oral and genital ulcers led to the consideration of BD. This case underscores the importance of detailed clinical history-taking-particularly regarding mucocutaneous symptoms-and highlights both the value and limitations of International Criteria for Behçet's Disease (ICBD) in complex, multisystem presentations.

Keywords: *Behçet, Neuro Behçet, Diagnostic Challenges, International Criteria for Behçet's Disease (ICBD)*

Introduction

Behçet's disease (BD) is a rare, chronic inflammatory disorder classified as a systemic vasculitis affecting both small and large vessels. It is most commonly characterized by recurrent oral and genital ulcers and can also involve the eyes, skin, joints, gastrointestinal tract, blood vessels, and central nervous

system (Alpsoy *et al*., 2021). Neurological involvement occurs in a minority of patients and presents a wide spectrum of symptoms, making diagnosis challenging (Zhan *et al*., 2025).

Currently, no diagnostic test exists for BD. Clinicians rely on the International Criteria for Behçet's Disease (ICBD), which provide a valuable framework but have limitations. The ICBD assigns points to the most common manifestations-oral ulcers, genital ulcers, ocular lesions, skin lesions, vascular involvement, and neurological symptoms-with a total score of ≥4 required for diagnosis (Davatchi *et al*., 2014). While capturing the core features of BD, the scoring system may be insufficient in complex multisystem presentations. This case highlights both the utility and the constraints of the ICBD in guiding diagnosis, particularly in patients with multisystem involvement, where delayed recognition may lead to severe and potentially irreversible complications.

Case Presentation

A 23-year-old patient from Italy was admitted to the internal medicine ward for evaluation of cognitive decline and recurrent fever.

Six months before admission, after a long journey by car to visit relatives in Sicily and upon returning home, he developed lower extremity vein thrombosis (LEVT). Initial treatment with rivaroxaban was started at 15 mg twice daily for induction, followed by 20 mg once daily for maintenance. Shortly after initiating rivaroxaban, the patient experienced a severe decline in visual acuity. Ophthalmological examination revealed retinal haemorrhages in both eyes. Consequently, rivaroxaban was discontinued and replaced by subcutaneous enoxaparin injections. However, the patient developed a severe local skin reaction, leading to cessation of enoxaparin and reintroduction of rivaroxaban.

Three months prior to admission, the patient began experiencing recurrent fevers occurring two to three times daily, reaching up to 39 °C, two to three times per week. Concurrently, cognitive impairment emerged.

Two months prior to admission, he presented twice to the emergency department for recurrent urinary retention. No clear aetiology was identified. Despite normal urinalysis, a urinary tract infection was suspected. Ciprofloxacin was prescribed twice daily for two weeks, and an indwelling urinary catheter was placed. A follow-up appointment with an urologist was scheduled. Shortly afterwards, he was again admitted to the emergency department due to an altered mental status. A transient ischemic attack was suspected, based on the spontaneous resolution of cognitive symptoms. Brain CT scan was normal.

DOI: https://dx.doi.org/10.47746/FMCR.2025.6501

The patient's family medical history included a Factor II mutation in his mother; his father had no relevant medical history. His personal medical history was marked by cannabis abuse, which he had discontinued one year prior to the onset of symptoms. At admission, he reported being single and denied unprotected sexual activity. His treatment at the time included rivaroxaban 20 mg once daily and tamsulosin 0.4 mg once daily.

Upon admission, physical examination revealed normal cardiac and pulmonary auscultation and diffuse abdominal tenderness. The patient was lethargic, but further neurological examination revealed normal results. There were no skin lesions observed and the oropharyngeal examination was normal.

Blood analysis revealed anaemia (haemoglobin 12.5 g/dL), mildly elevated C-reactive protein (CRP) at 5.5 mg/L (decreased from 40 mg/L two weeks earlier), and ferritin at 288 mcg/dL (upper limit 275 mcg/dL). Electrolytes and renal function were within the normal range. Arterial blood gases were normal and showed no acidosis. Autoimmune serologies, including rheumatoid factor, anti-cyclic citrullinated peptide antibody, antiphospholipid antibodies, antineutrophil cytoplasmic antibodies, and antinuclear antibody, were negative, as were infectious serologies for syphilis, HIV, Borrelia, brucella, and HCV.

Urinary toxicology screening was negative for cannabis, opiates, cocaine, amphetamines, methamphetamines, MDMA (ecstasy), barbiturates, benzodiazepines, tricyclic antidepressants, and tramadol.

Spinal fluid analysis showed major leucocytosis with 800/mm^3 white blood cells, for an upper normal range of 5/mm^3, with a predominance of neutrophils (68%) and normal glucose levels. The culture was negative, as well as the Multiplex PCR.

An MRI of the brain showed involvement of the basal ganglia and midbrain, associated with a mass effect on the third ventricle. This involvement extended to the optic tracts, predominantly on the right side. No associated contrast enhancement was observed. There was no evidence of vascular or ischemic lesions, and the arteries of the circle of Willis remained intact. No haemorrhagic complications were noticed (Fig. 1).

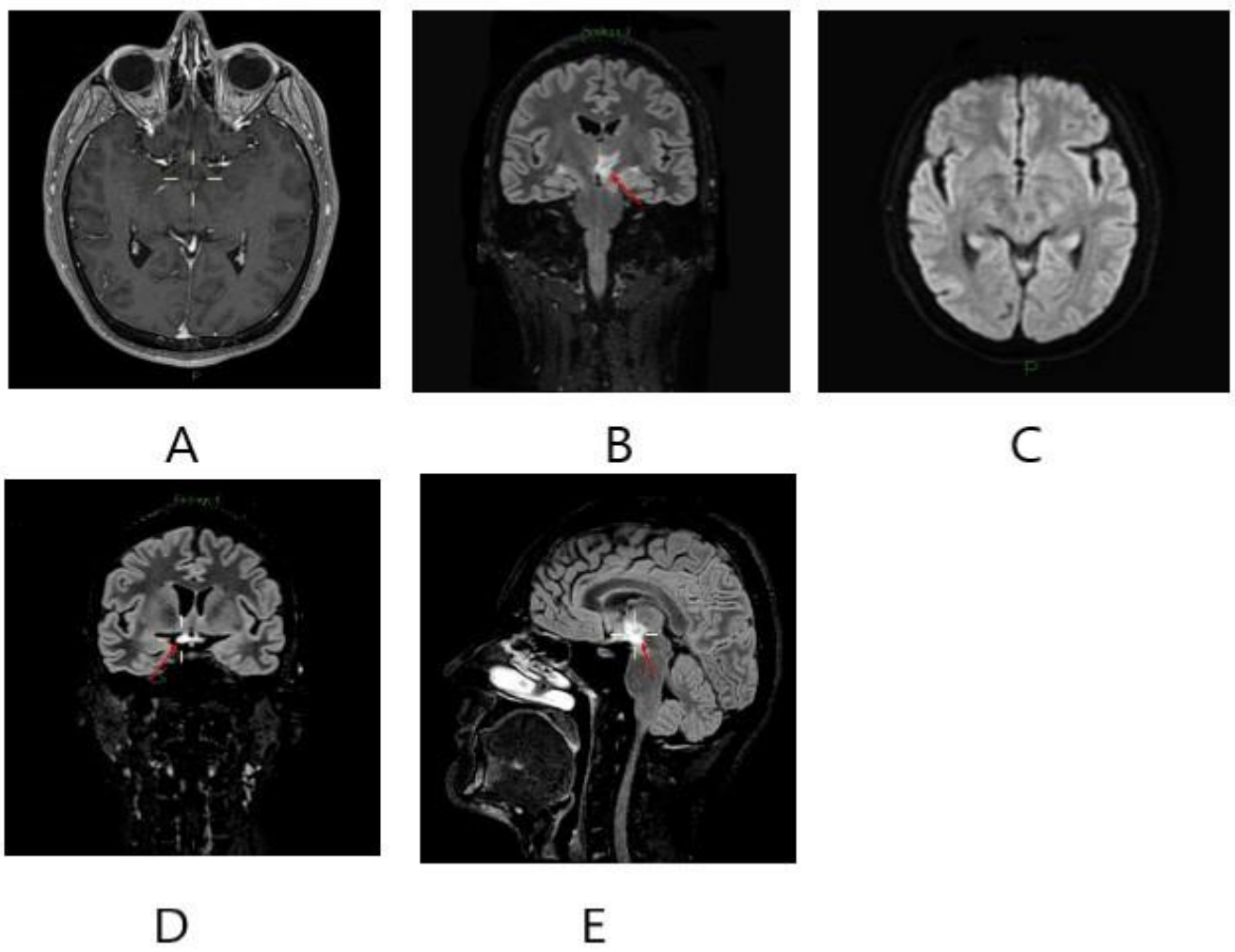

Figure 1: A. axial T1-weighted post contrast MRI examination shows no enhancement; B. coronal T2 Flair weighted shows hyperintensity of the basal ganglia; C. diffusion weighted imaging: no hyperintensity; D. coronal T2Flair weighted shows hyperintensity of the optical tracts; E. sagittal T2 Flair weighted shows hyperintensity of midbrain.

Ophthalmologic evaluation confirmed a significant decrease in vision in both eyes due to posterior uveitis with retinal vasculitis. After further questioning, the patient reported a history of recurrent oral ulcers during adolescence and a single genital ulcer one year prior. Based on these findings, the diagnosis of neuro-Behçet's disease was evoked, and the patient was referred to a university hospital for specialised treatment as well as further evaluation.

A spine MRI performed upon admission to the university hospital showed hyperintensity of the spinal cord in T2/STIR weighting, particularly at the level of C6-T10, consistent with longitudinally extensive transverse myelitis, as well as an oedematous appearance of the spinal cord. No significant leptomeningeal enhancement was observed, with no evidence of meningitis. There were no signs of disc disease, canal stenosis, or foraminal narrowing (Fig. 2).

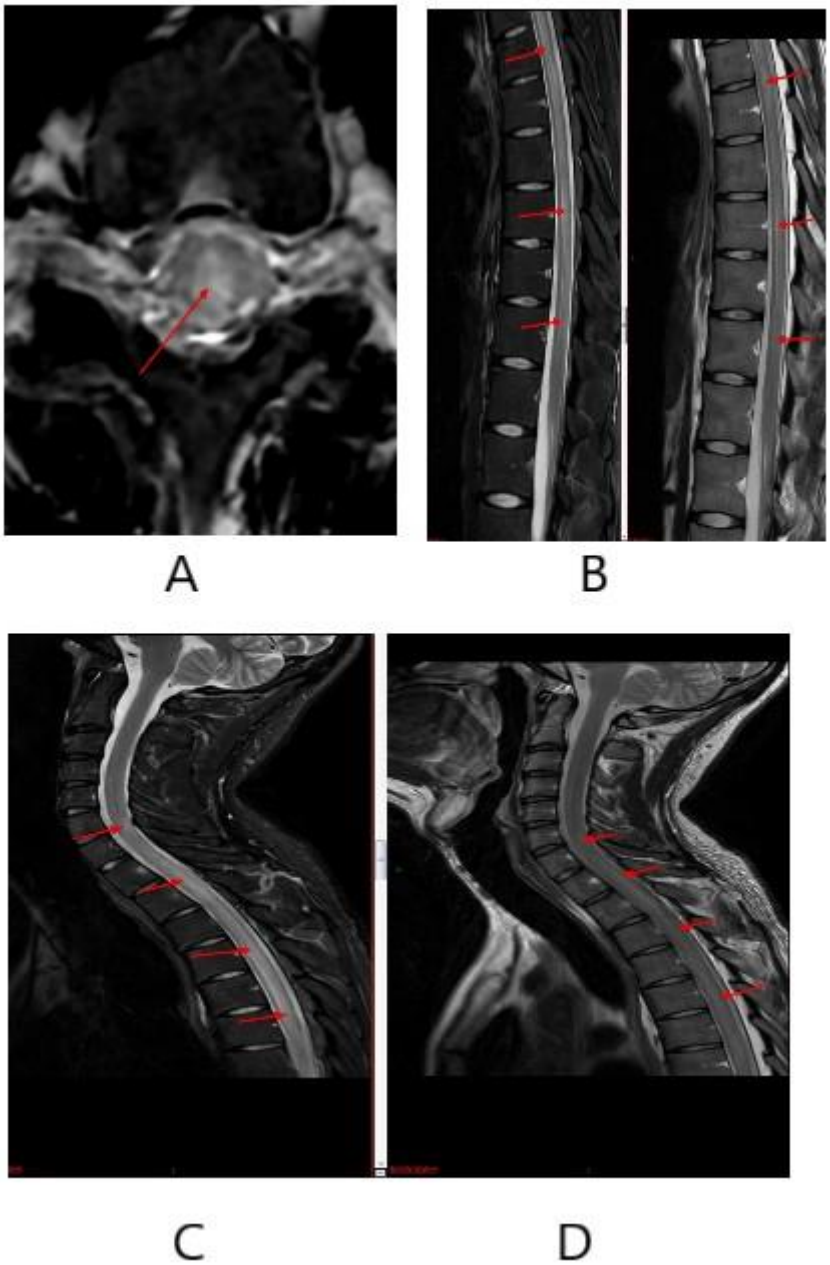

Figure 2: A. axial T2-weighted imaging shows hyperintensity; B. sagittal T2/STIR images show long-segment hyperintensity of the thoracic spine; C. and D. sagittal T2/STIR images show hyperintensity involving the distal cervical and thoracic spine.

Discussion

BD is a systemic vasculitis primarily characterised by recurrent oral and genital ulcers, which occur in approximately 97–99% and 85% of patients respectively (Al-Araji and Kidd, 2009). Vascular involvement can affect both the arterial and venous systems, presenting as deep vein thrombosis, arterial occlusions, or aneurysms (Demirtürk *et al*., 2017). Gastrointestinal and joint involvements are also frequently observed. Since there is no specific laboratory test for BD, the diagnosis relies on established

clinical criteria (Kiafar *et al*., 2021). The exact etiology of BD remains unclear. However, a genetic predisposition has been associated with the HLA-B51 allele, particularly in populations with high disease prevalence. Environmental triggers have also been proposed, suggesting a multifactorial origin involving both genetic and external factors (Mattioli *et al*., 2021).

Over the years, several criteria have been developed for BD screening, including the Japanese revised (1972), ISG (International Study Group, 1990), Iran traditional and Iran classification tree (1993), Korea (2003), and ICBD (International Criteria for Behçet Disease, 2013). ICBD, which is the updated version of the ISG criteria, has the highest estimated sensitivity at 94.8%, compared to 85% for ISG. However, there is a slight decrease in specificity, 90.5% versus 96% for the ISG. Notably, the ICBD criteria uniquely include neurological involvement, although they do not specify which neurological signs or symptoms should be evaluated (Table 1) (Davatchi *et al*., 2014).

Table 1: International Criteria for Behçet Disease, 2013; Davatchi, *et al*., 2014.

Clinical Feature	Points	Description
Oral ulcers	1 point	Recurrent aphthous ulcers (≥3 episodes/year).
Genital ulcers	2 points	Recurrent genital ulcers or scarring.
Ocular lesions	2 points	Uveitis or retinal vasculitis (confirmed by an ophthalmologist).
Skin lesions	1 point	Erythema nodosum, papulopustular lesions, or acneiform nodules (in patients not on corticosteroids).
Vascular lesions	1 point	Includes superficial phlebitis, large vessel thrombosis, or arterial involvement.
Neurological manifestations	1 point	Parenchymal or non-parenchymal neurological signs suggestive of Neuro-Behçet's Disease.
Positive pathergy test	1 point	Skin hypersensitivity reaction to a needle prick (optional but supportive if positive).

Diagnosis Criteria

A total score of ≥4 points confirms the diagnosis of Behçet's Disease.

Fever is not included in the diagnostic criteria for BD, probably because it occurs often alongside major manifestations such as vasculitis or neurological involvement. A study investigating fever in BD patients found that the onset of fever varies with disease stage. Among 163 patients (51 males, 112 females), 110 reported a history of recurrent fever, representing 22% of the cohort. Those with involvement of one or more organs had a higher prevalence of recurrent fever (83%) compared to patients with only skin or mucosal involvement (27%). It is uncommon for patients with BD to have fever as the only symptom (Seyahi *et al*., 2013).

Vascular involvement in BD has a prevalence ranging from 15% to 40% (Demitürk *et al*., 2017). Vascular involvement is categorised into arterial and venous types, with the latter being more frequent

(Ozguler *et al*., 2020). The most common venous complication is LEVT, accounting for approximately 60–80% of all vascular lesions in BD. Bilateral LEVT appears to occur more frequently in BD patients compared to controls (Seyahi and Yurdakul, 2011).

Among arterial lesions, aneurysms are more common than occlusions (Demitürk *et al*., 2017). The artery that is most frequently affected is the aorta, followed by the pulmonary arteries (Giannessi *et al*., 2022). BD is the only vasculitis known to cause pulmonary artery aneurysms, which represent the leading cause of death in patients (Chadli *et al*., 2023).

Vascular involvement may also affect the central nervous system (CNS). Venous complications include cerebral venous sinus thrombosis (CVST). Arterial lesions in the CNS can present as aneurysms or arterial dissections. When these vascular abnormalities occur intracranially, they contribute significantly to the neurological manifestations of BD (Borhani-Haghighi *et al*., 2020).

Ocular involvement occurs in 30–70% of patients with BD, with a higher prevalence reported in endemic regions such as Turkey and the Middle East. Vision-threatening posterior segment involvement, including retinal vasculitis and panuveitis, is common and may result in permanent visual impairment in up to 25% of cases (Tugal-Tutkun *et al*., 2004; Kitaichi *et al*., 2007). Retinal vasculitis is considered a hallmark of BD, which is why it is included in the diagnostic criteria and assigned two points. Peripheral branch occlusions accompanied by intraretinal haemorrhages and macular oedema are frequent and pose a significant threat to vision. Central retinal vein occlusion and arterial occlusion are less commonly observed. The diagnosis of retinal vasculitis is primarily clinical and therefore depends heavily on physician expertise. Diagnostic tools include fluorescein angiography and optical coherence tomography angiography (Agarwal *et al*., 2022).

Neurological involvement is uncommon in the initial presentation of BD, typically emerging several years after the onset of other systemic manifestations. According to an epidemiological review, approximately 6% of patients presented with neurological features at disease onset (Al-Araji and Kidd, 2009). When neurological symptoms occur in isolation, diagnosis may be delayed due to the absence of other characteristic signs.

The same review highlighted a wide variation in the reported frequency of neurological involvement, ranging from 1.3% to 59% across different studies. In three prospective studies conducted in Turkey (Serdaroglu *et al*., 1989), Iran (Ashjazadeh *et al*., 2003), and Iraq (Al-Araji *et al*., 2003) - based on

data from multidisciplinary centers specializing in BD, neurological involvement was observed in approximately 3% of patients (Al-Araji and Kidd, 2009).

Neuro-Behçet's disease (NBD) presents with a range of neurological symptoms, depending on the type and location of lesions. These are broadly classified into parenchymal and non-parenchymal forms (Borhani-Haghighi *et al*., 2020).

Parenchymal lesions primarily affect the brainstem, hemispheres, or spinal cord. Hemispheric involvement may lead to headaches, motor and sensory deficits, or acute confusional states (Banerjee *et al*., 2021). Spinal involvement, though less common, often presents as transverse myelitis, as illustrated in the present case. Cerebrospinal fluid (CSF) analysis in the parenchymal form typically reveals elevated protein levels with neutrophil predominance and normal glucose concentrations. Non-parenchymal NBD is more often associated with venous pathology, such as cerebral venous sinus thrombosis. CSF findings in non-parenchymal cases are often normal, although elevated opening pressure may be observed (Banerjee *et al*., 2021).

In this case, the diagnosis of BD was unfortunately delayed. The patient initially presented with LEVT, and given a family history of factor II mutation on the maternal side, a hereditary thrombophilia was presumed. Several subsequent manifestations were misattributed: recurrent fever to infection, posterior uveitis to NOAC-related retinal haemorrhage, neurological symptoms (including cognitive decline, headaches, and urinary retention) to cannabis abuse, and cutaneous reactions at heparin injection sites to allergy rather than to a pathergy reaction. Each of these interpretations diverted attention from a systemic inflammatory condition, postponing the correct diagnosis.

Treatment

The treatment of BD depends on the stage of the disease and the specific organ systems involved. In cases of isolated mucocutaneous involvement, topical therapies such as corticosteroids may be sufficient. When symptoms are refractory to topical treatment, systemic agents are recommended. Colchicine is commonly used to prevent oral and genital ulcers, while corticosteroids like prednisone are used to manage active lesions. If flares persist despite these treatments, azathioprine may be added. In severe or refractory cases, particularly those with neurological or ocular involvement, anti-TNF agents are considered a third-line option (Alpsoy *et al*., 2021).

In our case, the patient presented predominantly with neurological and vascular manifestations. Once BD was suspected, high-dose intravenous corticosteroid pulses were administered, which caused a great clinical improvement. Given the severity of both neurological and ophthalmological involvement, azathioprine and adalimumab were initiated as part of long-term immunosuppressive therapy. Although the neurological symptoms and lesions resolved completely, the patient suffered significant vision loss in one eye, an outcome likely related to the delayed diagnosis and initiation of appropriate treatment.

The patient's LEVT was initially managed with anticoagulation. However, the long-term use of anticoagulants in BD remains a topic of debate. A non-controlled retrospective study comparing immunosuppressive agents with anticoagulants for the treatment of deep vein thrombosis in BD suggested that immunosuppressive therapy is essential, whereas anticoagulation may not be necessary. Some clinicians advocate for the combined use of immunosuppressants and anticoagulants in vascular BD to reduce recurrence risk, while others support short-term anticoagulation, with long-term management relying primarily on immunosuppression to control the underlying vasculitis. This approach is based on the premise that effective control of inflammation prevents vascular complications (Ahn *et al*., 2008; Emmi *et al*., 2019).

Conclusion

Neurological involvement, or neuro-Behçet's, can lead to severe and potentially irreversible complications including cognitive decline, stroke-like events, and long-term disability if not promptly diagnosed and treated. In cases of unexplained vascular, ocular, or neurological findings, it is necessary to evaluate the possibility of BD and to systematically ask about recurrent oral and genital ulcers. Fever, although not part of current diagnostic criteria, can further complicate the diagnosis if misinterpreted as a sign of infection. Greater awareness among first-line physicians is essential, as delayed recognition may lead to avoidable morbidity. While the International Criteria for Behçet's Disease (ICBD) provide a useful framework, they should be applied with caution in complex presentations, and further refinement may help enhance diagnostic accuracy. As clinical experience and research continue to expand, the existing diagnostic criteria may benefit from future review to ensure they remain effective in guiding diagnosis across complex multisystem cases.

References

Agarwal A, Rübsam A, Zur Bonsen L, Pichi F, Neri P, Pleyer U. A comprehensive update on retinal vasculitis: etiologies, manifestations and treatments. *J Clin Med* 2022; 11: 2525.

Ahn JK, Lee YS, Jeon CH, Koh EM, Cha HS. Treatment of venous thrombosis associated with Behçet's disease: immunosuppressive therapy alone versus immunosuppressive therapy plus anticoagulation. *Clin Rheumatol* 2008; 27: 201-205.

Al-Araji A, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. *Lancet Neurol* 2009; 8: 192-204.

Al-Araji A, Sharquie K, Al-Rawi Z. Prevalence and patterns of neurological involvement in Behçet's disease: a prospective study from Iraq. *J Neurol Neurosurg Psychiatry* 2003; 74: 608-613.

Alpsoy E, Leccese P, Emmi G, Ohno S. Treatment of Behçet's disease: an algorithmic multidisciplinary approach. *Front Med* 2021; 8: 624795.

Ashjazadeh N, Borhani Haghighi A, Samangooie S, Moosavi H. Neuro-Behçet's disease: a masquerader of multiple sclerosis. A prospective study of neurologic manifestations of Behçet's disease in 96 Iranian patients. *Exp Mol Pathol* 2003; 74: 17-22.

Banerjee S, Hamzoui K, Safari A, Borhani-Haghighi A. The cerebrospinal fluid presentations of Neuro-Behçet disease, a way to know the etiopathogenesis and improve armamentarium. *Iran J Immunol* 2021; 18: 170-178.

Borhani-Haghighi A, Kardeh B, Banerjee S, Yadollahikhales G, Safari A, Sahraian MA, Shapiro L. Neuro-Behcet's disease: an update on diagnosis, differential diagnoses, and treatment. *Mult Scler Relat Disord* 2020; 39: 101906.

Chadli S, Khibri H, Firdaous SF, Moatassim N, Ammouri W, Maamar M, Harmouche H, Adnaoui M, Tazi Mezalek Z. Pulmonary artery aneurysms in Behçet's syndrome: a case series of 51 patients. *Rheumatology* 2023; 62(Suppl 2): kead104.246.

Davatchi F, Assaad-Khalil S, Calamia KT, Crook JE, Sadeghi-Abdollahi B, Schirmer M, *et al*. The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. *J Eur Acad Dermatol Venereol* 2014; 28: 338-347.

Demirtürk O, Tünel H, Alemdaroğlu U. Vascular manifestations of Behçet's disease. In: Behçet's Disease. *IntechOpen*; 2017: 149-189.

Emmi G, Bettiol A, Silvestri E, Di Scala G, Becatti M, Fiorillo C, Prisco D. Vascular Behçet's syndrome: an update. *Intern Emerg Med* 2019; 14: 645-652.

Giannessi C, Smorchkova O, Cozzi D, Zantonelli G, Bertelli E, Moroni C, Cavigli E, Miele V. Behçet's disease: a radiological review of vascular and parenchymal pulmonary involvement. *Diagnostics* 2022; 12: 2868.

Kiafar M, Faezi ST, Kasaeian A, Baghdadi A, Kakaei S, Mousavi SA, Nejadhosseinian M, Shahram F, Ghodsi SZ, Shams H, Davatchi F. Diagnosis of Behçet's disease: clinical characteristics, diagnostic criteria, and differential diagnoses. *BMC Rheumatol* 2021; 5: 2.

Kitaichi N, Miyazaki A, Iwata D, Ohno S, Stanford MR, Chams H. Ocular features of Behçet's disease: an international collaborative study. *Br J Ophthalmol* 2007; 91: 1579-1582.

DOI: https://dx.doi.org/10.47746/FMCR.2025.6501

Mattioli I, Bettiol A, Saruhan-Direskeneli G, Direskeneli H, Emmi G. Pathogenesis of Behçet's syndrome: genetic, environmental and immunological factors. *Front Med* 2021; 8: 713052.

Ozguler Y, Hatemi G, Cetinkaya F, Tascilar K, Hamuryudan V, Ugurlu S, Seyahi E, Yazici H, Melikoglu M. Clinical course of acute deep vein thrombosis of the legs in Behçet's syndrome. *Rheumatology* 2020; 59: 799-806.

Serdaroğlu P, Yazici H, Ozdemir C, Yurdakul S, Bahar S, Aktin E. Neurologic involvement in Behçet's syndrome: a prospective study. *Arch Neurol* 1989; 46: 265-269.

Seyahi E, Karaaslan H, Ugurlu S, Yazici H. Fever in Behçet's syndrome. *Clin Exp Rheumatol* 2013; 31: 64-67.

Seyahi E, Yurdakul S. Behçet's syndrome and thrombosis. *Mediterr J Hematol Infect Dis* 2011; 3: e2011026.

Tugal-Tutkun I, Onal S, Altan-Yaycioglu R, Altunbas HH, Urgancioglu M. Uveitis in Behçet disease: an analysis of 880 patients. *Am J Ophthalmol* 2004; 138: 373-380.

Zhan H, Cheng L, Li Y. Neuro-Behçet's disease: an update of clinical diagnosis, biomarkers, and immunopathogenesis. *Clin Exp Immunol* 2025; 219: uxae123.