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Atypical Presentation of Neurobehcet's Disease: A Case Report

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Abstract: ***Introduction**: Behcet's disease (BD) is a complex multisystem autoimmune relapsing vasculitis with an enigmatic etiology, affecting both large and small vessels. Central nervous system (CNS) involvement is infrequent and categorized into two principal subtypes: parenchymal and non-parenchymal. The peripheral nervous system is typically preserved, with involvement occurring in exceedingly rare instances. The onset of this condition commonly manifests in the second decade of life, with a higher prevalence observed in males compared to females. **Case report**: Herein, we present the clinical scenario of a female patient in her fifth decade of life who presented with symptoms of emesis, vertigo, and visual disturbances, alongside a history of fever and cough persisting for three days approximately fifteen days prior to her presentation, which appeared as the initial manifestation of Neuro-Behçet's Disease (NBD). Magnetic Resonance Imaging (MRI) revealed hyperintensities on T2 FLAIR sequences within the bilateral posterior limb of the internal capsule, midbrain, and dorsal pons. The patient exhibited a favorable response to a regimen of antibiotics, antivirals, and corticosteroids. This case underscores the diagnostic challenges and the critical importance of considering Neuro-Behçet's in atypical presentations. **Discussion**: Behçet's syndrome (or disease) is a chronic multisystemic inflammatory disorder distinguished by systemic vasculitis accompanied by perivascular inflammatory infiltrates. This condition is characterized by recurrent and relapsing oral ulcers, genital ulcers, skin lesions, ocular manifestations (notably uveitis), and broader systemic implications, including arthritis and involvement of the gastrointestinal or central nervous systems (4, 5). Behçet's disease (BD) is particularly notable among systemic vasculitis due to its capacity to impact both arterial and venous circulation, as well as all sizes of blood vessels- large, medium, and small. HLA-B51 is regarded as a defining feature of Behçet's syndrome, despite the ambiguity surrounding its role in pathogenicity. HLA-B51 may play a significant role in the genetic clustering of Behçet's syndrome, particularly given the disease's prevalence in Eastern Asia and the Mediterranean regions, and could also influence the determination of clinical phenotypes within this heterogeneous condition (9, 10). **Conclusion**: This case report underscores the multifaceted challenges of managing Behçet's disease with neurological involvement. It emphasizes the importance of early recognition, the potential effectiveness of immunosuppressive therapy, and the necessity of a coordinated multidisciplinary approach to optimize patient outcomes. Despite the complexities of neurological Behçet's disease, continued research and collaborative clinical practices hold promise for advancing treatment strategies and improving long-term prognosis.*

Keywords: Neuro-Behçet's disease, multisystem vasculitis, central nervous system, HLA-B51, immunosuppressive therapy

1. Case Report

A woman in her 50s referred from primary care for further management following multiple episodes of vomiting, lethargy, and progressive neurological symptoms including giddiness and diplopia. MRI revealed T2/FLAIR hyperintensities in the internal capsules, midbrain, and dorsal pons. As her condition worsened with declining sensorium and desaturation, she was intubated and transferred to the emergency department, arriving on ventilator support. MRI showed extensive brainstem, thalamic, and cerebellar involvement with mild tonsillar herniation, raising suspicion of acute rhombencephalitis (viral, autoimmune, paraneoplastic) and atypical PRES. Neuro-Behçet's disease was considered based on imaging and HLA-B5 positivity, although systemic features were absent.

She was admitted to the ICU and started on antivirals, pulse steroids, antibiotics, and IVIG. CT CAP ruled out malignancy, and CSF analysis showed mild lymphocytic pleocytosis with negative infectious and autoimmune panels. A repeat MRI showed a small acute infarct in the left thalamus, and antiplatelet therapy was initiated. The patient improved steadily, was extubated, and shifted to the ward after stabilization. She later developed intravascular hemolysis, likely drug-induced (Bactrim DS), which resolved upon drug withdrawal. Swallow assessment revealed difficulty; appropriate interventions were advised. Hyperglycemia was managed with antidiabetics.she later improved, was haemodynamically stable and was discharged on tapering steroids.

These were the investigations done:

Category	Investigation	Result
Autoimmune Markers	ANA by IFA	Weakly positive (1:100)
	HLA-B51	Detected (suggestive of Behçet's)
	SSA-Ro / SSB-La IgG	Negative
	SMO IgG / RNP-Sm	Negative
	Jo-1, Scl-70 IgG, Centromere IgG	Negative
	DNA strand antibody	Negative
	p-ANCA / c-ANCA	Negative
Infectious Workup	Leptospira IgG	Negative
	HSV 1 & 2	Negative
	CSF India Ink	No yeast found

	MTB (Mycobacterium tuberculosis)	Negative
	Meningoencephalitis panel (viral/bacterial/fungal/ parasitic)	Negative
Other Neurological Markers	NMO-MOG (CSF)	Negative
	Autoimmune encephalitis panel (NMDA, VGKC)	Negative
	Paraneoplastic antibodies	Negative
Imaging	MRI Brain – Day 2	T2 FLAIR hyperintensities in bilateral posterior internal capsule, midbrain, and dorsal pons
	MRI Brain – Day 7	Extensive edema in brainstem, cerebellum, thalami, basal ganglia, corona radiata, mild tonsillar herniation
Other Imaging	CT Chest & Abdomen	Normal
	CT Aortogram	Normal

2. Discussion

Neuro-Behçet's Disease (NBD) represents one of the most serious manifestations of Behçet's Disease (BD), a chronic, relapsing, multisystem vasculitis. While BD is classically characterized by mucocutaneous findings such as recurrent oral and genital ulcers, skin lesions, and uveitis, neurological involvement occurs in approximately 5–10% of cases, typically several years after the onset of systemic disease [7,12]. In rare instances, such as in our case, NBD may present as the initial and predominant manifestation in the **absence of classical systemic features**, creating a diagnostic dilemma.

This patient, a woman in her 50s, presented with acute-onset neurological symptoms including giddiness, diplopia, vomiting, and altered sensorium. MRI brain revealed symmetrical T2/FLAIR hyperintensities in the brainstem, internal capsules, and thalami- findings that are characteristic of **parenchymal NBD**, the most common subtype of neurological involvement in BD. Parenchymal NBD typically involves the **brainstem, basal ganglia, thalami, and internal capsule**, and is associated with progressive neurological deficits [2]. Non-parenchymal forms, such as cerebral venous sinus thrombosis (CVST), were ruled out radiologically.

The **diagnostic challenge** in this case was the **absence of mucocutaneous, ocular, or systemic signs**, which precluded the patient from meeting the **International Criteria for Behçet's Disease (ICBD)** [8]. However, **HLA-B51 positivity** provided a valuable diagnostic clue. HLA-B51 is associated with a significantly increased risk of BD, especially in Asian, Middle Eastern, and Mediterranean populations. While not diagnostic in isolation, its presence in the context of compatible imaging and clinical findings strengthens the likelihood of BD [27].

Extensive evaluation excluded other infectious, autoimmune, and paraneoplastic causes of rhombencephalitis. The **CSF profile**, showing mild lymphocytic pleocytosis with normal glucose and protein, is typical of NBD but non-specific. The infectious workup, including bacterial, viral (e.g., HSV, enterovirus), fungal, and mycobacterial tests, was negative. Autoimmune encephalitis panels (including NMDA, VGKC, AMPA, and GABA receptors) and paraneoplastic antibodies were also unremarkable. Similarly, neuromyelitis optica (NMO) and myelin oligodendrocyte glycoprotein (MOG) antibody testing were negative, ruling out common mimickers such as **NMO spectrum disorders or autoimmune encephalitis** [28].

Given the rapid neurological decline and imaging findings, the patient was empirically started on **broad-spectrum antivirals, antibiotics, corticosteroids, and intravenous immunoglobulin (IVIG)**. Once infectious and neoplastic causes were excluded, a diagnosis of **probable Neuro-Behçet's Disease** was favored, supported by HLA-B51 positivity and dramatic clinical response to **high-dose corticosteroids**, consistent with treatment guidelines [29]. Follow-up MRI showing a small left thalamic infarct led to initiation of **antiplatelet therapy**, acknowledging the prothrombotic tendency in BD.

A notable complication during hospitalization was **drug-induced intravascular hemolysis**, most likely from **sulfamethoxazole-trimethoprim (Bactrim DS)**, which has been reported to cause oxidative stress–mediated hemolysis, especially in predisposed individuals [30]. Hemolysis resolved after the drug was discontinued. Additionally, the patient developed **dysphagia**, likely secondary to brainstem involvement, which was managed through multidisciplinary swallowing assessments and rehabilitation. **Steroid-induced hyperglycemia** was controlled with antidiabetic agents.

This case highlights the **diagnostic complexities of NBD**, especially in patients who lack systemic features of BD. The value of **neuroimaging**, **genetic markers like HLA-B51**, and the exclusion of mimics is critical. Moreover, it underscores the importance of **early immunosuppressive therapy**, which can result in significant neurological recovery and prevent irreversible damage. Given the potential severity and heterogeneity of NBD, a **multidisciplinary approach** involving neurology, rheumatology, infectious disease, and rehabilitation specialists is essential for optimal outcomes.

3. Conclusion

This case illustrates a rare and diagnostically challenging presentation of Neuro-Behçet's Disease (NBD) manifesting with rapidly progressive brainstem dysfunction in the absence of classical mucocutaneous or ocular features typically associated with Behçet's Disease. The initial neuroimaging findings mimicked rhombencephalitis, and an extensive workup for infectious, autoimmune, and paraneoplastic causes yielded negative results. The presence of HLA-B51, in conjunction with characteristic MRI findings and clinical deterioration, was pivotal in raising suspicion for NBD. A prompt and aggressive immunosuppressive approach- comprising corticosteroids,

antivirals, IVIG, and supportive care- led to marked clinical improvement, highlighting the reversibility of neurological deficits when treated early.

This case underscores the need for heightened clinical vigilance for NBD in patients with unexplained brainstem or thalamic lesions, even in the absence of systemic features. It reinforces the diagnostic value of early MRI, HLA typing, and CSF analysis, while also demonstrating the importance of a multidisciplinary, patient-tailored approach in managing complex neuroinflammatory disorders. Ultimately, timely recognition and treatment of atypical NBD presentations can significantly influence outcomes and prevent long-term neurological morbidity.

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