

Symptomatic Intracranial Hypertension Secondary to Superior Vena Cava Thrombosis as the Presentation of Behçet's Disease

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Abstract

Introduction:

Behçet's disease (BD) is a rare inflammatory autoimmune disorder characterized by recurrent oral and genital ulcers, uveitis, and other systemic manifestations. Reported neurological manifestations of BD include meningoencephalitis, cerebral venous thrombosis, intracranial hypertension (ICH), and cranial nerve palsies. Involvement of the superior vena cava (SVC) is rare but should be considered in patients with BD with suspected ICH.

Case Report:

A 32-year-old man presented with ICH as the initial manifestation of BD. He presented with a one-week history of facial and neck edema, headache, and blurry vision, followed by fever, sore throat, and oral blisters a few days later. Lumbar puncture (LP) was performed, and opening pressure was found to be elevated at >50 cmH₂O and closing pressure of 36 cmH₂O. The work-up included a chest CT, which identified thrombosis of the SVC extending into the brachiocephalic veins, and blood work which revealed elevated inflammatory markers. Further probing revealed a history of genital ulcers and a family history of a cousin with BD. The patient underwent mechanical thrombectomy and was treated with oral prednisone with symptom resolution.

Conclusion:

BD has a wide spectrum of symptomology and may present without common manifestations, making it challenging to diagnose. The aim of our report was to emphasize the importance of exploring the rarer vascular, neurological, and cardiac symptoms of BD in order to avoid potentially dangerous sequelae. A system approach may be necessary to diagnose and optimally treat these patients.

Keywords: Behçet's disease, neuro-Behçet disease, SVC syndrome, ICH, case report

1. Introduction

Behçet's disease (BD) is a rare clinically diagnosed autoimmune and inflammatory vasculitis commonly seen in the Mediterranean, Chinese, Japanese, and Korean populations (1,2). BD is unique in that it affects vessels of all sizes resulting in a large spectrum of vessel related symptomology including recurrent oral aphthous ulcers, genital ulcers, ocular disease (typically uveitis), skin lesions like erythema nodosum and folliculitis, and other systemic findings (1). In about 5 to 10 percent of cases, neurological involvement is also present (1,3). Vascular and neurological manifestations of BD, although rare, can make the initial diagnosis of the disease difficult especially when characteristic findings like ulcers are not present as seen in our patient.

2. Case Report

A 32-year-old black/white, non-Middle Eastern man who presented with a one-week history of face and neck swelling, and severe bitemporal headache associated with blurry vision. He had a significant medical history of ulcerations over the proximal thigh bilaterally, recurrent sore throat, and aphthous ulcers of the mouth and lips the year prior, and has a family history of a cousin with BD. He reported subjective fevers and night sweats a few days prior to symptom onset. He visited the emergency room twice in the week prior, due to sore throat and fevers, which was treated with NSAIDs and amoxicillin for presumed upper respiratory tract infection. Over the preceding 4 weeks, he reported experiencing generalized weakness, nausea, dizziness, and a 15lb unintentional weight loss. Worsening facial and neck swelling, and an intractable headache associated with nausea, photophobia, and phonophobia, prompted admission to the hospital.

Significant physical exam findings included diffuse swelling of the face and neck, whitish discharge on bilateral anterior palatine tonsil, and tender bilateral posterior cervical adenopathy. The Pemberton test was positive, with elevation of his arms bilaterally resulting in facial plethora. His eye exam was negative for papilledema or any signs of uveitis. An LP was concerning for intracranial hypertension with opening pressure of >50 cmH₂O and a closing pressure of 36 cmH₂O. Several lab studies were performed summarized in Table 1. Cerebral spinal fluid (CSF) studies found normal protein and cell counts, meningitis panel was unremarkable, infectious workup for human immune deficiency virus, tuberculosis, syphilis, hepatitis (A, B, and C) and Epstein Barr virus were negative. Autoimmune markers C3 and C4 were abnormal as seen in Table 1. Other autoimmune workup, including anti-nuclear antibody, extractable nuclear antigen panel, rheumatoid factor, antiphospholipid antibodies, anticardiolipin antibodies, antineutrophil cytoplasmic

antibodies, paroxysmal nocturnal hemoglobinuria, and JAK2 mutations, were unremarkable.

Initial head CT scan without contrast was negative for bleeding or masses. Head MRI with and without contrast found moderate cervical lymphadenopathy and a filling defect in the proximal internal jugular vein (IJV). Head and neck MR Venography (MRV) was negative for thrombosis. Carotid CTA and chest CT with contrast found thrombotic obstruction of superior vena cava (SVC) (Figure 1). Abdomen and pelvis CT was negative for any malignancy, ruling out SVC thrombosis secondary to paraneoplastic syndrome. An echocardiogram revealed dilated cardiomyopathy with an ejection fraction (EF) of 20%-25% and filling defect in the proximal IJV. A cardiac stress test was negative for ischemia and determined a mildly reduced EF of 55%. Cardiac MRI was performed due to EF discrepancy and was negative for fibrosis or endocarditis with an EF of 52%.

3 days into the 12-day hospital stay, the patient developed oral ulcers. A clinical diagnosis of BD was made, strengthened by the history of recurrent oral ulcers and ulcers on bilateral upper thighs, SVC thrombosis in presence of negative thrombophilia workup, absence of known risk factors for SVC thrombosis, elevated inflammatory markers, and family history of BD. No genetic testing was performed as the clinical presentation was highly suggestive of the diagnosis.

The patient was started on an intravenous heparin drip for SVC obstruction, and the thrombus was eventually removed via catheter-directed thrombolysis 5 days later. He was subsequently anticoagulated with enoxaparin which was then bridged to warfarin. The patient was placed on prednisone for BD treatment. Headache and nausea improved with the LP, and was subsequently started on acetazolamide, intravenous acetaminophen, and ondansetron for further symptom control. He was also placed on valsartan-sacubitril and carvedilol to treat new-onset heart failure with mildly reduced ejection fraction. Prior to discharge, the patient's facial and neck edema improved significantly, and his headache and blurry vision resolved. Acetazolamide was discontinued and the patient was sent home on warfarin and prednisone. In the outpatient setting, warfarin was replaced with apixaban for long-term anticoagulation therapy and colchicine was added for BD symptom prevention.

3. Discussion

Only about 5 to 10 percent of Behçet's disease patients have neurological manifestations, referred to as neuro-Behçet disease (NBD) (1,3). Some cases are difficult to diagnose because of the propensity of BD to present without the usual mucocutaneous and genital ulceration. Hence, concerning NBD symptoms can be missed or confused for other diseases which poses a diagnostic challenge. NBD can be classified as



Figure 1. CT chest with contrast displaying the 116.1 mm size thrombosis of the superior vena cava.

either parenchymal or nonparenchymal, depending on involvement of CNS parenchyma. One report (4) claims BD with parenchymal involvement is thought to be 2.4 to 7.3 times more common than BD without parenchymal involvement while another study (1) reports 80% of NBD cases have parenchymal involvement. Parenchymal involvement usually has accompanying T2 weighed MRI hyperintensities in the cerebral hemispheres, basal ganglia, brainstem, and spinal cord (3). Common symptoms include hemiparesis, hemisensory loss, cognitive dysfunction, brainstem disease causing ataxia, cranial nerve palsies like optic neuropathy, and meningoencephalitis (1,5,6). About 20% of NBD cases are non-parenchymal, of which 10-40% have vascular manifestations with a predilection for the venous system (80-90% of cases) (1,7). Non-parenchymal NBD has been associated with venous thrombosis and resulting ICH manifesting as headache, blurry vision, and papilledema (1,8,9). LPs performed on these patients usually demonstrate an increased opening pressure, but CSF inflammatory and fluid studies often vary (1). The literature has noted several different types of vascular involvement in this type of NBD including acute meningeal syndrome, cerebral venous thrombosis (CVT), SVC

syndrome, arterial thrombosis leading to stroke, and extracranial dissections or aneurysms of large arteries (7,10). Our patient's findings are consistent with non-parenchymal NBD with the presence of vascular involvement with the SVC syndrome and ICH without imaging and neurological symptoms associated with parenchymal involvement.

BD rarely has cardiac manifestations, but, if present, are usually associated with poor prognosis (12). BD can be associated with a spectrum of different cardiac problems including coronary artery aneurysms, aortic aneurysms, conduction system abnormalities, endomyocardial fibrosis, pericarditis, cardiomyopathies, and valvular dysfunctions such as mitral valve prolapse with mitral regurgitation (11,12). Therefore, a proper workup would include an echocardiogram and cardiac stress test in addition to a cardiac MRI if needed for an abnormal/unclear echocardiogram or stress test (12). Our relatively young patient had heart failure with reduced ejection fraction and dilated cardiomyopathy likely due to their BD. Some cases of young BD patients with cardiac involvement have been reported in geographical regions with high BD prevalence but are overall quite rare (2,11).

Screening for large venous thrombosis using MRI/MRV and CTA in BD patients with elevated intracranial pressure is

Laboratory Results on Admission	Value (Range)
Complete Blood Count (CBC)	
White Blood Cells (WBC)	*14.7 (4.8-10.8 x 10 ⁹ /L)
Hemoglobin	11.9 (13.1-17.3 g/dL)
Hematocrit	*34.7 (39-49%)
Platelets	*506 (150-450 x 10 ⁹ /L)
Comprehensive Metabolic Panel (CMP)	
Aspartate Aminotransferase (AST)	*62 (0-41 U/L)
Alanine Transaminase (ALT)	*92 (0-40 U/L)
Other Results	
Lactic Acid	*2.9 (0.4-2.0 mmol/L)
Lactate Dehydrogenase (LDH)	*264 (100-235 U/L)
Erythrocyte Sedimentation Rate (ESR)	*67 (0-15 mm/h)
C-Reactive Protein (CRP)	*7.3 (0.000-0.744 mg/dL)
C3 Component	*190 (86-184 mg/dL)
C4 Component	*65 (16-47 mg/dL)

Table 1. Summary of significant lab findings. *Outside the normal range

worthwhile to rule out dangerous sequela even though these manifestations are quite rare. Furthermore, performing an eye exam (including fundoscopic) to evaluate for papilledema secondary to ICH and signs of anterior uveitis is important to identify harmful manifestations of BD – fortunately our patient did not have these symptoms (1,8,9).

BD has been correlated with HLA-B*51 which is commonly carried amongst Japanese, Middle Eastern and Turkish populations (13). This gene has an overall low prevalence in patients from non-endemic regions like the United States (1,13). BD is a clinical diagnosis so genetic testing are not always performed (1). Our patient is not a member of a high-risk population and his symptoms closely resembled non-parenchymal NBD. Genetic testing was therefore deemed unnecessary. However, future genetic studies for BD may be useful in building a database for other potential genetic causes for the disease and may be a useful source of future study.

Our patient experienced significant improvement with thrombectomy and the addition of heart failure medications. The decision to treat with steroids and colchicine was made based on the evidence for their use as preventative treatments in BD (7).

4. Conclusion

BD has a wide spectrum of symptomology and may present without common manifestations making it a challenge to diagnose. The aim of our report was to emphasize the importance of exploring the rarer vascular, neurological, and cardiac symptoms of BD in order to rule out potentially dangerous sequela. A systems approach may be necessary to diagnose and optimally treat these patients.

Conflicts of Interest:

Authors declare no conflicts of interest

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