CASE REPORT

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Neuro Behcet's Disease Presenting as Hemiparesis

Sana Parvez, Pallaavi Goel*, Mukesh K Sarna**, Amit Agarwal***, Ishank Goel*****

Abstract

Neuro-Behcet's disease (NBD) is one of the grave manifestations of Behcet's disease (BD), which is a multisystem vasculitis disorder of unknown aetiology, characterised by recurrent oral-genital ulcers, arthritis, and uveitis. Neuro-Behcet's disease is rare, but one needs to consider it in the differential diagnosis of other neuro-inflammatory conditions. We report the case of a 26-year-old male who presented with classical history of oral ulcers, right-sided hemiparesis, and gastrointestinal manifestations. The immunogenetic HLA typing was positive for HLA-B51 genotype.

Introduction

Behcet's disease (BD) is a multisystem vasculitis disorder of unknown aetiology that is characterised by recurrent oral-genital ulcers, arthritis, and uveitis. The age of onset is between 20 and 40 years and is more common in males (3:1). HLA - B51 genotype is seen in 40 - 65%. The central nervous system involvement in Neuro-Behcet's disease (NBD) is either parenchymal or non-parenchymal. Primary presentation with NBD is seen in up to 10% of all patients[1]. NBD needs to be differentiated from other neuro-inflammatory conditions; therefore, its clinical manifestations, and management are important.

Case report

A 26-year-old male presented with a history of recurrent oral ulcers for 7 years, progressive decrease in appetite since 1-year, fresh bleeding per rectum for last 7 months, joint pain from past 1-month, intermittent constipation for 15 days and rashes on chest and back from last 7 days. He developed acute onset numbness and weakness in right leg while irrigating the fields during evening hours followed by dull aching headache for 1 day, which progressed to weakness in right half of the body. There was no complaint of slurring of speech, sweating or palpitation at the time of development of weakness. Bladder control were normal. Patient did not have any history of genital ulceration, nausea, vomiting, fever, weight loss. He had taken several medical regimes for oral ulcers but did not get any relief. No significant family history was present. He was admitted and further work-up was done.

Following are the examination findings: PR = 98 bpm, BP = 130/90 mmHg, afebrile. No oral lesions at the time of presentation, maculo-papular rashes were present on the trunk, swelling and marked tenderness in bilateral wrist joints.

Higher mental functions were normal, speech was intact, motor system findings of limbs are mentioned in Table I.

Table I: Motor examination of right upper and lower limbs.

Motor system examination	Right upper limb	Right lower limb
Power	Grade 1	Grade 3
Tone	Increased	Increased
Deep tendon reflexes	3+	3+
Plantar reflex	Not applicable	Mute

Right upper motor neuron type facial palsy was present. Sensory system was intact. Respiratory and abdominal examination were normal. Per rectal examination was done to rule-out haemorrhoids and fissures. Ophthalmological examination ruled-out uveitis and optic neuropathy. Pathergy test was done, which was negative.

Differential diagnosis

- Acute ischaemic stroke
- Multiple Sclerosis
- Infectious Meningoencephalitis
- Neuro-sarcoidosis
- Systemic lupus erythematosus

Case management

Diagnosis: Laboratory investigations are listed in Table II and Table III.

**Junior Resident, **Professor, Department of General Medicine, ***Professor, ****Senior Resident, Department of Neurology, Mahatma Gandhi Medical College and Hospital, MGUMST, Jaipur - 302 022, Rajasthan.*

Corresponding Author: Dr Sana Parvez, Junior Resident, Department of General Medicine, Mahatma Gandhi Medical College and Hospital, MGUMST, Jaipur - 302 022, Rajasthan. Phone: 8696699567, E-mail: drsana977@gmail.com.

Table II: Laboratory investigations.

Investigations	Result	Reference range
TLC	11.6 × 10^9/l	4.5 - 11.0 × 10^9/l
Haemoglobin	14 g/dl	13.5 to 17.5 g/dl
Platelets	3,20,000/µl	1,50,000 to 4,50,000/µl
ESR	43 mm/hr	< 15 mm/hr
Total bilirubin	0.6 mg/dl	0.2 to 1.3 mg/dl
SGOT	22 U/L	15 to 46 U/L
SGPT	38 U/L	13 to 69 U/L
Urea	30 mg/dl	15 to 45 mg/dl
Creatinine	0.7 mg/dl	0.5 to 1.25 mg/dl
Uric acid	4.8 mg/dl	2.5 to 6.2 mg/dl
Total protein	7.0 g/dl	6.3 to 8.2 g/dl
Albumin	4.0 g/dl	3.5 to 5.0 g/dl
Total cholesterol	166 mg/dl	< 200 mg/dl
HDL cholesterol	52.2 mg/dl	40 to 60 mg/dl
Triglycerides	110 mg/dl	< 150 mg/dl
LDL	98 mg/dl	< 180 mg/dl
RA factor	< 8.6 IU/ml	< 12 IU/ml
Anti-CCP	< 20 u/ml	< 20 u/ml
CRP	110.79 mg/l	0 - 10 mg/l
Urine routine	Negative for bilirubin, glucose, protein, blood, leucocyteNo RBC, WBC	
ECG	Normal	
2D ECHO	Normal	
HIV 1 and 2	Non-reactive	
HbsAg	Negative	
Anti-HCV antibody	Negative	
VDRL	Negative	

Table III: CSF analysis.

CSF examination	Result	Reference range
Appearance	clear	
Protein	55 mg/dl	12 - 60 mg/dl
Sugar	94 mg/dl	40 - 70 mg/dl
Cell count	350 cells/mm^3	0 - 5 cells/mm^3
Cell type	Lymphocytes 98%	
Cytology	No malignant cells	
Oligoclonal bands	Not seen	

Neuroimaging – MRI brain with contrast study was done (Fig. 1 and 2).

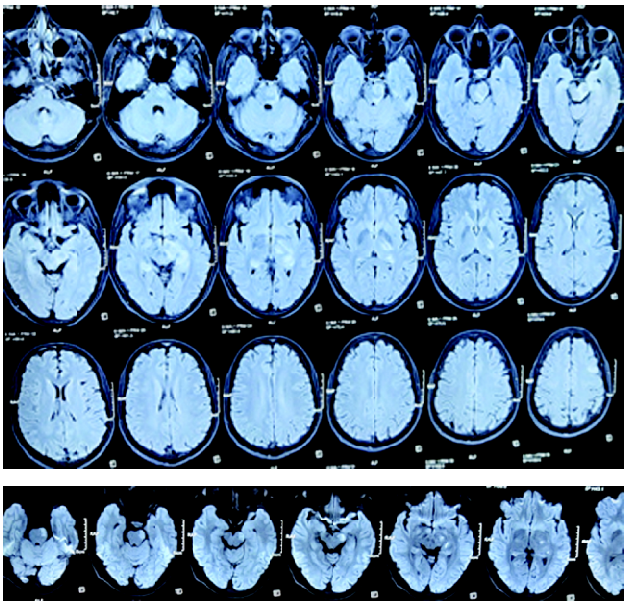

Fig. 1 and 2: *Altered signal intensity within left half of pons, midbrain, left cerebral peduncle, thalamus, posterior limb of internal capsule, left medial temporal lobe and in left basal ganglia with expansion of brainstem and mild mass effect. Hyperintensity is seen to extend in left optic tract. Minimal extension of hyperintensity is seen in right half of pons in paramedian region.*

Ultrasonography of abdomen and CT scan of chest were done to rule-out any other associated disease and revealed no abnormality.

Sigmoidoscopy was done for per rectal bleed evaluation, Fig. 3. Colonic biopsy was suggestive of non-specific colitis.

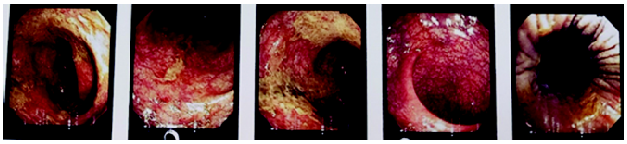

Fig. 3: *Shows erythematous mucosa with erosions and multiple linear white-based ulcers in colon and rectum.*

ENA profile tested negative.

HLA typing revealed HLA-B51 positive status.

Treatment

IV methylprednisolone pulse therapy was initiated in a dose of 1 mg/kg for 5 days. Along with that, limb physiotherapy was done. This led to subsequent improvement in power to grade 3 in the right upper limb and grade 4+ in the right lower limb. Other symptoms were managed symptomatically. There was subsidence of rash and per rectal bleed. Patient was discharged on oral prednisolone 40 mg once a day. Patient is on follow-up and we are gradually tapering the steroids.

Discussion

Behcet's disease is a rare immune-mediated variable vessel systemic vasculitis that is characterised by a triad of aphthous ulcers, genital lesions, and ocular involvement. The pathogenesis of BD is not fully known. Risk factors include genetic and environmental factors. It is associated with autoimmune responses, autoinflammation and vascular injury in the form of neutrophilic angiocentric infiltrates with leukocytoclastic or lymphocytic vasculitis, with or without mural thrombosis and necrosis. Oral ulcers are present during the disease course in almost all patients, are usually the first symptom and may appear years before the diagnosis is made. Other cutaneous lesions include papulopustular lesions, erythema nodosum, cutaneous vasculitis, pseudo-folliculitis, and pyoderma gangrenosum. Nervous system involvement, also called as cerebral angio-Behcet's syndrome, is one of the most serious manifestations of BD. Joint involvement in BD is present in the form of non-erosive mono- or polyarthritis and commonly involved joints are hands, ankles, knees, and feet. Gastrointestinal involvement causes pain, bleeding *per rectum* due to haemorrhage or gut mucosal ulcerations[2]. Patients primarily presenting with neurological symptoms will have history of recurrent oral ulcers and one or more symptoms of systemic involvement.

The two major forms of neurologic involvement in BD are parenchymal involvement (central nervous system involvement) and cerebral venous sinus thrombosis (CVST). They are also described as "intra-axial NBD" and "extra-axial NBD". In CNS-NBD, small vessels are affected causing focal or multifocal manifestations. Extra-axial NBD is due to large vessel involvement, leading to thrombosis of the major cerebral venous sinuses and has limited symptoms with better prognosis. About 75 - 80% of patients with NBD present with parenchymal involvement, commonly affecting the brainstem and/or corticospinal tract especially the telencephalic/diencephalic junction and the brainstem, which are usually large. The major symptoms and signs of CNS-NBD include headache, hemiparesis, dysarthria, cerebellar ataxia and cranial neuropathies (mainly involving motor-ocular and facial nerves) or signs of meningeal irritation and these usually develop in a subacute manner[3].

The revised international criteria for BD include – ocular lesions, oral aphthae and genital aphthae (each assigned 2 points); skin lesions, CNS involvement and vascular manifestations are assigned 1 point each. The pathergy test, when used, was assigned 1 point. A score $\geq$ 4 points suggests BD[4]. CSF findings may show elevated protein level and prominent pleocytosis during the acute phase of CNS-NBD. Neutrophilic predominance is typically seen in acute phase, but later replaced by a lymphocytic form. Many CNS-NBD patients have a relapsing-remitting course initially, with some ultimately developing a secondary progressive course and a few have a progressive CNS dysfunction from the onset. The differentials to be considered are mainly autoimmune and demyelinating illnesses such as multiple sclerosis, granulomatosis with polyangiitis (Wegener's), Polyarteritis Nodosa, Systemic lupus erythematosus and Rheumatoid arthritis[5]. Our case represents the characteristic history and clinical presentation of a young male with MRI brain findings typical of NBD, and it adds on to the existing literature.

Our patient had associated gastrointestinal symptoms which have not been reported very frequently in the published literature of NBD[6]. Though BD is commonly associated with ulcer formation and large bowel bleeding as reported in many case reports[7], it can also present with other gastrointestinal manifestations like colitis[8]. The ileocaecal region is most commonly affected, with ulcerations that may penetrate or perforate. Rarely, the oesophagus and stomach may have ulcerations. Bowel wall thickening is the most common finding on a computed tomography (CT) scan. Pathology shows a vasculitis mainly involving the small veins or, alternatively, nonspecific inflammation[9]. Sometimes NBD can also present with psychiatric symptoms like hallucinations, anxiety, poor communication, rather than neurological symptoms as was seen in our case that presented with sudden onset weakness of one side of body[10]. A case series on pseudo-tumoral NBD was published which differentiated it from classical form of NBD, it revealed that pseudo-tumoral type is more severe and life-threatening and immunosuppressive therapy was the treatment of choice[11]. NBD can also mimic a cerebral tumour, though there was no such presentation in our case[12,13]. NBD is classically recognised on MRI brain. In MRI sequences, DWI is useful for differentiating an acute exacerbation of neuro-behçet's disease from acute infarction[14].

The treatment of parenchymal NBD primarily consists of high-dose intravenous methylprednisolone pulses for 5 - 10 days, followed by the gradual tapering of oral doses over 3 - 6 months. Azathioprine, cyclophosphamide, cyclosporine-A, methotrexate, mycophenolate mofetil, tacrolimus, interferon-α or TNF-α inhibitors can also be used. It has been previously reported that treatment with high dose of steroids has shown good results, as was seen in our case[15]. There have been case reports of use of infliximab in patients of NBD, but results were equivocal, hence not used in our case[16]. Refractory cases of NBD have been reported to improve with infliximab[17]. Long-standing cases of NBD have also been successfully treated with infliximab[18]. Low dose rituximab was also effective for treating relapsing NBD[19].

Conclusion

NBD can cause a high degree of morbidity and mortality. Early recognition and diagnosis help to initiate appropriate treatment, thereby modulating the course of the disease and preventing complications.

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