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RESEARCH

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Neuro-Bechet's disease: a case series from India

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Abstract

Background: There are several studies which have studied large cohort of Neuro-Bechet's disease (NBD) patients worldwide However, there is sparse literature about NBD from India. We aimed to characterize the clinical, radiological characteristics, treatment response and outcome in NBD.

Methods: The study was a retrospective descriptive analysis of a cohort of patients with NBD evaluated between January 2017 to June 2021, fulfilling the International Consensus Recommendation (ICR) criteria for NBD.

Results: Twelve patients were diagnosed as NBD during the study period. The mean age of the patient was 34.7 ± 11.1 (range 21–59 years). The mean duration of illness was 1.4 ± 1.2 years. All 12 patients had neuroparenchymal NBD. Systemic symptoms were present in 6 patients (50%). Pyramidal tract involvement (67%) was the most common symptom and sign followed by cranial nerve, spinal cord and visual involvement. Pathergy test was positive in 6 patients (50%). Human leucocyte antigen (HLA) B51 positivity was seen in all patients. Thalamus (100%) was the most common area involved followed by pons (80%). Favourable outcome (modified Rankin Scale scores ≤ 2) was seen in 7 patients, poor outcome in 3 patients and 2 patients were lost to follow-up after first attack.

Conclusion: NBD is prevalent in India and there is need for clinical suspicion. Brainstem and cerebral syndrome are the most common presentation of NBD and thalamus is the most common site of involvement in NBD.

Keywords: Neuro-Behcet's disease, HLA B51, Pathergy test

Background

Behcet's disease (BD) was first described in 1937 by Turkish dermatologist, Hulusi Behcet [1]. It is a multisystemic vasculitis disorder of almost unknown etiology involving small and large vessels including veins [2]. The basic pathophysiology is inflammatory perivasculitis, which can occur in almost any tissue [3]. The neurological involvement in BD (NBD) usually occurs following the systemic manifestation of BD with mean delay of 3 to 6 years. However, NBD can occur together or precede (6%) other manifestations of BD [2]. CNS is the predominant target in NBD which is either parenchymal (80%) or non-parenchymal. The brainstem and basal ganglia are the commonest area affected in parenchymal NBD but spinal cord and cerebral hemispheres have been reported to be affected [4]. The neurological manifestations due to parenchymal NBD depends on the area of the involvement by the inflammatory process. The non-parenchymal NBD presents with dural sinus thrombosis, intracranial and extracranial aneurysm formation, and arterial vasculitis [5]. The peripheral nervous system involvement is rare and cause peripheral neuropathy, mononeuritis multiplex, myopathy, and/or myositis [6]. It is challenging making an accurate diagnosis of NBD as the definitive diagnosis often requires histologic confirmation of the affected neural tissue which is not readily accessible for pathologic examination. There are no definitive validated

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criteria for NBD. However, in 2014, a practical clinical diagnostic criterion termed as the International Consensus Recommendation (ICR) criteria for NBD diagnosis were developed [7]. There is sparse literature about NBD from India except few anecdotal case reports. The objective of our study was to characterize the clinical, radiological characteristics, treatment response and outcome in patients diagnosed with NBD.

Subjects and methods

The study was a retrospective descriptive analysis of a cohort of patients with NBD admitted under the neurology unit at the dedicated quaternary care hospital for neurological disorders in south India. Patients older than 18 years of age, evaluated between January 2017 to June 2021, fulfilling the diagnostic criteria for NBD according to the International Consensus Recommendation (ICR) criteria for NBD with a minimum follow-up of 6 months were included in the study (Additional file 1: Table S1). The hospital records of the patients fulfilling the inclusion criteria were reviewed. The patients were classified according to ICR criteria as parenchymal (pNBD), non-parenchymal (npNBD), mixed (mNBD) and peripheral nervous system NBD (pnsNBD). The baseline demographic data, clinical presentation, biochemical profile, serological profile, cerebrospinal fluid (CSF) profile, microbiological profile, histopathological data (if available), radiological profile, treatment details and outcome were obtained from the hospital case records of the patients were taken. Patients with other causes of infective and non-infective granulomatous inflammation like neurosarcoidosis, Wegener's granulomatosis, neurotuberculosis, neurobrucellosis, neurosyphilis etc., primary CNS vasculitis, demyelinating disorders like multiple sclerosis, neuromyelitis optica spectrum disorders were excluded from the analysis. The degree of disability of the patients was assessed using the modified Rankin scale (mRS) [8]. A mRS score 0 represents no symptoms, 1 as no significant disability, 2 as slight disability, 3 as moderate disability, 4 as moderately severe disability, 5 as severe disability and 6 as death. A mRS ≤ 2 was considered as favourable outcome and ≥ 3 as poor outcome. The pathergy test was done by pricking the flexor aspect of forearm with a blunt gauge 20 needle and reading the result 48 h later. Magnetic Resonance Imaging (MRI) of the brain and spine were analyzed by an independent and qualified neuroradiologist blinded to the clinical details. Institute Ethics Committee approval was obtained for the retrospective analysis of the data. The study was conducted in accordance with the Declaration of Helsinki (1964).

Statistical analysis

Data was expressed using descriptive statistics. Continuous variables were expressed as mean/median with standard deviation/ Inter-quartile range respectively whereas categorical variables were expressed as frequencies and percentages. Statistical analysis was performed using IBM SPSS software version 22.

Results

A total of 12 patients of NBD satisfying the inclusion and exclusion criteria were analysed. Seven patients belonged to definite and 5 to probable NBD. Six patients were male and six patients were female. The mean age of the patient at presentation was 34.7 ± 11.1 (range 21–59 years). The mean duration of illness was 1.4 ± 1.2 years (range 0.5–6 years). The median duration of symptoms at presentation was 2.25 months (IQR 1.25–10.5 months).

Clinical features

All 12 patients (100%) had pNBD. There were no npNBD, mNBD and pnsNBD patients. The episode was acute in 3 patients, relapsing–remitting pattern in 6 patients (60%) and chronic progressive in 3 patients. Six patients (50%) had a single clinical attack. Patients with single attack had multifocal clinical presentation in 1 patient, brainstem syndrome in 2 patients, cerebellar syndrome in 2 patients and myelopathic presentation in 1 patient. The median number of attacks was 2.5 (IQR 1–3.25). Six patients had ≥ 2 attacks. Pyramidal involvement (67%) was the most common symptom followed by cranial nerve, spinal cord and visual involvement. Systemic symptoms were present in 6 patients (50%). Uveitis and recurrent oral ulcers in 3 patients, only uveitis in 2 patients and only oral ulcers in 1 patient. The systemic symptoms preceded neurological symptoms in 5 patients (83.4%) and were concurrent in 1 patient. The clinical features of the patients are summarised in Table 1.

Laboratory data

The mean erythrocyte sedimentation rate was 10.1 ± 8.2 (range- 4–45). In the CSF mean protein was 39.1 ± 28.1 (range 24–127 mg/dl), mean glucose was 83.7 ± 12.5 (range 64–104 mg/dl). pleocytosis (range- 5–45 cells) was seen in 6 patients (50%) and normal in remaining patients. Pathergy test was positive in 6 patients (50%). Human leucocyte antigen (HLA) B51 positivity was seen in all patients. One patient underwent biopsy of mesencephalic lesion and histopathology showed foci of non-granulomatous non-caseous necrosis with diffuse macrophage and lymphocytes infiltration.

Table 1 Brief summary of clinical, radiological profile and outcome of patients

Patient No	Age (years)/ Gender	Duration of illness (years)	Clinical attacks	Description of attacks	MRI findings	mRS score
1	46/M	3	4	1.Right facial weakness 2. left hemianopia 3. Reduced right facial sensation 4. Reduced right facial sensation	T2/FLAIR hyperintense lesions in thalamus, midbrain, pons, subcortical white mater, Right occipital lobe infarct	0
2	42/F	1	1	1. Diplopia, left 3rd nerve palsy, quadriparesis, seizures	Left thalamus, midbrain, subcortical white mater with contrast enhancement	NA
3	47/F	1	1	1. Spastic paraparesis with urge incontinence	Thalamii, medial temporal lobe, hippocampus, basal ganglia, brainstem, cord	3
4	45/F	0.5	1	1. Left abducens nerve palsy	Subcortical white mater, pons, medulla, thalamus	0
5	30/M	3	3	1. Right ataxic hemiparesis 2. Left ataxic hemiparesis 3. Right hemiparesis	Bilateral basal ganglia, thalamo-mesencephalo-pons	2
6	25/M	6	3	1. Left hemiplegia 2. Status dystonicus with encephalopathy 3. Mood disturbances	Bilateral thalamus, pons, midbrain, basal ganglia	2
7	21/M	2	2	1. Right ataxic hemiparesis 2. Quadriplegia due to cervical myelopathy	Bilateral thalamus, pons, midbrain, medulla, cord, subcortical WM	NA
8	59/M	3	3	1. Headache with fever- meningitis 2. headache 3. Encephalopathy	Subcortical WM, pons, medulla with brainstem atrophy	3
9	31/F	1	1	1. Cerebellar ataxia with dysarthria	Cerebellum, pons, medulla	3
10	35/M	6	5	1. Left ataxic hemiparesis 2. Optic neuritis 3. Paraplegia due to long segment myelitis 4. Left ataxic hemiparesis 5. Cognitive and mood disturbances	Thalamus, basal ganglia, midbrain and subcortical WM	2
11	30/F	0.5	1	1. Cerebellar ataxia	Cerebellum, pons	0
12	35/M	0.5	1	1. Right hemiparesis	Bilateral thalamus, pons, midbrain	0

M male, *F* female, *WM* white mater, *NA* not available, *FLAIR* fluid-attenuated inversion recovery, *mRS* modified Rankin scale

MRI features

Brain and spine MRI was done in all patients (Figs. 1, 2, 3). All the patients had T1 iso-intense and T2/Fluid-attenuated inversion recovery (FLAIR) hyper-intense parenchymal lesions with or without contrast enhancement with or without diffusion restriction. Thalamus (100%) was the most common area involved followed by pons (80%), subcortical white mater (80%), midbrain (70%), medulla (60%), basal ganglia (30%) and spinal cord (30%). Five patients had persistent old lesions with new lesions, 4 patients had resolution of old lesions, one patient had cerebral and brainstem atrophy on follow-up MRI. Two patients did not have follow-up MRI.

Treatment profile

All patients received intravenous methylprednisolone as treatment for acute attack followed by oral prednisolone for 6 months. Three patients received intravenous cyclophosphamide as second line treatment for acute attack. Three patients requiring intravenous cyclophosphamide had poor outcome. Five patients received azathioprine and 3 mycophenolate mofetil as maintenance therapy. Two patients were lost to follow-up.

Outcome

The median mRS score was 2. Favourable outcome (mRS scores ≤ 2) was seen in 7 patients, poor outcome in 3 patients and 2 patients lost to follow-up after first attack.

Discussion

This was a hospital-based study which was aimed at studying the clinical, radiological profile, treatment response and outcome in patients diagnosed with NBD from India. We studied 12 patients who were diagnosed as NBD as per the ICR criteria for NBD diagnosis. The reported frequency of NBD from India is relatively low probably due to low prevalence, lower rate of suspicion by the treating physician and neurologist. BD is commonly characterised by recurrent oral aphthae which is the main and recurrent symptom, genital ulcers, skin lesions, arthritis,

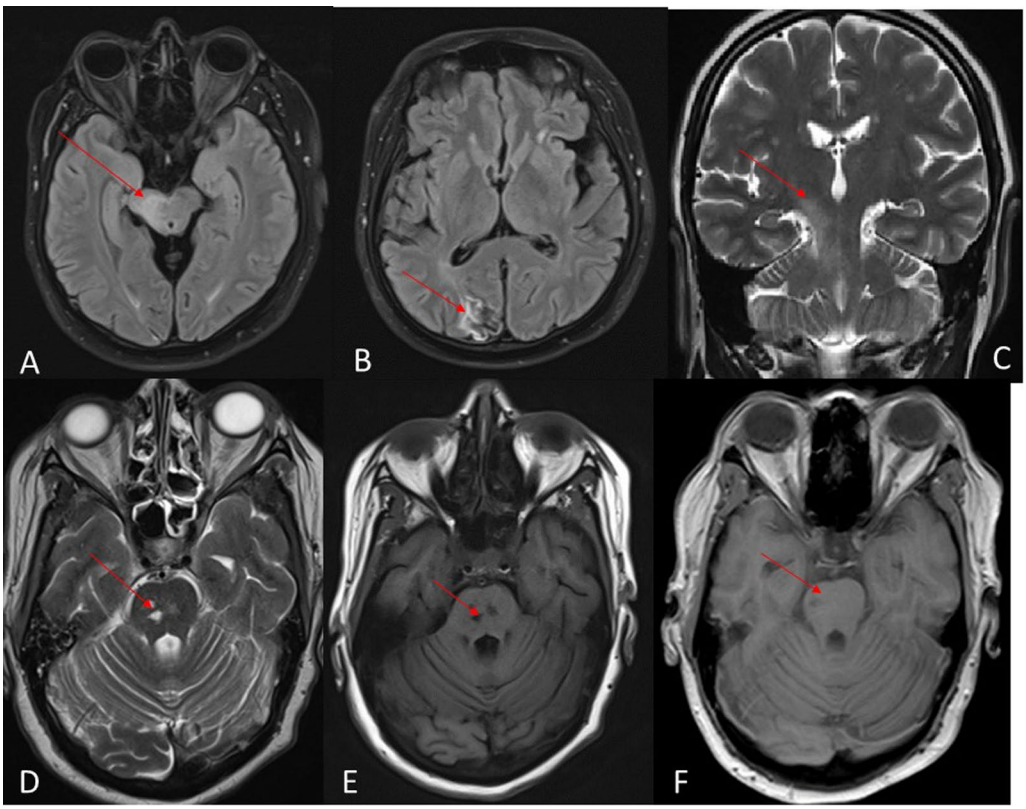

Fig. 1 Magnetic resonance imaging (MRI) brain of patient 1 (**A**–**C**). **A**, **B** Fluid-attenuated Inversion Recovery (FLAIR) axial images showing hyperintense lesion in midbrain and gliosis in right occipital area (red arrows); **C** coronal *T2* image showing cascade sign (red arrow). MRI of patient 3 (**D**–**F**), (**D**, **E**) axial *T2* and *T1* image showing pontine base discrete hyperintense and hypointense lesion (red arrow); **F** axial *T1* image showing decrease in lesion with treatment

uveitis, and thrombophlebitis [9]. The first report of neurological involvement in BD was described in 1941. NBD is seen in 10–20% of BD patients [10]. NBD is relatively uncommon but potentially treatable, and should be considered in the differential diagnosis of inflammatory, infective, or demyelinating central nervous system (CNS) disorders and one of the causes of long-term morbidity in BD. Genetic susceptibility has been reported in BD which has ethnic group susceptibility. The HLA B5 genotype is seen in 40–65% of patients diagnosed with BD in studies from Turkey and Eastern Asia and the prevalence of HLA-B51/B5 among subjects with NBD is not dissimilar to that found in patients with BD without neurological involvement [11].

There are several studies which have studied large cohort of NBD patients worldwide including Mediterranean, European, Middle East and South East Asian countries. Akman-Demir et al. from Turkey reported one of the largest series on the neurological involvement in BD and assessed the pattern of involvement and prognosis in NBD. They analyzed 200 cases of NBD and found male predominance. The mean interval between onset of BD and NBD was 5.6 years after onset of BD. The skin pathergy test was positive in 83% of patients. The parenchymal involvement was the most common manifestation of NBD. The brainstem involvement was the most common area of parenchymal NBD. Hemiparesis, pyramidal involvement and behavioural change was the most common clinical manifestation in pNBD. Dural sinus thrombosis was the most common presentation of npNBD. CSF pleocytosis was seen in 60% of cases with pNBD. The indicators for favorable prognosis were normal CSF, npNBD, number of attacks less than 2 and functional independence at admission whereas abnormal CSF, pNBD, more than 2 attacks, progressive course, dependent at admission and relapse during steroid tapering were poor prognosis indicators [12]. Al-Araji et al. from Iraq studied the prevalence of neurological involvement and described the clinical patterns of neurological presentation in NBD. Twenty patients of NBD were studied and pNBD was most common presentation with pyramidal signs as the most common clinical sign. CSF pleocytosis with raised protein was seen in 50% of pNBD patients. However, MRI lesions were more frequent in

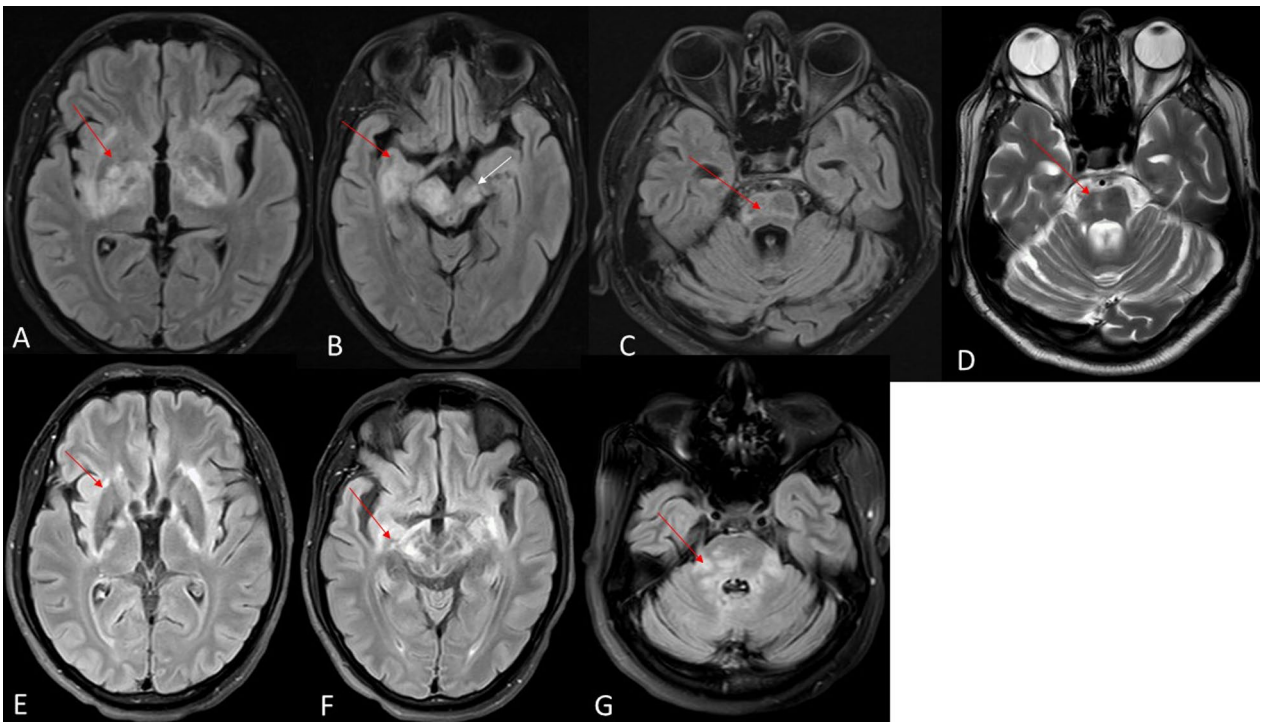

Fig. 2 MRI brain of patient 6 (**A**, **B**, **E**, **F**). **A**, **B** axial FLAIR images show hyperintense lesion in bilateral basal ganglia, right medial temporal lobe and midbrain (red and white arrows); **E**, **F** axial FLAIR images showing decrease in lesion with treatment; **C**, **D** axial FLAIR and *T*2 images of patient 8 showing pontine hyperintense lesion with ponto-cerebellar atrophy (red arrows); axial FLAIR images of patient 9 showing pontine, bilateral middle cerebellar peduncles and cerebellar lesion (red arrows)

cerebral white matter (92%) than brainstem and thalamus [13]. Hirohata et al. from Japan studied the clinical characteristics of NBD. They reviewed 76 patients with acute NBD, 35 with chronic progressive (CP) NBD, and 33 with non-NBD. They found high-intensity lesions frequently in the pons, midbrain, and basal ganglia in acute NBD as well as CP NBD. Brainstem atrophy was more frequently occurred in CP NBD [14]. Talarico et al. from Italy assessed the prevalence of neurological involvement in BD and the clinical patterns of presentation in NBD. They studied 44 patients with NBD (35 pNBD) and brain MRI showed pons-mesencephalon lesions in 19 patients and meningoencephalitis with brainstem involvement in 16 patients [15]. Sorgun et al. from Turkey studied treatment response and prognosis in patients with NBD. They studied 60 NBD patients and parenchymal NBD was the most common presentation. The time to NBD was 8 years. HLA B51 positivity was very low (5%) whereas positive pathergy test was 50%. Brainstem (60%) was most common site of parenchymal lesion followed by cerebral hemisphere (30%). Patients with severe NBD had older age at onset and longer time to NBD [16]. Kim et al. from South Korea studied 110 patients with NBD. HLA B51 positivity was 50% but positive pathergy test was 16%. pNBD was the most common presentation with brainstem syndrome as the predominant clinical manifestation. Acute pNBD (72%) was more common presentation than cpNBD. Abnormal CSF findings were noted in 70% of patients. Pons, midbrain followed by deep white matter was most common sites of lesions on MRI [17]. Bolek et al. retrospectively reviewed the charts of 77 patients (definite NBD = 61, probable NBD = 16) of NBD. The most common presentation in their cohort was parenchymal NBD (61%). The most frequently affected parenchymal area was brainstem (72.9%) followed by cerebellum and diencephalon. The median time for NBD onset after BD onset was 6 years. Acute onset pNBD was more frequent than CP NBD. All patients with npNBD had favourable outcome whereas 57% of patients with pNBD had favourable outcome [18].

Based on the findings from large cohort of NBD patients, we can infer that NBD shows male predominance, mean time of onset of 6–8 years after BD onset, parenchymal involvement predominance, brainstem and cerebral white mater as the most common affected areas, acute attacks and relapsing–remitting as the predominant pattern with favourable prognosis in npNBD as compared to cp NBD. The literature of NBD is very

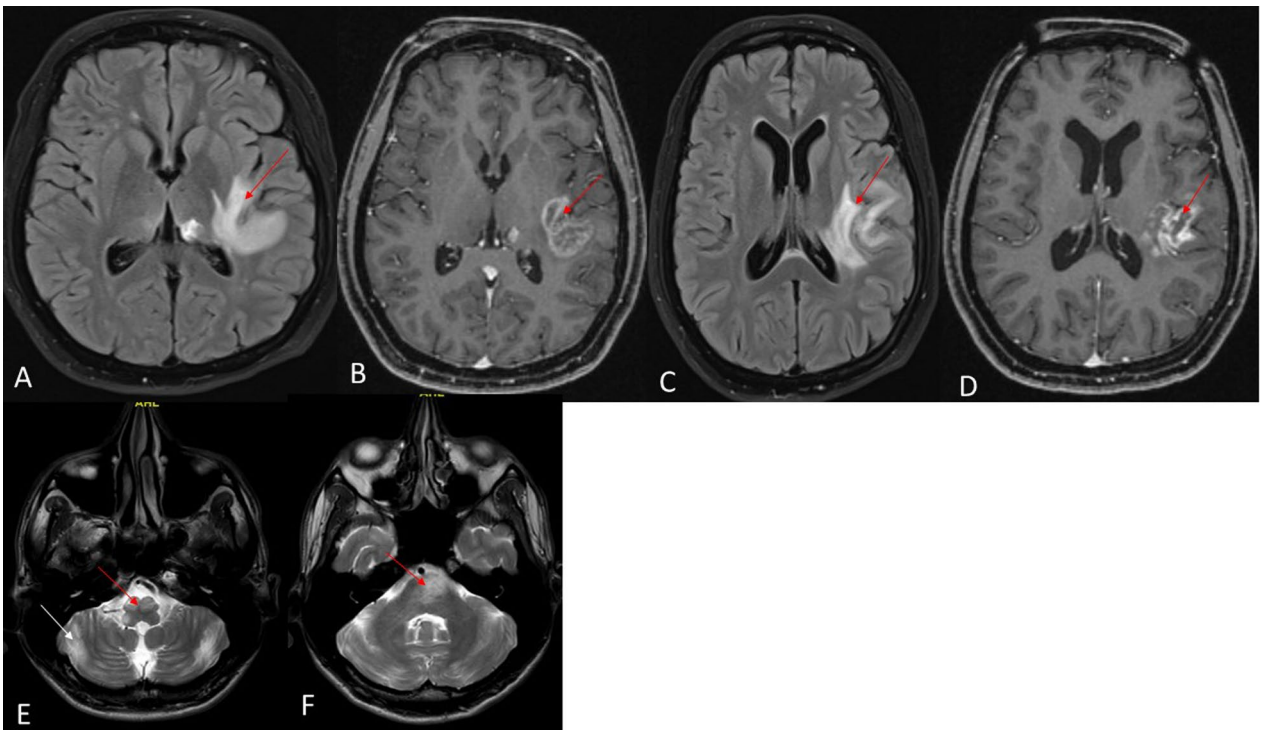

Fig. 3 MRI brain of patient 2 (**A**–**D**). **A**, **C** axial FLAIR images show hyperintense lesion in left thalamus, internal capsule and peri-insular region (red arrows); **B**, **D** *T*1- contrast images show contrast enhancement in left thalamus, internal capsule and peri-insular region (red arrows); **E**, **F** axial *T*2 images of patient 7 shows hyperintense lesions in medulla, cerebellum and pons (red and white arrows)

limited from India with few anecdotal case reports. We reviewed our patients who were diagnosed as NBD and studied the clinical, radiological, treatment profile and outcome. As compared to above studies, we found similar age at onset, equal gender distribution, parenchymal NBD and pyramidal symptoms predominance, CSF abnormalities, HLA B51 and pathergy test positivity. However, thalamus involvement was seen in all patients followed by pons, subcortical white matter unlike in above studies wherein the brainstem and cerebral white mater involvement is predominant. Poor prognosis was seen in cp NBD in our cohort as demonstrated in other studies.

The management of neuro-Behçet's disease includes treatment of acute attacks and prevention of relapses. The treatment of acute attacks is achieved by high-dose intravenous corticosteroids followed by maintenance treatment with oral steroids for 6–12 months depending on the type and severity of the neurological involvement. Immunosuppressants are used to prevent relapses. Oral immunosuppressants such as azathioprine and mycophenolate are the most commonly used. Patients who are refractory or who cannot tolerate these medications can be managed by cyclophosphamide, interferon alpha, or anti-TNF-α monoclonal antibodies such as infliximab, etanercept, and adalimumab [19–21]. All our patients received high-dose intravenous corticosteroids and 3 patients cyclophosphamide for acute attack. Patients requiring cyclophosphamide had poor outcome. The pro-inflammatory cytokines IL-6 and IL-8 are reported to be elevated in the acute and chronic progressive NBD with significant decrease following initiation of treatment and levels of IL-17, IL-21 has also been found to be increased in NBD [22, 23].

The strength of the study is the detailed description of patients with NBD from India wherein the prevalence and index of clinical suspicion is low. The limitation of this study was very small sample size of 12 patients, non-representation of npNBD, lack of detailed medical evaluation for systemic BD and short follow-up. NBD as etiology of dural sinus thrombosis in Indian sub-continent is very rare and NBD is not considered as a cause for dural sinus thrombosis in routine clinical practice. Hence, there was non-representation of npNBD in our cohort.

Conclusion

Patients presenting with lesions in basal ganglia, thalamus, brainstem and cerebellum should be evaluated for NBD. The positive HLA-B5 test and pathergy test is seen

in less than 50% of patients. NBD should be considered as a differential diagnosis in demyelinating CNS disorders, CNS vasculitis in India. The disease is not limited to Middle East and Mediterranean countries. Brainstem and cerebral syndrome are the most common presentation of NBD and thalamus is the most common site of involvement in NBD. Acute and relapsing–remitting pattern of illness has favourable prognosis than the chronic progressive pattern of NBD. HLA B51 testing should be included in the evaluation of CNS demyelinating and vasculitic illness.

Abbreviations
NBD: Neuro-Behcet's disease; HLA: Human leucocyte antigen; mRs: Modified Rankin scale.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s41983-022-00586-3.

Additional file 1: Table S1. International Consensus Recommendation Criteria for NBD

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References:

1. Behcet H. Uber rezidivierende Aphthose durch ein Virus-veursachtr Geschwur am Mund, am Auge und an den Genitalien. Dermatol Monatsschr. 1937;36:1152–7.
2. Kural-Seyahi E, Fresko I, Seyahi N, Ozyazgan Y, Mat C, Hamuryudan V, et al. The long-term mortality and morbidity of Behcet syndrome: a 2-decade outcome survey of 387 patients followed at a dedicated center. Medicine (Baltimore). 2003;82:60–76.
3. Borhani-Haghighi A, Kardeh B, Banerjee S, Yadollahikhales G, Safari A, Sahraian MA, et al. Neuro-Behcet's disease: an update on diagnosis, differential diagnoses, and treatment. Mult Scler Relat Disord. 2019;23(39): 101906.
4. Peño I C, De las Heras Revilla V, Carbonell B P, Di Capua Sacoto D, Ferrer M E F, García-Cobos R, et al. Neurobehçet disease: clinical and demographic characteristics. Eur J Neurol 2012;19:1224–7.
5. Al-Araji A, Kidd DP. Neuro-Behcet's disease: epidemiology, clinical characteristics, and management. Lancet Neurol. 2009;8:192–204.
6. Saip S, Akman-Demir G, Siva A. Neuro-Behcet syndrome. Handb Clin Neurol. 2014;121:1703–23.
7. Kalra S, Silman A, Akman-Demir G, Bohlega S, Borhani-Haghighi A, Constantinescu CS, et al. Diagnosis and management of Neuro-Behçet's disease: international consensus recommendations. J Neurol. 2014;26:1662–76.
8. Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: implications for stroke clinical trials: a literature review and synthesis. Stroke. 2007;38:1091–6.
9. Zhang L, Wang X, Liu F, Zhang Z. Neuro-Behcet disease. Arch Med Sci. 2021;17(2):569–73.
10. Takeuchi H. Acute Neuro-Behçet's disease. Brain Nerve. 2021;73:560–7.
11. Yazici H, Tuzun Y, Pazarli H, Yalcin B, Yurdakul S, Muftuoglu A. The combined use of HLA-B5 and the pathergy test as diagnostic markers of Behçet's disease in Turkey. J Rheumatol. 1980;7:206–10.
12. Akman-Demir G, Serdaroglu P, Tasçi B. Clinical patterns of neurological involvement in Behçet's disease: evaluation of 200 patients. The Neuro-Behçet Study Group. Brain. 1999;122:2171–82.
13. Al-Araji A, Sharquie K, Al-Rawi Z. Prevalence and patterns of neurological involvement in Behcet's disease: a prospective study from Iraq. J Neurol Neurosurg Psychiatry. 2003;74:608–13.
14. Hirohata S, Kikuchi H, Sawada T, Nagafuchi H, Kuwana M, Takeno M, et al. Clinical characteristics of neuro-Behcet's disease in Japan: a multicenter retrospective analysis. Mod Rheumatol. 2012;22:405–13.
15. Talarico R, D'Ascanio A, Figus M, Stagnaro C, Ferrari C, Elefante E, et al. Behçet's disease: features of neurological involvement in a dedicated centre in Italy. Clin Exp Rheumatol. 2012;30:S69–72.
16. Sorgun MH, Kural MA, Yücesan C. Clinical characteristics and prognosis of Neuro-Behçet's disease. EurJ Rheumatol. 2018;5:235–9.
17. Kim SW, Kim T-G, Oh J, Kim D-Y, Choi Y-C, Kim SM, et al. Clinical and radiological characteristics of neuro-Behcet's disease in South Korea. J Clin Neurol. 2019;15:429–37.
18. Bolek EC, Sari A, Kilic L, Kalyoncu U, Kurne A, Oguz KK, et al. Clinical features and disease course of neurological involvement in Behcet's disease: HUVAC experience. Mult Scler Relat Disord. 2020;38: 101512.
19. Caruso P, Moretti R. Focus on neuro-Behçet's disease: a review. Neurol India. 2018;6:1619–28.
20. Uygunoglu U, Siva A. An uncommon disease included commonly in the differential diagnosis of neurological diseases: Neuro-Behçet's syndrome. J Neurol Sci. 2021;15(426): 117436.
21. Hatemi G, Silman A, Bang D, Bodaghi B, Chamberlain AM, Gul A, et al. Management of Behcet disease: a systemic literature review for the EULAR evidence based recommendations for the management of Behcet's disease. Ann Rheum Dis. 2008;67:1656–62.
22. Hirohata S, Kikuchi H. Changes in biomarkers focused on differences in disease course or treatment in patients with neuro-Behçet's disease. Intern Med. 2012;51(24):3359–65.
23. Ben Dhifallah I, Borhani-Haghighi A, Hamzaoui A, Hamzaoui K. Decreased level of IL-37 correlates negatively with inflammatory cytokines in cerebrospinal fluid of patients with Neuro-Behcet's disease. Iran J Immunol. 2019;16(4):299–310.

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