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Tumefactive Neuro-Behçet's Disease: A Case Report and Review of the Literature

Zeynep Kuzu^{1*}, Incisule Ozer¹, Canan Yucesan¹ and Ayse Dursun²

¹Department of Neurology, Ankara University School of Medicine, İbni Sina Hospital, Samanpazarı, Ankara, Turkey

²Department of Pathology, Gazi University School of Medicine, Beşevler, Ankara, Turkey

*Corresponding author: Zeynep Kuzu, Department of Neurology, Ankara University School of Medicine, İbni Sina Hospital, Samanpazarı, Ankara, Turkey, 49500, Tel: 9005393823394, E-mail: drzeynepkuzu@hotmail.com

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Abstract

Aim: Behçet's disease is a multi-systemic autoimmune disease, characterized with recurrent oral-genital ulcers and uveitis. Neuro-Behçet's disease (NBD) may rarely cause tumour like brain lesions.

Methods: Here we present a case of forty-two-year-old Turkish male with tumour like brain lesion whose tissue biopsy result was compatible with necrotic inflammation, perivascular polymorphonuclear leukocytes (PMNL), lymphocytes and other inflammatory cells infiltration. Bacterial and fungal blood cultures were negative. The patient was diagnosed with NBD and was treated with intravenous methylprednisolone 1000 mg/day for 5 days. His neurologic examination improved significantly with the treatment. We evaluated histopathological properties of all biopsy proven cases reported so far in the literature including our case.

Results: When tumour-like lesions were seen in patients who had Behçet's disease in past medical history, NBD should be considered for preventing unnecessary brain operation. Seventy-three percent of all biopsy proven tumefactive NBD cases had inflammatory cell infiltration in the tumour like lesion area.

Conclusion: After excluding infectious aetiology, high dose IV methylprednisolone should be begun as soon as possible in spite of mass effect that is compatible with tumour in brain magnetic resonance imaging (MRI); the good response to steroid supports to the diagnosis of tumefactive NBD. Although most tumefactive NBD patients have inflammatory infiltration in biopsy material why some cases do not have any inflammatory cell infiltration in acute lesion area needs to be clarified in further research.

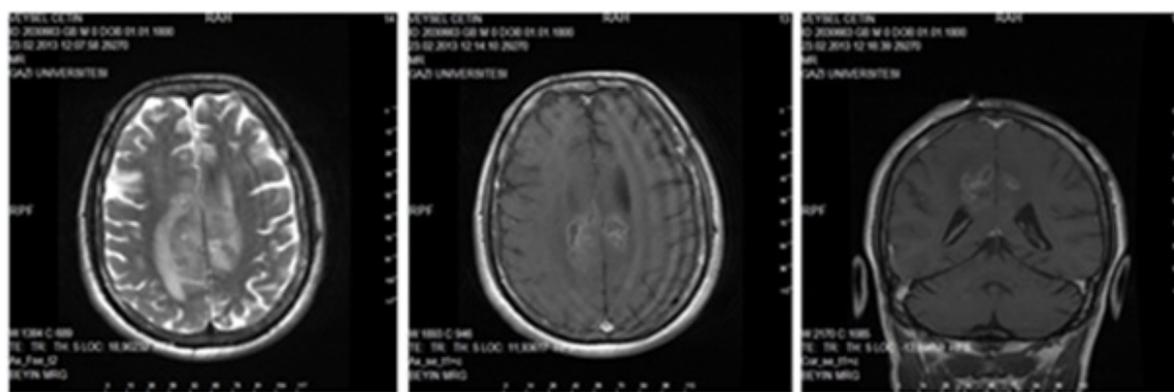
Keywords: Neuro-Behçet's disease; Tumour-like lesions

Introduction

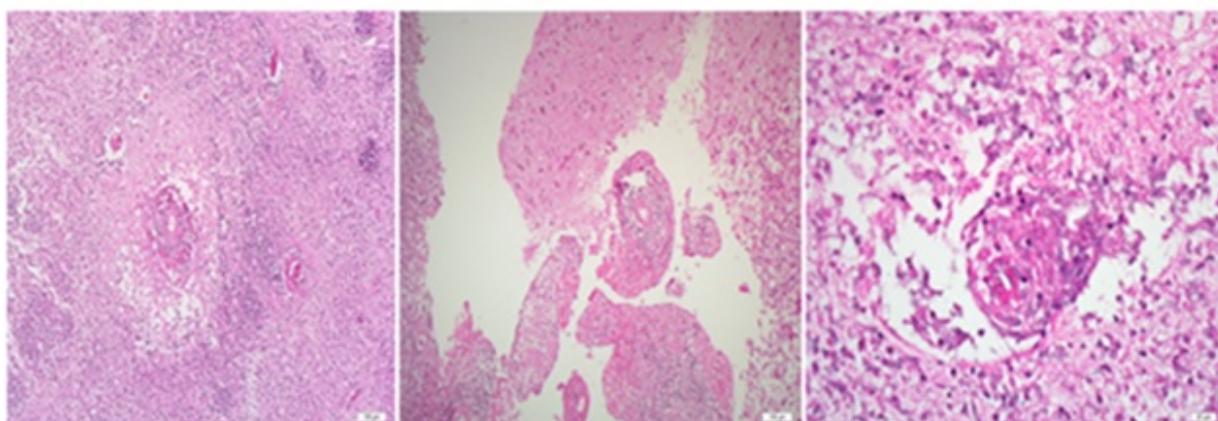
Behçet's Disease (BD) is a multi-systemic autoimmune disease, characterized with recurrent oral-genital ulcerations, uveitis and skin lesions such as erythema nodosum, folliculitis, ulceration and skin pathergy reaction [1]. Neurological involvement (Neuro-Behçet's Disease, NBD) is one of the leading causes of mortality and morbidity in Behçet's Disease [2]. Central Nervous System (CNS) lesions in BD are polymorph and occur in 5.3% of Turkish cases [3]. In addition, men were 2.8 times more likely to experience NBD than women [2]. Clinical patterns of neurological involvement can be categorized as two main groups; those with parenchymal CNS involvement (encephalitis, encephalomyelitis) and those with non-parenchymal CNS involvement. The latter group consisted of cases who had CNS dysfunction due to involvement of major vessels and those who did not show any CNS parenchymal involvement (essentially cerebral venous thrombosis and, rarely, intracranial aneurysms) [3]. The brain magnetic resonance imaging (MRI) lesions are usually localised in brainstem and basal ganglia in parenchymal NBD. There have been 10 biopsy-proven tumefactive NBD case reports in English based literature so far [4-13]. We evaluated histopathological properties of all the cases including our case. We think this may be helpful to comprehend different neuropathological involvement pattern of NBD and may trigger future researches

Case Presentation

Forty-two-year-old Turkish male admitted to a Neurosurgery clinic with a complaint of weakness in the left extremities, sleepiness and secondary generalized seizures in February 2013. Because of contrast enhancing lesions with necrotic core and extensive oedema around the lesions in brain MRI (**Figure 1a**) he was undergone an operation and the result of tissue biopsy was compatible with necrotic inflammation, perivascular polymorphonuclear leukocytes (PMNL), lymphocytes and other inflammatory cells infiltration (**Figure 1b**). Then, he was admitted to our clinic in March 2013.



a)



b)

Figure 1: (a) T2 weighted brain MRI showing hiperintense lesions and T1 weighted images with contrast showing contrast enhancement with necrotic cores in the lesions. **(b)** Lesion biopsy showing perivascular mixed type inflammatory cells infiltrating vessels, causing paraneuronal necrosis and apoptosis. There is not any sign compatible with fibrinoid necrosis. Haematoxylin and Eosin stain (H&E stain) 100x.

Except for erythema nodosum his physical examination was normal. Confusion, amaurosis in the both eyes, left spastic hemiparesis (1/5 in the upper and 3/5 in the lower extremity), Babinski's and Hoffman's signs in the left were found in the neurologic examination. Past medical history revealed that he had Behçet's disease since 1998 and had blindness due to eye involvement of BD since 2009.

Routine complete blood counting and biochemical tests were all normal. C-reactive protein level (45 mg/dl) and erythrocyte sedimentation rate (30 mm/h) were relatively high. Bacterial and fungal blood cultures were negative. Infectious causes including toxoplasma, galactomannan and criptococcus neoformans were also excluded. Brain MRI showed that there was huge increase of previous lesions sizes and numbers (**Figure 2**).

The patient was diagnosed with NBD and was treated with intravenous (IV) methylprednisolone 1000 mg/day for 5 days. His left spastic hemiparesis improved significantly; muscle

power became 3/5 and 4/5 in the upper and lower left extremities, respectively, on the fifth day of the treatment. He was discharged from hospital with oral steroid and pulse cyclophosphamide as maintenance treatment. Control brain MRI three months later showed significant reduction in all the lesions (**Figure 3**).

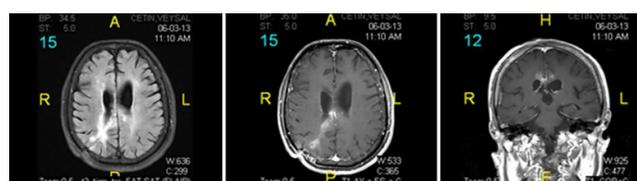


Figure 2: (a) Tumor like lesions at axial FLAIR weighted image, **(b and c)** Peripheral contrast enhancement and necrotic core at T1 sections of MRI with gadolinium.

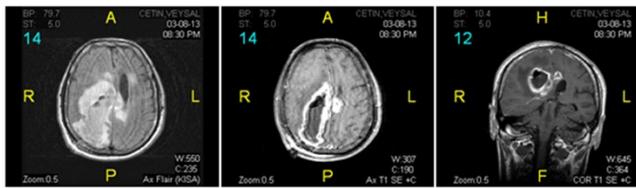


Figure 3: (a) On post treatment images there was significant reduction in lesion size at FLAIR sequence (b and c) Less contrast enhancement and absence of necrotic core in T1 weighted MRI images with gadolinium.

Discussion

CNS lesions in BD are polymorph and occur in 5.3% of cases in Turkey [3]. CNS involvement is one of the most severe manifestations of BD [14]. Sometimes it is difficult to

differentiate from multiple sclerosis, stroke, intracranial hypertension, meningoencephalitis and myelitis. Concomitant systemic signs and symptoms are helpful in differential diagnosis [15].

Because of space-occupying lesion our case was operated at first. Since histopathologic examination revealed perivascular inflammatory infiltration, after excluding infectious causes, he was diagnosed with tumefactive NBD. As previously suggested, he was given high dose steroid and he improved significantly [4].

NBD may rarely cause tumour-like lesion, tumefactive NBD. We searched tumefactive NBD case reports in English based literature and found 10 biopsy proven cases that had mass effect in brain MRI by means of midline shift and/or ventricular compression so far [4-13]. Data regarding age, gender, complaints at admission, neurological symptoms, CNS imaging, histopathologic findings and treatment response were summarized including our case in **Table 1** (11 cases).

Table 1 Characteristics of biopsy proven tumour-like NBD.

Case No	Age/ gender	Complaints at admission	Neurological examination	Brain MRI	Biopsy	Treatment prophylactic	Acute attack/	Response to steroid
1(4)	59/F	Headache, progressive left hemiparesis, lethargy and temporal fits as characterized by sensations of bad smell for the last 24 hours	Left hemiparesis and bilateral papilloedema	Right fronto-temporal mass causing shift of the midline structures suggestive of high-grade glioma	Reactive gliosis associated with panvasculitis, thrombosis, extensive infarction and vascular proliferation	Surgery		Not given
2(5)	47/M	Right hemiparesis, dysarthria, headache and vomiting	Mild right hemiparesis of MRC grade IV and dysarthria	Ring enhancing lesions with subtle perilesional oedema both at the left side of the pons and at the left parietal cortex	Perivascular lymphocytic cuffing, focal necrotic lesion, microglial nodules, foci of necrosis, foamy histiocytic collections, and reactive gliosis	Steroid		Recovery
3(6)	43/M	Headache, photophobia and asthenia	Drowsiness, mild left arm and facial paresis and right eyelid ptosis, without pupillary abnormalities.	2 cm thalamic lesion with mass effect and contrast enhancement	Gliosis with gemistocytic astrocytes, without signs of tumour or vasculitis	Steroid/cyclophosphamide		Recovery
4(7)	50/M	Left hemiparesis and dysarthria	Left hemiparesis and dysarthria	Large neoplasm-like lesion affecting the brainstem, basal ganglia, and white matter of the cerebral hemisphere	Invasion of inflammatory cells in the white matter, especially around the blood vessels.	Steroid		Recovery

5(8)	34/M	Right hemipyramidal syndrome and diffuse headache	Right hemipyramidal signs	Large left capsulo-thalamic lesion with oedema and peripheral contrast enhancement	Necrotic lesions with inflammatory infiltration in the white matter. Multifocal lymphocytic, neutrophilic and macrophagic infiltrate with perivascular distribution.	Steroid/cyclophosphamide	Recovery
6 (9)	33/M	Nausea, vomiting, and headache	Mild right hemiparesis, somnolans	Mass lesion at the left basal ganglia extending to the ventral site of the midbrain, causing compression to the surrounding tissue with cerebral edema.	Mild reactive gliosis without inflammatory cell infiltration	Steroid	Recovery
7(10)	23/M	Headache, fever and progressive right-sided weakness.	Right homonymous hemianopia and mild right spastic hemiparesis	Mass lesion involving the left temporal lobe with signal change extending into the left cerebral peduncle, thalamus, internal capsule, basal ganglia, and corona radiata posteriorly	Perivascular inflammatory infiltrate	Steroid/azathiopirin	Recovery
8(11)	41/F	Mental deterioration and right hemiparesis	Poor mental activity, dysarthria and right hemiparesis.	Lesion of the left lenticulo-thalamic region	Tissue ruled out a tumor but did not show any specific diagnosis	Steroid	Recovery
9(12)	52/F	Dizziness, nausea, and headache, confusion, poor feeding and vomiting	Brun's nystagmus, mild attention deficit, immediate memory impairment, visuo-spatial disorientation, and wide-based unsteady gait	In the right cerebellar hemisphere, posterior medulla, and pons with an isosignal central mass.	Lymphocytic vasculitis involving small and medium-sized vessels (mainly veins) of white matter	Steroid/azathioprin	Not responded and died
10 (13)	38/M	Confusion	Left third nerve palsy, right spastic hemiparesis	Mass-like lesion deep in the left side of the brain. The epicenter was in the left cerebral peduncle with extension into the basal ganglia and the frontal corona radiata, left optic tract, midbrain, left pons, left inferior cerebellar peduncle and left cerebellar hemisphere	Patchy inflammatory infiltrates composed primarily of mononuclear lymphocytic cells and microglial rod cells.	Steroid/azathioprine	Recovery
11 (own case)	47/M	Weakness in the left extremities, sleepiness and seizure	Confusion, amaurosis in the both eyes, left spastic hemiparesis	Right parietal subcortical region, ranging to the body of and corpus callosum and leading to mass effect	Necrotic inflammation, perivascular PMNL, lymphocytes and other inflammatory cells	Steroid/cyclophosphamide	Recovery

CYC: Cyclophosphamide; AZA: Azathioprine

The median age was 43 (range 23-59) years, with a male predominance (72.7%) in patients with tumefactive NBD (**Table 1**). Admission complaints included headache (n=7), paresis (n=7), ataxia (n=5), seizure (n=2), and mental changes (n=5). Other abnormal findings in neurologic examination were aphasia, disturbed consciousness, cerebellar ataxia, hemianopia, memory deficit (**Table 1**). Lesion localisation was mainly in brain stem, basal ganglia or thalamus. Only two cases had lobar lesions (frontotemporal and parietal) without brain stem involvement (1st and 11th cases).

Seventy-three percent of all the cases had inflammatory cell infiltration in the tumour like lesion area. However, 27% of the cases did not have any inflammatory infiltration in spite of acute brain lesion; biopsy may not have taken from acute lesion area in those cases. Otherwise, although blood brain barrier was broken in acute lesion (because all tumefactive lesions were contrast enhancing) inflammatory cell infiltration might not be seen in all cases. May this be related pathologic investigation technique, or may inflammatory infiltration not develop in some acute lesion area? This issue needs to be explained in future researches.

The chosen treatment modalities were mainly corticosteroids during acute attacks (n=10; 91%) and immunosuppressive agents (n=6; 54.5%) such as cyclophosphamide and azathiopurine for preventive treatment (5-13). One patient who had panvasculitis in biopsy material was just operated, not given any medical treatment [4]. Nine out of ten patients (90%) improved completely or partially with steroid; however, one patient did not respond the treatment in her third attack and since she had transtentorial herniation, temporal lobectomy was done and she died later on [12].

For differential diagnosis of tumefactive NBD, space occupying lesions such as glioblastoma multiforme, lymphoma, bacterial abscess or tuberculoma must be considered. Rarely, an inflammatory condition such as sarcoidosis, Wegener's disease, multiple sclerosis (Balo's type) or granulomatous pseudotumour may lead to similar lesions [8]. It has been suggested that histopathological examination may be done to rule out infectious or tumoural diseases and to avoid the inadequate use of immunosuppressive agents in previous reports [14,16,17].

In summary, headache and paresis were the most frequent admission complaints, just compatible with classical parenchymal NBD. The most frequent lesion localisation was brain stem, basal ganglia or thalamus, also was compatible with classical parenchymal NBD; lobar lesions were seen less commonly in tumefactive NBD. Most cases had perivascular inflammatory cell infiltration in biopsy material and respond steroid very well. However, it should be kept in mind that inflammation may not be seen in biopsy material and some cases may not give good response to steroid treatment. Panvasculitis may be seen rarely (9%) in acute tumefactive NBD lesion.

Conclusion

We thought that when tumour-like lesions were seen in patients who had Behçet's disease in past medical history, NBD should be considered for preventing unnecessary brain operation. After excluding infectious aetiology with appropriate investigations, high dose IV methylprednisolone should be begun as soon as possible; the good response to steroid supports to the diagnosis of tumefactive NBD. If there is not good response, then, surgery should be planned as soon as possible. Although most patients have inflammatory infiltration in biopsy material why some cases do not have any inflammatory cell infiltration in acute lesion area needs to be clarified in further research.

Ethics Considerations

On behalf of all authors, the corresponding author states that this research complies with the guidelines for human studies and animal welfare regulations. The subject in our case report has given informed consent and we confirm that the study protocol has been approved by the institute's committee on human research.

On behalf of all authors, the corresponding author states that there is no conflict of interest.

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