Int J Acad Med Pharm, 2021; 3 (1); 64-69

International of Academic Medicine and Pharmacy

Neuroimaging Manifestations of Behcet's Disease: A Retrospective Study from the Eastern Mediterranean Region of Turkey**

Gülen Burakgazi [1]* , Fatma Duman [2]

[1] Recep Tayyip Erdoğan University, Faculty of Medicine, Department of Radiology, Rize, Turkey
[2] Hatay Mustafa Kemal University, Faculty of Medicine, Department of Anatomy, Hatay, Turkey

ORCID; 0000-0003-4913-4838, 0000-0001-5747-9989

Article info **Research article**

Received :22.08.2020
Received in revised form :07.11.2020
Accepted :02.11.2020
Available online :05.01.2021

Keywords

Headache
Neuro-Behçet's disease
Magnetic resonance imaging

Abstract; In this article, we aimed to emphasize the importance of neuroimaging together with neurological examination in the early diagnosis and treatment of cerebrovascular pathologies in Behçet's disease (BD), in terms of diagnosis, differential diagnosis and prevention of complications. A retrospective evaluation was made of cases diagnosed with BD disease who presented at our hospital with neurological findings between 2010 and 2017. Multi-slice computed tomography and magnetic resonance images obtained from these patients were retrospectively evaluated. Retrospective evaluation was made of a total of 121 patients (63 males, 58 females) with neurological symptoms who underwent neuroimaging. The most common symptom was headache and the most common finding (89%) determined was in the brain parenchyma. Of the vascular origin pathologies, thrombus in the superior sagittal sinus was most often determined (15%). Early diagnosis of neurological findings in BD is important in respect of preventing cerebrovascular complications.

INTRODUCTION

Behçet's disease (BD) is a systemic disease characterized by recurrent oral and genital ulcers, uveitis, arthritis, arterial aneurysms, venous thrombosis, skin lesions and gastrointestinal lesions. In this chronic vasculitis disease, the etiology of which is not known, neurological symptoms are seen in 4%-49% of patients. These can include, meningitis, meningoencephalitis, cranial nerve paralysis, and psychiatric symptoms [1,2].

Neurological involvement is seen in approximately 11% of BD patients and this involvement is one of the most destructive findings of BD [3]. BD may emerge first with neurological symptoms and findings. The first finding of Neuro -Behçet's disease (NBD) in BD patients is usually headache of a benign nature. Although headache types have been defined for NBD, careful neurological examination must be made of BD patients with headache and neuroimaging should be applied. In the differential diagnosis of NBD, intracranial tumor, aseptic meningitis and multiple sclerosis should be considered. This condition in BD can mask the potentially fatal complication of NBD findings [4,5]. In most cases, diagnosis with clinical examination alone is difficult. Neuroimaging in addition to clinical findings plays an important role in both diagnosis and in the evaluation of complications [6]. Neuroimaging is typically applied for headache that is suggestive of intercranial (intracranial?)pathology. Previous studies have shown that imaging of headache in the absence of neurological symptoms in BD or atypical characteristics does not reveal a visible abnormality. The widely accepted view for neuroimaging in cases with headache, is that of red flag symptoms and findings, the presence of focal neurological findings despite appropriate treatment, and sudden onset and progressive neurological findings during the course of systemic disease [7].

The aim of this study is to present the neuroimaging findings of BD patients with neurological symptoms in the light of the literature.

MATERIALS and METHODS

Ethical approval

Approval was obtained from the relevant university clinical research ethics committee (Ethics No: 2018/156). The study was also carried out in accordance with the Helsinki

*Corresponding author: Gülen Burakgazi, E-mail; burakgazigulen@gmail.com, http://dx.doi.org/10.29228/jamp.47105
** The manuscript has been oral presented in 26th international symposium on morphological sciences, 05/07/2018, Prag.

Declaration of Principles.

Patients and study design

A retrospective evaluation was made of 121 patients (63 males, 58 females), with neuroimaging and without systemic disease from 197 patients, diagnosed with BD who presented at our hospital with neurological symptoms between 2010 and 2017. Cases diagnosed by a senior neurologist or internal medicine physician were selected from the archive. Since it is a retrospective study, there is no information about their treatment.

The multi-slice computed tomography (MSCT) and magnetic resonance images (MRI) acquired from these patients were evaluated retrospectively. The MSCT images were obtained using a 64-detector Toshiba device, and the MRI using a 1,5 Tesla Philips Achieva device. The images were evaluated on a workstation by a specialist radiologist. The brain arterial and venous vascular structures were evaluated on 3-dimensional reformatted images obtained from MR angiography (MRA) and MR venography (MRV).

RESULTS

Retrospective evaluation was made of 121 patients comprising 63 (52.1%) males and 58 (47.9%) females with a mean age of 36±1.17 years (range, 18-77 years). When the clinical symptoms were examined, 89.26% of patients were seen to have presented at hospital with complaints of headache (Table 1). Other symptoms were neck pain, dizziness, fainting, loss of balance and speech impairment.

Table 1. Associated clinical symptoms

	N	%
Headache	108	89.26
Neck pain	3	2.48
Dizziness	25	20.66
Position dizziness	1	0.83
Fainting	1	0.83
Loss of balance	2	1.65
Speech disorder	2	1.65

On the brain MRI, parenchymal involvement was observed in 30.6% of cases, vascular involvement in 8.3%, and both vascular and parenchymal involvement in 7.4% (Table 2). The brain MRI, MRA, MRV, diffusion MRI and MSCT findings of all the patients were examined in detail (Table 3). From the findings observed on the images obtained from the cases, pathology was determined at the rate of 56.20% on MRI, 5.78% on MRA, 40.50% on MRV, 13.22% on diffusion MRI and 4.96% on MSCT. The presence of pathology was determined most on conventional brain MRI. The most common finding on MRI was non-specific ischemic focus in 71.90% (Figure 1). On the MRV examination, sinus thrombus (Figure 2) and hypoplasia were determined. In the transverse sinus of one patient, widespread collaterals were observed to have developed secondary to chronic thrombus (Figure 3).

Table 2. Classification of MRI findings according to location

	N	%
Parenchymal finding	37	30.6
Vascular finding	10	8.3
Parenchymal and vascular finding	9	7.4
Normal	63	52.1
No conventional MRI	2	1.7
TOTAL	121	100.0

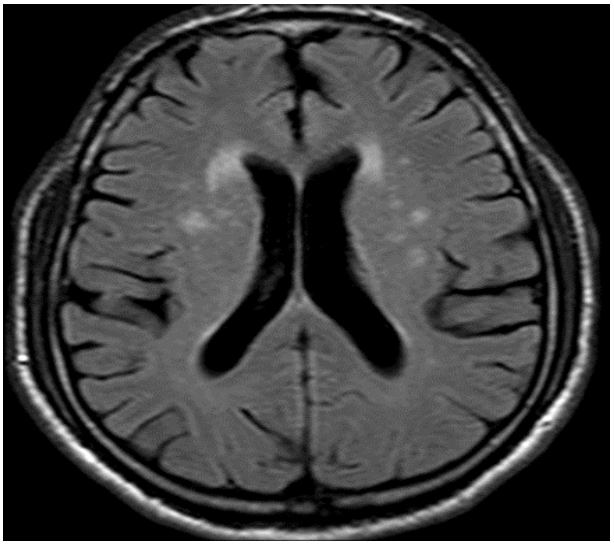

Figure 1. Axial FLAIR sequence; there are hyperintense non-specific foci in the bilateral periventricular area

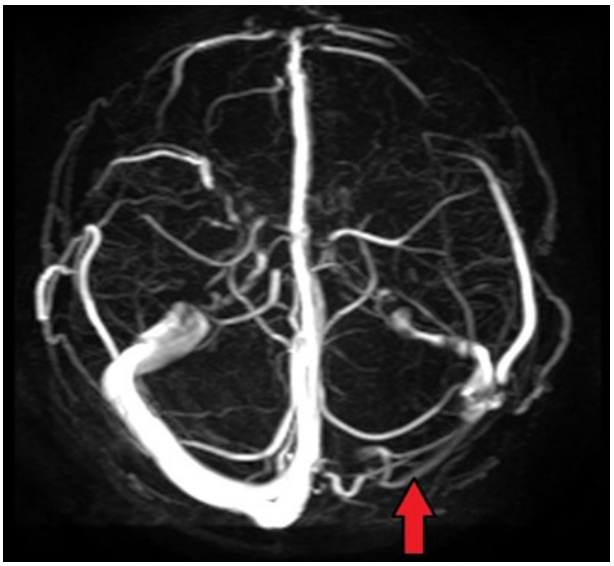

Figure 2. In the patient with Behçet's disease, the absence of flow indicating the presence of thrombus in the left transverse sinus is observed in MRV images.

Table 3. Findings of different imaging methods of the cases.

		MRI		MRA		MRV		DİF-MRI		MDCT	
		N	%	N	%	N	%	N	%	N	%
Normal		68	56.20	7	5.78	49	40.50	16	13.22	6	4.96
Intensity increase in brainstem and cerebellum		1	0.83	-	-	-	-		-	-	-
Nonspesific focus		87	71.90	-	-	-	-		-	1	0.83
Atrophy	Cerebral	8	6.61	-	-	-	-	-	-	3	2.49
	Cerebellar	1	0.83	-	-	-	-	-	-	-	-
	Brainstem	2	1.65	-	-	-			-		-
	Diffuse	1	0.83	-	-	-	-	-	-	-	-
	Thalamus	2	1.65	-	-	-	-	-	-	-	-
Capsula interna infarction		-	-	-	-	-	-	-	-	1	0.83
Thrombus	Transverse sinus	-	-	-	-	15	12.40	-	-	-	-
	Sigmoid sinus	-	-	-	-	1	0.83			-	-
Hypoplasia (Transverse sinus)		-	-	-	-	4	3. 31	-	-	-	-

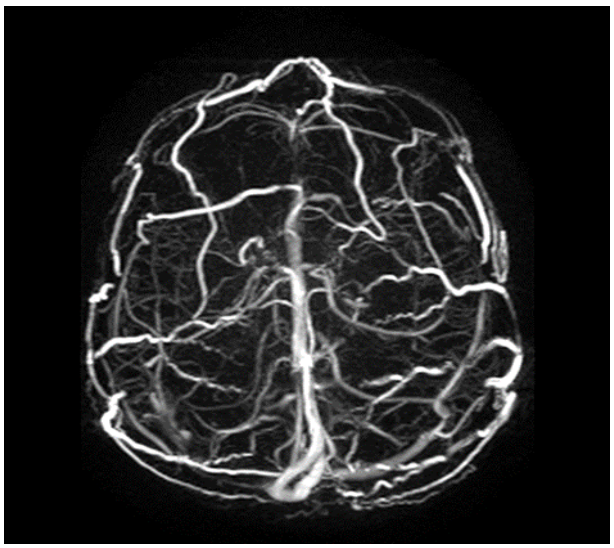

Figure 3. In patients with Behçet's disease, absence of current in the bilateral transverse sinus secondary to chronic thrombosis and widespread collateral flow are observed in MRV images.

On the brain MRI analysis, non-specific ischemic focus were seen most at the rate of 27.59% with periventricular localization (Table 4). In the MSCT taken first because of neurological symptoms in one case, other than chronic ischemic changes, no pathological finding was determined radiologically.

In 10 (8.26%) patients, pathology was determined on conventional brain MRI, and the MRV examinations of the same patients were observed to be normal. In 12 (9.92%) patients, pathology was determined on MRV, and the conventional MRI examinations were evaluated as normal. While diagnosing of cerebral venous thrombosis (CVT), we evaluated MRV with conventional MRI examinations, clinical and laboratory findings of the cases. In addition, there were findings such as collateral circulation developing secondary to thrombus and presence of reanalyzed flow in the control MRV examinations of the cases.

When the formation of thrombus or findings of parenchymal or vascular involvement were examined, no statistically significant difference was determined between the genders (p>0.05) (Table 5).

Table 4. Location of nonspecific ischemic foci in MRI examination

	Bilateral		Unilateral Left		Right	
	N	%	N	%	N	%
Frontal	2	2.30	2	2.30	-	-
Parietal	-	-	1	1.15	-	-
Occipital	-	-	2	2.30	-	-
Periventricular	24	27.59	2	2.30	1	1.15
Sentrum semiovale	15	17.24				
Brainstem	1	1.15				
Subkortical white matter	1	1.15				
TOTAL	79	90.81	7	8.05	1	1.15

Table 5. Gender distribution of findings

	Female		Male			
	N	%	N	%	X^2	P
Thrombus	6	10.3	10	15.9	0.804	0.370
Parenchymal involvement	14	24.1	23	36.5	2.305	0.129
Vasculer involvement	4	6.9	6	9.5	0.307	0.580

DISCUSSION

The most important findings of this study were; parenchymal involvement was observed in the majority of cases, cerebral atrophy observed more common, non-specific foci were seen high percentage and specially in the periventricular area, the

most widespread symptom was headache, thrombus mostly seen in transverse sinus and there was no significant difference in findings between gender ($p>0.05$).

Neuro-Behçet's disease (NBD) generally emerges in two forms as parenchymal or non-parenchymal (vascular) involvement. There may also be a mixed type of parenchymal and non-parenchymal involvement together [8]. Although parenchymal involvement was observed in the majority of the current study patients, there were also recorded cases of vascular and mixed-type involvement. Parenchymal disease primarily affects the brain stem, cerebral hemisphere and the spinal cord [9].

The most common form of NBD (80%) is an inflammatory perivasculitis in the form of subacute meningoencephalitis usually involving the brain stem. Involvement in this form is typically in the unilateral thalamus and basal ganglions. Thalamus involvement was determined in 2 cases in the current study, which was consistent with findings in literature of parenchymal involvement (Figure 4).

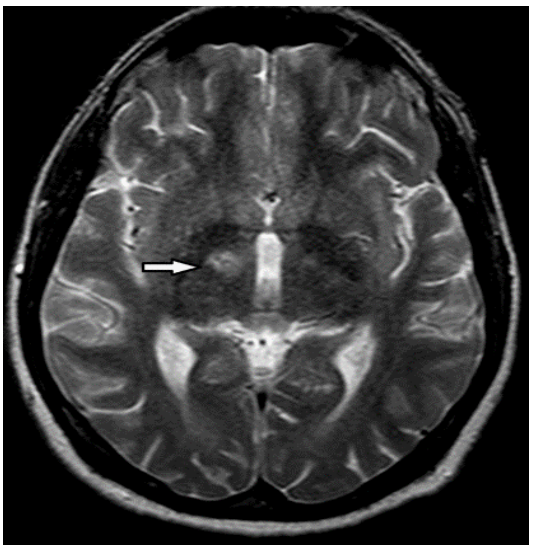

Figure 4. A patient with Behçet's disease has a hyperintense appearance in the axial T2W sequence secondary to involvement in the right thalamus.

Recent studies have shown that there is inflammatory cellular infiltration around the peripheral small venules and arterioles of parenchymal lesions in NBD, and the consequent demyelinisation leads to edema [10,11]. In vascular involvement, cerebral venous thrombus is often seen (20%), and thrombus can cause increased intracranial pressure. In the current study, although pathological findings of the parenchyma were determined most, there were also vascular findings at a noteworthy rate.

MSCT has been reported to be non-diagnostic in parenchymal brain lesions [12]. In the MSCT evaluations of the current study cases, capsule interna infarct was observed in one patient and cerebral atrophy in eight. Although cerebral atrophy could be a finding of chronic BD and it is known that it could accompany several neurological diseases, it is a non-diagnostic finding. In 6.6% of the current study patients, findings consistent with atrophy were observed, usually in the cerebrum. The average age of the patients with atrophy was 51.7 year (the range of 27-77 year). In the youngest case, cerebral, cerebellar and brainstem atrophy was observed. All cases were in the chronic stage and in some of them, there was concomitant atrophy in the cerebellum and brain stem [13,14].

Brain MRI is the most frequently used imaging method in patients with suspected NBD. In the acute disease course, lesions are seen in the basal ganglion or the brain stem, extending to the diencephalic structures, and in some, an increase in central contrast is seen with the mass effect. MRI T2-weighted and FLAIR (fluid-attenuated inversion recovery) sequences are used for the determination of ischemic or gliotic changes and ischemic white matter lesions. On T2-weighted images, the MRI findings are usually high signals from areas of the cerebral central structures with scattered localization affecting the cerebral peduncle and pons [10,13,14]. In the MRI examinations of the current cases, non-specific foci were generally seen. These were most often in the periventricular area and were observed bilaterally at a high rate. Hyperintense foci can be seen at a high rate in T2A in MRI examination in the normal population [15]. Therefore, this finding in present study cannot be associated primarily with Neuro-Behçet disease.

In the diffusion MRI and MRA examinations obtained from the cases with acute neurological findings, no pathological findings were determined. In cases with neurological findings on diffusion MRI and MRA, advanced imaging methods should be applied.

Although no consensus has been reached on NBD, diagnosis is generally made from the presence of lesions consistent with neuroimaging in BD patients with neurological symptoms or headache. A relationship has been found between NBD and the frequently seen symptom of headache in 10%-15% of BD patients, and even if there is no central nervous system involvement, it has been emphasized in literature that headache can be seen as a widespread symptom [8,14,16-18]. In the majority of the current study patients (89%), headache was

seen to be the first symptom on presentation at the polyclinic. Headache is important in parenchymal involvement and in vascular involvement. The most typical feature of headache in our cases is sudden onset, and was not in a typical localization.

Headache has been reported to be the most common and the most important symptom in 80% of cases with cerebral venous thrombosis. Generally in BD, it is the first, and sometimes the only finding, which is severe, general, and progressive and increases with the Valsalva maneuver. Furthermore, in 2% of patients with venous thrombosis an association has been found with NBD [19,20]. In the current study, it was noticeable that headache was the most frequent symptom in the cases determined with cerebral venous thrombosis. In addition to headache, other complaints of the cases were recorded as neck pain, dizziness, fainting, loss of balance and speech impairments.

CVT may be seen at the rate of 3.6% in BD and it may be the first finding before diagnosis or it may emerge in the course of the disease. CVT is seen in the superior sagittal sinus, transverse sinus, sigmoid sinus and the straight sinus [8,21,22]. In the present study, CVT was seen most often in the transverse sinus and thrombus was observed in the sigmoid sinus in only one patient.

In neuroimaging using MRI and MRV together, dural sinus thrombosis and parenchymal lesions can be easily determined [23,24]. When the MRI and MRV tests were evaluated, the findings were determined to show a difference. In cases determined with pathological signal intensity increase at the rate of 8.26% on MRI, the MRV examination was normal, and in cases with pathological change determined on MRV at 9.6%, the MRI tests were normal. Therefore, for NBD diagnosis in BD patients, MRI and MRV must be evaluated together. This evaluation can be considered useful for both early diagnosis and differential diagnosis.

CONCLUSION

In BD, the symptom of headache is an important symptom showing intracranial pathologies. Several studies have shown that in the absence of neurological symptoms or atypical clinical characteristics, imaging methods in cases with headache have revealed findings of the rarely seen Neuro-Behçet's disease. Therefore, in BD cases with headache and no accompanying neurological symptoms, neuroimaging should be performed. When there is new onset of headache in BD, and when the severity of headache increases, NBD should be considered without examination for the presence of neurological findings, and neuroimaging should be performed. Neuroimaging is extremely important in diagnosis, differential diagnosis, early initiation of treatment, and in the prevention of complications. As NBD can be seen secondary to parenchymal and/or vascular involvement, advanced imaging methods and MRV should be added to conventional MRI.

Conflict of interest

No conflict of interest was declared by the authors.

Financial disclosure

The authors declared that this study hasn't received no financial support.

REFERENCES

1. Hegde AN, Mohan S, Lath N et-al. Differential diagnosis for bilateral abnormalities of the basal ganglia and thalamus. *Radiographics*. 2011; 31(1):5-30.
2. Tunc R, Saip S, Siva A: Cerebral venous thrombosis is associated with major vessel disease in Behcet's syndrome. *Ann Rheum Dis.* 2004; 63:1693-1694.
3. Davatchi F, Chams-Davatchi C, Shams H et al. Adult Behcet's disease in Iran: Analysis of 6075 patients, Int. *J. Rheum Dis.* 2016; 19(1):95-103.
4. Topcuoglu OM, Topcuoglu ED, Altay CM, Genc S. Imaging pearls of pediatric Behçet's disease. *Eur J Radio*l. 2017; 94:115-124.
5. Fountain EM, Dhurandhar A. Neuro-Behçet's disease: an unusual cause of headache. *J Gen Intern Med.* 2014; 29(6):956-960.
6. Mehdipoor G, Davatchi F, Ghoreishian H, Arjmand Shabestari A. Imaging manifestations of Behcet's disease: Key considerations and major features. *Eur J Radiol.* 2018; 98:214-225.
7. Tsushima Y, Endo K. MR Imaging in the evaluation of chronic or recurrent headache. *Radiology.* 2005; 235(2):575–579.
8. Al-Araji A, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. *Lancet Neurol.* 2009; 8 (2):192–204.
9. Kabukcu T, Edemci S, Ucan H, Celik C, Gunes HN, Yoldas T, Whole thoracal spinal cord involvement in case of neuro-Behcet's disease. *Rheumatol*. Int. 2009; 29(6):707–709.

   Akman-Demir G, Serdaroglu P, Tasçi B. Clinical patterns of neurological involvement in Behçet's disease: evaluation of 200 patients. *Brain*. 1999;122(11):2171–2182.

11. Haghighi AB, Sharifzad HR, Matin S, Rezaee S. The pathologicalpresentations of neuro-Behcet disease: a case report and reviewof the literature. *Neurologist*. 2007;13:209-214.
12. Banna M, El-Ramahl K. Neurologic involvement in Behcet disease: imaging findings in 16 patients, *AJNR Am. J. Neuroradiol.* 1991; 12 (4):791–796.
13. Abdel Razek AA, Alvarez H, Bagg S, Refaat S, Castillo M. Imaging spectrum of CNS vasculitis. *Radiographics.* 2014; 34(4):873-894.
14. Al Kawi MZ, Bohlega S, Banna M. MRI findings in neuro-Behcet's disease. *Neurology.* 1991; 41(3):405–408.
15. Figatowska MB. T2-hyperintense Foci on Brain MR Imaging. *Med Sci Monit*. 2004 ;10 Suppl 3:80-87.
16. Siva A, Kantarci OH, Saip S, et al. Behçet's disease: diagnostic and prognostic aspects of neurological involvement. *J Neurol.* 2001; 248(2):95–103.
17. Farahangiz S, Sarhadi S, Safari A, Borhani-Haghighi A. Magnetic resonance imaging findings and outcome of neuro-Behçet's disease: the predictive factors. *Int J Rheum Dis*. 2012;15(6): e142 -149.
18. Ndıaye M, Sow AS, Valıollah A et al.: Behçet's disease in black skin. A retrospective study of 50 cases in Dakar. *J Dermatol Case Rep*. 2015; 9:98-102.
19. Ferro J.M, Canhao P. Cerebral venous sinus thrombosis: update on diagnosis and management, Curr. *Cardiol.* Rep. 2014; 16 (9):523.
20. Souirti Z, Messouak O, Belahsen F. Cerebral venous thrombosis: a Moroccan retrospective study of 30 cases. *Pan Afr Med J.* 2014;14;17:281.
21. Rottenstreıch A, Machol K, Eısenstein EM et al. Behçet's disease and cerebral sinus vein thrombosis in children: a case study and review of the literature. *Clin Exp Rheumatol*. 2015;33 (Suppl. 94): S163-8.
22. Aguiar de Sousa D, Mestre T, Ferro J.M. Cerebral venous thrombosis in Behcet's disease: a systematic review, *J. Neurol.* 2011; 258(5): 719–727.
23. Bonneville F. Imaging of cerebral venous thrombosis, *Diagn. Interv. Imaging.* 2014; 95(12):1145–1150.
24. Kocer N, Islak C, Siva A et al. CNS involvement in neuro-Behçet syndrome: an MR study. *AJNR Am J Neuroradiol*. 1999; 20:1015-24.