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Research Paper

Manifestations of Neuro- Behçet Disease: Acase Series Study

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ABSTRACT:

BACKGROUND:

Behçet disease is an idiopathic chronic relapse multi-systemic vascular-inflammatory disease of unknown origin. Central nervous system involvement is considered one of the most severe manifestations of the disease, and it is categorized into primary or secondary. The primary neuro-Behçet disease can be sub-classified into parenchymal and non-parenchymal disease.

OBJECTIVE:

To identify neuro-Behçet disease clinical and radiological manifestations, and categorize the various presentations into characteristic patterns.

PATIENTS AND METHODS:

A case series study was conducted in Iraqi hospitals and outpatient clinics from March 2022 to December 2022. Demographic data of the patients and the duration of BD at the time of NBD diagnosis were recorded. The patients were clinically re-assessed for the fulfillment of Behçet disease diagnostic criteria. The enrolled patients were evaluated by neurologists in each province, for the manifestations of neuro-Behçet disease, whether current or previous presentation. Henceforth, a revision of patients' radiological reports was recorded.

RESULTS:

There were 80 patients in this study; the mean age of patients was 31.7 ± 9.1, with male predominance (62%). The mean duration of Behçet disease at neuro-Behçet diagnosis was 2.8 ± 2.4 years.

Regarding cumulative clinical manifestations, parenchymal symptoms were the most common, predominantly brainstem syndrome (67.5%). Non-parenchymal manifestations such as venous sinus thrombosis and pseudotumor cerebri presented in 46.3% of patients with Behçet disease. MRI findings reflected the clinical picture, with parenchymal involvement (55.1%) and brainstem hyperintensity being the most common (40%), followed by venous sinus thrombosis (43.8%).

CONCLUSION:

Behçet disease neurological manifestations occurred mainly in men in their thirties to forties, and the majority of them presented within 2.8 years of Behçet disease onset. Brainstem involvement is the most common presentation. However, the disease can also present with a wide range of symptoms. CVST pattern of the disease was prevalent in Iraq. Radiologically, brainstem hyperintensity is the most common finding in parenchymal NBD.

KEYWORDS: Neuro- Behçet disease, Brainstem syndrome, cerebral venous sinus thrombosis, Behçet disease.

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INTRODUCTION:

Behçet's disease (BD) is an idiopathic chronic relapsing vascular-inflammatory disease that affects multiple systems(1).

The diagnosis of Behçet disease is clinically based. According to the work of the International Study Group, the criterion set assigns 2 points for oral ulcer, genital ulcer, and ocular lesions and 1 point for neurological, vascular, and positive pathergy test results. Scoring 4 points or more is required to diagnose the patient with Behçet disease(2).

Neurological manifestations of Behçet's disease are presented variously and reported in 1% to 49% of cases(3). These manifestations can be categorized further into primary or secondary(3). Primary

nervous system involvement in Behçet disease, "neuro-Behçet syndrome" (NBS), is defined as the development of neurologic features in a patient with Behçet disease that cannot be explained by another disease or treatment and in which objective abnormalities are found either on neurological examination or supported neuroimaging or cerebrospinal fluid (CSF) findings consistent with NBS[4]. Clinical data and neuroimaging demonstrate two main patterns of primary NBD parenchymal and non-parenchymal. Clinical, therapeutic, and prognostic implications are presumed to be associated with this classification[4].

The most common neurological pattern of Behçet disease is parenchymal CNS involvement, which can be focal or multifocal. Parenchymal involvement of NBD frequently presented with brainstem or corticospinal tract syndromes, with subacute brainstem syndrome representing the most common presentation, which may involve all or some of the neurological signs and symptoms[16].

Cognitive-behavioral changes and sphincter dysfunctions usually precede or accompany other brainstem symptoms (brainstem-plus type). Remarkably, cranial nerve palsies have not frequently presented as would be expected, and sensory symptoms are rarely reported (5,6). Other manifestations that may presented include myelopathy either in isolation or accompanying other CNS findings (spinal-plus type)[7], urinary sphincter dysfunction, and, to a much lesser degree, extrapyramidal signs and seizures.

Cerebral venous sinus thrombosis (CVST) or, rarely, extra-parenchymal major arteries involvement are the main presentations of non-parenchymal disease. 10% to 20% of patients with Behçet disease who have neurological involvement present with cerebral venous sinus thrombosis (CVST)[8]. The superior sagittal sinus is the most frequently affected; however, a significant percent of these patients also have lateral sinus thrombosis, which is the most common involvement site in female patients with Behçet disease, as has been reported[9,10].

Despite the rarity of the mixed pattern (parenchymal and non-parenchymal) occurrence, it had been reported in the previous study by Al-Araji[18].

MRI findings may include parenchymal lesions within the brainstem, which may have occasional extension to the diencephalon, and less frequently periventricular and subcortical white matter involvement (11); non-parenchymal venous sinus thromboses, in which the occluded dural sinus is frequently observed on MRI with the relative absence of venous infarcts that expected to be present with other causes of dural sinus thrombosis[12] ; and spinal cord involvement can affect the spinal cord with inflammatory lesions that in the majority of patients are longitudinally extensive, affecting three segments or more[9,13,14].

The manifestations of NBD in Iraq have been studied previously by Al-Fahad in 1999 and Al-Araji in 2003[16,18]. However, there was no other study that addressed NBD in Iraq since. In our study, we tried to shed light on NBD and determine changes in patterns of presentation that have occurred particularly with the better awareness and diagnostic tools that are available now.

PATIENTS AND METHODS:

A descriptive case series study was conducted in neurology units of tertiary centers and clinics in Iraqi provinces from March 2022 to December 2022. The study recruited 80 patients who met the inclusion criteria of the study. The age of patients involved in the study was 18 years or older. All the patients were diagnosed with Behçet disease by rheumatologists and re-evaluated by neurologists according to the International Study Group's major diagnostic criteria for Behçet disease to fulfill Behçet disease diagnosis. Exclusion of the conditions or medications that might simulate NBD presentation was ensured before recruitment.

We used a modified structure questionnaire paper when evaluating the patients after obtaining their written consent. Neurologists performed a clinical evaluation for all participants. The data collected involved the demographic data (age, gender), duration of Behçet disease before neuro-Behçet disease diagnosis, and clinical manifestations such as parenchymal involvement (brainstem syndrome, stroke-like, cognitive, and spinal cord involvement) and non-parenchymal involvement (CVST and pseudotumor cerebri), meningitis-like episodes, seizure, and peripheral nervous system involvement.

A revision of the patient's MRI, using a 1.5 tesla MRI scanner (Philips Achieva nova, dual 16 channel, Netherlands) was recorded by neurologists in each province, in addition to reviewing of MRI brain with gadolinium contrast, MRV, and spinal cord MRI from the time of their neurological manifestations.

The diagnosis of Behçet disease was confirmed by

Rheumatologists in the provinces and reviewed by the assessing neurologists.

Statistical analysis:

Microsoft Excel 2010 and IBM SPSS version 24 were used for data entry, management, and analysis. Descriptive statistics of the variables were expressed as percentages and Mean±SD. The X2 test was used to test for associations between variables. P value at < 0.05 was considered to be significant.

RESULTS:

The demographic characteristics of the study population are shown in (figure 1). The mean age of patients was 31.7 ± 9.1 years (range 18 – 59 years) and males presented 62.5% of patients with a male-to-female ratio of 2:1.

The mean duration of Behçet disease at Neuro-Behçet disease diagnosis was 2.5 ± 2.4 years (Ranging 0 – 10 years) (Table 1).

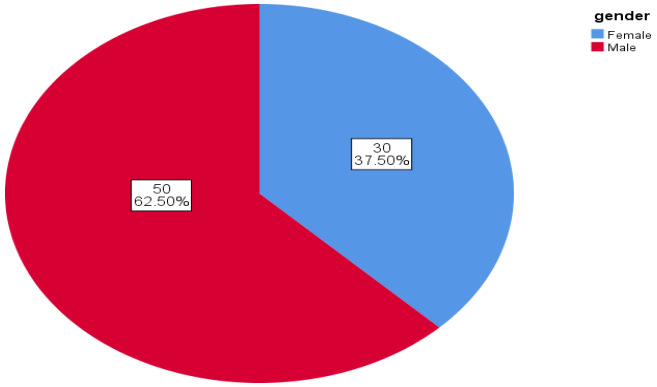

Figure 1: Gender distribution across participants.

Table 1: Descriptive Statistics of mean duration of Behçet disease at Neuro- Behçet disease diagnosis.

Duration of DB at NBD Diagnosis	n	n%	Minimum	Maximum	Mean
After BD diagnosis	70	87.50%	0.08	10	2.82
At presentation	10	12.50%			

The cumulative frequency of Neuro-Behçet disease manifestations is given in the table below, showing that the majority of the patients developed brainstem manifestations (67.5%).

Table 2: Cumulative frequency of all neurological signs and symptoms in 80 patients with Neuro-Behçet disease.

Neurological signs and symptoms	n	n%
Brainstem involvement	54	67.50%
Cranial nerves involvement	35	44.10%
Sphincter disturbance	18	22.50%
Cognitive-behavioral changes	14	17.50%
Spinal cord involvement	11	13.80%
Increase ICP and CVST	37	46.30%
Stroke like event	28	35.00%
Meningitis like event	3	3.80%
Seizure	25	31.30%
Sensory manifestations	1 (CIDP)	1.30%
	1 (Lumbosacral neuritis)	1.30%

Regarding brainstem involvement, the pyramidal signs and symptoms were the most common feature (figure 2).

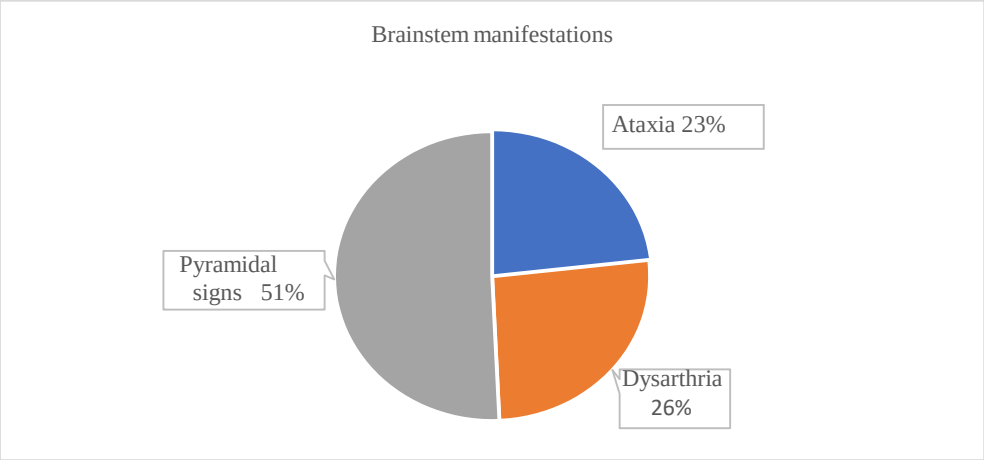

Figure 2: Brainstem involvement in NBD.

The MRI characteristics for patients are given in the table below.

Table 3: MRI CNS involvement patterns.

Radiological features	n	n%
Brainstem hyperintensity	32	40.00%
cortical hyperintensity	3	3.80%
periventricular/ subcortical hyperintensity	9	11.30%
Increased intracranial pressure	3	3.80%
venous thrombosis	35	43.80%
myelitis	10	12.50%
normal	2	2.50%

Neuro- Behçet disease diagnostic criteria are given in (table 4).

Table 4: Diagnosis criteria for Neuro-Behçet disease.

Major criteria	n%
Oral ulcer (3/ year)	97.50%
Genital ulceration	88.80%
Skin lesions	28.70%
Eye involvement	51.2% (Anterior uveitis)
	2.5% (both)
	11.3% (posterior uveitis)
Pathergy test	75.00%

DISCUSSION:

The primary central nervous system involvement of Behçet disease (BD) is heterogeneous. It can potentially present with two clinical patterns; parenchymal or non-parenchymal venous sinus thrombosis lesions[1,16,18].

In this study, the males were prevalent (62.5%). This finding comes along with other studies that showed NBD was significantly more common in men, as men are more likely to develop a severe disease course and to be more likely to be hospitalized [15,16].

The age of patients in this study was comparable with other studies that showed the mean age in the third to fourth decades [16,17,18].

In this study, most patients developed neurological manifestations after BD diagnosis in a period ranging from 1 month to 10 years (in 2 patients in this study). This period of disease development was similar to previous studies. Similarly, 10 of the enrolled patients presented with NBD at the onset of Behcet disease, such an early presentation was reported in the previous studies [16,19].

Regarding NBD manifestations, the majority of patients had parenchymal disease, with brainstem manifestations being the most common, which was comparable to reports from previous studies [16,18]. However, CVST in our study was a relatively common presentation, a pattern that has been reported by both Al-Fahad 1999 and Al-Araji 2003[16,18] and also frequently reported in the Middle East and France but less often in other countries[20,21,22]. CVST prevalence in these regions might be explained by a genetic predisposition for CVST or environmental factors.

Spinal cord involvement, stroke-like and meningitis-like events in this study were higher than previously reported by Al-Fahad 1999 and Al-Araji studies[16,18]. However, it was close to what was reported in another study in the Middle East[20]. This difference might be attributed to a greater awareness among neurologists of the prevalence and variable manifestations of the disease, as well as the larger number of patients in this study.

Sensory involvement was rare, which was similar to other studies[18]. The two reported cases of sensory involvement in this study were chronic inflammatory demyelinating polyneuropathy and lumbosacral neuritis.

Cranial nerve involvement in NBD was common in our study, which is similar to the study previously conducted by Al-Fahad (1999) and Al-Araji in 2003 in Iraq[16,18]. However, this finding was in contrast to other studies. The frequent involvement of the abducens nerve secondary to CVST might be the reason for cranial nerve involvement's high prevalence.

In this study, seizures (31.3%) were more frequently reported in comparison with the previous studies by Al-Araji (5%)[18] and Turkish studies (16.7%)[23]. the larger number of CVST cases as the cause of seizures in our study might explain the seizures' higher frequency.

In this study, the majority of patients had a parenchymal involvement (55.1%) with brainstem hyperintensity on MRI (40%), while cerebral venous thrombosis came second (43.8%). These findings correlate with the previous studies[18,19].

Regarding Behçet disease diagnostic criteria. 97.5% of the patients have oral ulcerations, followed by genital ulceration at 88.8%, while 75% have positive pathergy tests. The involvement of the anterior part (51.2%) was the most common pattern of eye involvement in the disease. These results were similar to previous studies[16,18].

CONCLUSION:

Based on the study results, Behçet disease neurological manifestations occurred mainly in men in their thirties to forties, and the majority of them presented within 2.8 years of Behçet disease onset. Brainstem involvement was the most common presentation. However, the disease can also present with a wide range of symptoms. CVST pattern of the disease was prevalent in our study, as in the previous national studies. Radiologically, brainstem hyperintensity is the most common finding in parenchymal NBD, and a minority of the patients have cortical and periventricular/ subcortical hyperintensities.

Author's contributions:

All the authors have directly participated in the preparation of this manuscript and have approved the final version submitted. AA and IA have recruited and evaluated the patients and participated in its design and interpretation.

Conflict of interest:

Authors have no conflict of interest

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REFERENCES:

1. FEIGENBAUM A. Description of Behçet's syndrome in the Hippocratic third book of endemic diseases. Br J Ophthalmol. 1956;40:355-57.
2. International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD). The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countries on the sensitivity and specificity of the new criteria. J Eur Acad Dermatol Venereol. 2014 ;28:338-47.
3. Yoon DL, Kim YJ, Koo BS, Kim YG, Lee CK, Yoo B, et al. Neuro-behçet's disease in South Korea: clinical characteristics and treatment response. Int J Rheum Dis. 2014;17:453-58.

4. Siva A, Saip S. The spectrum of nervous system involvement in Behçet's syndrome and its differential diagnosis. J Neurol. 2009;256:513-29.

5. 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.

6. Siva A, Kantarci OH, Saip S, Altintas A, Hamuryudan V, Islak C, et al. Behçet's disease: diagnostic and prognostic aspects of neurological involvement. J Neurol. 2001;248:95-103.

7. Yesilot N, Mutlu M, Gungor O, Baykal B, Serdaroglu P, Akman-Demir G, et al. Clinical characteristics and course of spinal cord involvement in Behçet's disease. Eur J Neurol. 2007;14:729-37.

8. Essaadouni L, Jaafari H, Abouzaid CH, Kissani N. Les manifestations neurologiques de la maladie de Behçet : étude de 67 patients [Neurological involvement in Behçet's disease: evaluation of 67 patients]. *Rev Neurol (Paris)*. 2010;166:727-33. PMID: 20451941.

9. Uluduz D, Midi I, Duman T, Colakoglu S, Tüfekci A, Bakar M, et al. Behçet's disease as a causative factor of cerebral venous sinus thrombosis: subgroup analysis of data from the VENOST study. Rheumatology (Oxford). 2019;58:600-8.

10. Aguiar de Sousa D, Mestre T, Ferro JM. Cerebral venous thrombosis in Behçet's disease: a systematic review. J Neurol. 2011;258:719-27.

11. Atasoy HT, Tunc TO, Unal AE, Emre U, Koca R, Esturk E, et al. Peripheral nervous system involvement in patients with Behçet disease. Neurologist. 2007;13:225-30.

12. Park JH, Jung MK, Bang CO, Park HK, Sung KB, Ahn MY, et al. Neuro-Behçet's disease mimicking a cerebral tumor: a case report. J Korean Med Sci. 2002;17:718-22.

13. Siva A. Common Clinical and Imaging Conditions Misdiagnosed as Multiple Sclerosis: A Current Approach to the Differential Diagnosis of Multiple Sclerosis. Neurol Clin. 2018;36:69-117.

14. Lee HS, Kim do Y, Shin HY, Choi YC, Kim SM. Spinal cord involvement in Behçet's disease. Mult Scler. 2016;22:960-63.

15. Borhani Haghighi A, Pourmand R, Nikseresht AR. Neuro-Behçet disease. A review. Neurologist. 2005;11:80-89.

16. Al-Fahad SA, Al-Araji AH. Neuro-Behcet's disease in Iraq: a study of 40 patients. J Neurol Sci. 1999;170:105-11.

17. Sakane T, Takeno M, Suzuki N, Inaba G. Behçet's disease. *N Engl J Med*. 1999;341:1284-91.

18. Al-Araji A, Kidd DP. Neuro-Behçet's disease: epidemiology, clinical characteristics, and management. Lancet Neurol. 2009;8:192-204.

19. Gökçay F, Celebisoy N, Gökçay A, Aksu K, Keser G. Neurological symptoms and signs in Behçet disease: a Western Turkey experience. Neurologist. 2011;17:147-50.

20. Fadli ME, Youssef MM. Neuro-Behçet's syndrome in the United Arab Republic. Eur Neurol. 1973;9:76-89.

21. Daif A, Awada A, al-Rajeh S, Abduljabbar M, al Tahan AR, Obeid T, et al. Cerebral venous thrombosis in adults. A study of 40 cases from Saudi Arabia. Stroke. 1995;26:1193-95.

22. Wechsler B, Dell'lsola B, Vidailhet M, Dormont D, Piette JC, Blétry O, et al. MRI in 31 patients with Behçet's disease and neurological involvement: prospective study with clinical correlation. J Neurol Neurosurg Psychiatry. 1993;56:793-98.

23. Kutlu G, Semercioglu S, Ucler S, Erdal A, Inan LE. Epileptic seizures in Neuro-Behcet disease: why some patients develop seizure and others not? Seizure. 2015;26:32-35.