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Clinical and imaging features of spinal cord type of neuro Behçet disease

A case report and systematic review

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Abstract

Rational: To investigate the clinical and MRI characteristics of spinal cord nerve Behçet's disease.

Patient concerns: One patient with spinal cord nerve Behçet's disease was admitted to our hospital at October 20, 2015.

Diagnose: Spinal cord nerve Behçet's disease.

Interventions: Retrospective analysis was performed on such case as well as 16 cases of spinal cord nerve Behçet's disease reported in China or abroad.

Outcomes: Seventeen cases of spinal cord type of neuro Behçet's disease include 13 men and 4 women, with an average age of onset of 34.8 years old. The mean time from Behçet's disease symptoms to spinal cord involvement were 10.8 years. The initial symptom in one case was spinal cord injury, and another 4 cases had a recurrence course. The most common performance of spinal cord injury was sensory disturbance (82.4%), following by weakness (76.5%), sphincter or sexual dysfunction (58.8%), and pain in back, backside of neck or lower chest (29.4%). The number of cells was slightly increased or the protein level was increased in cerebrospinal fluid test. And the water channel protein antibody and oligoclonal band of serum levels were all negative. The spinal cord injury involved more than 3 vertebral bodies in 10 cases, and involved more than half of spinal cord in sagittal plane in 8 cases. In acute stage, shock therapy with large dose of glucocorticoid was generally applied both in China and abroad.

Lessons: The clinical features of spinal cord nerve Behçet's disease were various, making it easily misdiagnosed. Longitudinal extensive transverse myelitis performs as a characteristic manifestation.

Abbreviations: BD = Behçet disease, CSF = cerebrospinal fluid, LETM = longitudinal extensive transverse myelitis, MRI = magnetic resonance imaging, mRS = modified Rankin scale, NBD = neuro-Behçet disease, OB = oligoclonal band.

Keywords: longitudinal extensive transverse myelitis, neuro Behçet disease, neuromyelitis optica, spinal cord

1. Introduction

Behçet disease (BD) is a heterogeneous, multisystem relapsing inflammatory disorder of unknown cause, which is characterized by recurrent oral and genital ulcers, skin and mucosa, eyes, joints, vascular, gastrointestinal and neurological manifestations.[1] The main histopathological feature is of widespread vasculitis of arteries or venules of any size and the involvement of many other organs has been described, but the exact pathogenesis in BD has not been fully elucidated. Besides, BD mainly affects young men, and has a peculiar geographic distribution in the ancient Silk Road, including countries in the Mediterranean, the Middle East, and the Far East.[2] However, it has been reported that neuro-Behçet disease (NBD) refers to the neurological manifestations of the disease from most countries across the globe.[3]

The neurological involvement of BD is called NBD, especially in invasion of the brainstem and diencephalon region.[1] NBD causes devastating central nervous system complications and occurs in 5% to 30% of patients with BD, which can be divided into 2 main subtypes: parenchymal, an inflammatory meningoencephalitic process and nonparenchymal, a condition secondary to vascular involvement such as dural sinus thrombosis.[4] However, the NBD involved spinal cord is very rare, and only 16 cases were reported in China and abroad before.[5–16]

In recent years, NBD patients were required to conduct paraclinical diagnostic tests and an increasing range of immunomodulatory treatments. The diagnostic process and the quality of care were improved, sensible use of resources was encouraged, and a balanced consideration of potentially harmful medications was measured by practice guidelines. Therefore, we performed a systematic review to describe the clinical and imaging features of spinal cord type of NBD in this study. Accordingly, the information of the clinical and magnetic resonance imaging (MRI) features of NBD involved spinal cord analyzed to improve the understanding of this disease.

2. Patients and methods

A total of 17 patients were retrospectively analyzed in our study (13 men, and 4 women). This study was approved by The

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H-ML and CD contributed equally to this work.

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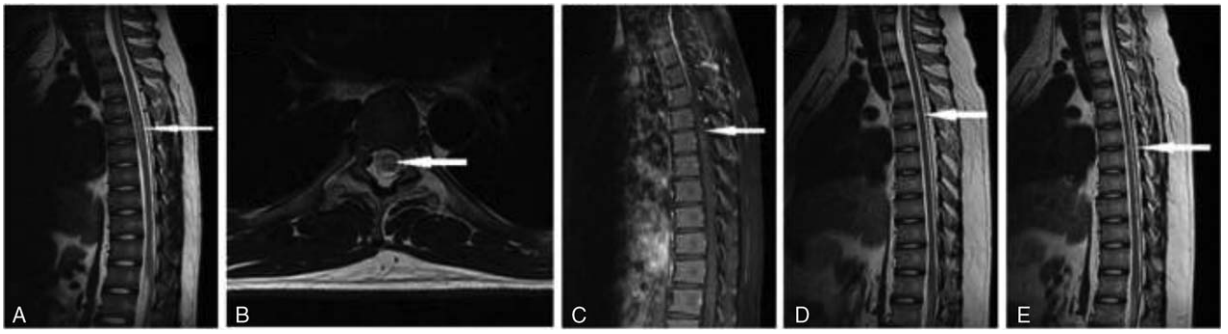

Figure 1. MRI of myelitis lesion with spinal cord involvement in a Behçet disease patient. A, T2-weighted MRI scan showing high signal intensities from 4 to 7 thoracic vertebral body level. B, Axial T2-weighted images demonstrating the entire diameter of the extensive cord lesion. C, After 2 months, T2-weighted magnetic resonance imaging scan showing high signal intensities in the fifth thoracic vertebral level. D and E, Four months after discharge, T2-weighted MRI scan indicating high signal intensities in the fifth thoracic vertebral level and the spinal cord of 6 to 7 thoracic vertebral levels. MRI = magnetic resonance imaging.

Institutional Review Board of Ethics Committee of the First Hospital of Hebei Medical University. One patient was admitted to our hospital at October 20, 2015. The other 16 cases with complete data were searched from "PubMed," "MEDLINE," "Chinese Technology Periodical Database," or "Wanfang database" between 1995 and 2016. All the studied patients fulfilled the diagnostic criteria of the International Study Group for BD. The age of 17 cases ranged from 16 to 65 years (average 34.8 years). Among these, 8 cases were reported with interval time from BD symptoms to the spinal cord involvement ranging from 3 months to 40 years (average 10.8 years). In addition, 17 cases were reported with interval time from spinal cord symptoms to treatment ranging from 3 days to 1 year (average 68.3 days). The follow-up period was 6 months to 25 years (average 6.8 years).

3. Results

3.1. Clinical findings

Among the 17 case, spinal cord injury acted as initial symptoms in only 1 case. Four cases of patients showed recurrence of the disease, of which 2 cases reported interval time of 7 months and 2 years respectively.

The most common performance of spinal cord injury was sensory disturbance with main symptom of decreased sensation (82.4%). The following performance was weakness (76.5%) and 41.2% patients displayed limb weakness. 58.8% patients showed sphincter or sexual dysfunction while 29.4% patients showed pain in back, backside of neck or lower chest, and the distribution region was relevant to location of spinal cord injury.

3.2. MRI characteristics

All of the 17 patients underwent MRI scan of spinal cord, and the lesions were mainly located in the spinal cord from lumbar to medulla. The lesion length of spinal cord involvement ranged from 1 segment to the whole spinal cord, including 3 cases of only 1 vertebral level, 1 case of all the spinal cord, and 3 cases of the medulla. The median lesion length was 6.8 vertebral bodies, and 10 patients had more than 3 vertebral body lesions. In the axial image, the lesion area showed transverse lesion along the sagittal axis, and 8 patients showed involvement of more than half of the spinal cord in the sagittal plane.

The patient of our hospital received MRI plain and enhancement scanning after admission. Abnormal medulla signals were observed from 4 to 7 thoracic vertebral body level (Fig. 1A and B). After 2 months, the patient had no discomfort, and the MRI scan of thoracic vertebra showed the range of small patchy abnormal in the spinal cord of the fifth thoracic vertebral level was significantly narrower compared with the image before (Fig. 1C). Four months later, no discomfort was complained. Moreover, MRI plain scan also indicated abnormal signals in the fifth thoracic vertebral level and the spinal cord of 6 to 7 thoracic vertebral levels (Fig. 1D and E).

3.3. Laboratory findings

Cerebrospinal fluid (CSF) test was performed in 14 patients, indicating that the cell numbers and/or protein level were increased. Nine cases were tested by oligoclonal band (OB), and 6 cases were tested by antiaquaporin-4 antibody (AQP-4Ab). However, all the results of OB and AQP-4Ab test were negative.

3.4. Treatment and outcomes

In acute stage, 14 patients were treated with shock therapy of high dose of glucocorticoid, and 12 cases among them were given methylprednisolone treatment. The other 2 patients were treated with infliximab. One patient was not treated because of mild neurological deficit (Table 1).

The modified Rankin scale (mRS) was utilized to evaluate the recovery of neurological function in patients. Three patients were completely recovered (mRS 0). Nevertheless, 14 patients had sequelae, including 11 cases with mild neurological disability (mRS 1 to 3) and 3 cases with severe neurological disability (mRS 4). Spinal cord injury was less than 3 vertebral in 7 patients, and their functional outcomes were better than others (mRS 0–3).

4. Discussion

The widespread damage of spinal cord acts as the most typical characteristic of spinal cord type NBD patients that is in young male patients, which is characterized by abnormal sensory, motor dysfunction, sphincter function, or sexual dysfunction. In addition, there are some common manifestations of BD, such as repeated attacks of oral and genital ulceration, inflammation of the eye, skin lesions, and so on. NBD can be seen in 2 different patterns: parenchymal and nonparenchymal involvement.[17] Though NBD is relatively uncommon and potentially treatable, doctors need to consider it in the differential diagnosis of

Table 1

Clinical features of spinal cord involvement in neuro-Behçet disease.

No.	Sex	Age†	Clinical course	Spinal cord involvement		MRI lesions			CSF (WBC, cell/mm^3; protein, mg/mm^3)	OB	AQP-4Ab	Treatment of acute phase	FU (y)	mRS
				Clinical manifestations	Symptom onset to MRI	Sagittal section	Axial section	Enhancement						
1	M	38	Spinal → BD	Spinal, SD, SphD	6 mo	T7-T8	Localized (central)	None	ND	ND	Negative	Not done (observation)	25	1
2	F	23	BD → spinal	Back pain, sensory, motor, SphD	3 d	T8-L1	Extensive	T8-L1	WBC 1320, protein 20	NR	Negative	IVMP	20	2
3	F	45	BD → spinal	Sensory	1 mo	C7-T1	Extensive	C7-T1 (rim enhance)	WBC 9, protein29	NR	ND	IVMP	18	0
4	M	25	BD → spinal	Sensory, SphD, moter,	6 d	Medulla -T7	Localized (central)	T2,T5	WBC 16, protein69	NR	Negative	IVMP	16	4
5	M	31	BD → 1st spinal → 2nd spinal	Moter (1st) Motor, SphD, SD (2nd)	7 d 2 wk	T5- L1 (1st) C2-T10 (2nd)	Extensive (1st) extensive (2nd)	None (1st) C3 (2nd)	ND WBC 51, protein60 (2nd)	NR ND	ND	IVMP (1st) IVMP (2nd)	4	4
6	F	43	BD → spinal	Posterior neck pain, sensory, moter	3 wk	Medulla-C5	Extensive	C1	WBC 9, protein 40.3	NR	ND	IVMP	1.5	4
7	M	32	BD → 1st spinal → 2nd spinal	SphD, SD (1st) Sensory, moter (2nd)	5 mo 2 wk	C3-T10 (1st) T3-T6 (2nd)	Extensive (1st) Extensive (2nd)	None (1st) T5 (2nd)	WBC 15, protein10 (1st) ND	ND ND	ND	IVMP (1st) CyP (2nd)	5	3
8	M	28	BD → spinal	Chest pain, Sensory	7 d	T5-T6	Localized (central)	T5-T6	WBC 10, protein 700	ND	ND	Dexamethasone	NM	0
9	M	33	Spinal → BD	Moter, SD, SphD, Sensory	4 mo	C3	Localized (central)	ND	WBC 5, protein 1103	ND	ND	IVMP	1	2
10	M	19	BD → spinal	Moter, SD, SphD, Sensory	3 d	L1	Localized (central)	ND	ND	ND	ND	IVMP	NM	2
11	M	52	BD → spinal	Sensory	1 mo	C5	Localized (central)	ND	WBC 1, protein 94	ND	ND	Glucocorticoid	NM	1
12	M	50	BD → spinal	Sensory moter	1day	T4-T5	Localized (central)	ND	WBC 16, protein 800	ND	ND	IVMP	NM	1
13	F	65	BD → spinal	Moter	2 mo	All spinal cord	Extensive	All spinal cord	WBC 39, protein 144	NR	Negative	IVMP	1	2
14	M	30	BD → 1st spinal → 2nd spinal	Moter, headache, SphD, sensory	1 y	C4-T4	Localized (central)	C4-T4	ND	ND	ND	Infliximab	3	0
15	M	43	BD → 1st spinal → 2nd spinal	Moter, headache, SphD, sensory	NM	T6-T10	Extensive	T6-T10	WBC 23, protein 78	NR	Negative	IVMP	0.5	3
16	M	18	BD → spinal	Moter, SphD, sensory	3 mo	T3-T6	Localized (central)	T3-T6	WBC 438, protein 950	NR	Negative	Infliximab	NM	3
17*	M	16	BD → spinal	Moter, back pain, SphD, sensory	2 wk	T4-T7	Localized (central)	T4-T7	WBC 62, protein 402	NR	ND	IVMP	0.5	1

AQP-4 Ab = anti-aquaporin-4 antibody, C = cervical, CSF = cerebrospinal fluid, CyP = cyclophosphamide, FU = follow-up, IVMP = intravenous methylprednisolone, L = lumbar, M = months, mRS = modified Rankin Scale, ND = not done, NM = not mention, NR = not remarkable, OB = oligoclonal band, SD = sexual dysfunction, SphD = sphincter dysfunction, T = thoracic.

* Patient in our hospital.

† Age at spinal cord involvement.

inflammatory, infective, or demyelinating CNS disorders. Remarkably, the clinical manifestation of BD eye lesion is similar to neuromyelitis optica (NMO), which all present with decreased visual acuity. However, BD usually involve the retina or uveal,[8] while NMO mainly involve the optic nerve.

The proposed diagnostic criteria for NBD include 2 levels of certainty, but with strict requirements including objective neurological signs to reduce false positive diagnosis and improve accuracy. There are many diagnostic methods for NBD, but we have considerable difficulty finding a specific laboratory, radiological or histological findings to help in diagnosing the spinal cord type NBD. It is particularly important to conduct a thorough neurological examination and attention to the redflag symptoms, when deciding if BD patients presenting with new-onset headache were detected by neuroimaging.

CSF test has limited specificity for the diagnosis of spinal cord type NBD, which mostly indicates slight to moderate increase in number of cells.[18] In addition, it is likely to be mistaken for infectious meningitis, the simultaneous presence of meningeal signs and symptoms commonly seen in NBD, because a pleocytosis with elevated protein levels in parenchymal NBD was observed in CSF analysis.[1] MRI is currently the most sensitive tool for diagnosing NBD. T2-weighted and FLAIR MRI scan can show high signal intensities, while T1-weighted MRI scan can show high or normal signal intensities. The characteristics of long segmental spinal cord involvement are very similar to NMO.[19] More women suffer from NMO than men, and the positive rate of Ab AQP-4 detection is relatively higher. A secondary progressive course of disease is common in the spinal cord type of NBD. In the present study, 4 cases developed with progressive disease, while Wingerchuk et al[20] found such a progressive course is rare in the development of NMO. Therefore, AQP-4 Ab detection, gender, optic neuritis, BD symptoms, and course characteristics might help distinguish NMO and the spinal cord of NBD in patients with longitudinal extensive transverse myelitis (LETM).

The common therapy for the published cases was that shock therapy with high dose of glucocorticoid was traditionally utilized for the treatment of the acute phase of spinal cord NBD, followed by combined treatment with immunosuppressive drugs was also used to prevent recurrence of disease in long-term treatment.[21] Previous studies reported that the treatment of infliximab could improve the condition of patients with significant effect and slight side effects.[5,16] However, some studies found that NBD usually indicated poor prognosis. Noel et al[22] held a follow-up of 115 cases of NBD, and found the disability rate was as high as 40%. Furthermore, the 5 and 7 year survival rates were only 65% and 53%. In the present study, the spinal cord NBD patients showed high disability rate as 82.4%. Hence, NBD involving the spinal cord is an important cause for disability.

In general, LETM is a common inflammatory manifestation in patients with spinal cord type NBD. Accordingly, recurrent oral or genital ulcers, eye lesion, and other BD manifestations should be emphasized in patients with LETM. Early diagnosis and treatment should be performed in NBD to reduce recurrence and improve prognosis.

5. Conclusion

The clinical features of spinal cord NBD were various, making it easily misdiagnosed. Besides, LETM performs as a characteristic manifestation. Therefore, neurological involvement may be suggested by the associated clinical features and classical MRI findings. In light of the evidence of poor prognosis in patients with BD and spinal cord involvement, we suggested an early steroid therapy upon recognition of such patients.

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