Case report

Recurrent longitudinal extensive transverse myelitis in a neuro-Behçet syndrome treated with infliximab

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Background: Spinal cord involvement is not common, but can be seen in neuro-Behçet's syndrome (NBS). The major site of involvement is the cervical spinal cord with the myelitis-like inflammatory lesions continuing more than two segments, and extending to the brainstem.

Case: A 30-year-old male patient who has been followed with a diagnosis of Behçet's syndrome admitted to our neurology department clinically and radiologically suggestive of recurrent and extensive longitudinal myelitis. His anti-aquaporine antibody was negative. Because of insufficient effect of azathioprine, cyclophosphamide, and corticosteroids, infliximab was started. His clinical and radiological status is stationary for 3 years under infliximab treatment.

Discussion: Myelitis such as that occurring in our patient may have a similar presentation like neuromyelitis optica (NMO), which should therefore be included in differential diagnosis. Myelitis observed in both NMO and NBS shows spinal cord lesions longer than three or more vertebrae. Anti-aquaporine antibody must be evaluated in all patients presenting with longitudinal myelitis. Anti-tumor necrosis factor agent infliximab might be an alternative treatment in severe form of NBS such as myelitis.

Conclusion: In our case, successful treatment of recurrent and extensive longitudinal transverse myelitis in NBS with infliximab was demonstrated.

Keywords: Neuro-Behçet syndrome, Neuromyelitis optica

Introduction

Behçet syndrome (BS) is a multisystem disease of unknown cause, in which an inflammatory perivascularitis can arise in almost any tissue.¹ The majority of patients with neurological involvement due to BS present with parenchymal central nervous system involvement, most commonly affecting the brainstem diencephalic region. Spinal cord involvement, on the other hand, is a rare condition of parenchymal involvement in neuro-Behçet's syndrome (NBS).² Although many reports have reported longitudinal spinal cord involvement in NBS affecting more than two segments, currently there is no published paper about recurrent and

extensive longitudinal myelitis imitating neuromyelitis spectrum disorder.

Case report

A 30-year-old male initially presented with painful anorectal bleeding, for which he had to have bowel resection. Three months later, the patient developed oral and genital ulcers together with blurred vision and uveitis. He was diagnosed with BS with gastrointestinal involvement (GI) in 2004 and started on 100 mg of azathioprine daily. In 2008, the patient admitted to our neurology department due to left arm weakness and tonic spasms. The spinal magnetic resonance imaging (MRI) performed within a few days showed an extensive longitudinal lesion extending from the level of fourth cervical vertebra (C4) to the level of fourth thoracic vertebra (T4) (Fig. 1).

Upon this finding, daily azathioprine dose was increased to 150 mg, and intravenous (IV)

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Figure 1 Cervical and upper thoracic spinal MRI: sagittal T2-weighted images show an extensive longitudinal lesion from C4 to T4 without gadolinium enhancement.

methylprednisolone treatment was given at a dose of 80 mg/day, stopped in 3 months by tapering the dose.

The patient was followed in our outpatient clinics with a stable course for 2 years. In March 2010 he presented with severe weakness in his right leg (2/5 at the Medical Research Council scale), flaccid tone, loss of vibration and position sense in both feet and decreased sensation below T6, and urinary retention. Spinal MRI with gadolinium enhancement demonstrated multiple confluent hyperintense lesions spanning between T4 and T10 levels with gadolinium enhancement (Fig. 2).

All vasculitis markers including antinuclear antibody (ANA), anti-dsDNA, cytoplasmic antineutrophil cytoplasmic antibodies (cANCA), perinuclear antineutrophil cytoplasmic antibodies (pANCA), rheumatoid factor (RF), anti-SSA-SSB, anti-phospholipid antibodies, and anti-cardiolipin antibodies were negative.

The patient was given 10 days of 1 g IV methylprednisolone treatment followed by 64 mg per oral prednisone. The symptoms of the patient were resolved completely. However, the patient admitted to our outpatient clinic soon after in May 2010, complaining of headache,

Figure 2 Cervical and upper thoracic spinal MRI: sagittal T2-weighted images reveal a longitudinal lesion from T1 to T7, which shows gadolinium enhancement at the level of T5.

Figure 3 Cervical and upper thoracic spinal MRI: sagittal T2-weighted images reveal an extensive longitudinal lesion from the level of T1 to T7, with gadolinium enhancement at the levels of T3–T4 and T6–T7.

fever, bilateral lower-extremity muscle weakness (2/5), and urinary retention. Repeated spinal MRI showed contrast-enhancing extensive longitudinal involvement of the spinal cord (Fig. 3). Because of recurrent and extensive longitudinal myelitis, anti-aquaporine antibody was performed but resulted as negative.

Intravenous methylprednisolone was given for 10 days, although headache and fever was resolved a poor response was observed for motor weakness. Cyclophosphamide IV 1 g was given three times, also with limited response. The regimen was then switched to infliximab with a dose of 5 mg/kg administered by IV infusions at weeks 0, 2, 6, and every 8 weeks then. Under infliximab treatment, lesions observed in spinal MRI showed prominent improvement. The clinical table of the patient is stable with no recurrent attack and he has still been treated with infliximab for 3 years.

Discussion

Neurological involvement in BS occurs in ~2.2–2.5% of the patients primarily consisting of parenchymal or non-parenchymal.^{1,2} Non-parenchymal involvement usually results from thrombosis within the dural venous sinuses. Parenchymal NBS primarily involves the brainstem, but a small subset of these patients displays spinal cord involvement. Although many reports have reported longitudinal spinal cord involvement in NBS affecting more than two segments, there are no data regarding recurrent and extensive longitudinal myelitis to our

knowledge.³ In our unique case, recurrent and extensive longitudinal transverse myelitis was demonstrated. Patients with spinal involvement often demonstrate a primary or secondary progressive course and overall have a worse prognosis as compared to other NBS presentations. This pathology commonly results in motor, sensory, and autonomic dysfunction. The relative frequency of such type of myelitis is 4% among patients with NBS.³ Myelitis such as that occurring in our patient may have a similar presentation in conditions like neuromyelitis optica (NMO), which should therefore be included in differential diagnosis. Myelitis observed in both NMO and NBS shows spinal cord lesions spanning greater than three or more vertebrae in length. In a paper by Wingerchuck *et al.*, the authors have discussed the NMO related to systemic inflammatory syndromes such as systemic lupus erythematosus. The connection between these two heterogeneous groups is still being investigated, but both may also coexist in one patient with a genetic tendency towards autoimmunity. Interestingly, few case reports have also suggested that BS may also be included within this spectrum of systemic inflammatory syndromes related to NMO presentations, as well.⁴

Finally, we would like to discuss the use of infliximab treatment in our patient. There is no established treatment protocol for myelitis in NBS. In most NBS patients with myelitis, high-dose systemic corticosteroid therapy was reported to be effective for both acute and subacute

phases.⁵ Our patient presented multiple times with longitudinally extensive transverse myelitis. At his last presentation, he failed to respond to multiple high doses of steroid treatment, but eventually showed a good response with infliximab, which indicates a beneficial use of this drug in a unique neurological presentation of this disease. Serum tumor necrosis factor (TNF) alpha is increased in active BS, indicating a role for TNF alpha in disease pathology.⁶ Anti-TNF alpha monoclonal antibodies, producing a TNF alpha blockade, have shown significant improvements in various manifestations of BS, such as oral ulcerations and GI involvement.⁷ A recent paper by Pipitone *et al.*⁸ has discussed the use of infliximab treatment for NBS, evidencing decreased cerebrospinal fluid (CSF) levels of inflammatory cytokines TNF α , interleukin-1 β , and IL-6 as well as symptomatic resolution of disease in several patient cases of NBS. Also recently, Coulter *et al.*⁹ published a paper emphasizing the effect of infliximab in a patient with neuro-Behçet presenting with longitudinal extensive transverse myelitis. On the light of these data, infliximab appears to be beneficial in the various presentations of NBS, as in our patient with recurrent extensive longitudinal myelitis.

Disclaimer statements

Contributors UU: physician who treated and followed patient presented in our report. MP: medical student

working with UU to write the report, but was not directly involved in patient care.

Conflicts of interest None.

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Ethics approval Not required.

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