Rare disease

Diagnostic dilemma in CNS Behçet's disease

Orla Ni Mhuircheartaigh,¹ Christopher Hunt,² Josephine Huang,³ Neeraj Kumar,³ Eric L Matteson¹¹Department of Rheumatology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA²Department of Radiology, Mayo Clinic College of Medicine, Rochester, Minnesota, USA³Division of Neurology, Mayo Clinic Rochester, Rochester, Minnesota, USA

Correspondence to Dr Orla Ni Mhuircheartaigh, orla.nimhuircheartaigh@gmail.com

Summary

A 23-year-old gentleman presented to the emergency department with new onset neurological dysfunction and painful oral and genital ulcers. Biopsies of the lesions noted non-specific inflammatory changes. MRI of the brain revealed a large mass-like lesion involving the pons, medulla, midbrain and surrounding cerebral tissue with T2 signal enhancement that was not amenable for biopsy. Both the ulcer biopsy results and the MRI findings could be attributed to either central nervous system (CNS) lymphoma or CNS Behçet's disease. A diagnosis of CNS Behçet's disease was thought to be most likely based on the clinical presentation and MRI findings. He was treated with high-dose immunosuppression and made a significant recovery.

BACKGROUND

Involvement of the nervous system occurs in between 2% and 50% of patients with Behçet's disease¹ and may indeed be the presenting feature in up to 5% of cases. The lesions encountered occur in a variety of presentations, both clinically and radiologically. Diagnosis of central nervous system (CNS) Behçet's disease can be challenging for this reason. CNS Behçet's can often be misdiagnosed for alternative pathologies such as CNS tumours and demyelinating disease. Correct detection is necessary to commence appropriate immunosuppressive treatment and prevent progression of the disease.

CASE PRESENTATION

A 23-year-old gentleman of northern European descent presented with acute neurological dysfunction, consisting of a right-sided cranial nerve (CN) III palsy, dysarthria, solemnness and difficulty with ambulation. He had associated deep, painful oral and scrotal ulcers.

In the year preceding his presentation he had complained of an intermittent low-grade headache and recurrent oral ulcerations. Three months prior to presentation, he was diagnosed with a right sided CN VII palsy which subsequently regressed. He also noted paraesthesia and weakness of the left upper and lower limbs and started to develop recurrent low-grade fevers. He had no significant medical or surgical history. He was a non-smoker, minimum alcohol consumer and denied any prior illicit drug use. His family history was non-contributory.

His symptoms fluctuated for 3 months ultimately resulting in a rapid decline in function which precipitated his presentation. At the time of admission he was severely somnolent, ataxic and uncoordinated. He was pyrexia at 38°C.

He was admitted for further investigation and management of his condition.

INVESTIGATIONS

CT brain

This noted a low attenuation lesion in the right basal ganglia measuring 4 × 2.5 × 3 cm³.

MRI brain and spine

This noted an expansile mass centred in the right aspect of the pons with extension into the left body of the pons as well as inferiorly into the dorsal aspect of the medulla with superior extension into the midbrain, right cerebral peduncle, right thalamus and the posterior limb of the internal capsule (figure 1). There was significant enhancing T2 signal. Similarly, the MRI cervical and thoracic spine noted multiple small areas displaying signal abnormalities with subtle enhancement.

CSF fluid analysis

CSF fluid was retrieved by means of a lumbar puncture procedure, which revealed a CSF white cell count of 7 cells/mm³, a protein content of 39 mg/dl, a negative infectious work-up and the absence of oligoclonal bands.

Biopsy of the ulcerated lesions

Non-specific inflammatory changes were noted but no evidence of vasculitis or lymphoma was seen.

Ophthalmology examination

He was reviewed by ophthalmology where suboptimal visual acuity, bilateral retinal haemorrhages, bilateral optic neuropathy (left > right) and a left-sided abducens nerve palsy were noted.

Other investigations performed

Relevant basic laboratory work-up

Mild leukocytosis of 13.5 cells/L with differential of 82% neutrophils, 12% lymphocytes. Elevated aspartate aminotransferase 183 IU/L, alanine transaminase 231 IU/L and a total bilirubin of 0.9 mg/dL.

Infectious work-up

Studies for West Nile, varicella zoster virus, toxoplasma, fungal serology, syphilis serology, cytomegalovirus, tuberculosis QuantiFERON test, Lyme serology, as well as PCR for Whipple's disease were all negative. Of note,

Figure 1 MRI brain at diagnosis. Increased T2 signal seen on fluid attenuated inversion recovery sequence (A) involving the cerebral peduncles and inferior thalamus demonstrates patchy, asymmetric enhancement (B and C, coronal and axial T1-weighted postgadolinium sequences). Differential from the radiologist was limited and this was felt most likely to represent primary central nervous system lymphoma even though the somewhat patchy enhancement might argue against lymphoma which typically is more uniform in an immunocompetent host.

immunoglobulin (Ig) G Epstein-Barr virus PCR was positive, but the IgM serology result was negative.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis at this point was between inflammatory, infectious, demyelinating, neoplastic or granulomatous conditions. CNS Behçet's disease, CNS lymphoma and disseminated encephalomyelitis were at the top of the differential list. The lesion was reviewed by the neurosurgery service and unfortunately was not amenable for biopsy to assist with confirming the diagnosis.

TREATMENT

Based on his clinical presentation and radiological findings the most likely diagnosis was felt to be Behçet's disease with CNS involvement. He was started on a 5-day course of intravenous methylprednisolone 1000 mg/day. The symptoms rapidly improved, so that he was able to ambulate, eat and converse within 72 h. He was discharged on a regimen of oral prednisolone 60 mg daily and azathioprine 100 mg daily.

OUTCOME AND FOLLOW-UP

At 2 weeks postdischarge he was reviewed in the outpatient setting. He had some gait difficulty due to a left-sided hemiparesis and left-sided foot drop, which was

much improved. He also had some persistent diplopia. However, his scrotal ulcers had completely resolved and his oral ulcers were barely visible. His prednisolone therapy was tapered from 60 to 40 mg daily and he was continued on maintenance azathioprine therapy, 100 mg daily.

At 4 weeks postdischarge he was reviewed again. His clinical course continued to improve. Residual left-sided hemiparesis, foot drop and some difficulty with coordination remained. His diplopia was resolving and his ophthalmological exam revealed less retinal haemorrhages and improvement in his optic atrophy. He had a repeat MRI brain performed, which noted an interval improvement in the lesions seen and the T2-contrast enhancement. The images were felt to be consistent with CNS Behçet's disease (figure 2).

He was continued on oral prednisolone and azathioprine with the plan to taper off the steroids slowly and maintain on steroid sparing agents with close follow-up.

DISCUSSION

Initial features of CNS Behçet's disease are often non-specific, making diagnosis difficult until severe neurological damage occurs.

In this case, this young gentleman had symptoms that could be attributable to Behçet's disease when reviewed

Figure 2 MRI of the brain at 5 weeks after starting of immunosuppression. Interval improvement of the previously seen mass-like expansion involving the cerebral peduncles with reduction in the degree of T2 signal on fluid attenuated inversion recovery sequence (A) and near complete resolution of the previously seen associated enhancement on the axial and coronal views (B and C).

retrospectively. These included his year-long history of recurrent oral and genital ulceration and his previous presentation with a CN VII palsy. However, his neurological decline was rapid and unpredictable. Appropriate and expeditious administration of treatment was essential. The appropriate treatment differs significantly between the different possible diagnoses. Unfortunately, as the lesion was not amenable for biopsy, confirmation of the diagnosis was challenging. Therefore, diagnosis was made in this case based on his clinical presentation, which was indeed consistent with a diagnosis of Behçet's disease, and the investigations performed, which were more inconclusive. To add complexity to his case, his age, clinical presentation and the MRI findings could also be consistent with either of the two most likely diagnoses; CNS lymphoma or CNS Behçet's disease.

Different diagnostic criteria are used to assist diagnosis for Behçet's disease. The international Behçet's criteria, that was published in 1990², is the most commonly used and has a relatively high sensitivity and specificity. Unfortunately, no diagnostic tool exists for CNS Behçet's disease. The association with positive serology including human leucocyte antigen (HLA) B-51 and HLA-B serotype, an elevated protein count in the absence of oligoclonal bands on CSF analysis and MRI can assist in the diagnosis. CNS Behçet's disease is commonly omitted in the differential for rapidly progressive neurological decline, often resulting in a delay in diagnosis.

CNS Behçet's disease can be divided into parenchymal and non-parenchymal disease. Radiological findings in parenchymal disease can be characterised into typical and atypical involvement.³ MRI classically notes small foci of high signal intensity on T2-weighted imaging.³ The diencephalon, brain stem and spinal cord are the most commonly affected areas.⁴ Our case presented in a very atypical manner with no prior case reports documenting similar lesions. Other commonly seen varieties include; presentation as a space occupying lesion, a unilateral brain tumour or with involvement of the leptomeninges. Atypical manifestations are commonplace and require a more extensive work-up. The clinical presentation reflects the area of the brain involved. Stereotactic-guided biopsy of the involved area is often essential to rule out other possible pathologies.⁵ Primary CNS lymphoma can also often present in a variable fashion.⁶

Genital ulceration can also occasionally be a manifestation of an underlying lymphomatous disease. This further complicated the diagnosis in this case.

Neurological involvement in Behçet's disease is a poor prognostic indicator. It was the third most common cause of death (12.2%) in a cohort of patients that was assessed in Paris, France.⁶ Other poor prognostic indicators include male gender, arterial involvement and recurrent flares. This supports the urgency of treatment in the patient in this case and the need for familiarity with the diversity of lesions that have been previously documented.

CONCLUSION

CNS Behçet's disease is a frequently seen manifestation of Behçet's disease. There is no validated diagnostic tool to assist with confirming the diagnosis, which may often be challenging. It can present in an atypical manner and progress rapidly. Expeditious treatment is essential to halt progression and prevent permanent neurological damage or potential mortality. This case demonstrated a classic diagnostic challenge seen in CNS Behçet's disease and highlights considerations that may need to be taken to ensure the most appropriate management is applied.

Learning points

- ▶ Central nervous system (CNS) Behçet's disease is Behçet's disease where there is neurological involvement which can result in severe neurological impairment.
- ▶ If untreated, CNS Behçet's disease can progress rapidly.
- ▶ CNS Behçet's disease can present in a wide variety of presentations making diagnosis challenging.
- ▶ CNS lymphoma often presents with cerebral lesions or orogenital lesions that may be identical to that seen in CNS Behçet's disease.
- ▶ A decision is occasionally required in complex cases, such as the case outlined in this report, to proceed with treatment for the most likely condition without a definite diagnosis being confirmed.

Competing interests None.

Patient consent Obtained.

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