Neuro-Behcet's Disease: A Case with Acute Neurological Manifestation with Parenchymal Involvement

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Neuro-Behcet's disease (NBD) is a rare disease with variable neurological features including silent progressive neurological involvement. The prompt and accurate diagnosis of NBD remains a clinical challenge as not all neurological features are due to NBD. Due to this, diagnosing NBD is a clinical dilemma encountered in clinical practice.

A twenty-five-year-old Bahraini male presented with symptoms of headache, diplopia, left partial ptosis and increased somnolence. The headache was progressive, severe. The initial CT brain was normal. MRI brain revealed changes consistent of neuro-behcet's disease.

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Behcet's disease is a relatively uncommon vascular, autoimmune inflammatory disorder of unknown origin with characteristic urogenital ulceration and uveitis described as the triple-symptoms complex and multi-organ involvement[1]. The precise etiology has yet to be determined but occurs due to combined environmental and genetic factors[2]. It is more prevalent along the ancient Silk Road, including countries in the Far East, Middle East and Mediterranean Basin, in which the population has a high incidence of HLA-B51 allele[2,4]. The clinical signs varies according to age, sex, and ethnicity[2,5]. In general, it is considered to be more common in males and with more severe manifestations[5].

The prevalence of neuro-Behcet's remains between 5-30% of all patients with Behcet's disease and classified into: parenchymal and non-parenchymal[6]. Neuro-Behcet's disease is an adverse prognostic factor[3].

The aim of this presentation is to report a case of Behcet's disease with acute neurological manifestation and the importance of prompt diagnosis and management.

THE CASE

A twenty-five-year-old male with five years history of Behcet's disease and migraine headache was admitted to the medical ward with a history of severe progressive headache, increased somnolence, diplopia, imbalance and left partial ptosis for five days. He was not compliant to prednisolone and colchicine.

He was hemodynamically stable and afebrile. There was no evidence of skin rash or joint involvement. The neurological assessment showed left partial ptosis and left facial palsy. Meningeal signs were absent and no other neurological findings. The following differential diagnoses were contemplated: CNS infection, multiple sclerosis, stroke, adverse treatment of Behcet's disease and Neuro-Behcet's disease.

Laboratory investigations showed neutrophilia with no leukocytosis, elevated ESR and normal coagulation profile, renal and liver function tests. Routine serological markers for viral infection including HIV, hepatitis B and hepatitis C were negative. Serological marker of anti-EBV (EBNA 1) IgG and anti-EBV (VCA) IgG were positive. Anti EBV (VCA) IgM was negative. Syphilis antibody was negative. He was not immune to toxoplasmosis IgG. He was immune to varicella-zoster virus. Anti-nuclear antibody and double-stranded DNA antibodies by enzyme-linked immunosorbent assay (ELISA) were negative. Anti-CCP was negative. Urine dipstick was negative for protein and urine microscopy showed 11-20 red blood cells. Blood culture was sterile. The chest x-ray was normal. CT brain ruled out hemorrhage and reported as a normal study. MRI brain revealed white matter changes mainly in the left basal ganglia involving the posterior limb of the left internal capsule, medial aspect of the left temporal lobe, left cerebral peduncle, heterogeneous T2 hyperintense lesions in brainstem and pons with cystic changes in the center of the lesions, see figures 1 and 2. There was a mass effect on the inferior aspect of the third ventricle. Diffusion showed slight fluid restriction and contrast showed irregular peripheral enhancement mainly in the pons and left basal ganglia. There were multiple signal void holes mainly in the left basal ganglia and pons bilaterally.

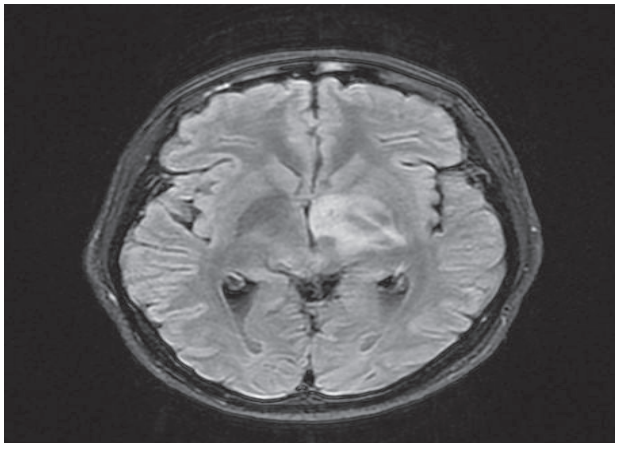

Figure 1: Heterogeneous T2 Hyperintensity in the Left Basal Ganglia, Brain Stem and the Pons with Peripheral Enhancement

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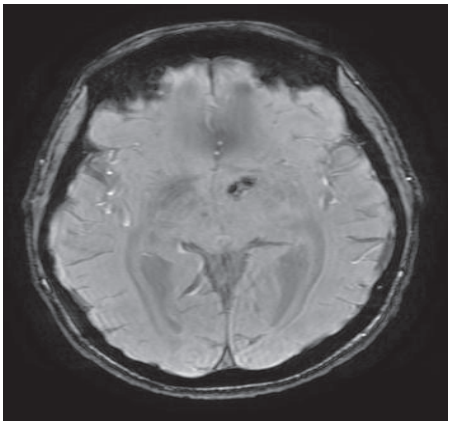

Figure 2: Swan Series Showed Black Holes Suggestive of NBD

The clinical manifestation and the neuroimaging were suggestive of neuro-Behcet's disease. He was managed with pulse methylprednisolone for five consecutive days and then started on prednisolone (1mg/kg) 60mg PO OD and methotrexate 15mg PO once per week with folic acid 10mg PO once a week. Physiotherapy sessions were initiated. The patient was discharged with residual ptosis and partial facial weakness. Follow-up treatment consisted of tapering dose of prednisolone, methotrexate 15mg once per week and folic acid 10mg PO once a week. He completed 10 sessions of cyclophosphamide. One year later, follow-up MRI brain with IV contrast revealed no heterogeneous lesions with peripheral enhancement described before in the left basal ganglia and brainstem, see figure 3.

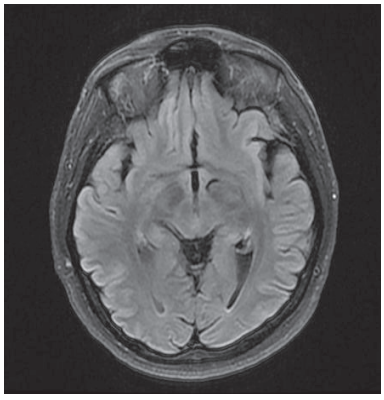

Figure 3: The Previously Described Heterogenous Area at the Left Basal Ganglia, Brain Stem and Pons, and Peripheral Enhancement is No Longer Seen

DISCUSSION

The definitive diagnosis of neuro-Behcet's disease has to meet the three criteria: 1) To meet the international study group criteria 2) Neurological symptoms and signs known to be caused by BD and supported by distinguishing abnormalities in neuroimaging or cerebrospinal fluid (CSF) fluid analysis 3) No other explanation of the neurological findings[1,4].

Studies revealed distinct clinical features between acute and chronic parenchymal NBD. Fever and high CSF cell count were more frequently seen in acute parenchymal NBD, whereas sphincter dysfunction, ataxia, dementia, confusion, brainstem atrophy and abnormal MRI findings in the cerebellum were frequently seen in chronic parenchymal NBD[8].

MRI brain is the standard neuroimaging modality in the diagnosis of NBD. The incremental pattern in the number of lesions and MRI burden in parenchymal NBD indicate the ongoing inflammatory process[7]. Parenchymal lesions are usually located within the brainstem extending to diencephalon and less commonly seen in periventricular and subcortical white matter. Acute or sub-acute parenchymal lesions are hypointense in T1 weight images, hyperintense in T weight images, heterogenous enhancement with contrast in T1 images, fluid-attenuated inversion recovery with edematous extension images[1,4,6]. Chronic parenchymal lesions are isointense to hypointense in T1 and slight hyperintense in T2. Brainstem atrophy is common in chronic parenchymal NBD[1,4,6]. All of these features support the hypothesis of small vessel vasculitis with venular involvement. The lesions can be hemorrhagic and this supports the venous pathology as well[1]. It is important to distinguish NBD from others, such as brain tumors if the mass effect is present or multiple sclerosis when the lesions are periventricular or sub-cortical[1,4,6]. Relapses are more commonly seen in parenchymal NBD compared to non- parenchymal NBD[3].

Treatment of NBD is a clinical challenge due to the lack of controlled or comparative trials on the treatment of NBD. In one study, early aggressive treatment in acute parenchymal NBD with combined pulse steroid and cytotoxic agents was associated with a reduced negative effect of neurological involvement[9].

Treatment of acute parenchymal involvement includes pulse IV methylprednisolone 1 gram per day for up to 7 days followed by oral prednisolone (1mg/Kg/day) for one month and then tapered by 5-10 mg every 10-15 days along with immunosuppressive drugs[10]. Success was reported with azathioprine, methotrexate, mycophenolate mofetil, chlorambucil and cyclophosphamide[4,10,11].

Biological agents are reserved for severe parenchymal NBD (at onset), persistent or relapsing course of NBD despite being on steroids and azathioprine or chronic progressive disease[10]. The clinical experience with infliximab is extensive than other biological agents[4].

Tocilizumab has been reported in case reports as a biological agent in refractory NBD but yet to be included in the recommendation.

CONCLUSION

The clinical course of our patient showed a clinical neurological remission. The early and prompt diagnosis and administration of steroids and cytotoxic drug has altered the course of the disease. Neuro-Behcet's disease is rare, but the clinicians should consider it in their differential diagnosis.

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