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CASE REPORT

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Brain tumor-like lesion in Behçet disease

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Abstract We report a patient with longstanding Behçet disease who presented sudden onset of headache and facial paresis. The magnetic resonance imaging (MRI) showed a mass in the right thalamus, extending to the lentiform nucleus, subthalamic area, right cerebral peduncle and deep subcortical white matter. Stereotactic brain biopsy disclosed gliosis with no signs of malignancy. The diagnosis of a pseudotumoral form of neuro-Behçet disease was done and she was treated with pulse methylprednisolone and intravenous cyclophosphamide. After 8 weeks she had improved and a new MRI showed disappearance of the tumor-like lesion. The differential diagnosis, especially with central nervous system tumor is emphasized.

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Introduction

Behçet disease (BD) is an inflammatory multisystem syndrome, characterized by recurrent oral and genital ulceration and relapsing inflammation of the eye [1]. Since there are no specific tests for BD, the diagnosis is based on clinical criteria [2]. Central nervous involvement [neuro-Behçet disease (NBD)] was first recognized in 1941, but the first autopsy findings were reported only in 1944. Up to now, several cases of NBD have been reported and the frequency has ranged from 2.2 to 50% of the cases of BD [3–11]. However, a pseudotumoral form of NBD is a very rare condition [3, 5].

We report a case of thalamic mass on magnetic resonance imaging (MRI) in a patient with a longstanding Behçet disease with sudden onset of headache. A stereotactic brain biopsy was required to exclude a central nervous system (CNS) tumor. The patient was treated for NBD with pulse methylprednisolone and intravenous cyclophosphamide with significant improvement of clinical and MRI features.

Case report

In January 2002, a 43-year-old white woman with BD was referred to the rheumatology outpatient clinic. Her disease started 20 years ago, when she had bilateral anterior uveitis, and oral and genital ulcers. She had been treated with prednisone and cyclosporine, because of the recurrence of the uveitis. Despite the treatment, the patient remained with bilateral low visual acuity. On that occasion, she has been taking cyclosporine for 8 years, without recurrence of the ocular or mucocutaneous symptoms. On physical examination, the patient presented good general health, with body index mass of 25.21 kg/m^2, blood pressure 140×80 mmHg and heart

rate 70 bpm. No abnormalities were noted on the skin, mucosa, cardiorespiratory or abdominal examination. Ophthalmologic examination revealed bilateral subcapsular cataracts, vitreal turvation and retinal vascular atrophy. Immunological tests for toxoplasmosis, syphilis, tuberculosis, cytomegalovirus and human immunodeficiency virus were negative. Total blood count, blood chemistry, urinalysis and chest radiographs were normal. Because of absence of clinical activity of the disease, cyclosporine was discontinued.

The patient had no new symptoms until October 2002, when she developed sudden bilateral progressive throbbing headache, photophobia and asthenia. On examination, no evidence of clinically active BD was noted. Neurological examination showed drowsiness, mild left arm and facial paresis and right eyelid ptosis, without pupillary abnormalities. Muscle stretch reflexes, tactile and pain sensibility were unremarkable. Cranial computadorized tomography showed a 2×2 cm thalamic lesion with mass effect and contrast enhancement. On MRI, the lesion was hypointense in T1 and hyperintense in T2, involved mainly the right thalamus, extending ipsilaterally to the lentiform nucleus, subthalamic area, cerebral peduncle and deep subcortical white matter, and led to third ventricle compression and midline deviation (Fig. 1). Magnetic ressonance angiography was normal. Stereotactic brain biopsy demonstrated gliosis with gemistocytic astrocytes, without signs of tumor or vasculitis (Fig. 2). The patient received intravenous dexamethasone (4 mg/day), when she developed a progressive psychomotor aggressiveness, memory and sleep disturbances and polyphagia. No metabolic abnormalities were detected. The patient was treated with pulse methylprednisolone (1 g/day for 3 days) and maintained with oral prednisone (60 mg/day). Nevertheless the patient showed neuropsychological worsening and reevaluation suggested organic psychosis secondary to corticotherapy. Prednisone was tapered to 20 mg/day and a monthly pulse of cyclophosphamide was given for 6 months. After 8 weeks of treatment, she had marked improvement, with complete remission of paresis and ptosis. MRI at this time yielded no evidence of the previous mass (Fig. 3). She has been followed up for 1 year and the disease did not relapse.

Discussion

The frequency of CNS involvement in BD is around 15–25% in most studies [6–9], with a range from 2.9% in Taiwan [1] to 44% in Saudi Arabia [3]. It is considered a disease of young adults mainly in the third and fourth

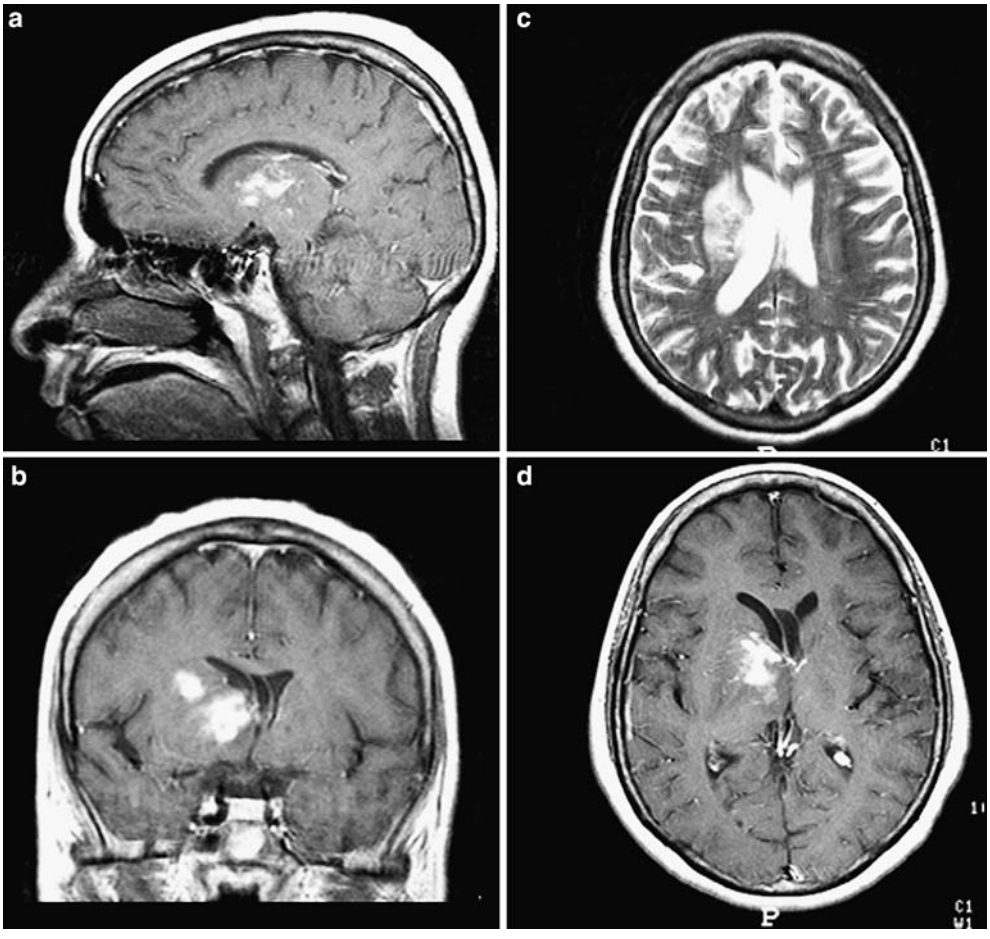

Fig. 1 MRI in sagittal T1 (**a**), coronal T1 (**b**), axial T2 (**c**) and FLAIR (**d**) showing an extensive tumor-like mass with gadolineum enhancement extending from right thalamus, extending to the lentiform nucleus, subthalamic area, ipsilateral cerebral peduncle and deep subcortical white matter

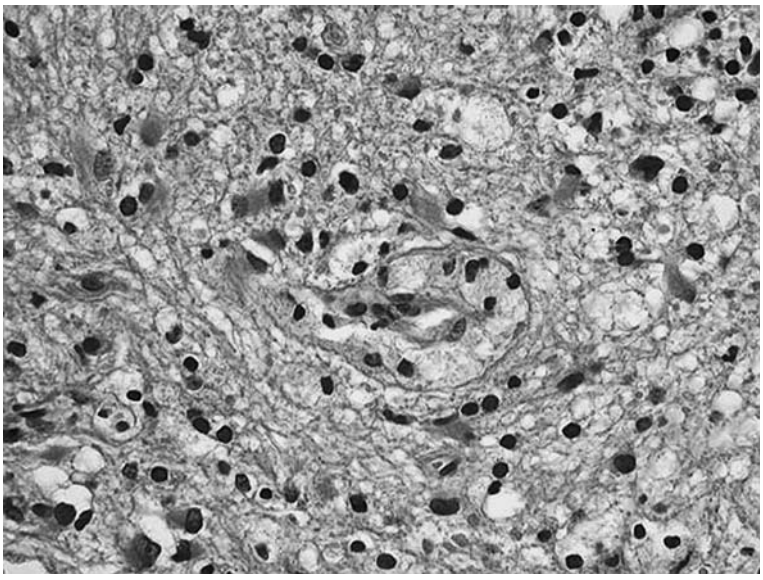

Fig. 2 Extensive gliosis and perivascular cuffing by foamy macrophages, without evidence of malignancy or vasculitis. H and E, × 100

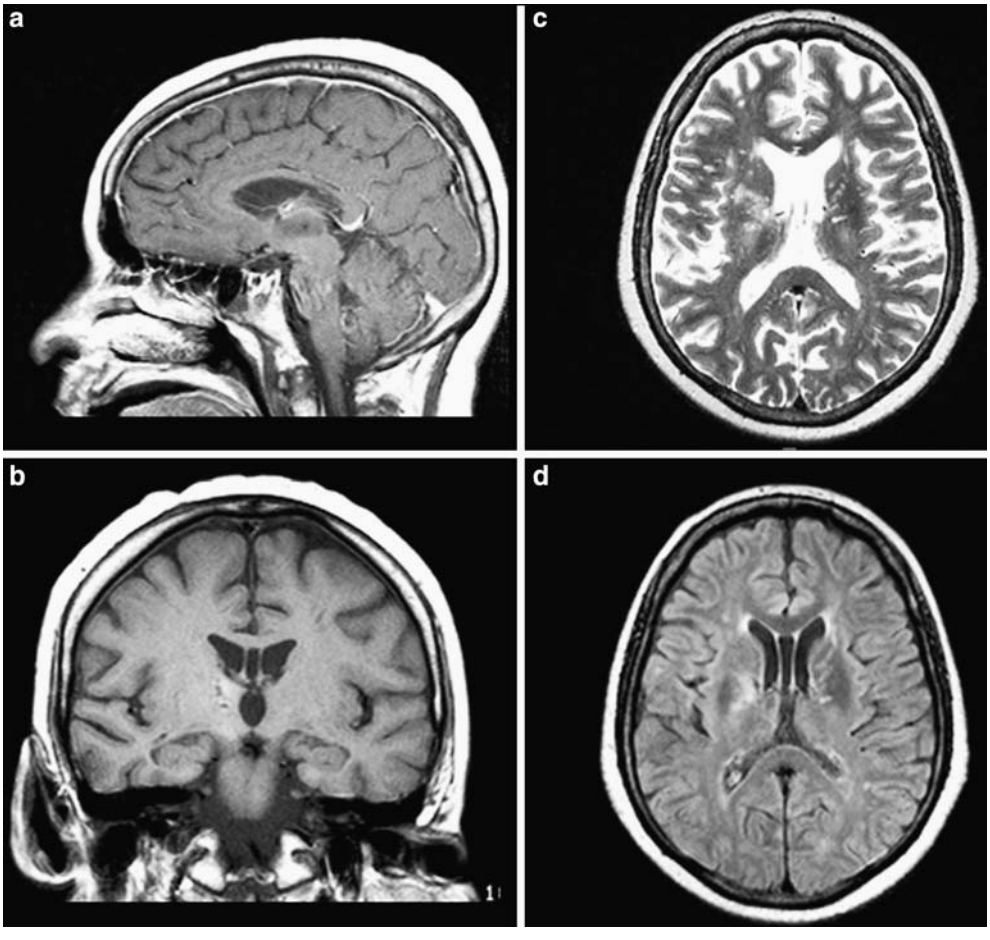

Fig. 3 MRI in sagittal T1 (**a**), coronal T1 (**b**), axial T2 (**c**) and FLAIR (**d**) showing absence of tumor-like lesion and biopsy scar on right thalamus

decades [8]. In recent reports, men with BD were considered at much higher risk of developing neurological complications than women [7, 8].

Neurological presentation and clinical course of NBD are variable. Some patients have an acute attack followed by a relapsing–remitting or secondary progressive course. Others, as our patient, have a primary progressive course without a clear-cut attack. There are also patients without neurological complaints, but with abnormalities on MRI [1, 12]. NBD has been classified into three types according to the presentation [1]: (1) Brain stem disturbance with cranial neuropathy, ocular motor dysfunction, nystagmus and gaze palsies. Headache, meningism and CSF pleocytosis are frequently seen. (2) Meningomyelitis

and (3) meningoencephalitis which may be chronic and progressive leading to dementia, parkinsonism, pseudobulbar palsy and quadriparesis. Tumor-like masses are a rare form neuro-Behçet [3, 5].

In our case, the diagnosis of BD was based on International Study Group criteria for BD. She was treated with corticosteroids and cyclosporine for 8 years prior the development of acute neurological symptoms. Initially, the main difficulty was to distinguish NBD from other CNS diseases, especially malignancies. However, stereotactic biopsy showed no evidence of neoplasic cells, therefore the patient was treated with methilpredinisolone pulse and intravenous cyclophosphamide for NBD. She experienced a significant neurological improvement and the tumor-like image on MRI had also disappeared.

Histopathogical changes in NBD can vary with age of the lesion. However, a non-specific low-grade inflammatory reaction with mononuclear and/or neutrophilic infiltrate appears most commonly [10]. Vasculitis is usually considered to be a central pathological feature in NBD [9–11], but cannot always be demonstrated. Multifocal necrotic foci, predominantly in the brainstem and basal ganglia, may be seen. In our case, histological examination demonstrated gliosis with gemistocytic astrocytes, but signs of inflammation were lacking. The absence of neoplastic cells and the good response to corticosteroids makes the diagnosis of NBD likely.

The differential diagnosis of NBD should include multiple sclerosis, infections, vascular disease and tumors. Previously, multiple sclerosis was one of the leading causes of misdiagnosis, but MRI findings are now distinctive in most cases. In NBD, the major abnormality is usually in the brain stem–diencephalon–basal ganglia region [6–9, 12]. However sometimes the predominant lesion may be in the periventricular white matter, in which case it will be difficult to distinguish from multiple sclerosis, mainly in the absence of the other features of BD [10]. CNS infections are usually ruled out by CSF cultures. Because of the mass effect of the lesion in our patient, CSF examination was not indicated. Although the longstanding corticosteroid use prior to development of neurological symptoms predispose to premature atherosclerosis, cerebrovascular disease was ruled out by MRI and MR angiography findings. The main differential diagnosis, CNS tumor, was only discarded after CNS biopsy. Previous cyclosporine A (CyA) therapy has also been associated with the development of NBD [13]. CyA is a potent immunosuppressive agent which is widely used for patients with graft-vs-host disease and various autoimmune diseases. CyA use is associated with numerous side effects; nephrotoxicity and hypertension are the most common, but neurotoxicity is also known to occur in up to 40% of patients receiving CyA. The most common neurological complication is postural tremor, posterior leucoencephalopathy and generalized seizure. The mechanism underlying the neurotoxicity of CyA remains unclarified. CyA also induces neurological complications in patients with BD in up to 30%. Whether the permeability of the CNS to CyA increases or not in the presence of vasculitis, the reason for the similarity between neurological complications in patients with CyA-induced NBD and the symptoms of typical NBD remain unclarified [13]. Our patient received longstanding CyA treatment, but CyA was stopped 9 months before CNS manifestations, making the hypothesis of CyA-induced CNS manifestations less probable.

There are few reports regarding pseudotumoral neuro-Behçet which emphasize the rarity of this neurological complication [2]. Diagnosis is difficult and a wide range of different diagnosis should be considered, including CyA-induced CNS manifestations and CNS malignancy. When treated with steroids, the prognosis of this neurological presentation seems to be favorable in the short-term. Because of the presence of steroid-induced psychosis, we introduced pulse cyclophosphamide to control CNS manifestations. Because both medications were introduced in a short period of time, we were not able to determine if corticosteroid or cyclophosphamide alone or both were effective in our patient.

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