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Neuro-Behçet's disease mimicking cerebral abscess complicated by metronidazole-induced encephalopathy

[1]Ayse Guler, [2]Ece Cinar, [3]Tuncer Turhan, [4]Husnu Pullukcu, [5]Taner Akalin, [1]Figen Gokcay, [1]Nese Celebisoy

[1]Neurology Department, [2]Physical Medicine & Rehabilitation Department, [3]Neurosurgery Department, [4]Clinical Microbiology & Infectious Disease Department, [5]Pathology Department, Faculty of Medicine, Ege University, Bornova, Izmir, Turkey

Abstract

This is the report of a 32-year-old man with Behçet's disease described dizziness, double vision and headache. The cranial MRI demonstrated a ring enhancing nodular lesion in left medial occipital lobe, and T2 hyperintense lesion in diencephalon mimicking abscesses. A stereotactic biopsy was performed. The histology showed features of neuro-Behçet's disease and an abscess was ruled out. During the procedure till the histopathologic results were gathered he was given ceftriaxone and metronidazole when cerebellar signs appeared. Cranial MRI showed additional symmetrical hyperintensities in bilateral cerebellar dentate nuclei which was attributed to metronidazole toxicity. Repeat MRI performed forty days later showed complete resolution of both dentate hyperintensities and diencephalic and occipital ring enhancing lesions. This is the first case of neuro-Behcet's disease complicated by metronidazole-induced encephalopathy. This case also showed that nodular ring enhancing lesions can be seen in neuro-Behçet's disease and can lead to difficulties in diagnosis and management.

INTRODUCTION

Behçet's disease (BD) is a chronic, relapsing multisystem inflammatory disorder first described by the Turkish dermatologist Hulusi Behçet in 1937.[1] Inflammatory perivasculitis can arise in almost any tissue. Nervous system involvement is one of the most serious manifestations of BD and has been reported to occur in 5.3%[2] up to 59%[3] in hospital based series, usually after systemic manifestations from months to years. Two different patterns of Central nervous system (CNS) involvement have been defined: parenchymal and nonparenchymal or vascular.[4] Vascular BD can be confirmed by computed tomographic angiography, magnetic resonance angiography, or magnetic resonance venography. Magnetic resonance imaging (MRI) is the examination of choice for the study of parenchymal involvement in BD. Mesodiencephalic junction, cerebellar peduncles, pons, medulla, basal ganglia, internal capsule, and cerebral hemispheres are the commonly involved sites.[5] We describe a case of parenchymal BD with nodular abscess-like lesions who was diagnosed with stereotactic brain biopsy. As an infection could not be excluded before the histopathologic examination he was treated with ceftriaxone and metronidazole which caused metronidazole-induced encephalopathy.

CASE REPORT

A 32-year-old man presented with dizziness, double vision and headache that had started four days earlier. BD had been diagnosed 8 years prior with recurring oral and genital ulcers and two previous uveitis attacks. He was on colchicine since then. The medical history was otherwise nonspecific. Other than restriction of the upward gaze, neurological examination was normal. Complete blood count and biochemistry revealed leukocytosis with neutrophilia (17.64 10^3/μL). Sedimentation rate, C-reactive protein levels, thyroid functions were normal. The cranial MRI demonstrated a ring enhancing lesion with internal hypointensity on the left medial occipital lobe next to the interhemispheric fissure on T1-weighted images with gadolinium injection. T2-weighted and FLAIR sequences revealed an additional nodular occipital and a left diencephalic lesion which were hyperintense. Diffusion weighted imaging (DWI) and apparent diffusion coefficient (ADC) map revealed central hyperintensity on

Address correspondence to: Nese Celebisoy, M.D., Ege University Faculty of Medicine, Neurology Department, Ankara Street, 35100, Bornova, Izmir, Turkey. Tel:+905332654508, e-mail:neşe.celebisoy@ege.edu.tr, ncelebisoy@gmail.com

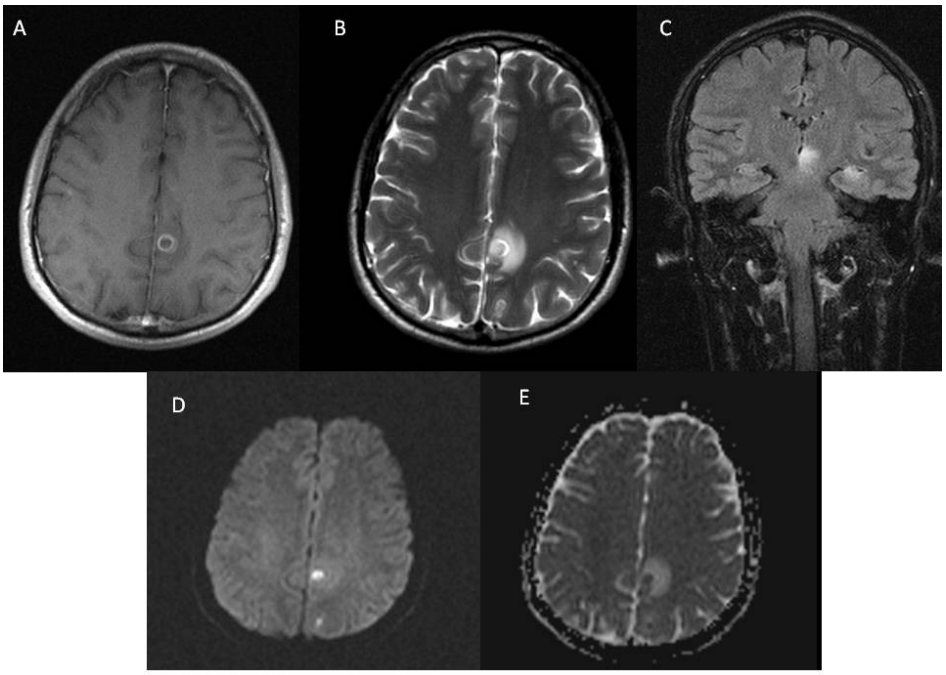

Figure 1: First cranial MRI: A) Ring enhancing lesion with internal hypointensity on the left medial occipital lobe next to the interhemispheric fissure on T1-weighted magnetic resonance images with gadolinium injection, B-C) T2-weighted and FLAIR sequences revealed another nodular occipital and a left diencephalic lesion, D-E) DWI and ADC map revealed central hyperintensity on DWI B1000 with hipointensity on ADC for occipital lesions.

DWI B1000 with hypointensity on ADC for occipital lesions (Figure 1).

Lumbar puncture performed demonstrated normal results. As an infectious etiology could not be ruled out the patient was started on ceftriaxone 2x1g and metronidazole 4x0.5g. A stereotactic biopsy was performed at the left occipital ring enhancing lesion. Biopsy specimen showed a necrotic focus containing histiocytes and also lymphocytic vasculitis characterized with perivascular lymphocytic infiltration (immunohystochemical staining revealed T lymphocytes (CD3 (+), CD20 (-)) and reactive gliosis (Figure 2). Cultures for bacteria, tuberculosis and viruses were negative. Antibiotic therapy had been continued for 14 days when the patient began to complain increasing imbalance. The neurological examination showed

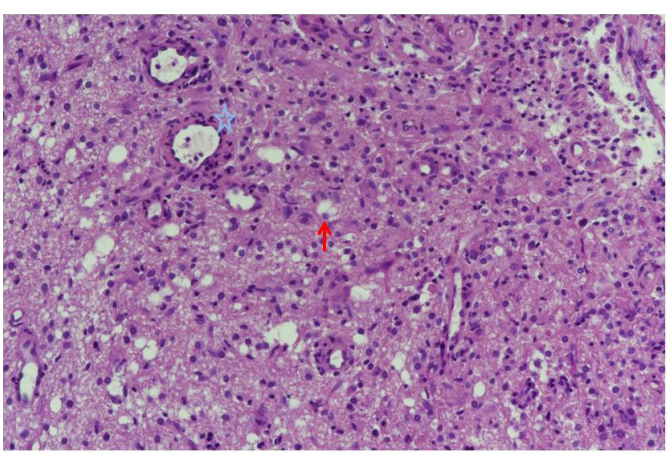

Figure 2: Biopsy specimen: (HE, X200) foamy histiocytes (arrow) and lymphocytic vasculitis characterized with perivascular lymphocyte infiltration (star) with reactive gliosis.

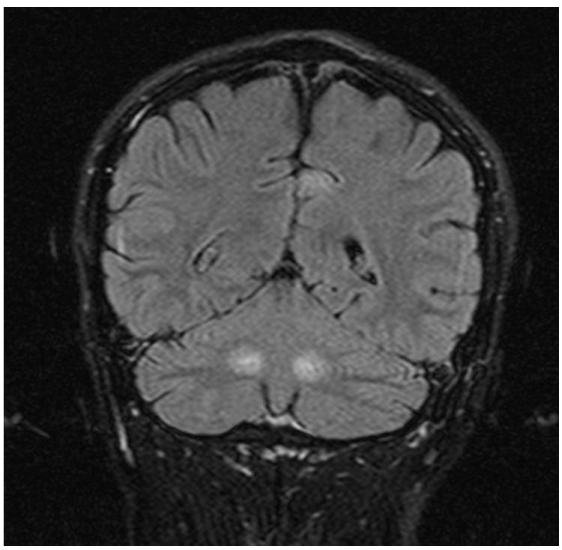

Figure 3: Cranial MRI performed after development of the cerebellar findings: FLAIR sequences showed hyperintensities in bilateral cerebellar dentate nuclei.

dysarthria, dysmetria and an ataxic wide-based gait. Control cranial MRI showed no decrease in the size of previous lesions. In addition, T2 FLAIR sequence showed hyperintensities in bilateral cerebellar dentate nuclei which was attributed to metronidazole toxicity (Figure 3). The drug was stopped immediately and intravenous methyl prednisolone 1g/day was given for five days which was followed by oral prednisone 60mg/g daily. Control MRI performed forty days later showed complete resolution of both dentate hyperintensities and diencephalic and ring enhancing lesions (Figure 4).

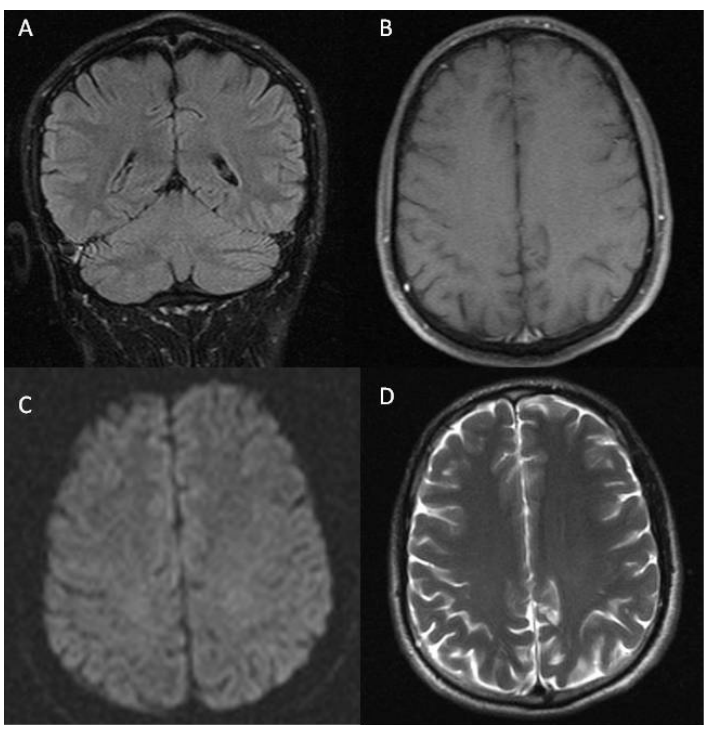

Figure 4: Control MRI performed forty days later: FLAIR (A), T1 (B), DWI (C) and T2 (D) sequences showed complete resolution of both dentate and diencephalic hyperintensities and also ring enhancing lesions.

DISCUSSION

The most common imaging lesion seen in the acute or subacute stage of parenchymal involvement in BD is an asymmetric mesodiencephalic junction lesion, which is hyperintense on T2-weighted images often associated with edema and shows contrast enhancement.[5-8] Mass-like lesions mimicking cerebral tumors have also been described.[9-12] Nodular ring enhancing lesions as it was the case in our patient have been described in just one previous case.[13] In another patient with similar imaging features an abscess involving gram-positive cocci has been identified.[14] Central hyperintensity on DWI and hypointensity on ADC map is known to be associated with brain abscess due to the impeded water mobility of pus. Necrotic tumors on the other hand are characterized by central hypointensity on DWI and hyperintensity on ADC map.[15] Although our patient's diencephalic involvement supported neuro-Behçet's disase, occipital lesions made it difficult to rule out an accompanying abscess, therefore antibiotic therapy was started before stereotactic surgery and it was continued till histopathologic results were obtained.

The neuropathologic findings of neuro-Behçet's disease in the acute phase involves meningoencephalitis with an intense inflammatory infiltration including polymorphs, eosinophils, lymphocytes and macrophages with areas of necrosis and apoptotic neuronal loss.[16,17] It is not a cerebral vasculitis as the blood vessels are not infiltrated; rather it is an inflammatory perivascultis.[17] Our patient's biopsy specimen revealed histopathologic features of neuro-Behçet's disease and an abscess was ruled out. During this period he was on metronidazole for two weeks when cerebellar symptoms and signs appeared.

Metronidazole is a commonly used drug against protozoal and anaerobic bacterial infections. Metranidazole toxicity has been reported to induce neurologic side effects including peripheral neuropathy, encephalopathy, cerebellar dysfunction and seizures.[18-21]Cumulative doses usually required to elicit cerebellar symptoms has been reported as 25-110 g.[18] In our patient, total doses of metronidazole were 28 g. Though the mechanism of metronidazole toxicity remains unclear most lesions show complete resolution.[18,19,22] This has been proposed to be associated with acute axonal swelling with increased water content rather than a demyelinating process.[18] Symmetric and bilateral T2 hyperintense lesions in the cerebellar dentate nuclei, typical for metabolic encephalopathy are the most common MRI findings.[18,19] After discontinuation of the drug, both the clinical and MRI findings of our patient showed complete resolution.

To our knowledge, this is the only reported case with co-existing neuro-Behcet's disease and metronidazole-induced encephalopathy. Ring enhancing lesions made it difficult to rule out an abscess and metronidazole was initiated after admission to the hospital and was continued till the histopathologic results were gathered which induced cerebellar dysfunction associated with typical MRI findings. Neuro-Behcet's disease is a serious condition requiring aggressive immunosuppressive treatment to prevent mortality and permanent neurological sequelae. Co-existence of metronidazole toxicity as we report here is a rare but possible complication of treatment and may lead to difficulties in diagnosis and management of this already complicated clinical picture.

DISCLOSURE

Conflict of interest: None

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