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Case Report

Neuro-Behçet disease mimicking brain tumor: A case report

Pedro L. Tramontini[1], Alessandro Finkelsztejn[2], Juliana Á. Duarte[3], Guilherme T. Santos[1], Rafael Roesler[4,5], Gustavo R. Isolan[1,6]

[1]Neurosurgery Department, Hospital de Clínicas de Porto Alegre, [4]Department of Pharmacology, Institute for Basic Health Sciences, Federal University of Rio Grande do Sul, [2]Neurology Department and [3]Radiology Department, Hospital de Clinicas de Porto Alegre, [6]Advanced Center of Neurology and Neurosurgery (CEANNE)-Brazil, Porto Alegre, RS, [5]Cancer and Neurobiology Laboratory, Experimental Research Center, Porto Alegre Clinical Hospital, Federal University of Rio Grande do Sul, Brazil

E-mail: *Pedro L. Tramontini - pl.tramontini@gmail.com; Alessandro Finkelsztejn - alessando.finkels@gmail.com; Juliana Á. Duarte - juavila2003@yahoo.com.br; Guilherme T. Santos - guilhermetomsantos@gmail.com; Rafael Roesler - rafaelroesler@hcpa.edu.br; Gustavo R. Isolan - gisolan@hcpa.edu.br
*Corresponding author

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Abstract

Background: Behçet's disease (BD) is an inflammatory multisystem disease with unknown etiology, and consists of a TRIAD comprising recurrent oral ulcers, genital ulcers, and uveitis. In some cases, the disease affects the central nervous system, called Neuro-Behçet Disease (NBD). Few cases of NBD simulating a brain tumor have been previously reported.

Case Description: Here, we describe the case of a 46-year-old male patient with a previous diagnosis of brain tumor who was later diagnosed for BD.

Conclusion: This case highlights the importance of differential diagnosis of lesions with tumoral features. Checking for the possibility of NBD may help avoiding biopsy in these types of cases.

Key Words: Behçet syndrome, brain tumor-like lesions, brain disease diagnosis, neuro-Behçet Disease

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INTRODUCTION

Behçet's disease (BD) is an inflammatory multisystem disease of unknown etiology with periods of relapses and remissions. The disease was named in the memory of "Hulusi Behçet," a Turkish dermatologist who has described a trisymptom complex, characterized by recurrent oral ulcers, genital ulcers, and uveitis.[8] Later, studies demonstrated the multisystemic pattern of this condition, which can compromise vessels, joints, the gastrointestinal tract, the heart, lungs, and central nervous system (CNS). The disease can affect all sizes of blood vessels, on both arterial and venous sides.

Few cases of NBD mimicking a brain tumor have been reported. We report a case of a patient with a previous diagnostic of brain tumor who was diagnosed as BD. We discuss the case and review the literature regarding this rare presentation of BD.

CASE REPORT

MR, male, 46-year-old, came to the hospital with a complaint of subacute hemiparesis in the left lower limb, accompanied by mental confusion.

In the past, he had the same clinical presentation associated to oral ulcers. He was submitted to brain MRI and to lumbar

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puncture. The brain MRI showed a T2-hyperintense lesion in the regions of mesencephalon and right parahippocampus [Figure 1]. The cerebrospinal fluid (CSF) showed sterile monocytic pleocytosis. In the past, it was suspected of herpetic encephalitis, and he completed a treatment with intravenous Acyclovir, with improvement of the symptoms. One year later, the patient had a similar clinical and radiologic condition, being treated again with acyclovir and showing resolution of symptoms. Seven months later, there was a new relapse, and prophylactic Valacyclovir was started. When the patient entered the hospital, he showed paralytic mydriasis in the right eye, left supranuclear facial paresis, and paresis in the left lower limb with hyperreflexia. Ophthalmologic evaluation was unremarkable. In the previous medical history, there was a clear story of recurrent painful oral ulcers (6 episodes/month – in the worst moment of the disease) that healed in seven days and acneiform lesions in dorsum. No genital ulcers or visual alterations were reported. At this time in the hospital, the patient has no oral ulcers. Cell blood count, rheumatologic tests, syphilis, HIV, hepatitis serology, and Mantoux's reaction were performed. All were negative. A pathergy test was also performed, with negative results. CSF showed 28 leukocytes (66% neutrophils and 44% monocytes) and 46 mg/dL of proteins. Cultural tests and PCRs for infectious agents were negative. Brain MRI showed an hyperintense T2 lesion at midbrain peduncle, simulating a mesencephalic tumor [Figure 2]. A neurosurgical consultation was performed. A brain biopsy was discussed, but the team decided to submit the patient to a conservative treatment, administering corticosteroids for a possible BD. He was submitted to IV methylprednisolone in a dose of 1 g daily during 5 days. His symptoms remitted completely after 10 days.

DISCUSSION

Epidemiology

Generally, BD starts in the third or fourth decade of life,[2] with similar rates for males and females. There is a higher prevalence in countries along the "Silk Route", extending from Asia (Japan, China, Russia) to the Middle Eastern and Mediterranean countries.[4] Turkey has the highest prevalence (42/10,000) in population with 12 years or older *et al*.[7] In the western countries, the prevalence is much lower.[29] Environmental and genetic factors found in eastern countries may influence the frequency of the disease. For example, HLA-B51, a kind of human leucocyte antigen, has a higher prevalence among the inhabitants of the "silk route".[4] However, BD appears to be less frequent among Japanese immigrants in the US and Turkish immigrants in Germany, suggesting the role of environmental factors in the development of the disease.[4]

Pathophysiology

In spite of the several immunological components demonstrated, the exact mechanism which leads to the inflammatory changes remains obscure. A plausible hypothesis is that an infectious agent or an autoantigen, such as heat shock proteins (HSP), triggers an inflammatory reaction that leads to the disease, in genetically predisposed individuals.[23] Oral microbial flora also has been implicated in the pathophysiology, as BD starts mostly with symptoms of the oral mucosa.[27]

Genetic factors play an important role in the development of BD. Ohno *et al*. has first described the association between the disease and HLA-B5(51) in 1973.[28] A meta-analysis showed that carriers of HLA-B51/B5 have an increased risk of developing the disease when compared with non-carriers (OR: 5.78).[26]

It has been proposed that the genetic susceptibility induces the overexpression of pro-inflammatory cytokines, such as Th1 and Th17, thus enhancing the inflammatory reaction in BD.[12] The organs affected by the disease show significant infiltration by lymphocytes and neutrophils.[10]

Clinical features

The typical features of BD include mucocutaneous lesions. Oral and genital ulcers, together with cutaneous,

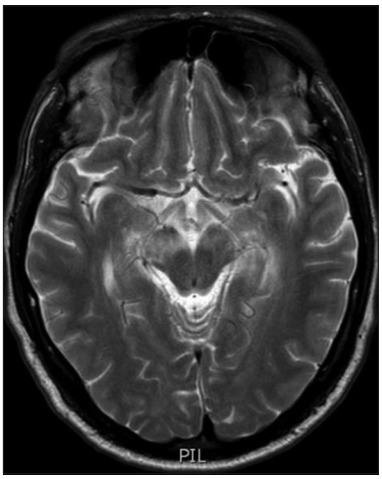

Figure 1: Lesion with hypersignal on T2 in the regions of midbrain and right parahippocampus

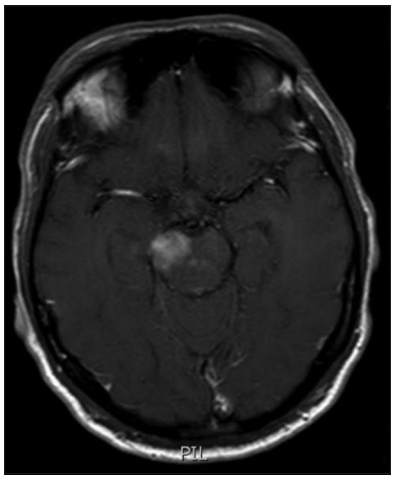

Figure 2: Hyperintense lesion on T2 at the midbrain peduncle, mimicking a mesencephalic tumor

ocular, and articular lesions are the most frequent features of the disease in all countries.[4] Oral ulcers consist of recurrent and painful ulcerations of the oral mucosa. The most common sites include lips, buccal mucosa, tongue, and soft palate. It starts as a slightly raised and erythematous area with vesicle-pustules, evolving into an ulcer within 2–3 days, with rolled borders and a grayish yellow necrotic base.[5] These lesions can be debilitating, affecting eating, drinking, and swallowing. Healing is typically spontaneous within one to three weeks.

The genital ulcers are similar in appearance and course to the oral ones. They are most commonly found on the scrotum in men and the vulva in women. They are usually deeper and have a tendency to scar and are also debilitating.[5] Other important cutaneous lesions are erythema nodosum-like lesions, papulopustular lesions, and superficial thrombophlebitis.[5]

Other symptoms of BD include ocular, vascular, gastrointestinal, and neurological involvement. Recent studies demonstrated that these other lesions can have their onsets later in the course of the disease (5–10 years).[6] Usually, BD starts with relatively milder manifestations.

Diagnosis

The diagnosis of BD is primarily based on clinical criteria following the exclusion of other conditions. The International Study Group for Behçet's Disease Criteria consists of presence of recurrent oral ulcers, plus any two of recurrent genital ulcers, typical ocular lesions, typical cutaneous lesions, or a positive skin pathergy test (SPT).

An international team developed new criteria under the name International Criteria for Behçet's Disease, briefly "ICBD" criteria, which were published in 2006. These new criteria were revised in 2013, becoming the 17th set of classification/diagnosis criteria for BD. In this criteria, oral ulcers (OU), genital ulcers (GU) and ocular manifestations get each 2 points, and others (skin lesions, neurological manifestations, vascular manifestations, and positive SPT) get 1 point. If a patient gets 4 points or more, the patient is diagnosed as having BD.[18]

Neurological features

Neurological involvement is one of the most serious causes of morbidity and mortality in BD.[21] The frequency of neurological involvement varies, based on the sample studied and the definition of neurological involvement. It seems that neuro-Behçet's disease (NBD) is more frequent in men than in women.[2,19] The age of onset is usually 20–40 years. Neurological manifestations commonly develop a few years after the onset of BD. Few patients with BD starts systemic manifestations with neurological symptoms.[1,19]

There are two categories of CNS involvement in BD: parenchymal or non-parenchymal. In the first, the principal finding is meningoencephalitis. Lesions can occur in brainstem, spinal cord, in the brain, or be diffuse.[2] At the end, vascular complications involving thrombosis of large vessels (typically veins) occur.[2] Every time that an initial diagnosis of NBD is predicted, infectious and neoplastic disorders must be ruled out.

It is important to note that NBD is an inflammatory perivasculitis.[14] So, the blood vessel walls are not infiltrated and there is no evidence for endothelial cell necrosis. The structures affected can be confirmed by MRI, where striking atrophy can be seen.[20,22]

Making a NBD diagnosis is easier when the patient has systemic findings of the disease. Also, it is uncommon for BD to arise in the absence of systemic features. No validated criteria exist.[2]

The characteristic MRI lesion in parenchymal involvement is an upper brainstem lesion that extends into the thalamus and basal ganglia on one side. Bilateral lesions are less common.[20,22] Hyperintense T2 gives a better visualization and are often associated with edema.[20,22] Comparing the findings of MRI studies, these lesions were hyper intense on both gadolinium enhanced T1-weighted images (WI) and T2WI.[16]

In the acute phase, most patients have single lesions, but in the chronic phase, more diffuse involvement is noted, making it difficult to differentiate between NBD and multiple sclerosis.[9] The most common neuropathological findings in patients with BD are focal necrotic lesions in the brain.[17] Severe and acute inflammation consisting mainly of lymphocytic and neutrophilic infiltrations of the perivascular spaces and parenchyma can lead to necrotizing and disseminated encephalitis.[11,15]

CSF constituent are altered in around 70–80% of patients with parenchymal complications.[2] CSF protein is modestly raised in most cases.[6] Cell count is often raised and CSF, and neutrophilia is found in the early stages, being replaced later by lymphocytosis.[2]

Subacute meningoencephalitis accounts for 75% of cases in parenchymal NBD.[2] Usually, this feature accompanies the exacerbation of systemic features of BD.[3] Headache is common before and during the attack. Many syndromes might be encountered during the course of parenchymal NBD. Signs of brainstem involvement include ophthalmoparesis, cranial neuropathy, and cerebellar or pyramidal dysfunction.[2] Symptoms suggestive of cerebral hemispheric involvement include encephalopathy, hemiparesis, hemisensory loss, seizures and dysphagia, depending of the location of the lesion. Ischemic stroke and epilepsy are uncommon in BD.[2]

Brain tumor-like NBD

Few cases of NBD mimicking a brain tumor have been reported. The earliest case was reported in 1987.[24]

Matsuo *et al*. have reported a case and reviewed previous reports.[25] These were predominantly large lesions, involving the commonly affected areas in NBD (braistem, diencephalon, basal ganglia, and internal capsule).[2,24,30] Most cases have been diagnosed after lesion biopsy, and respond to treatment with corticosteroids.

Differential diagnosis is extensive. It includes infectious causes (viral, bacterial, fungal), uveomeningitic syndromes (sarcoid, SLE, Sjögren), Neoplastic causes, complications of other systemic diseases or complications of treatment for BD (drug induced-meningitis, infections with immunosuppression).

Patients who have an acute parenchymal inflammatory episode usually recover well with corticosteroid treatment.[2] Around 20–30% of them stands with residual neurological impairment.[1,32] The chief pathological changes of vascular BD is aneurysm formation of the peripheral arteries.[13,16] CNS involvement occurs mostly late in the course of the disease.[17,31] The mortality reported by Wolf *et al*. in patients with NBD was 41%.[33] Our case report shows the importance of differential diagnosis in lesions with tumoral characteristics in mesencephalon and thalamus. History of recurrent oral ulcers should suggest Neuro-Behçet, avoiding biopsy in this cases and being initiated empiric treatment with corticosteroids.

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Conflicts of interest
There are no conflicts of interest.

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