



CASE REPORT

Optic neuritis as presenting manifestation of Behçet's Disease with multisystem involvement

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Special Issue on Inflammatory Demyelinating Diseases of the Central Nervous System

Abstract

Introduction: Optic nerve damage unrelated to uveitis, retinal disease and intracranial hypertension are extremely rare in Behçet's Disease (BD). We report a case of BD with systemic manifestations in which the initial neurological expression was an optic neuritis.

Case Report: A 20-year-old woman, with recurrent oral aphthosis, presented with acutely right blurred vision and was diagnosed with an optic neuritis. One year later she complained of lack of strength in the left limbs and had a mild left hemiparesis. Two years later she presented with a pancreatitis, skin ulcers and rectal bleeding, and she was diagnosed with multisystemic BD.

Discussion: We present a case where the clinical and laboratory features were very typical of inflammatory damage to the optic nerve in a patient with a later diagnosis of BD. Recognition of this clinical syndrome, although uncommon, might help clinicians to remember BD in the differential diagnosis of patients presenting with optic neuritis.

Keywords: Optic neuritis, Multisystemic, Behçet's Disease.

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Citation: Barros et al. Optic neuritis as presenting manifestation of Behçet's Disease with multisystem involvement. *International Journal of Clinical Neurosciences and Mental Health* 2016; 3(Suppl. 1):S03

DOI: [http://dx.doi.org/10.21035/ijcnmh.2016.3\(Suppl.3\).S03](http://dx.doi.org/10.21035/ijcnmh.2016.3(Suppl.3).S03)

Published: 20 Oct 2016

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Open Access Publication Available at <http://ijcnmh.arc-publishing.org>

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Introduction

Behçet disease (BD) is a rare inflammatory disease of unknown cause in which any organ can be involved. Neurological involvement, which may affect up to 49% of patients, is an important cause of long-term morbidity and takes mainly one of two forms: parenchymal (most often meningoencephalitis) and non-parenchymal (most often vascular thrombosis within large veins).

The age of onset of neuro-BD (NBD) is usually 20–40 years and it commonly develops a few years after the onset of the other systemic features of BD [1]. However, the first systemic symptoms of BD might coincide with neurological presentation and in some uncommon cases, the neurological presentation can precede systemic features. In such cases, diagnosis can be very difficult, because some cases may never develop mucocutaneous manifestations [2].

Optic nerve damage unrelated to uveitis, retinal disease and intracranial hypertension is extremely rare but has been reported in a few patients with BD. It can be bilateral and can be recurrent over many years. Kansu et al reported two patients with BD and a diagnosis of retrobulbar neuritis [3]. However, it is still considered that the most likely pathophysiological hypothesis to optic nerve lesion is secondary invasion after retinal vasculitis or a consequence of destruction after glaucoma and uveitis. So, optic neuritis is an exceedingly rare presentation of BD; by contrast, inflammatory eye disease affects up to 70% of patients.

Here, we present a case report of BD in which the initial neurological expression (and one of the first manifestations) was an optic neuritis without concomitant ocular disease.

Case Report

A 20-yr-old, white, Portuguese woman, with a history of recurrent oral aphthosis (>3 episodes/month) and purpura after “flu-like” syndrome at age 7, presented with acutely right blurred vision and impaired color vision. The visual disturbance developed over a period of hours and was associated with pain with eye movements; visual acuity was 6/10 in the right eye. A central scotoma was present in the right eye on confrontation testing, and ophthalmoscopy revealed swelling of the right optic nerve head, with no evidence of uveitis, retinal vasculitis or optic atrophy. Visual evoked potentials showed increased latency in the right eye. The remainder of the neurologic and systemic examination was normal. Brain MRI (Figure 1) revealed numerous foci of hyperintense signal on long TR sequences in the subcortical white matter (periventricular frontal, parietal, occipital lobes and corpus callosum); there was not any infratentorial lesion and none of these lesions had gadolinium enhancement. There was also no evidence of venous thrombosis on magnetic resonance venography.

The spinal cord MRI was normal. The CSF sample was acellular, with glucose and protein concentration within the normal range, and later proved negative by polymerase chain reaction for herpes simplex virus, cytomegalovirus, borrelia and varicella zoster virus; oligoclonal bands (OCB) were negative. A pathergy test was performed and was positive. The day after admission, the patient developed an oral ulcer (Figure 2) that was biopsied; histology revealed an inflammatory infiltrate of mixed type with lesions compatible with a vasculitis. The diagnosis was optic neuritis secondary to probable BD and the patients started treatment with intravenous

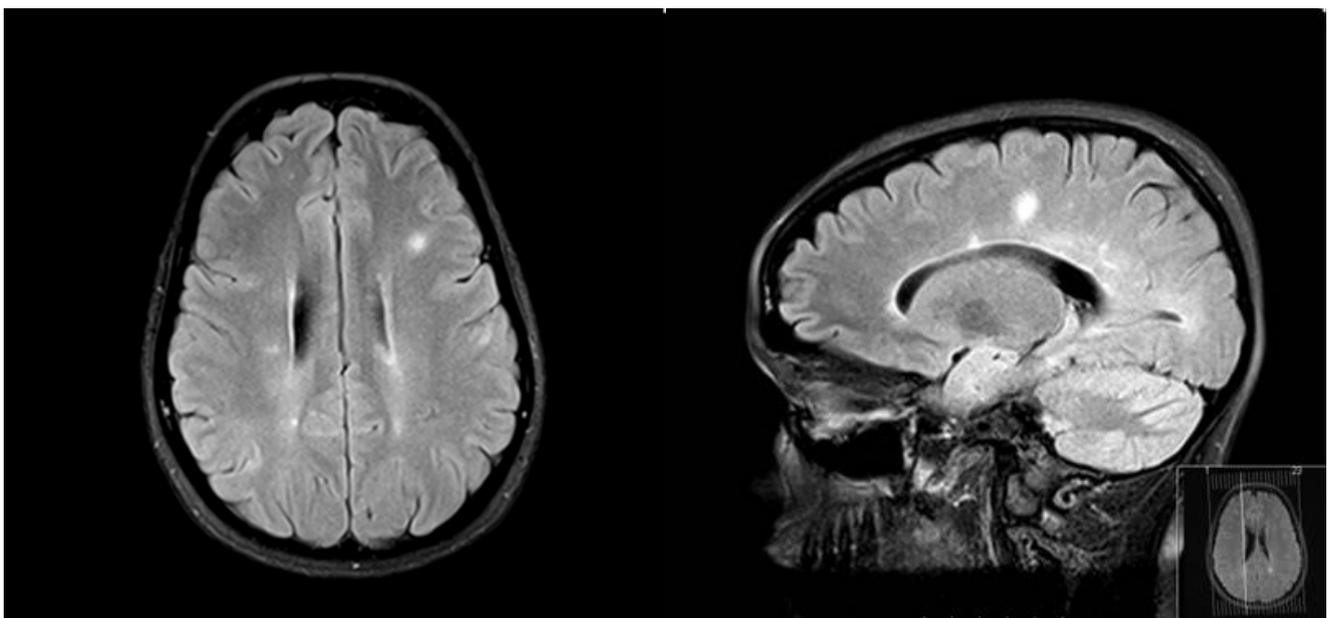


Figure 1. Brain MRI revealed numerous foci of hyperintense signal in the subcortical white matter in a total of 17 lesions.



Figure 3. Oral ulcer.

methylprednisolone at a dose of 1 g daily/5 days. Clinical response was noted within 72 h, but recovery was not complete and a 5-day cycle of intravenous human Immunoglobulin (0,4 g/Kg/day) was performed, with visual acuity returning to 10/10 in the right eye and partial resolution of papillitis seen on ophthalmoscopy. At follow-up, visual acuity was 10/10 in both eyes, with full visual fields and normal ophthalmoscopic appearances. It was decided to start Colchicine, 1 mg/day.

One year later, the patient was admitted with dizziness and imbalance; neurological examination revealed a mild left hemiparesis. A new brain MRI was performed: there was persistence of the lesions previously described (some with decreased size) and two new frontal white matter lesions, subcortical at right and sub-insular at left. A 5-day cycle of intravenous methylprednisolone (1 g/day) was performed and the patient achieved full recovery. It was decided to initiate therapy with azathioprine 100 mg/day.

Twelve months later, the patient complained of abdominal pain, haematochezia and skin ulcers. Colonoscopy showed a change in the vascular pattern in the rectum with erythema and friability; histology was suggestive of ulcerative colitis. The patient started mesalazine and required 2 cycles of prednisolone (0.5 mg/kg/day) to achieve disease control. Azathioprine was increased to 150 mg/day. One year later, the patient was hospitalized with acute pancreatitis. On the suspicion of drug toxicity, azathioprine and mesalazine were stopped. Two days later the patient reported the onset of oral and skin ulcers, abdominal pain, haematochezia and fever with increased inflammatory markers. A new colonoscopy showed linear and star ulcers with exudate, more prominent at the hepatic angle, suggesting the diagnosis of multisystemic BD. Due to the severity of the disease, the ineffectiveness of azathioprine and the need to reduce the dose of glucocorticoids, the patient started infliximab 5 mg/kg (each 8 weeks), with an increase of the dose to 10 mg/kg (each 6 weeks).

The patient had a significant clinical and analytical improvement since then, with reduction of prednisolone dose. Colonoscopy performed 12 months later revealed healing of intestinal ulcers. Azathioprine was resumed about 9 months uneventfully.

No neurological events occurred; 6 years after the initial neurological expression with optic neuritis the patient presents a normal neurological examination and cerebral MRI showed no progression of the lesions.

Discussion

We present a case where the clinical and laboratory features were very typical of inflammatory damage to the optic nerve. Mitra et al [4] published a report of a 10-year-old girl with BD and acute unioocular visual loss associated with papilledema, also describing several neurological separate presentations over the course of 3 years, associated with cerebral MRI abnormalities. A very good response to systemic corticosteroids was noted, similarly to our patient. As reported in a recent review of neurological involvement in BD, early recognition and treatment of optic neuropathy can limit the degree of permanent visual loss, and there is usually a significant response to steroids [5]. Beyond cerebral venous thrombosis and meningocephalitis, the neurological involvement in BD is usually due to parenchymal brain and spinal cord focal lesions. In the acute phase, most patients have single lesions; however, in the chronic phase, more diffuse involvement can be seen, with multiple lesions affecting the periventricular and subcortical areas. Thus, in an atypical clinical context, the differential diagnosis with multiple sclerosis can be extremely difficult [6].

There have been no controlled trials of treatment of any aspect of neurological involvement in BD. There is a consensus that EV corticosteroids should be used as first-line treatment. Whether immunosuppressive agents or tumour necrosis factor (TNF) antagonists should be used at the same time or later depends on the severity of disease and the response to steroids. In this case, and given the good initial response to a cycle of corticosteroids, it was decided to delay the onset of immunosuppressive therapy, which was then initiated after the second neurological event. It is now recommended that patients should move on to anti-TNF α earlier with aggressive disease, such as the case that responds poorly to steroids, or if relapse is not prevented by regular immunosuppression. Once more, that is what happened in this case: when intestinal involvement occurred, it was decided to escalate therapy and initiate an anti-TNF α .

We emphasize that a diagnosis of BD was only possible many months after the visual disturbance, when other systemic features appeared. According to the International BD Study Group (ISGBD) criteria, a patient with recurrent oral aphthosis and neurological manifestations cannot be diagnosed with BD. Some patients can take several years

for other systemic manifestations to appear and these cases may lead to an improper diagnosis with adverse therapeutic consequences if diagnosis is conducted strictly on ISGBD criteria.

In conclusion, optic neuritis without inflammatory eye disease should be considered as part of the spectrum of NBD. Recognition of this clinical syndrome, although uncommon, might help clinicians to remember BD in the differential diagnosis of patients presenting with optic neuritis.

Abbreviations

BD: Behçet disease; ISGBD: International BD Study Group; NBD: Neuro-BD (NBD); TNF: Tumour necrosis factor

Competing interests

The authors declare no conflict of interest.

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