

An unusual case of meningitis

Un caso inusuale di meningite

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INTRODUCTION

Behçet Disease (BD) is a multisystem relapsing disease of unknown cause in which an inflammatory perivasculitis can arise in almost any tissue. The most widely accepted criteria for the diagnosis of BD are the presence of recurrent oral ulceration in addition to two other features among recurrent genital ulceration, eye lesions, skin lesions and a positive pathergy test [1]. Oral and genital ulcers are the most frequent signs of this disease with a frequency of 97-99% and 85% respectively [1-3].

HLA type B51 has been reported to be present in 60-70% of Turkish and Japanese patients, although in only 10-20% of European patients. Neurological involvement (neuro-BD, NBD) is observed in up to 30% of patients, commonly develops a few years after the onset of BD and is the most serious cause of short-term mortality and disability BD-related [1, 2].

There are two categories of CNS involvement in BD that are generally accepted: parenchymal and non-parenchymal involvement. In the parenchymal category, meningoencephalitis occurs, whereas in the non-parenchymal one vascular complications involving thrombosis within large veins and occasionally arteries occur. We here report the case of a patient with an atypical presentation of NBD.

CASE REPORT

A previously healthy, caucasian, 38-year-old female was admitted to the emergency department of our hospital three days after the onset

of fever, headache, neck pain with partial rigidity and impaired vision of the left eye. On examination, she had a temperature of 38.9°C, an oxygen saturation of 100% on room air, a blood pressure of 140/85 mmHg, a heart rate of 98 beats per minute and a respiratory rate of 18 breaths per minute.

Complete blood counts revealed a haemoglobin of 13.6 g/dl, a white blood cell count of $10.37 \times 10^3/\mu\text{l}$ (neutrophil 88.6%, lymphocyte 9.1%), a platelet count of $256 \times 10^3/\mu\text{l}$ and a pro-inflammatory state (CRP 21.4 mg/dl).

A lumbar puncture was performed, which revealed pleocytosis (white cells 185/ μl , 2% granulocytes and 98% monocytes), mild hypoglycorrhachia (54 mg/dl) and increased protein level (168 mg/dl). Due to the suspicion of meningitis, she was started on ceftriaxone (2 g x 2/die), ampicillin (4 g x 3/die), acyclovir (800 mg x 3/die) and dexamethasone (8 mg x 2/die), and she was transferred to the department of infectious diseases.

MRI of the brain was normal (Figure 1A and B), but fluorescein angiography showed bilateral retinal vasculitis with hemorrhages (Figure 1C and D). All microbiological analysis performed on CSF and blood (both culture and neurotropic virus PCR, VDRL and TPHA, *Mycobacterium tuberculosis* PCR, *Streptococcus pneumoniae* and *Neisseria meningitidis* urinary antigens), as well as specific blood tests aimed to diagnose autoimmune or clotting disorders, yielded negative results.

Although at the presentation of the patient and during the recovery the orogenital mucosa was normal a detailed anamnesis of the patient revealed some oral aphthous episodes and, nine

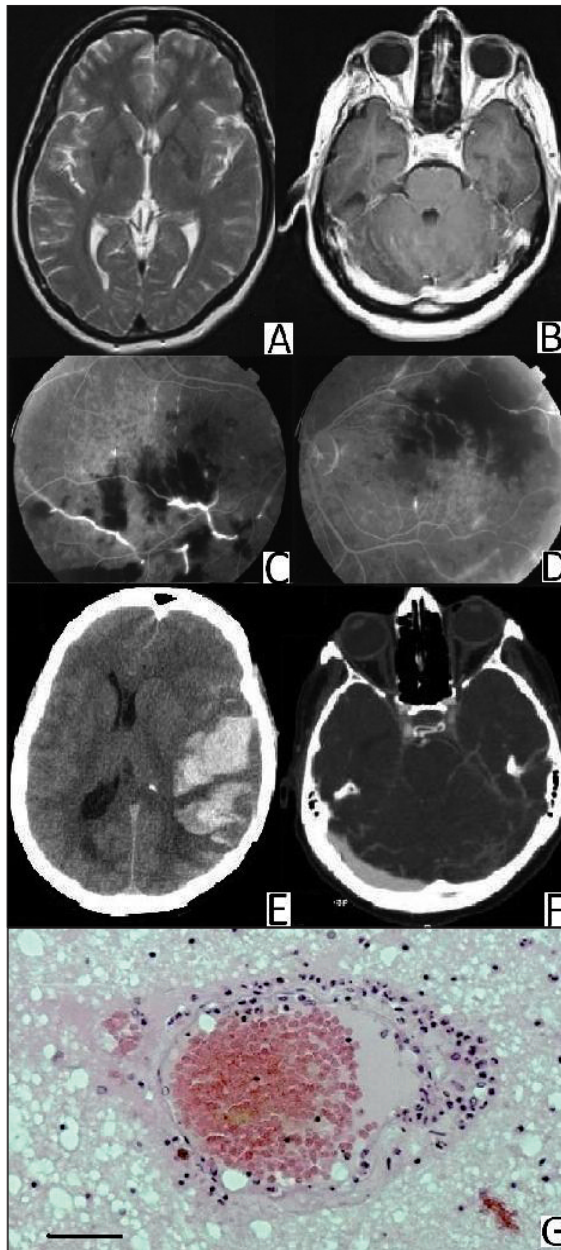


Figure 1 - Normal MRI signal of brain stem, basal ganglia and white matter on axial T2 weighted images (A) and regular contrast uptake of the transverse sinus with echo contrast MRI (B). Bilateral retinal hemorrhages and retinal vasculitis of the posterior pole of the right (C) and left (D) eye detected by fluorescein angiography. Temporal-occipital haemorrhagic stroke consequent to a left sigmoid transverse sinus thrombosis on CT scan (E, F). To note, the mass-effect with compression on left lateral ventricle and initial dilatation of the occipital horn of the right lateral ventricle (F). Histologic specimen of brain tissue stained with hematoxylin and eosin (G). A small vessel with mononuclear inflammatory infiltration, mainly lymphocytes, surrounding it. Scale Bar = 50 microns.

months before hospitalization, a self-limiting episode of genital ulceration. BD screen was undertaken: the pathergy test was negative, but immunogenetic analysis showed positivity for HLA-B51 allele.

Cyclosporine (300 mg die) was therefore started, while going on with antibiotic and steroid therapy, and the clinical conditions of the patient began to improve.

Three days thereafter, however, the patient became suddenly drowsy and CT scan of the brain revealed a wide temporal-occipital haemorrhagic stroke related to the presence of left sigmoid transverse sinus thrombosis and causing a marked cerebral oedema with transtentorial herniation of the left hippocampus and mass effect on the brain stem (Figure 1E and F). In spite of intensive care treatment, the patient's general conditions critically deteriorated and she finally died 12 days after hospitalization.

Although the *post-mortem* examination of the visceral organs of the patient did not show any other systemic signs of vasculitis, no evidence of oro-genital ulceration or skin lesions, the main histological feature of the brain tissue examined was the presence of perivascular inflammatory cell cuffs, mainly lymphocytes, around the middle-sized and small blood vessels without wall necrosis or evidence of inflammatory cells invading it (Figure 1G). These vessels, mainly part venules and small veins, often showed micro thrombi inside them. This histological and neuropathological appearances in our patient confirmed the hypothesis of Neuro Behçet disease.

DISCUSSION

In the patient we described, three main aspects deserve special considerations. First of all, although autopsy did not show evidence of either systemic vasculitis or oro-genital ulceration and although criteria for the diagnosis of BD were not completely fulfilled, the clinical, immunological and neuropathological features together were consistent with NBD.

To our knowledge, these atypical findings have been previously described in literature in only one case by Lueck et al. [4].

The above-mentioned patient had a history of relapsing uveitis and retinal vasculitis and cranial nerve palsies. As in our patient, there were no systemic signs of vasculitis and no evidence

of oral or genital ulcerations, but MRI of the brain showed a deep lesion close by thalamus whereas neuropathological examination revealed multiple small necrotic lesions affecting both grey and white matter as well as diffuse perivascular inflammation.

Authors defined a new clinical condition, which called "Behçet's-MINUS" (Multifocal, Intermittent Neurological and Uveitic Syndrome). Secondly, neurological involvement of our patients had features of both parenchymal (alterations of CSF constituents) and non-parenchymal (thrombosis of the left sigmoid transverse sinus) NBD.

Patients with cerebral venous thrombosis have usually normal CSF characteristics, but in some series up to 20% of patients present with coexisting parenchymal and vascular complications, making the diagnosis more difficult [5-8]. Finally, the syndrome had an unusual, rapid progression and our patient died despite prompt and appropriate treatment.

We can suppose that in some cases the neurological involvement precedes so rapidly that systemic features of BD do not have time to appear, which could explain why our patient did

not have either systemic signs of vasculitis or typical aphta.

■ CONCLUSION

NBD is a multifaceted disease characterized by many different clinical onsets and no validated criteria for its diagnosis exist.

Moreover diagnosis can be intricate, as on our case, because NBD can present itself as an acute meningeal syndrome that mimics central nervous system infections.

Whether diagnostic criteria would help to reduce the risk of incorrect diagnosis or therapeutic failure is not clear. Nevertheless, we believe that efforts at developing such criteria should be pursued, in order to help clinicians faced with difficulty in diagnosis.

Key words: Behçet Disease, Neuro-Behçet-Disease, oral ulcers

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SUMMARY

We report on a patient who presented at our hospital with fever, headache, neck pain, partial nuchal rigidity and decreased vision of the left eye. The clinical history, biochemical and instrumental exams performed suggested meningitis but the final hypothesis achieved was an unusual case of Neuro-Behçet-Disease (NBD) without orogenital ulcerations at presentation and with normal MRI

findings, whose course was complicated by fatal cerebral venous sinus thrombosis and intracranial haemorrhage. The post-mortem results confirmed the diagnosis. This is a rare case confirmed by anatomo-pathological findings where NBD can present itself as an acute meningeal syndrome that mimics central nervous system infections, making diagnosis difficult and delaying treatment.

RIASSUNTO

Riportiamo il caso di una paziente ricoverata per febbre, cefalea, dolore al collo con parziale rigidità nucale e calo del visus dell'occhio sinistro. La storia clinica iniziale e i primi accertamenti strumentali sembrano suggerire una meningite ma ulteriori approfondimenti condurranno alla diagnosi di Neuro-Behçet-Disease (NBD) dall'esordio inusuale perché in assenza di afte oro-genitali e con

reperti neuro-radiologici iniziali pressoché normali, il cui decorso però si complicherà rapidamente con una trombosi dei seni cerebrali ed infarcimento emorragico. I reperti anatomo-patologici confermeranno la diagnosi. Il caso descritto illustra un episodio di NBD che esordisce con la sintomatologia tipica di una meningite acuta, rendendo difficile la diagnosi e il successivo trattamento.

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