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Case Report Open Access

Neuro-Behcet's-Disease with Severe Brainstem Affection: A Case Report of a Successful Intensive Medical Care Management

Oikonomou P* and Bäzner H

Neurological Clinic, Klinikum Stuttgart, Katharinen Hospital, Kriegsbergstr, Germany

***Corresponding author:** Oikonomou P, Neurological Clinic, Klinikum Stuttgart, Katharinen Hospital, Kriegsbergstr, Germany, Tel: 49711-278-42460; E-mail: p.oikonomou@klinikum-stuttgart.de

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Abstract

Neuro-Behcet's-disease (NBD) refers to any neurological involvement of Behcet's-disease (BD), which is a multisystemic vasculitis, presumably of autoimmune etiology. Few cases of neuropsychiatric manifestation of BD with severe parenchymal lesions have been reported. Clinicians who are unaware of this fact can neglect a fatal complication of BD. With respect to this diagnostic and therapeutic challenge we report of a 38-year-old man with a history of BD, who presented to our emergency department with hyperactive delirium, dysarthria, deterioration of vision, headache and nausea due to pronounced brainstem affection. After symptomatic and causal treatment in our neurological intensive care unit the patient improved clinically, reflected in the decline of pathological findings in the neuroimaging.

Keywords: Neuro-Behcet's-disease; Delirium; Brainstem affection; Diagnosis; Management; Neurological intensive medical care; Behcet's-disease; Neuropsychiatric disorder

Abbreviations: BBB: Blood-Brain Barrier; BD: Behcet's Disease; cMRI: Cranial Magnetic Resonance Imaging; CMV: Cytomegalovirus; CNS: Central Nervous System; CSF: Cerebrospinal Fluid; DD: Differential Diagnosis; e.g.: Exempli Gratia; EBV: Epstein-Barr-Virus; HHV4: Humanes-Herpes Virus-4; ECG: Electrocardiogram; HSV: Herpes-Simplex-Virus; i.e.: Id Est; I.V.: Intravenous; INT-α: Interferon-α; LP: Lumbar Puncture; NICU: Neurological Intensive Care Unit; NBD: Neuro-Behcet's-Disease; VZV: Varicella-Zoster-Virus; HHV3: Humanes Herpes Virus 3

Introduction

Behcet's-disease (BD) is a multisystemic vasculitis affecting vessels of different size, type and localisation [1]. The clinical course is characterized by recurrent oral and genital ulcerations, ocular manifestations such as uveitis and skin lesions e.g. erythema nodosum [2]. The pathogenesis of BD remains unknown, but autoimmunity initiated from infectious agents and other environmental factors, as well as genetic disposition, are suspected to play an important role [3].

Neuro-Behcet's-disease (NBD) is a term to describe every neurological involvement of BD [4]. NBD lesions occur more often in the central nervous system (CNS) than in the peripheral nervous system [5]. NBD can be classified into parenchymal and nonparenchymal; also referred to as vasculo-BD or angio-BD [6,7].

Delirium is one of the most common clinical syndromes occurring in the neurological intensive care unit (NICU) [7]. Few cases of neuropsychiatric manifestations of NBD in the form of delirium have been published [8,9].

Methodology

A search of relevant literature was performed in "PubMed" using the following strings; "Behcet's-disease", "Neuro-Behcet's-disease", "delirium and Neuro-Behcet's-disease" and "therapy of Neuro-Behcet's-disease".

Case Report

A 38-year old man was admitted to the emergency department of our hospital in an acute confusional state. Review of his medical history revealed high restlessness, agitation, dysarthria commencing 2 days prior, deterioration of vision, and a gait instability beginning weeks before.

The day of admission, the patient also suffered from acute headaches, nausea with vomiting and complained of not seeing clearly. The patient was awake, had normal vital signs and no hemodynamic instability. His neurological assessment revealed anisocoria with moderate mydriasis in the left eye and dysarthria. Examination of the heart, lungs and abdomen revealed no pathological findings. Inspection of the skin revealed pseudo-follicular changes in the thigh, aphthae on the scrotum and in the mouth. Psychopathological examination showed a psychomotor slowing, disorientation in every dimension, disorder of the content and flow of thoughts in the form of paranoia and optic hallucinations. The medical examination showed minor signs of hyperactive delirium.

The patient's medical record revealed that he was suffering from BD with ocular manifestation, i.e., panuveitis and occlusive retinal vasculitis. As a research trial participant over the past 5 years he was regularly prescribed interferon-α treatment.

To confirm the suspicion of NBD, a cranial MRI examination (cMRI) was performed. The cMRI showed gadolinium enhancing lesions mainly in the mesencephalic-diencephalic transition area with surrounding edema-equivalent signal demonstrating a typical image of parenchymal NBD (Figure 1).

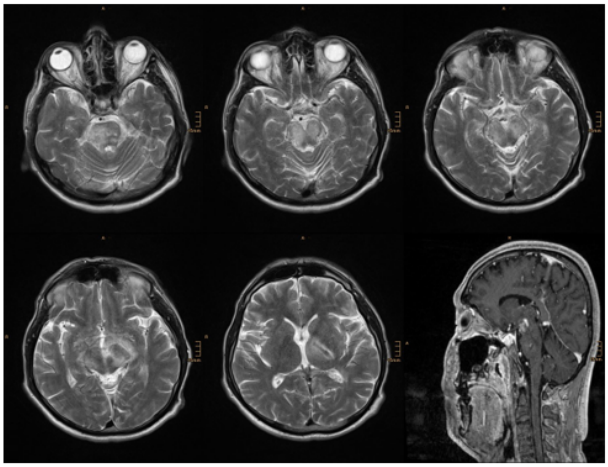

Figure 1: MRI-series of five T2-axial and one T1-sagital with gadolinium: Asymmetrically arranged lesions on the right in mesencephalic-diencephalic transition region with gadolinium enhancement, surrounding edema-equivalent signal, which discreetly extend along the long paths superiorly in the left-sided thalamus and the pontomedullary junction.

Due to the hyperactive delirium and risk of circulatory and respiratory dysregulation induced by the affection of brainstem, the patient was admitted to our NICU. After admission the patient remained very restless, showed poor insight and self-harming behavior. The cerebrospinal fluid (CSF) showed a total protein of 69,3 mg/dl and 88 leukocytes/µl, including 35 lympho-monocytic cells/µl and a lactate-level of 2.5 mmol/l. Infectious causes were excluded following negative examination in the CSF for syphilis, borrelia, toxoplasmosis, HSV, VZV, EBV and CMV. No antiviral prophylaxis was administered.

A disease-modifying treatment with methylprednisolone 1g/d was administered immediately after admission combined with thrombosis prophylaxis, gastric protection, regular measures of electrolyte and glucose, and continued for 5 days. A schema of oral prednisolone followed, beginning with 100 mg/d and was successively reduced by 10 mg every 3 days.

The prolonged hyperactive delirium was treated with benzodiazepine, clonidine and antipsychotics. Mobilization and physiotherapy contributed to remission of delirium symptoms.

A neuroimaging follow-up was conducted after 5 days of methylprednisolone treatment. The cMRI revealed a decline of the findings with recurrence of edema and space-occupying effect and declining contrast enhancement (Figure 2).

After multidisciplinary discussion and considering the patient's questionable compliance, we concluded to administer I.V. pulse therapy of cyclophosphamide 1000 mg/month for the following 6 months with additional clinical and MRI follow-ups.

The patient showed successive clinical improvement in our NICU and was transferred to our neurological ward and later to a neurological rehabilitation center. At the time of transfer no signs of delirium existed. The cMRI at that time showed a further improvement in the findings (Figure 3).

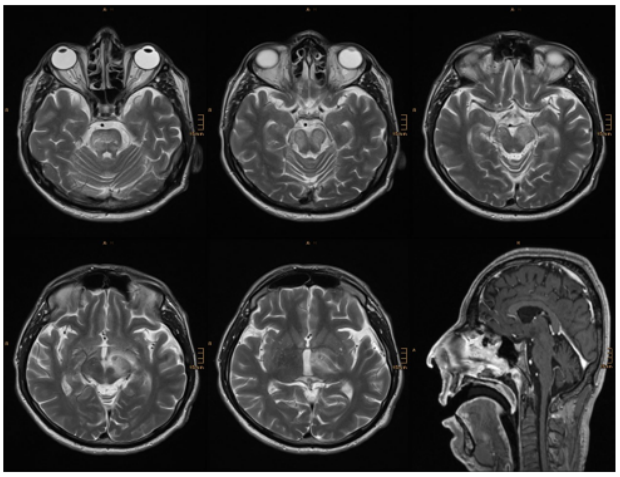

Figure 2: MRI-series of five T2 axial and one T1 sagital with gadolinium: After 5 days of methylprednisolone therapy, decline of the pathological findings with recurrent edema/space-occupying effect and a decline in gadolinium enhancement with further extensive high T2 signal changes focusing mesodiencephalic (bilaterally in the pons, the right cerebellar peduncle and cerebral peduncle, thalamus and left sided posterior capsule).

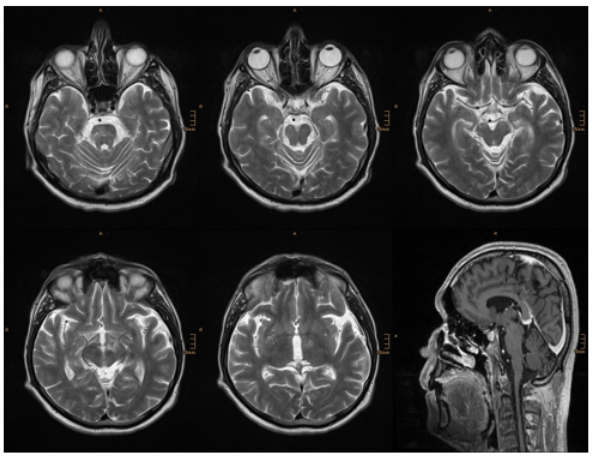

Figure 3: MRI-series of five T2 axial and one T1 sagital with gadolinium: Significant decline of the pathological findings with recurrent edema, no more mass effect and a further decline in gadolinium enhancement.

Discussion

BD has a worldwide prevalence of 0.1-1/10,000 with a significant geographical preference in patients from eastern Asia to the Mediterranean [1,3], with a higher prevalence in Turkey 80-420/100,000 [7]. The patient was of Turkish ancestry. Disease incidence amongst individuals of Turkish heritage in Germany was

found to be 21/100,000; which is significantly higher than that of the general German population (0.42–0.55/100,000) [10].

The diagnosis of BD is based on criteria including recurrent genital aphthae, eye and skin lesions and a positive pathergy test [11]. There are no existing pathognomonic laboratory tests for BD, hence the diagnosis is made on the basis of clinical findings. In our case the patient was already diagnosed with BD, therefore discussion of the diagnostics of BD is beyond the scope of this paper.

NBD is rare and remains difficult to diagnose. Several infections and other inflammatory diseases can produce similar symptoms and should be excluded. In fact, NBD occurs in 5-10% of patients with BD and is more frequent in males [1]. In our case NBD occurred approximately 5 years after the onset of the disease. This chronicle dissemination of 5 years between the manifestations of NBD after the diagnosis of BD has also been described in other demographic studies [4,12]. Importantly, MRI with MR angiography and MR phlebography is essential in order to exclude non-parenchymal lesions of NBD e.g. aneurysms, sinus vein thrombosis. Nonetheless the DD of an infectious cause, especially in a patient under an immune-modulatory treatment with IFN-α, has to be excluded. We recommend considering central nervous system involvement in patients with BD as soon as neuropsychiatric symptoms will occur. Follow-up cMRI examinations are needed to both confirm the diagnosis and demonstrate the response to treatment.

Whilst monitoring the patient's vital signs, we performed a symptomatic and causal treatment of the hyperactive delirium by modulating the immune response at the small cerebral vessels considered responsible for the parenchymal lesions apparent in the MRI. However, early mobilization, a normal circadian rhythm, and humanistic care of the patient remain standard practice for the best medical treatment of delirium at the ICU [13]. These practices, in combination with core-disease therapy, lead to a rapid improvement of the patient, facilitating the transfer to a neurological ward for the initiation of the chronic treatment of NBD.

Curative therapy of NBS is currently not available. Present treatment attempts to limit the neuroinflammation in order to reduce brain damage, to slow disease progress, and to avoid a life -threatening situation [3,14]. A variety of anti-inflammatory and immunosuppressive therapies have been reported [15]. General clinical experience with BD suggests the use of glucocorticoids, especially in cases such as ours, where acute life or organ threatening conditions present [12]. Nevertheless, no placebo-controlled trials of glucocorticoids for NBD have been performed. Some data suggested that the efficacy of glucocorticoids varies according to the regimen and route of administration [16]. We performed a high dose pulse corticosteroids treatment with methylprednisolone 1g/d administered intravenously for 5 days, followed by gradual reduction of orally administered prednisolone.

Disease-modifying treatment was also initiated with cyclophosphamide. This was an individual empirical decision based on the treatment of cerebral vasculitis as no placebo controlled, or comparative trials, of NBD treatment have been published [17]. A trial of 40 patients treated with cyclophosphamide suggested that an immediate and aggressive treatment by cyclophosphamide may ameliorate the prognosis of NBD [1]. New treatment strategies with anti-chemokine and anti-cytokine antibodies have also been suggested. Unfortunately, long-term treatments have not demonstrated a healing outcome [7]. The prognosis of NBS remains therefore, unfavorable [18,19].

Conclusion

To conclude, severe neurological manifestations in BD are rare in central Europe. However, in patients with the typical signs of BD and acute neuropsychiatric syndrome, NBD should be taken into consideration. Mandatory diagnostic measures include cMRI including cerebral vascular imaging with MR-angiography or conventional angiography, and CSF studies. Disease-modifying therapy of NBD is not yet sufficiently evidence-based; therefore, regular clinical and imaging follow-ups are indicated. The clinical characteristics of each form of NBD, along with the patient's individual compliance, should be also taken into consideration. Multicentre trials are needed in order to improve the evidence of our therapeutic strategies.

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