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CASE REPORT

A Changed Man: A Rare Case of Behcet's Disease Autoimmune Encephalitis

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Abstract

Behcet's disease (BD) is characterized by recurrent oral ulcers with concomitant systemic multi-organ involvement, which may include neurological disease, ocular disease, vascular disease, genital ulcers, skin lesions, and arthritis. The clinical symptoms arise from vasculitis that involves small, medium, and large blood vessels. We present the case of a young male who presented with atypical Behcet's autoimmune encephalitis with recurrent oral ulcers, neurological manifestations, HLA-B51 positivity, abnormal EEG findings, and improvement following multiple plasma exchange treatments.

Keywords: Behcet's, Autoimmune, Encephalitis, HLA-B51

1. Introduction

Behcet's disease (BD) is a vasculitis that involves small, medium, and large vessels leading to systematic multi-organ manifestations.[1] These presentations include oral ulcers; genital ulcers; skin findings such as erythema nodosum; uveitis; and rarely, neurological involvement.[1] The exact pathogenesis of Behcet's is not well understood, but there is a strong genetic link with BD and the presence of HLA-B51 allele.[2,3] We present the case of a 23-year-old male with no PMH who presented with recurrent oral ulcers, neurological involvement, positive HLA-B51 allele, abnormal EEG findings, and improvement following multiple plasma exchange treatments, which led to the diagnosis of atypical Behcet's autoimmune encephalitis.

2. Case presentation

A 23-year-old male with no PMH presented to the emergency department with worsening recurrent involuntary forehead tapping with his upper extremities associated with memory loss, multiple oral sores, appetite loss, and disengagement in activities for daily living to the point of being bedbound.

His symptoms appeared suddenly five years prior to presentation at 18 years old. His initial symptom was intermittent involuntary upper extremity movements which progressively increased in frequency. Subsequently, he became more disengaged in daily activities, had blunt affect, socially disconnected, and performed poorly academically. Prior to age 18, he performed his activities of daily living, was socially active, and performed well academically.

His symptoms, between the ages of 18–19, were attributed to depression, and he was placed on various psychiatric medications, including selective serotonin receptor inhibitors; however, he did not clinically improve. As a result, an infectious work-up was pursued when he was 20 which revealed elevated IgM titers for Lyme, Mycoplasma, and Rocky Mountain spotted fever (RMSF). After multiple evaluations by different infectious diseases specialists, he was deemed to not have any of these infections. Of note, the patient continues to have elevations of IgM and IgG titers to Lyme and

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Mycoplasma three years later along with elevations of IgM titers for RMSF disease and IgG titer elevations in Coxsackievirus and Human Herpesvirus 6. At the age of 20, he had CSF testing, EEG, and a brain MRI; the results were negative and ruled out meningitis, encephalitis, seizures, mass, stroke, multiple sclerosis, hydrocephalus, or other infectious causes. CSF results revealed cell count: 0, protein: 36, glucose: 61. Neurology evaluated him and diagnosed autoimmune encephalitis based on his clinical presentation; his neurological exam at the time was normal aside from his blunt affect and involuntary upper extremity movements. He received five rounds of intravenous immunoglobulin (IVIG) at a dose of 2 g/kg daily with minimal improvement to his autoimmune encephalitis. Subsequently he received plasmapheresis for 5 dosages every other day and had marked improvement; his involuntary movements decreased substantially and he was more active socially and physically. However, these improvements only lasted a few weeks. He was generally noncompliant with medical follow-up and had persistent symptoms for the 2–3 years prior to his current ED presentation.

On this current admission, his family brought him in for an evaluation because they believed his blunt affect and involuntary forehead tapping had worsened. On examination, he was alert and oriented ×3, had multiple oral ulcers, and persistently tapped his forehead; the remainder of his exam was unremarkable. Due to his previous improvement after plasmapheresis, he received plasmapheresis again and had similar improvement; he eventually received five plasmapheresis treatments every other day during his hospital course. Further testing revealed positive HLA B-51, and an EEG revealed diffuse theta waves suggestive of diffuse cerebral dysfunction and paroxysmal sharp and sharp contoured activities in bilateral frontotemporal regions. His brain MRI at this time revealed no acute abnormalities. Based on his presentation, he was diagnosed with Behcet's autoimmune encephalitis. His symptoms of blunt affect and involuntary movements would improve following every plasmapheresis session. Due to his positive response to plasmapheresis, the family opted to continue recurrent plasmapheresis treatment rather than utilizing other therapies. As an outpatient, he received plasmapheresis every other day for one week, followed by weekly for three months. His symptoms would slowly return by the end of the week prior to his next treatment. He has not returned to his baseline before his onset of symptoms that started at age 18, however he has shown improvement.

3. Discussion

BD is a systemic vasculitis of unclear etiology that can affect multiple organ systems. The prevalence of BD is highest in the Middle East and East Asia.[4] BD most commonly occurs in the third decade of life, and males are more likely to have the disease compared to females.[1]

Neurological involvement in BD occurs in less than 10% of all Behcet's cases.[5] The neurological manifestations of BD is diverse, including personality changes, memory loss, headaches, movement disorders, and psychiatric manifestations.[6] The HLA-B51 allele appears to be linked to BD; one study estimated that the odds of a patient with the presence of HLA-B51 allele developing BD were increased by a factor of 5.78[2] while another study found that 60% of patients with BD had the HLA-B51 allele.[3]

The diagnosis of BD is a clinical one. Per the International Study Group criteria, the diagnosis of Behcet's is made in patients with recurrent oral ulcers (at least three episodes in a twelve-month period) and with any two of the following: recurrent genital ulcers; eye lesions; skin lesions; and a positive pathergy test.[7] As discussed previously, HLA-B51 has shown to have a strong association with patients who have BD.[2,3] Our patient had an atypical presentation with recurrent oral ulcers without two other criteria from the ISG diagnostic criteria; however, he presented with neurological manifestations and HLA-B51 positivity. Patients with Behcet's can also present with EEG findings such as theta waves and sharp waves.[8,9] In one study, 8 out of 10 BD patients had an increase in mild-to-moderate theta waves.[8] Similarly, our patient was found to have diffuse theta waves on EEG (Fig. 1).

Treatment for BD is based on the organ systems involved and symptom severity. Patients with

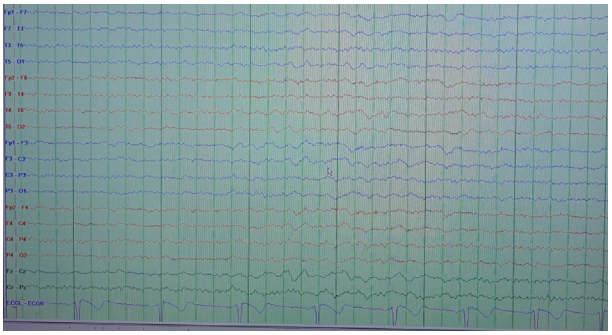

Fig. 1. EEG demonstrating diffuse theta activities suggestive of diffuse cerebral dysfunction and paroxysmal sharp and sharp contoured activities in bilateral frontotemporal regions.

Table 1. Laboratory results from his most recent hospitalization.

Serology	Results	Reference Range
Mycoplasma IgG Ab EIA	4.17	0.00–0.90
Mycoplasma IgM Ab EIA	1.85	0.00–0.90
Coxsackie Type A 16	1:200	Neg<1:100
Coxsackie Type A-24	1:800	Neg<1:100
Coxsackie Type A-7	1:200	Neg<1:100
Coxsackie Type A 9	1:200	Neg<1:100
Rocky Mountain Spotted Fever AB IgG	Negative	Negative
Rocky Mountain Spotted Fever AB IgM	1.14	0.00–0.89
Herpes Virus 6 Antibodies IgG	1.20	<1.10
NMDA Receptor Ab	<1.10	<1.10
Borrelia burgdorferi IgM	Positive	
Borrelia burgdorferi IgG	Positive	
Toxoplasma IgG	<3	<10
Toxoplasma IgM	<0.2	<0.9
HLA B51	Detected	
Antinuclear Antibody	Negative	<1:80
Thyroglobulin Antibodies	<20	<40
Thyroid Peroxidase Antibody	<10	<35
Immunoglobulin G	756 mg/dl	610–1660 mg/dl
Immunoglobulin A	184 mg/dl	84–499 mg/dl
Immunoglobulin M	135 mg/dl	35–242 mg/dl
Immunoglobulin E	11 mg/dl	<=100 mg/dl

isolated oral or genital ulcers can be treated initially with topical triamcinolone acetonide cream.[10] Patients with neurological involvement can be treated with intravenous corticosteroids and then slowly tapered.[11] For patients with severe neurological involvement, anti-TNF-a agents or cyclophosphamide can be first-line therapy.[11] Studies have shown that plasma exchange can be effective in treating BD including necrotizing vasculitis and ocular disease.[12,13] There are limited studies on the use of plasmapheresis in the treatment of BD, and has been typically used in refractory cases.[12,13]

The diagnosis of autoimmune encephalitis itself can be made when all three of the following criteria are met: 1) subacute onset of working memory deficits, altered mental status, or psychiatric symptoms; 2) at least one of the following: new focal CNS findings, seizures not explained by previous seizure disorder, CSF pleocytosis, or MRI findings of encephalitis; and 3) reasonable exclusion of other causes.[14] Our patient presented with memory deficits, focal CNS findings (his extremity movements), and the exclusion of other causes. CSF findings can be abnormal in autoimmune encephalitis with lymphocytic pleocytosis and/or raised CSF protein. Despite this, about one third of patients have normal CSF findings, as in our patient's case, therefore it does not exclude the diagnosis.[15] MRI results may also be normal in up to one third of cases; however, it typically will show medial temporal lobe signal changes.[15] The time course for follow-up may take years depending on clinical response to the immunotherapy.[15]

Other diagnoses were considered due to the atypical presentation of this patient's Behcet's autoimmune encephalitis. Antinuclear antibody (ANA) was negative, making many autoimmune disorders unlikely (Table 1). Multiple brain CT and MRI imaging studies did not reveal masses, strokes, multiple sclerosis, hydrocephalus, or evidence of infection. CSF studies did not reveal infection. He was found to have persistent IgM titer positivity to Lyme's disease, Mycoplasma, and RMSF for years (Table 1). He was also found to have IgG titer positivity to Lyme's, Mycoplasma, Coxsackievirus and Human Herpesvirus 6 (Table 1). Although his titers were positive, the patient had no history of having clinical manifestations of these infections. It is unknown if these antibodies played a role in the development of Behcet's in this patient; however, some literature has shown patients with antibodies against mycobacterial heat shock proteins are more likely to develop BD.[16]

There is sufficient literature to support a diagnosis of atypical Behcet's autoimmune encephalitis in light of the recurrent oral ulcers; his neurological manifestations; the recurrent, significant clinical improvement after plasma exchange and subsequent relapse afterwards; HLA-B 51 positivity; and his abnormal EEG.

4. Conclusion

Physicians should be diligent in history taking and keep a broad differential since BD autoimmune encephalitis is a rare entity which can present in a myriad of ways.

Disclaimers

The article has not been submitted to other places.

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Conflict of interests

There are no conflict of interests to report.

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