



Autoimmune rhomboencephalitis: A pediatric case report

Otoimmün rombensefalit: Pediatrik bir olgu bildirimi

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The known about this topic

Rhomboencephalitis is a severe and potentially life-threatening condition due to inflammation of the hindbrain (pons, medulla oblongata and cerebellum). Pediatric rhomboencephalitis is a very rare form of encephalitis in which autoimmune etiology is even rarer.

Contribution of the study

Herein, we describe a case of a child with autoimmune rhomboencephalitis successfully treated with a high dose of steroids.

Abstract

Rhomboencephalitis is a potentially life-threatening condition due to inflammation of the hindbrain with an unpredictable outcome depending on the wide spectrum of etiologies and the promptness of diagnosis and treatment. A 23-month-old Caucasian male presented with fever, clouding of consciousness, and trunk ataxia. Three weeks earlier he received active immunization against varicella-zoster virus. Routine laboratory tests were unremarkable. Cerebrospinal fluid showed slight elevation of leukocytes. The infection panel was negative. Brain magnetic resonance showed signal hyperintensity in the dorsal portion of the pons, which was consistent with a rhomboencephalitis. Autoimmune pathogenesis was supposed and a high dose of steroids was started. The patient's neurologic status progressively improved till full recovery and complete regression of previous magnetic resonance lesions after 1 year. Nevertheless, longer follow-up is needed in order not to miss any possible signs of an underlying autoimmune neurologic disorder.

Keywords: Autoimmune, brainstem encephalitis, rhomboencephalitis, steroid

Öz

Rombensefalit arka beyinin enflamasyonuna bağlı olarak gelişen ve yaşamı tehdit etme potansiyeli olan bir durum olup, geniş spektrumda bulunan etiyolojiler ve tanı ve tedavinin hızı ile bağlantılı olarak, sonuçları öngörülemez. Yirmi üç aylık beyaz bir erkek hasta ateş, bilinç bulanıklığı ve gövde ataksisi ile başvurdu. Üç hafta önce varicella zoster virüsüne karşı aşılanmıştı. Rutin laboratuvar testlerinde özellik saptanmadı. Beyin omurilik sıvısında lökositlerde hafif artış gözlemlendi. Enfeksiyon paneli negatif saptandı. Beyin manyetik rezonans incelemesi ponsun dorsal bölümünde sinyal hiperintensitesi gösterdi ve bu durum rombensefalit ile uyumlu idi. Otoimmün patogeneze varsayıldı ve yüksek doz steroid başlandı. Hastanın nörolojik durumu ilerleyici bir şekilde düzeldi ve tam iyileşme gözlemlendi. Bir yıl sonra, daha önce manyetik rezonans incelemesinde gözlenen lezyonlar tamamen geriledi. Bununla birlikte, altta yatan otoimmün nörolojik bir bozukluğun olası bulgularını atlamamak için daha uzun süreli izlem gerekmektedir.

Anahtar sözcükler: Beyinsapı ansefaliti, otoimmün, rombensefalit, steroid

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Introduction

Encephalitis refers to an inflammatory disorder of the brain characterized by alterations of consciousness and/or behavioral changes. Associated symptoms may include seizures, movement disorders and focal neurologic deficits (1). Clinical manifestations of encephalitis are usually accompanied by signs of inflammation in the cerebrospinal fluid and magnetic resonance imaging (MRI) findings, ranging from normal to wide-spread abnormalities (2). Among the encephalitides, rhomboencephalitis (RE) is a severe and potentially life-threatening condition due to inflammation of the hindbrain (pons, medulla oblongata and cerebellum). Rhomboencephalitis is rare, particularly in children, and it may be caused by an infection (mostly *Listeria monocytogenes*, enterovirus and herpes viruses) or an autoimmune dysregulation process (autoimmune diseases or paraneoplastic syndromes) (3). The outcome is unpredictable depending on the wide spectrum of etiologies and the promptness of diagnosis and treatment. Herein, we describe a case of a child with autoimmune RE successfully treated with a high dose of steroids.

Case

A 23-month-old Caucasian male presented with a four-day history of fever, prostration, and drowsiness. Three weeks earlier he received active immunization against varicella-zoster virus (VZV). The patient had no past medical diseases, normal psychomotor development and he was taking no medications. On admission, the child presented with clouding of consciousness, including slight difficulty in vigilance and attention. A neurologic examination showed neck stiffness and inability to sit without support owing to trunk ataxia. Both axial and appendicular hypotonia were evident. There were no oculomotor disturbances, movement disorders nor lateralizing signs. Routine laboratory tests revealed leukocytosis and thrombocytosis with normal inflammatory markers and electrolytes. A urine drug test was negative. Brain computed tomography (CT) was negative. Cerebrospinal fluid (CSF) was clear with elevated leukocytes, mostly monocytes (56/mm³, M 85%), and normal glucose and protein levels. Suspecting a meningoencephalitis, we started intravenous acyclovir along with ceftriaxone. Extensive infection panel was negative, including polymerase chain reaction (PCR) for enterovirus and herpes simplex virus, as well as blood and CSF cultures.

An electroencephalogram (EEG) showed slowing of background activity and transient 3-Hz slow-wave discharges on the occipital regions following eyes-closure. Brain magnetic resonance (MRI) showed signal hyperintensity in the dorsal portion of the pons, which was

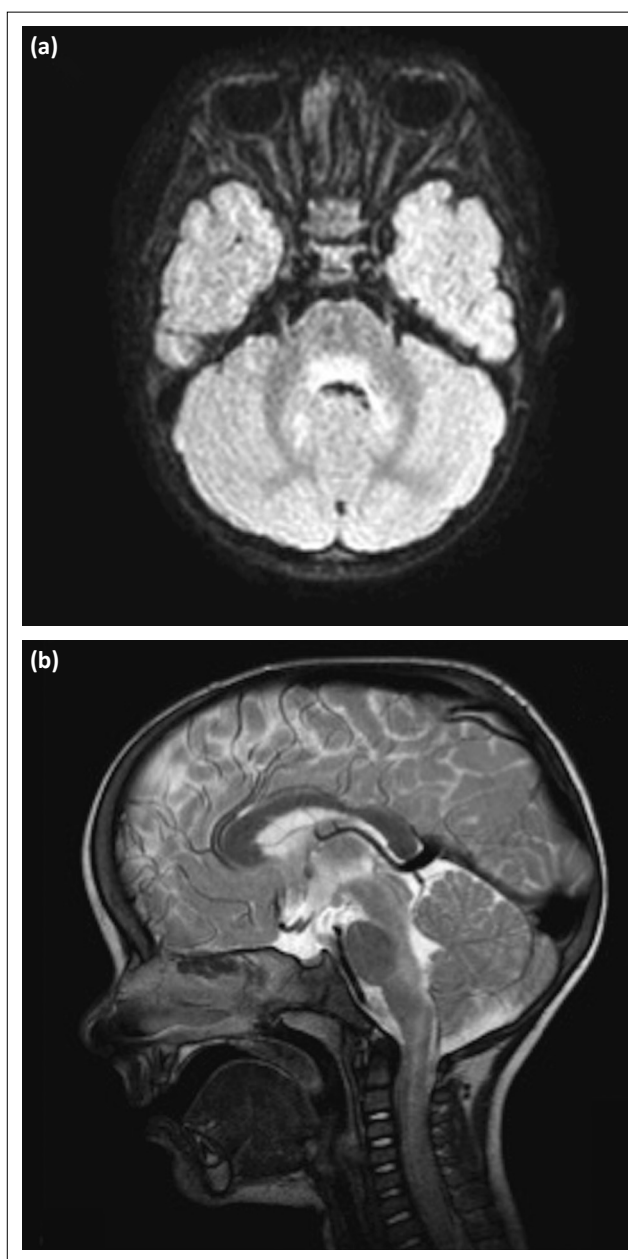


Figure 1. Signal FLAIR hyperintensity in the dorsal portion of the pons in axial (a) and T2 sagittal (b) view

consistent with a RE (Fig. 1). Spinal magnetic resonance was unremarkable.

In the setting of worsening mental status, the patient underwent a repeat lumbar puncture, which showed normal count of leukocytes (35/mm³), and molecular tests for other microorganisms including *Listeria monocytogenes* resulted negative.

Due to the lack of detectable infectious agents, an autoimmune pathogenesis was supposed, and immediately after the brain MRI result, a high dose of intravenous

methylprednisolone (IVMP) (30 mg/kg/day for 5 days) was started, followed by oral prednisone (2 mg/kg/day). After 2 days the child was awake and interactive, although he appeared still hypotonic. An extensive autoimmune encephalitis examination on serum, including antibodies against voltage-gated potassium and calcium channels, anti-GQ1b, anti-GAD, anti-MOG, anti-AQP4, and anti-NMDAR resulted negative. Cerebrospinal fluid results were not available due to technical issues.

The patient was discharged on tapering doses of oral steroids for the next 4 weeks and his neurologic status progressively improved till full recovery. Over a follow-up period of one year, he has not experienced any relapses and follow-up MRI at 6 months showed complete regression of the previous lesions. Written consent was obtained from the patient's parents.

Discussion

Few reports of children with RE, mainly caused by infections, have been published to date (4). However, RE may be the consequence of an autoimmune disorder such as Bickerstaff's brainstem encephalitis (BEE) (5) or be part of demyelinating diseases such as acute disseminated encephalomyelitis (ADEM) or neuromyelitis optica (NMO) (6, 7).

In our patient, clinical and MRI features were consistent with RE. Electroencephalogram (EEG) detection of intermittent slow activity in the occipital regions was a sign of cerebral dysfunction without implications for localization because posterior slowing distribution is commonly seen in children with a wide variety of lesions (8). However, EEG was useful to exclude the presence of some patterns suggestive for specific forms of encephalitis, such as extreme delta brush in anti-NMDA receptor encephalitis (2) and periodic lateralized epileptiform discharges (PLED) in herpes simplex encephalitis (9). Despite the absence of detectable glial and neuronal autoantibodies, an autoimmune form of RE was suspected in our patient owing to the negativity of infectious workup and rapid response to steroids. Although a recent study demonstrated that about 40% of pediatric patients with brainstem encephalitis had detectable neuronal and glial autoantibodies in their sera, there were no differences in outcomes between antibody-positive and antibody-negative groups (10). In a large retrospective study including both child and adult patients with RE, the most frequent cause was autoimmune/inflammatory and the majority of patients had a good response to high-dose steroid therapy, like our patient (3).

Once excluded the infections, BEE and ADEM should be considered into differential diagnosis giving their clinical and radiological affinity with the presented case. Bicker-

staff's brainstem encephalitis is characterized by the triad of ataxia, encephalopathy and ophthalmoplegia, whereas our patient did not present any oculomotor disturbance and anti-GQ1b antibodies were negative (5). Although acute disseminated encephalomyelitis lesions may include the hindbrain, the lack of subcortical and central white matter involvement makes this diagnosis questionable for our patient (6).

Indeed, the presence of a strictly localized lesion in the dorsal portion of the pons on brain MRI may be a peculiar finding. Considering the disease course of our patient, we cannot exclude the role of VZV immunization as a trigger; nevertheless, longer follow-up is needed in order not to miss any possible signs of an underlying autoimmune neurologic disorder.

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