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CASE REPORT

Acute disseminated encephalomyelitis: case report

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Abstract

To describe the case of a child diagnosed with Acute Disseminated Encephalomyelitis who presented recurrence. Child, from Belém, female, 10-years-old, started symptoms of hypoactivity and vomiting, evolving with altered level of consciousness, loss of sphincter control, decreased muscle strength, hemiparesis and aphasia. The cerebrospinal fluid was collected and meningitis was discarded. Was performed a computed tomography scan of the skull with a hypodense image in the deep parietal region. Corticosteroid therapy was started in low doses, showing a slight improvement. She was transferred to a referral hospital in pediatric neurology, with hypoactivity and altered neurological examination on the left. Magnetic resonance imaging of the brain and spinal cord showed images suggestive of Acute Disseminated Encephalomyelitis, and pulse therapy (methylprednisolone) was started. Afterwards, clinical progress was observed: improved speech, motor skills and sphincter control. Patient was discharged from hospital with corticosteroid maintenance and multidisciplinary rehabilitation. She remained clinically well, with good recovery. After five months, she evolved again with neurological manifestations, being considered a re-acute demyelinating condition, starting pulse therapy with methylprednisolone. She showed only partial improvement in symptoms. A new neuroimaging showing lesions still active. Chosen to perform immunoglobulin, evolving with significant clinical improvement. This disease starts with nonspecific prodromes and afterwards neurological symptoms will appears. The diagnosis is made through the neurological clinic and neuroimaging with classic alterations of the disease. Treatment is based on pulse therapy with methylprednisolone, followed by prednisolone. Intravenous human immunoglobulin is used as an option for cortic-resistant or relapsing patients.

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INTRODUCTION

Acute Disseminated Encephalomyelitis (ADEM) is an acute, inflammatory and demyelinating disease of the central nervous system (CNS) with multifocal involvement, affecting the cerebral white matter and spinal cord[1]. It has a rare incidence, being expected for pediatric patients an incidence of 0.23 to 0.4 cases per 100,000 children[2].

It is an autoimmune disease which pathogenesis is still not fully understood. Studies demonstrate an immune-mediated and transient response against myelin, by molecular mimicry or by the non-specific activation of T-cells associated with genetic predisposition[1,2]. Clinical manifestations may appear after infections, either by viral agents (Herpes viridae and Enterovirus group; by bacteria (Mycoplasma pneumoniae); or after vaccination (against measles, chickenpox, influenza, pertussis, rubella) and the use of drugs (amphetamine, sulfonamides, anthelmintics)[3].

Initially the clinical manifestations are nonspecific. In the prodromal phase there is headache, fever, vomiting, malaise, myalgia and anorexia, evolving with neurological alterations: alteration in the state of consciousness (lethargy to coma), focal or generalized seizures, psychoses and neurological symptoms multifocal (optic neuritis, visual field defects, aphasia, motor and sensory deficit, ataxia, abnormal movements, signs of acute meningoencephalitis with hemi, para, or tetraparesis; and cranial nerve paralysis)[2-4].

ADEM usually presents a typically monophasic course, although multiphasic forms have been described, which differential diagnosis is multiple sclerosis (MS), since the initial manifestation is practically identical. Therefore, long-term follow-up of cases is necessary[1,4].

Aiming to contribute to the early diagnosis and more appropriate clinical management of affected patients, this study carried out a literature review, based on a case report of a patient diagnosed with Acute Disseminated Encephalomyelitis admitted to a reference pediatric hospital in the Northern region.

CASE REPORT

Child, born in Belém, female, 10 years old, white, previously healthy, started in October 2019 with symptoms of hypoactivity and vomiting, evolving in one week with a change in the level of consciousness, loss of fecal and urinary continence, decreased muscle strength, left hemiparesis and aphasia. No history of recent vaccinations or contact with sick people.

Initially, she was admitted to a pediatric emergency room with cerebrospinal fluid (CSF) collection, meningitis being ruled out (colorless / clear / protein 23.6 / glucose 70 / cytometry 2 / mononuclear 100% / microbiological test without alterations / VDRL non-reactive). Computed tomography (CT) of the skull was performed, and an ischemic cerebrovascular accident (CVA) was suggested due to a 4 cm hypodense image in the deep parietal region on the right. Low-dose corticosteroid therapy was started, with slight improvement after treatment.

In 16 days, the patient was transferred to a reference hospital in pediatric neurology. Admitted with hypoactivity, dullness, impairment of expressive language, responding with gestures and dysarthric speech, receptive language, manifested by difficulty understanding commands, with alteration in the neurological exam in the left side; alterations in her Babinski signs and coordination), without alteration of the direct examination**.** After evaluation by a child neurologist, a brain magnetic resonance imaging (MRI) was ordered, which showed images suggestive of ADEM (marked signal changes in the periventricular regions, in the basal ganglia bilaterally, external capsule and right midbrain, characterized by hypersignal in T2 and FLAIR, with faint areas of enhancement after contrast).

Given the diagnostic hypothesis after clinical evaluation and complementary tests, treatment with pulse therapy (methylprednisolone 30 mg/kg/day for 5 days) was started. Serology for Herpes viruses I and II was performed, with a positive result (IgM 2.35/IgG >30), and acyclovir was prescribed for 21 days. After treatment, there was an important clinical progress, such as improvement in speech, motor skills, already signaling to caregivers about diuresis or evacuation, with improvement in sphincter control. The patient was discharged for outpatient follow-up, maintaining a dose of corticosteroids for five weeks with reduction and rehabilitation with a multidisciplinary team.

The patient remained clinically well, with good cognitive, behavioral and motor recovery, returning to perform activities that required greater motor planning (cycling). However, in March 2020 (five months after the first episode), she had ataxia, bilateral eyelid ptosis, right paresis, dysphagia, involuntary movements (choreoathetosis) in the left upper limb, expressive language deficit and loss of sphincter control. In this new admission, CSF was collected (without infectious alterations and absence of oligoclonal bands). As the symptoms indicated a recent encephalopathy, it was considered a worsening of the demyelinating condition. Thus, a new pulse therapy was prescribed (methylprednisolone 30mg/kg/day for five days), followed by maintenance with oral prednisolone.

However, the patient partially improved motor skills, involuntary movements and eyelid ptosis. She recovered speech, established dialogues, but she still had exertional fatigue and urinary incontinence. She was submitted to a new MRI of the brain after pulse therapy, with lesions still active, and lesions accentuating in the mesencephalic region. Thus, we decided to treat her with intravenous human immunoglobulin (2g/kg in 2 days), reducing the corticosteroid to 50mg/day. She had significant clinical improvement after treatment, being discharged from the hospital with referral for outpatient follow-up with a neuropediatrician and rehabilitation.

DISCUSSION

Acute disseminated encephalomyelitis (ADEM) is a demyelinating and inflammatory disease of the central nervous system (CNS)[4]. The prevalence of cases occurs in the first decade of life[1]; thus, the patient in this case report was in the pediatric age group, the one most commonly affected, in line with the literature. On the other hand, the involvement of this disease reveals a small predominance in males, ranging from 1.2 to 4.6 boys for every 1 girl[2,5,6]; but several series of cases in different countries have not shown differences between the sexes[5,7].

The period of greatest occurrence of ADEM covers the months of winter and spring, reinforcing the infectious etiology of the disease onset[1,8]. Although the North of Brazil does not have well-defined climatic seasons, the rainy period (December to May)[9] is considered as the most conducive for the dissemination of infectious diseases, mainly viral, a period corresponding to the beginning of the clinical condition of the patient described.

The initial clinical presentation of ADEM is quite variable, nonspecific prodromes (fever, headache and nausea)[2] may appear from 2 to 40 days after a viral infection or, more rarely, after vaccination[8]. Among the viruses most commonly associated with ADEM are the Herpes simplex virus[10]. In this sense, this clinical case agrees with the literature, as the patient initially presented nonspecific symptoms of a probable viral infection, which was confirmed with positive serology for Herpes virus I and II IgM.

After the period of general symptoms (3 to 4 days), the neurological symptoms of ADEM will appear[11]: encephalopathy (behavioral changes and/or altered level of consciousness), focal or multifocal deficits (hemiparesis, ataxia, dystonia, choreiform movements, aphasia , diplopia and dyslexia), cranial nerve involvement (especially the optic nerves, leading to optic neuritis)[7,8,11]. Finally, there may be signs of spinal cord involvement (flaccid paralysis, constipation and urinary disorders)[8].

Thus, from the initial clinical presentation with evolution to neurological signs and symptoms of the referred patient, the medical team should consider acute disseminated encephalomyelitis among the diagnostic hypotheses, while waiting for the confirmatory tests. Because it is a disease that triggers varying degrees of neurological deficits, significantly compromising the patient's cognition, it is necessary to intervene as early as possible.

The diagnosis of ADEM is carried out through clinical neurological and cranial MRI with classic images of the disease[1,2,8]. The diagnostic criteria are determined by the International Pediatric Multiple Sclerosis Study (International Pediatric Multiple Sclerosis Study Group – IPMSSG),[12] shown on Table 1.

The CSF study is performed to rule out or confirm central nervous system infections associated with ADEM, as there are no specific studies for CSF analysis in this disease. There may be pleocytosis (> 5 to > 20 cells/mL) in 29%-85% of cases, predominantly lymphocytes[13]. Intrathecal oligoclonal bands are present in up to 20% of cases[2]. Thus, the patient described presented the confirmatory criteria for ADEM, being one more case to corroborate with the literature about this disease.

Treatment is based on high doses of corticosteroids through pulse therapy with methylprednisolone (20-30mg/kg/day; maximum 1g/day) for 3-5 days, followed by oral prednisolone (1-2 mg/kg/day) for 1-2 weeks, with gradual reduction in 2-6 weeks[14]. As a treatment option for corticosteroid-resistant patients or in relapses, intravenous human immunoglobulin (2g/kg) is used for 2-5 days[8,14]. Thus, the clinical case described proves that the treatment with pulse therapy instituted in the patient's first hospitalization was essential for her complete recovery.

Cases of relapse may occur in ADEM: less than 3 months after the first episode, it is considered monophasic; over 3 months, multiphasic ADEM is determined[2]. This is limited to only two characteristic episodes of encephalomyelitis, over 3 suggest the diagnosis of multiple sclerosis, neuromyelitis optica or other neurological disease[2,12]. In this sense, the patient requires regular follow-up with a child neurologist.

In view of this, this clinical case is about a patient with multiphase ADEM due to the recurrence having occurred 3 months after the first episode, in addition to the good response after treatment with pulse therapy associated with intravenous human immunoglobulin, as already recommended in the current literature[8,14,15]. So far, the condition does not suggest a diagnosis of multiple sclerosis, both due to the clinical evolution presented and complementary tests such as the investigation of oligoclonal bands in the CSF, which was negative during the investigation in the second hospitalization.

Table 1. ADEM Diagnostic Criteria according to the IPMSSG.

1. A first clinical polyfocal CNS event with presumed inflammatory demyelinating cause
2. Encephalopathy NOT explained by fever, systemic illness, or postictal symptoms
3. Brain MRI is abnormal during the acute phase (3 months)
4. No NEW clinical or MRI findings appears 3 months or longer after onset
5. Brain MRI is abnormal during the acute phase (3 months) with diffuse lesions, badly outlined and large (> 1-2 cm) involving mainly the white matter (in FLAIR and T2 weighting).Hypodense T1 lesions in the white matter are rare. Deep lesions in the thalamus gray matter or in the basal ganglia may be present.

Source: Krupp LB, Tardieu M, Amato MP, et al. 2013[12].

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