CASO CLÍNICO/CASE REPORT

Acute Demyelinating Syndrome in a Child: When a Poor Evolution Suggests Combined Central and Peripheral Involvement

Síndrome Desmielinizante Agudo numa Criança: Quando uma Má Evolução Sugere Envolvimento Central e Periférico Combinado

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Abstract

The occurrence of a demyelinating event involving both the central and the peripheral nervous system in a child (simultaneously or sequentially) is rare. However, this can be underdiagnosed, since the manifestations involving the central nervous system can be more exuberant, dominating the clinical picture. A less favorable clinical evolution, in the medium and long term (despite acute treatment with corticosteroids) can lead to the retrospective diagnosis of an additional involvement of the peripheral nervous system, complicating the functional prognosis. We report the case of a 5-year-old child in which this happened, with important negative implications, particularly at the motor level.

Resumo

A ocorrência de um evento desmielinizante envolvendo simultaneamente o sistema nervoso central e periférico em idade pediátrica (simultânea ou sequencialmente) é pouco frequente. No entanto, pode dever-se ao facto de ser subdiagnosticado, uma vez que as manifestações envolvendo o sistema nervoso central podem ser mais exuberantes, dominando o quadro clínico. Uma evolução clínica menos favorável, a médio e longo prazo (apesar do tratamento agudo com corticosteróides), pode levar ao diagnóstico retrospetivo de atingimento adicional do sistema nervoso periférico, agravando o prognóstico funcional. Relatamos o caso de uma criança de 5 anos em que isso aconteceu, com implicações negativas importantes, principalmente a nível motor.

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Introduction

Guillain-Barré syndrome (GBS) (particularly its most common clinical expression, acute inflammatory demyelinating polyneuropathy [AIDP]) and acute disseminated encephalomyelitis (ADEM) are two common diseases affecting the pediatric population, which are usually recognized as separated entities involving different parts of the nervous system.[1,2] Having an autoimmune origin, these conditions are frequently described under the umbrella of pediatric acquired demyelinating syndromes, involving the peripheral and the central nervous system (CNS), respectively.[3]

The occurrence of these two entities, simultaneously or sequentially during a short period in the same patient, is not well understood and is probably underdiagnosed.[1] Occurring early in life, this situation naturally carries and increases risk of a poor neurologic outcome. We present a clinical case with a co-existence of ADEM and GBS resulting in severe disability in a 5-year-old child.

Case Report

A 5-year-old girl was admitted at a tertiary hospital in April 2016 with a febrile syndrome, encephalopathy and a generalized weakness, accompanied by hypokinetic myotactic reflexes. Initial work-up included blood analysis and a lumbar puncture, in which the following results were observed: cell count of 107/mm^3 (of mononuclear predominance), proteins of 60.0 mg/dL (15.0-45.0), normal glucose levels (taking into account the blood glucose measure) and an innocent microbiological study (including the screening for the following microorganisms: *Herpes simplex* viruses, enterovirus, *Escherichia coli* K1, *Haemophilus influenzae* type b, *Neisseria meningitidis* A, B, C, Y and W135, *Streptococcus agalactiae*, and *Streptococcus pneumoniae*). Later, blood and cerebrospinal fluid (CSF) cultures were shown to be negative. The electroencephalogram (EEG) revealed a diffuse encephalopathy and a magnetic resonance imaging (MRI) was compatible with the diagnosis of ADEM (**Fig. 1, A**). At that time, no anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibody was routinely screened.

She was treated with high-dose (30 mg/kg) intravenous methylprednisolone, with an insidious recovery of her previous mental status, albeit not accompanied by a straightforward motor improvement. However, given the need for a sustained and intense rehabilitation intervention, she was then transferred to the Hospital in the area of residence, presenting an asymmetric flaccid tetraparesis with greater involvement of the right side of the body (MRC 2/5) and was unable to sit without support, reason why she started immediately that said rehabilitation program.

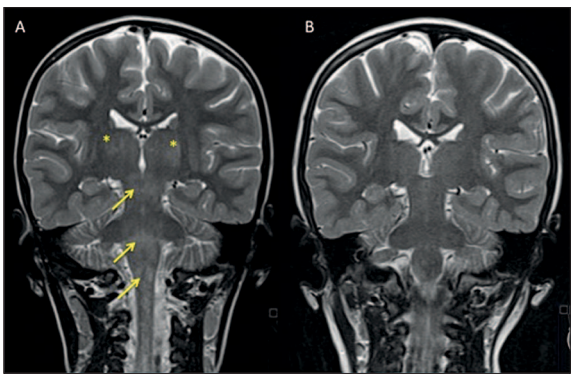

Figure 1. MRI (coronal T2) at the diagnosis (A, April 2016) and 6 months after hospital discharge (B, October 2016). (A) Several diffuse and poorly demarcated T2-hyperintense lesions can be seen, involving both white and grey matter, very suggestive of ADEM diagnosis (* - thalamus; arrows - lesions affecting distinct levels of the brainstem); (B) Six months after the diagnosis of ADEM, no new or chronic lesions were identified (radiological resolution). At no time were other spinal cord injuries or abnormal root enhancement identified.

In October (6 months after), a new brain MRI was performed, showing a complete resolution of the parenchymal hyperintensity areas without chronic lesions, suggestive of a monophasic ADEM, from an imaging perspective (**Fig. 1, B**). However, she maintained significant motor deficits, mainly at the pelvic girdle, but also distally, reinforcing the concept of a clinical-radiological dissociation. During rehabilitation program, despite the difficulties in standing without support and the need to walk with ankle-foot orthoses, there was an improvement.

Nevertheless, due to the dissociation between symptoms and imaging exams, the patient was referred for observation at a neuropediatrics outpatient clinic, where she was observed for the first time in June 2018. The neurological examination disclosed a girl with a nasal voice, a tetraparesis, predominant in right superior and left inferior limbs (proximal 4/5; distal 3/5); generalized myotactic hyperreflexia with ankle clonus and bilaterally indifferent plantar response; bilateral foot drop, more evident at the left side (2/5 in foot dorsiflexion), requiring bilateral orthoses; sensory exam was normal; fasciculations or signs of musculoskeletal fatigue were not detected, but muscle masses were not very developed. Suspecting the involvement of first and second motor neurons in the clinical picture, additional exams were requested to clarify the diagnosis. The analytical study showed: creatine kinase of 221 U/L (10-145), alkaline phosphatase of 264 U/L (30-120), gamma-glutamyl transferase of 248 U/L (100-247) and no other relevant changes. The electromyography revealed signs

of chronic and severe motor nerve damage, compatible with motor sequelae of an axonal variant of GBS. No sensory abnormalities were detected. At reassessment consultation, the signs of distal denervation of the lower limbs were slightly more evident, but the remaining neurological examination was similar. Thus, the electromyographic findings explained the clinical manifestations with the coexistence of first and second motor neurons dysfunction. The patient maintains an outpatient rehabilitation program with periodic neurological follow-up.

Discussion

This child had a single clinical event that allowed the diagnosis of an ADEM to be established, but the long-term evolution was not as expected, with many motor sequelae leading to a poor functional outcome. When reassessed at the neuropediatrics clinic, the neurophysiological study was compatible with sequelae of a GBS. Since there was no report of any clinical relapse since the first episode, altered mental status and motor deficits were admitted to be synchronous, with central and peripheral demyelination occurring as a single event. It should be noted that, at the beginning of the clinical picture, the suspicion of peripheral involvement would be difficult to sustain. Encephalopathy dominated the picture and the existence of CSF pleocytosis was much more favorable to the diagnosis of ADEM.

Nevertheless, although rare, simultaneous or sequential CNS demyelination and AIDP have been reported in children.[1,3] They are usually separated events, limited either to the CNS, presenting as ADEM, or to the peripheral nervous system (PNS), presenting as a form of GBS.[4] They share some features, such as autoimmune pathogenesis, previous history of viral infections or vaccination and myelin damage, leading to conduction abnormalities and being often accompanied by axonal loss.[2,3,5] In fact, it is presumed that the combination of central and peripheral demyelination could be explained by an immunological response against a common epitope component of both peripheral and CNS myelin, formally unknown.[1] Neurofascin, contactin and CASPR1 (contactin associated protein 1) have been proteins of interest in the eventual establishment of this relationship, as well as the MOG itself. However, in this case, antibodies against them were not evaluated at any time, as this was not routine (and possible) in our institution, that time.

The combination of these two diseases causes a broad spectrum of neurological abnormalities including consciousness impairment, arreflexia or hyperreflexia, hypotonia or hypertonia, sensory disturbances, neurogenic bowel and/or bladder, autonomic dysfunction and generalized weakness. Cerebrospinal fluid analysis, MRI and electrophysiologic studies have been frequently used to confirm the diagnosis. Acute treatment for this combined condition (ADEM and GBS) can include intravenous immunoglobulin, intravenous high-dose corticosteroids and sometimes plasma exchange.[3] Although isolated CNS or PNS demyelination usually portends a good outcome, the combination of two diseases may have a poorer prognosis, as we observed in this clinical case.[6] ■

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