RECIMA21 - REVISTA CIENTÍFICA MULTIDISCIPLINAR
ISSN 2675-6218

CHALLENGES IN THE MANAGEMENT OF EARLY MULTIPLE SCLEROSIS IN A 5-YEAR-OLD CHILD: CASE REPORT

DESAFIOS NO MANEJO DA ESCLEROSE MÚLTIPLA PRECOCE EM UMA CRIANÇA COM 5 ANOS DE IDADE: RELATO DE CASO

DESAFÍOS EN EL MANEJO DE LA ESCLEROSIS MÚLTIPLE TEMPRANA EN UN NIÑO DE 5 AÑOS: INFORME DE CASO

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e3122247
https://doi.org/10.47820/recima21.v3i12.2247

RECEIVED: 10/28/2022 APPROVED: 11/28/2022 PUBLISHED: 12/03/2022

ABSTRACT
Our study reports the case of a child with early Multiple Sclerosis. It is an inflammatory disease of the Central Nervous System more common in adults, considered very rare in the first decade of life. The patient had 5 years old when suffered acute attacks of ataxia and paparesis. Magnetic resonance imaging of the brain showed lesions compatible with the disease, although the cerebrospinal fluid did not detected typical changes. There was recovery from outbreaks and had difficulties to use immunomodulatory treatment. It reflects that the diagnosis and management in children and adolescents is more difficult, as they present nonspecific symptoms that open a range of different differential diagnoses. Therefore, our report highlights the differences between multiple sclerosis in adults and children and the difficulties in this specific population.

KEYWORDS: Multiple Sclerosis. Autoimmune disease. Children.

RESUMO
Este estudo relata o caso de uma criança com Esclerose Múltipla precoce. É uma doença inflamatória do Sistema Nervoso Central, mais comum em adultos, considerada muito rara na primeira década de vida. O paciente tinha 5 anos quando sofreu ataques agudos de ataxia e paparese. A ressonância magnética do encéfalo mostrou lesões compatíveis com a doença, embora o líquido cefalorraquidiano não tenha detectado alterações típicas. Houve recuperação dos surtos e dificuldades para utilizar o tratamento imunomodulador. Isso reflete o quanto o diagnóstico e manejo em crianças e adolescentes é mais difícil, pois apresentam sintomas inespecíficos que abrem um leque de diferentes diagnósticos diferenciais. Portanto, o relato destaca as diferenças entre a esclerose múltipla em adultos e crianças e as dificuldades nessa população específica.

PALAVRAS-CHAVE: Esclerose múltipla. Doença autoimune. Crianças.

RESUMEN
Este estudio reporta el caso de un niño con Esclerosis Múltiple temprana. Es una enfermedad inflamatoria del Sistema Nervioso Central, más común en adultos, considerada muy rara en la primera década de vida. El paciente tenía 5 años cuando sufrió ataques agudos de ataxia y paparesis. La resonancia magnética del cerebro mostró lesiones compatibles con la enfermedad, aunque el líquido cefalorraquídeo no detectó cambios típicos. Se retrataron los brotes y se tuvieron dificultades para utilizar el tratamiento inmunomodulador. Esto refleja cuánto diagnóstico y manejo en niños y adolescentes es más difícil, ya que presentan síntomas inespecíficos que abren una gama de

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ISSN 2675-6218

diferentes diagnósticos diferenciales. Por lo tanto, el informe destaca las diferencias entre la esclerosis múltiple en adultos y niños y las dificultades en esta población específica.

PALABRAS CLAVE: Esclerosis múltiple. Enfermedad autoinmune. Niños.

INTRODUCTION

Multiple sclerosis (MS) is an inflammatory disease of the Central Nervous System associated with demyelination and neurodegeneration[1]. It presents a variable clinical course, which difficulties the diagnosis and the treatment [2]. Brasil´s prevalence is 1.36 to 27.2/100,000 inhabitants and grows regions furthest from the Equator line [3]. The onset of the disease occurs mainly in the economically productive phase of the individual's life. [4]

MS is thought to be an immune-mediated disorder that occurs in genetically susceptible people. However, the sequence of events that initiate the disease remains largely unknown. Given the considerable clinical, genetic, imaging, and pathology heterogeneity, there may be more than one pathogenetic mechanism that contributes to tissue damage. This possibility has therapeutic implications, because more than one treatment approach may be required to effectively treat this disease. [5]

The 2017 McDonald's diagnostic criteria take into account the number of outbreaks, clinical lesions, and the results of laboratory tests. Lesions represent demyelination and axonal loss; and magnetic resonance imaging (MRI) is the test of choice to show them.[6]

In summary, it is a heterogeneous disease where there are few certainties regarding the pathophysiological basis, and which requires individualized treatment.

CASE REPORT

Male child, 5 years old, brown, was born in Santarém-PA by cesarean section with meconium aspiration, at 42 weeks and weighing 3 Kg. During pregnancy, her mother had Hypertensive Disease of Pregnancy. In neuropsychomotor development, she acquired gait at 12 months and spoke words after 1 year and a half.

In June 2019, he presented sudden ataxic gait, right lateralization and falls; appendicular incoordination and lower limb paresis, was hospitalized for 27 days. Skull computadorized tomography showed bilateral subcortical hypodensity. Pulse therapy with methylprednisolone was performed and the child regained normal gait.

A brain magnetic resonance image (MRI) demonstrated a bilateral middle cerebellar peduncle hypersignal and bilateral asymmetrical peritrigonal white matter lesions. Three months later, the patient presented imbalance and change behavior (agitation, aggressiveness). A new scan revealed the emergence of a new lesion in the left internal capsule without Gadolinium enhancement (figure 1); this last scan reinforced multiple sclerosis as a probable diagnosis, as it showed the spread of lesions in space and time. There was lymphocytic pleocytosis, normal protein electrophoresis and negative

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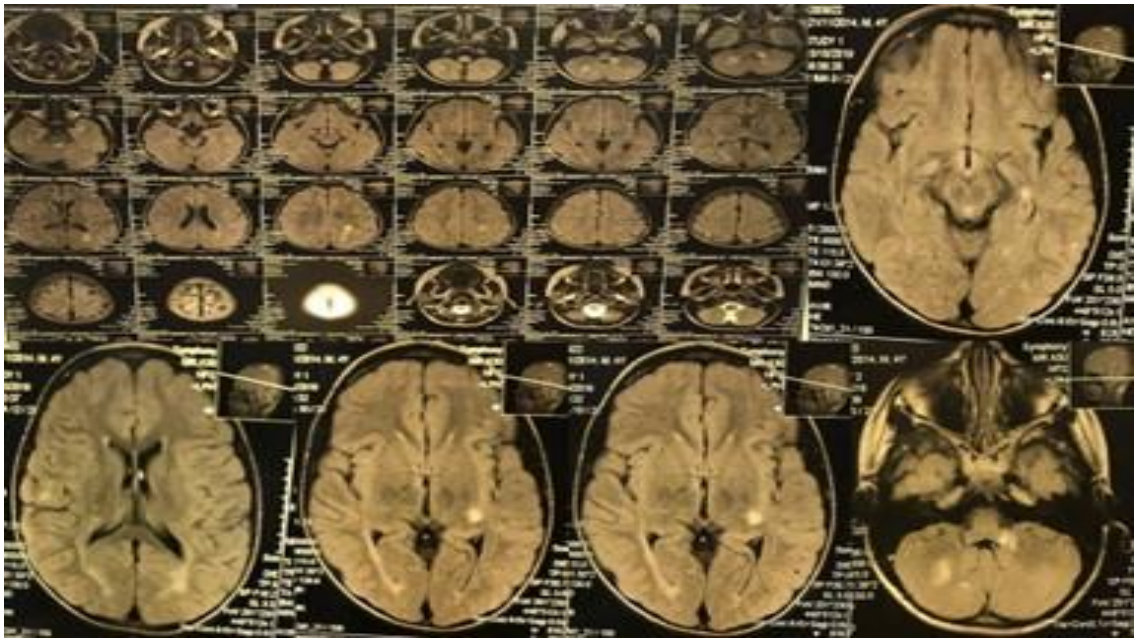
ISSN 2675-6218

oligoclonal bands in the cerebrospinal fluid. He achieved good functional recovery after pulse therapy with methylprednisolone.

FIGURE 1: Hyperintense lesions in the flair sequence, located in the right cerebellar hemisphere, left middle cerebellar peduncle, left internal capsule, left mesial temporal region and posterior periventricular regions bilaterally without expansive effect.



After the diagnosis of MS, immunomodulatory treatment was instituted with glatiramer acetate 40mg, subcutaneously, twice a week, but it presented some side effects, such as pain in the lower limbs, requiring the exchange for beta interferon.

In August 2020, he presented a new outbreak of the disease, now with medullary topography, characterized by paraparesis and sphincter dysfunction, requiring a new hospitalization to perform pulse therapy. He continues to be followed up with a specialist at an outpatient clinic, having recovered the neurological deficit again.

DISCUSSION

The patient in question presented focal neurological signs that pointed to cerebellar involvement in the first attack, raising the hypothesis of cerebelitis, but the neuroimaging indicated involvement of white matter in multiple sites. In the first episode of central nervous system demyelination in a child younger than 12 years of age, the most likely diagnosis is acute disseminated encephalomyelitis (ADEM), but was unlikely in the absence of encephalopathy (altered level of consciousness, seizures) or recent history of infection or vaccine [7]. So, multiple sclerosis was the most likely diagnosis, despite being a very rare disease in childhood.

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Multiple Sclerosis is a chronic autoimmune inflammatory disease that leads to demyelination of the central nervous system [8], mainly damaging the white matter. It typically occurs in early adulthood, but a minority of patients develop the disease in childhood [9], that is, before 16 years of age, being called Pediatric onset Multiple Sclerosis (POMS) or Juvenile Multiple Sclerosis. Between 3 and 10% of MS patients are younger than 16 years of age and less than 1% are younger than 10 years of age. [10]

Several factors seem to play a role in the genesis of POMS: genetic, geographic, sociocultural, demographic factors, lifestyle (passive smoking, especially if older than 10 years), history of infections, hepatitis B vaccine, and changes in the intestinal microbiota, determining a pro-inflammatory environment. Such elements cause the loss of homeostasis of the organism, leading to the disordered activation of the immune system [1, 11, 12]. Regarding genetic factors, there is until 14.9% cases with positive familial history of MS[13]. When both parents are diagnosed with MS, their child has around a 30% risk of developing the disease, even early. On the other hand, if one of the parents is diagnosed with MS, this risk is between 2% and 5%, the risk being higher in the case of a daughter of a mother with MS[13]. There is a higher prevalence in black children compared to Caucasian children, in addition to a similar distribution for both sexes in ages younger than 10-12 years, and female predominance in older ages[14].

Early recognition of childhood MS remains difficult, particularly as the range of characteristics at onset is variable. Our case began with cerebellar ataxia, that was the first manifestation only in 5% of in 125 patients in a series case, where sensory disturbance (26.4%), optic neuritis (14%), diplopia (11%), motor loss (11%) and gait disturbances (8%) predominated [15].

The absence of oligoclonal bands in CSF of our patient did not make the diagnosis of multiple sclerosis unlikely, since they are positive in 90% of cases in adults, but only in one third of affected children[16].

The evolution in relapsing-remission presented by the child was a point in common with most cases in the literature. POMS usually has a relapsing-remitting disease course. In the first two years after the incident attack, the annual relapse rate is highest [17]. And it remains relatively high in the first 5 years [18]. The disability scores of pediatric patients with MS remain low early in the course of the disease [19]. In a French database analysis, patients took an average of 10 years longer to progress to secondary progressive MS, compared to the duration of the disease in adult patients. However, because the disease starts earlier in POMS, these patients usually accumulate deficiencies at a younger age [20].

Although physical impairment is not a prominent feature in POMS, cognitive deficits are measurable in approximately one-third of its patients. Deficiencies are most often observed in the areas of complex attention, in fine movements, processing speed, visual memory and language integration and skills (the latter being more frequent than in adults) [21].

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It was observed that the patient responded well to pulse therapy with corticosteroids but showed intolerance to the first immunomodulator used and still had side effects with the second drug. The treatment of children with MS is based on case series, consensus, and international guidelines, but none are robust enough to report efficacy. However, all published studies on interferon and glatiramer acetate demonstrate an important reduction in relapses and confirm a generally favorable safety profile [22-25]. Unfortunately, despite receiving these treatment options, many POMS patients like ours experience relapses and new lesions emerge, leading to changes in therapy [26, 27].

CONCLUSIONS

The diagnosis of early MS is difficult, since it depends on a high suspicion associated with imaging and laboratory tests of the tertiary health system. Added to this are the regional difficulties in the context of the Amazon interior and the lengthy procedural service in the public health services.

Anamnesis and a detailed neurological physical examination are key points in the diagnostic suspicion, selecting the smallest number of hypotheses and facilitating early diagnosis, as was the case with the patient under study.

Thus, the treatment of this rare neurological disease in children is still a challenge, especially due to differences in relation to cases in adults.

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