Reporte de caso / Case report

Early Onset Of Multiple Sclerosis In A Two-Year-Old Girl: A Case Report

Inicio temprano de esclerosis múltiple en una niña de dos años: reporte de un caso

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ABSTRACT

Introduction: *Multiple sclerosis (MS) is an immune-mediated demyelinating disorder that is extremely rare before the age of five. Its diagnosis is challenging due to its clinical and radiologic overlap with other pediatric demyelinating syndromes.* ***Case Presentation:*** *We describe a two-year-old girl with recurrent focal neurological deficits and multifocal MRI lesions showing dissemination in space and time. Alternative diagnoses including ADEM, NMOSD (AQP4-IgG-negative), infection, vasculitis, and MOGAD were excluded. She responded to high-dose IV methylprednisolone during relapses. After fulfilling McDonald criteria for MS, long-term therapy with interferon beta-1a was started, and she has remained clinically stable.* ***Conclusions:*** *This case highlights an exceptionally early presentation of pediatric-onset relapsing-remitting MS and underscores the need to consider MS even in very young children when clinical and radiologic findings are strongly suggestive.*

Keywords: *Pediatric demyelinating disease, multiple sclerosis, brainstem syndrome, neuroimaging.*

RESUMEN

Introducción: *La esclerosis múltiple (EM) es un trastorno desmielinizante mediado por el sistema inmunitario, extremadamente infrecuente antes de los cinco años de edad. Su diagnóstico resulta complejo debido al solapamiento clínico y radiológico con otros síndromes desmielinizantes pediátricos.* ***Presentación del caso:*** *Se describe una niña de dos años con déficits neurológicos focales recurrentes y lesiones multifocales en la RM que evidenciaron diseminación en espacio y en tiempo. Se descartaron diagnósticos alternativos como ADEM, NMOSD (AQP4-IgG negativo), infección, vasculitis y MOGAD. Durante los brotes, respondió favorablemente a metilprednisolona IV en dosis altas. Tras cumplir los criterios de McDonald para EM, se inició tratamiento a largo plazo con interferón beta-1a, manteniéndose clínicamente estable.* ***Conclusiones:*** *Este caso muestra una presentación excepcionalmente temprana de EM remitente-recurrente de inicio pediátrico y subraya la importancia de considerar EM incluso en niños muy pequeños cuando los hallazgos clínicos y radiológicos son altamente sugestivos.*

Palabras clave: *Enfermedad desmielinizante pediátrica, esclerosis múltiple, síndrome de tronco encefálico, neuroimagen.*

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INTRODUCTION

Multiple Sclerosis (MS) is a chronic, immune-mediated demyelinating disease of the Central Nervous System (CNS)[1]. Clinically, it is characterized by a heterogeneous array of signs and symptoms, reflecting its impact on the motor, sensory, visual, and autonomic areas of the CNS[1,2]. MS is the most common non-traumatic disabling neurological disease in young adults[3,4]. The age of onset typically ranges from 20 to 40 years; however, cases occurring outside this range have also been reported[5]. Prevalence is highest in female children aged 13 to 16 years[6,7,8].

Evidence suggests that susceptibility to MS may begin to develop as early as the prenatal period[9,10]. Observations such as the month-of-birth effect and the increased concordance in dizygotic twins compared with siblings support the role of the intrauterine environment in shaping MS risk[9,10].

MS can begin abruptly or insidiously, with symptoms that may be pronounced or subtle enough that medical attention is not sought immediately[5]. As the clinical presentation of MS varies considerably, its phenotypic classification was refined by Lublin et al. in 2013[11]. In pediatric patients, the first symptoms are predominantly sensory disturbances, and impaired coordination of movements[12,13]. Pediatric patients with MS have a greater accumulation of new MRI lesions[14]. As in adults, the diagnosis of MS in children requires evidence of CNS demyelination that is separated in both space and in time[15].

Here, we report the case of a two-year-old girl who presented with a clinical course of neurological events, followed by periods of incomplete remission, along with MRI patterns that were more likely associated with MS.

CASE REPORT

A previously healthy two-year-old girl first presented to the pediatric service in October 2014 with hemiparesis and tremors on the left leg that gradually worsened. The family history was notable for thyroid disorders on the maternal side, a first-degree cousin with Crohn's disease and another first-degree cousin with myasthenia gravis. The patient was initially evaluated by orthopedics, to rule out a pathology of the hip joints.

Upon physical examination, no relevant signs were observed. Subsequently, a hip MRI was conducted, revealing a small hypersignal lesion of about 2.5 mm in diameter, adjacent to the articular cartilage of the femoral head. This lesion was only visible on STIR sequences and not on T1 or T2. A head MRI was also conducted, revealing multiple lesions with hypersignal on T2 and hyposignal on T1. These lesions were found in various locations: the middle cerebellar peduncles on both sides, with a greater prominence on the left; the supratentorial region in the white matter adjacent to the left lateral ventricle; the white matter of the lenticular nucleus on the left; the white matter adjacent to the left occipital horn; and the hypothalamic area. Additionally, another suspicious lesion was detected in the left temporo-occipital region, along with a lesion on the right side of the thalamus with a faint hypersignal in T2, without T1 correlate and slight positivity on diffusion mapping, though not on primary sequences (Fig. 1 and 2). After ruling out other diseases, and with the pattern of the MRI images consistent with MS, pulses of IV methylprednisolone were started at 30 mg/kg/dose per day for a total of three days.

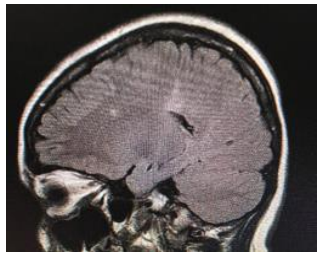


Figura 1. MRI showing demyelinating lesions (hypersignal on T2 and hyposignal on T1) in multiple locations.

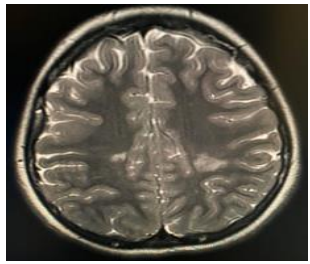
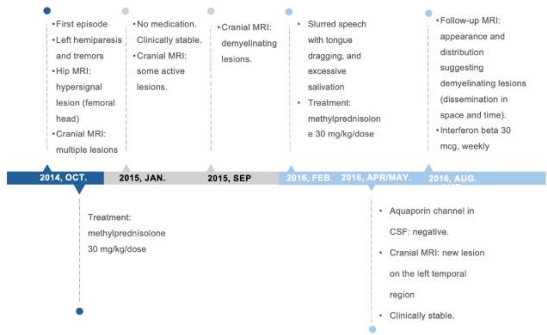


Figura 2. MRI showing demyelinating lesions (hypersignal on T2 and hyposignal on T1) in multiple locations.

In January 2015, the patient was no longer on any medication, and a subsequent head MRI was performed. There were indications of improvement, however, some active lesions remained. By 2016, at the age of 3 years and 4 months, the parents noticed slurred speech with tongue dragging, and excessive salivation. The patient was once again treated with IV methylprednisolone for a total of five days, with a good response. A head MRI was once again ordered, showing a new lesion on the left temporal region. In the same year, the patient was taken to Buenos Aires for testing of the antibodies of the aquaporin channel in CSF, which came back negative. For monitoring, another head MRI was conducted three months later, showing supratentorial white-matter lesions with hypersignal on T2 and hyposignal on T1. The appearance and distribution of the lesions were consistent with demyelinating pathology.



MRI – Magnetic Resonance Imaging CSF – Cerebrospinal Fluid

DISCUSSION

The patient was started on Avonex (interferon beta 0.5 ml or 30 mcg SC weekly) after presenting a relapsing pattern of focal neurological symptoms with MRI lesions demonstrating both dissemination in space and in time. Interferon beta remains one of the most commonly used first-line disease-modifying therapies in pediatric-onset MS because of its long-standing safety profile, extensive real-world experience, and acceptable tolerability in younger patients[16]. Although the patient's age was unusual for MS, the clinical course and imaging findings were consistent with this diagnosis. The McDonald criteria require evidence of Dissemination in Time (DIT) and Dissemination in Space (DIS) to establish the diagnosis, both of which were fulfilled in this case[17].

Acute Disseminated Encephalomyelitis (ADEM) was considered early in the diagnostic process[18]. However, the relapsing clinical course, absence of encephalopathy, and the temporal separation between episodes are inconsistent with ADEM, which typically presents as a monophasic, rapidly evolving illness with multifocal neurological deficits. Neuromyelitis Optica Spectrum Disorder (NMOSD) was also contemplated. However, anti-aquaporin-4 antibodies were negative, and based on the International consensus diagnostic criteria for NMOSD, the patient did not meet the required clinical, radiological, or serological features[19]. Other differential diagnoses including infection, vasculitis, and Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD) were subsequently ruled out.

CONCLUSIÓN

This case illustrates an exceptionally early presentation of relapsing-remitting multiple sclerosis, manifesting before the age of three and fulfilling the diagnostic criteria through clear dissemination in space and time. The patient's clinical course, characterized by recurrent focal neurological deficits and evolving MRI findings, underscores that MS may present even at ages traditionally considered outside the expected epidemiologic range. Prompt recognition, exclusion of mimicking conditions such as ADEM, MOGAD, and NMOSD, and early initiation of disease-modifying therapy contributed to clinical stabilization and highlight the importance of timely diagnosis. It is important to consider the diagnosis of multiple sclerosis in the pediatric population despite its rarity in patients under 2 years of age.

Author contributions

- Sebastián Martin Etchegaray (0009-0002-4978-5876): Manuscript writing and editing.
- Ana Recalde (0009-0009-2645-4178): Conception and design of the study; literature review; drafting of the initial manuscript.
- Jorge López-Benítez (0000-0003-1072-6131): Overall supervision of the study; critical revision and approval of the final version of the manuscript.

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