Letter

DOI: 10.5582/irdr.2020.01009

Multiphasic acute disseminated encephalomyelitis and differential with early onset multiple sclerosis

Arla Cinderella Stokes Brackett[1], Otto Jesus Hernández-Fustes[2,*], Carlos Arteaga Rodríguez[3], Olga Judith Hernandez Fustes[4]

[1] Neurology Service, Hospital San Juan de Dios, Guatemala;
[2] Neurology Department, InNeuro, Curitiba, Brasil;
[3] Neurology Department, Universidad Positivo, Curitiba, Brasil;
[4] Neurophysiology Department, Clínica das Américas, Curitiba, Brasil.

SUMMARY Multiple sclerosis is considered the most frequent demyelinating disorder of the Central Nervous System (CNS) among young adults, yet is very rare before 10 years old. Acute disseminated encephalomyelitis is a monophasic, polysymptomatic disorder that involves the CNS white matter with demyelinating lesions, which usually occurs after systemic viral infections. These two demyelinating diseases can present initially as an acute focal neurological syndrome and they can be difficult to distinguish. We describe a case of a nine-year-old girl that presented initially with dysphonia, gait ataxia, eyelid myokymia and brainstem disturbances. This was her second episode; the first episode was at the age of four years old. She recovered without neurological sequelae. The brain magnetic resonance imaging (MRI) demonstrated multiple demyelinating lesions in the white matter, cortical regions of the frontal lobe, periventricular distribution, internal capsule, corpus callosum and cerebellum. The purpose of the presentation of this case was to highlight the similarities between these two entities, since the clinical picture and neuroimaging are difficult to distinguish, mainly in relation to the first episode.

Keywords multiple Sclerosis, multiphasic acute disseminated encephalomyelitis, childhood

Multiple Sclerosis (MS) is considered the greatest demyelinating disorder in young adults, yet rare before 10 years. The overall incidence of acquired demyelinating syndromes in children and adolescents ranges from 0.6 to 1.66 per 100 000 children per year (*1,2*). Acute disseminated encephalomyelitis (ADEM) is a single-phase, polysymptomatic disorder involving central nervous system blanking, leading to demyelinating lesions secondary to systemic viral infections, often reaching the age of 5 years of age (*3*). For confirmation diagnosis, there is no specific biological marker test or confirmatory test, the MRI being considered the elected exam. Analysis of the cerebrospinal fluid may be useful, showing pleocytosis lymphocytic cells without oligoclonal bands and elevation of albumin. These pathologies may present with a focal neurological syndrome whose differential diagnosis is difficult to distinguish.

We describe a 9-year-old girl with a family health history, that eight days before admission she had gastroenteritis, and on admission presented difficulty walking, dysphonia and dysphagia. Neuro-psychomotor development was normal until that time. At the age of 4, she presented a similar condition accompanied by altered consciousness and coma that was interpreted as viral meningoencephalitis, evolving without sequelae.

Physical examination revealed eyelid myokymia on the right, ataxia, dysphonia, left upper limb monoparesis, left central facial paralysis and involvement of the X and XII cranial nerves.

Current brain MRI revealed multiple demyelinating lesions in the white matter in the frontal and peri-ventricular regions involving the internal capsule, corpus callosum and cerebellum (Figure 1). Cerebrospinal fluid found a slight increase in immunoglobulins (12.7%) and absence of oligoclonal bands. Our patient met the criteria for multiphasic acute disseminated encephalomyelitis (MDEM): *i*) Two clinical events meeting criteria for acute disseminated encephalomyelitis, separated in time by greater than 3 months, and *ii*) No evidence for clinically-silent new lesion formation on MRI between acute disseminated encephalomyelitis episodes (*4*). The patient was medicated with intravenous pulsotherapy of methylprednisolone and acyclovir, obtaining a good

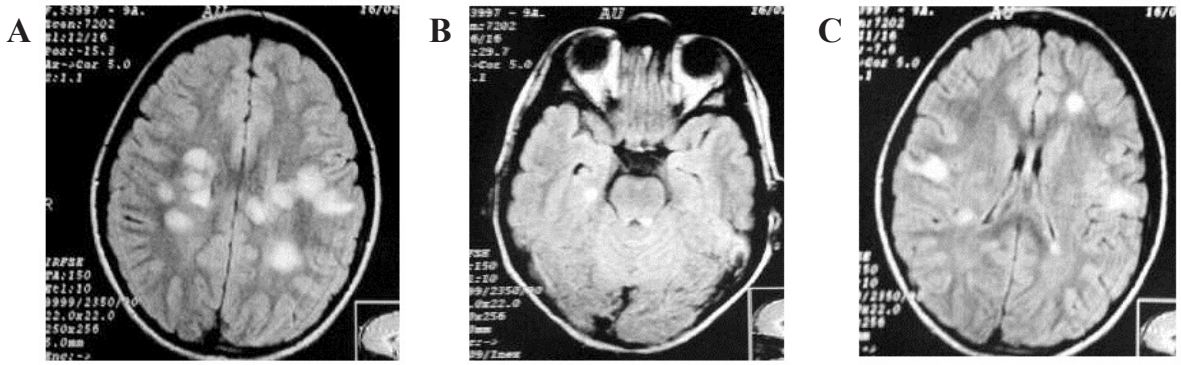

Figure 1. MRI showing multiple nodular, cotton-like images with hyperintense signal at T2 and in the long RT sequence and above all the flair sequence observed in the white matter of the semioval centers, as well as in the cortical regions of the left frontal lobe and suprasilvian regions, some of periventricular distribution in the corpus callosum. Hyperintense images were also observed in the right temporo mesial regions and in the left periaqueductal regions and in the path of the posterior legs of the internal capsules, the left middle cerebellar peduncle and the dentate nuclei of the cerebellum.

recovery in three weeks.

The International Paediatric Multiple Sclerosis Study Group defines ADEM as *i*) a first polyfocal, clinical CNS event with presumed inflammatory demyelinating cause; *ii*) encephalopathy not explained by fever, systemic illness, or postictal symptoms; *iii*) no new clinical and MRI findings emerging 3 months or more after the onset; *iv*) brain MRI is abnormal during the acute (3 mo) phase with diffuse, poorly demarcated, large (> 1-2cm) lesions predominantly involving the cerebral white matter (*5*).

The distinction between ADEM, MDEM or MS has been previously explored with no satisfactory consensus. Historically, ADEM was defined as the initial presentation of disseminated encephalomyelitis and MDEM as the occurrence of new symptoms in the setting of a history of ADEM.

The hallmark of this new category was the occurrence of two clinicoradiographic episodes of disseminated encephalomyelitis separated by at least three months. The clinical findings were defined as being new or a re-emergence of prior symptoms. If the patient sustained three or more episodes, it was classified as having a chronic inflammatory demyelinating disorder (*5*).

Our patient had an interval of five years between the first and the second clinical episode, the time between them can vary from three months to 33 years as reported by Numa *et al*. (*6*).

The presence of antibodies directed against anti-myelin oligodendrocyte protein (MOG) occurs in monophasic demyelinating disorders, particularly, in younger children and patients with ADEM. However, up to 1/3 of these children with MOG-abs will relapse within 2 years. Recent cohorts have suggested that a significant percentage of patients with recurrent optic neuritis, multiphasic demyelinating encephalomyelitis, ADEM associated with optic neuritis and neuromyelitis optica spectrum disorders have MOG-abs (*7,8*).

A diagnosis of MS can be confirmed by the presence of recurrent clinical demyelinating events and/or MRI evidence for new lesions involving different regions of the CNS. Implementation of the 2010 revised McDonald criteria may allow for diagnosis to be made at the time of the first demyelinating syndrome if imaging demonstrates silent lesions in two of the four regions typical for MS, at least one of which enhances with gadolinium. When criteria are not met at the time of the first event, new clinical attacks and/or serial imaging demonstrating accrual of lesions are needed to confirm the diagnosis of MS (*9*).

The purpose of the presentation of this case was to highlight the similarities between these two entities, since the clinical picture and neuroimaging are difficult to distinguish, mainly in relation to the first episode. Considering that 25% of cases with ADEM evolve to MS, evolutionary studies of neuroimaging are recommended.

Acknowledgements

In memory of Dr. Arla Cinderella Stokes Brackett, first author of this work, who left us early, for sharing her kindness and work with patients and with us during the three years of her residence, THANK YOU.

References

1. Waldman A, Ghezzi A, Bar-Or A, Mikaeloff Y, Tardieu M, Banwell B. Multiple sclerosis in children: an update on clinical diagnosis, therapeutic strategies, and research. Lancet Neurol. 2014; 13:936-348.
2. Sánchez-Calderón M, de Santos T, Martín S, Angulo T, Careaga J, Campos-Castelló J. Esclerosis múltiple en la infancia: nuestra experiencia y revisión de la literatura. Rev Neurol. 1998; 27:237-241.
3. Tenembaum S, Chitnis T, Ness J, Hahn JS; International Pediatric MS Study Group. Acute disseminated encephalomyelitis. Neurol. 2007; 68:S23-S36.
4. Banwell B, Ghezzi A, Bar-Or A, Mikaeloff Y, Tardieu

M. Multiple sclerosis in children: clinical diagnosis, therapeutic strategies, and future directions. Lancet Neurol. 2007; 6:887-902.
5. Krupp LB, Tardieu M, Amato MP, Banwell B, Chitnis T, Dale RC, Ghezzi A, Hintzen R, Kornberg A, Pohl D, Rostasy K, Tenembaum S, Wassmer E; International Pediatric Multiple Sclerosis Study Group. International Pediatric Multiple Sclerosis Study Group criteria for pediatric multiple sclerosis and immune-mediated central nervous system demyelinating disorders: revisions to the 2007 definitions. Mult Scler. 2013; 19:1261-1267.
6. Numa S, Kasai T, Kondo T, Kushimura Y, Kimura A, Takahashi H, Morita K, Tanaka A, Noto Y, Ohara T, Nakagawa M, Mizuno T. An adult case of anti-myelin oligodendrocyte glycoprotein (MOG) antibody-associated multiphasic acute disseminated encephalomyelitis at 33-year intervals. Intern Med. 2016; 55:699-702.
7. Hacohen Y, Banwell B. Treatment approaches for MOG-Ab-associated demyelination in children. Curr Treat Options Neurol. 2019; 21:2.
8. Hacohen Y, Mankad K, Chong WK, Barkhof F, Vincent A, Lim M, Wassmer E, Ciccarelli O, Hemingway C. Diagnostic algorithm for relapsing acquired demyelinating syndromes in children. Neurology. 2017; 89:269-278.
9. Yeshokumar AK, Narula S, Banwell B. Pediatric multiple sclerosis. Curr Opin Neurol. 2017; 30:216-221.

Received January 28, 2020; Revised February 22, 2020; Accepted February 26, 2020.

**Address correspondence to:*
Otto Jesus Hernández-Fustes, Neurology Department, InNeuro, Av. Marechal Floriano Peixoto 170, sl. 1509, Centro, Curitiba 80020-090, Brasil.
E-mail: otto.fustes@hc.ufpr.br