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Case Report

Enlarging the Spectrum of Inflammatory/Post-Infectious Acute Disseminated Encephalomyelitis: A Further Case Associated with Neurotoxocariasis

Jaime Lin,[1] Juliana Harumi Arita,[1] Antônio José Da Rocha,[2] Marcelo Rodrigues Masruha,[1] and Luiz Celso Pereira Vilanova[1]

[1]*Department of Neurology and Neurosurgery, Universidade Federal de São Paulo, SP, Brazil*
[2]*Department of Radiology, Faculdade de Ciências Médicas da Santa Casa de São Paulo, Brazil*
Address correspondence to Jaime Lin, linjaime@yahoo.com

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Abstract Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disorder with an acute or subacute onset, typically of a monophasic nature, which affects multifocal areas of the central nervous system. ADEM is commonly associated with an antecedent or concomitant infection that is usually viral. However, in the last few years, several published reports have indicated an association between ADEM and bacterial, fungal, or protozoal infections. Here, we present a case of ADEM associated with neurotoxocariasis, which, together with a previously reported case, enlarges the spectrum of inflammatory/post-infectious acute disseminated encephalomyelitis.

Keywords toxocariasis, encephalomyelitis, demyelination, white matter

1 Introduction

According to the latest consensus, ADEM is defined as a first clinical event with a presumed inflammatory or demyelinating cause and an acute or subacute onset that affects multifocal areas of the central nervous system (CNS). The clinical presentation, that typically follows a monophasic course, must be polysymptomatic and must include encephalomyelitis, with focal or multifocal lesions predominantly involving white matter that are evident in neuroimaging studies but without radiological evidence of previous destructive changes in the white matter [5].

ADEM is more commonly preceded by viral illness and vaccination, with measles, varicella, rubella, and mumps being the most frequently reported infections [7].

In the last decade, however, several articles reported different etiologies associated with ADEM, such as bacterial infection by *Borrelia bugdorferi*, fungal infection by *Cryptococcus sp.*, and protozoal infection by *Plasmodium falciparum*. Studies have also reported variations in the ADEM phenotype that are dependent upon the antecedent illness, with some etiologies being related to a more severe clinical phenotype, such as measles and others being associated with an excellent prognosis. Collectively, these reports have increased the clinical awareness of a typical cases of ADEM and have consequently expanded scientific interest in laboratory-based investigations of these cases [1].

In 2007, Marx et al. reported a case of ADEM associated with toxocariasis of the CNS [6], making the etiological spectra for ADEM even broader. Since then, no other case reports of ADEM related to helminthic infection have been published.

Herein, we describe an additional case of ADEM associated with toxocariasis of the CNS, exposing the need for further investigation of helminthic infection in cases of ADEM in countries, where parasitological infections are prevalent.

2 Case report

A 2-year-old, previously healthy boy with an uneventful familial history presented at the neuropediatric clinic of the Universidade Federal de São Paulo with an episode of sudden falling associated with somnolence. After this event, the patient slowly recovered his consciousness, revealing left hemiparesis that improved gradually over the course of several days. Fifteen days after the initial event, another episode of sudden falling occurred along with a worsening of the hemiparesis associated with dysarthria. During this period, the patient's parents reported mild behavioral changes.

The patient's epidemiological history was unremarkable except for a close contact with a pet dog. There was no history of previous infection.

Upon neurological examination, irritability, complete left hemiparesis, dysarthria, and left pyramidal signs were observed. There were no meningeal signs. A complete blood count showed 10.1×103 leukocytes with 40% neutrophils, 11% eosinophils, 2% basophils, 37% lymphocytes, and 10% monocytes. Blood electrolytes and metabolic analyses were within the normal range. Cerebrospinal fluid (CSF) analysis showed 10 cells (37% lymphocytes, 4% monocytes, 52% neutrophils, 5% eosinophils, and 2% plasmocytes) as well as a glucose level of 56 mg/dL and protein level of 43 mg/dL.

Magnetic resonance imaging (MRI) of the brain showed two large lesions compatible with imaging pattern of ADEM (Figure 1).

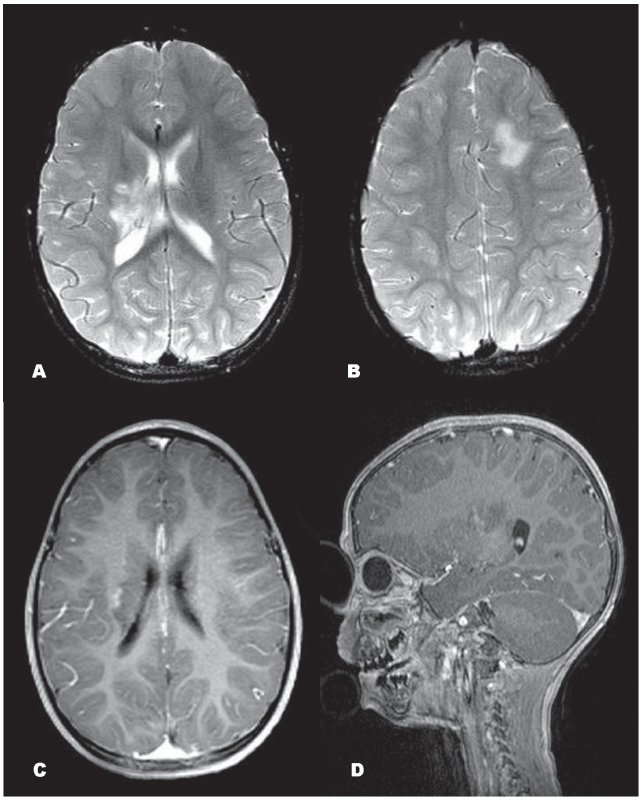

Figure 1: Magnetic resonance imaging (MRI) of the brain showing lesions characterized by hyperintensity on T2-weighted sequences located in the right internal capsule with extension to the right thalamus and caudate nucleus (A). The other lesion was demonstrated in the left frontal lobe (B). Both lesions compromised the periventricular white matter and presented minimal edema (C). Only the lesion in the right hemisphere exhibited a faint peripheral contrast enhancement ("open-ring pattern") (D).

An empirical treatment with albendazole was initiated before pulsotherapy. A few days later, results from blood and CSF analyses demonstrated a positive immunological reaction against Toxocara canis (immunoglobulin G [IgG]-ELISA and IgG4-ELISA). Serum samples were diluted to 1:100 before use, with a cutoff value (COV) of 0.477. CSF samples were diluted to 1:10 before use, with a COV of 0.477. The results of serum and CSF, expressed in optic density, were 1.149 and 0.837, respectively, confirming the diagnosis of neurotoxocariasis.

The patient was reevaluated after 1 month with a complete regression of his symptoms. The hospital's ethic commission approved this case report, and the parents gave informed consent for publication.

3 Discussion

Pathophysiologically, ADEM is characterized by both a primary autoimmune response and immune responses secondary to an infection contributing to CNS inflammation and subsequent demyelination [7].

The current knowledge indicates that ADEM is the consequence of either a direct CNS infection with a neurotropic pathogen, resulting in tissue damage, leakage of CNS-confined autoantigens into systemic circulation, activation of the T-cell response, and perpetuation of CNS inflammation, or structural mimicry between the inoculated pathogen and myelin proteins of the host [7]. In this sense, virtually any pathogen that invades the CNS may be capable of causing ADEM.

Since its first description in 1996 by Beautyman et al., the understanding of neurological infection by toxocariasis has vastly improved [4].

Clinical CNS disease is related to the number of larvae entering the brain, the severity of CNS damage, and the degree of inflammation. The clinical spectrum of CNS toxocariasis is broad, causing various syndromes: eosinophilic meningoencephalomyelitis, encephalitis, extramedullary space-occupying lesions, brain vasculitis, seizures, and possibly behavioral disorders [4].

The diagnosis of neurotoxocariasis is based on several findings: high serum titers of *T. canis* antibodies (measured with sensitive immunologic methods, such as ELISA or western blotting, that use *Toxocara* excretory-secretory antigens), eosinophilia in the blood or CSF, the demonstration of an intrathecal synthesis of anti-*T. canis* antibodies and close contact with dogs. The clinical and radiologic improvements, as well as the normalization of the CSF parameters during antihelminthic therapy, support the diagnosis [6].

Our patient presented with a subacute clinical event affecting multifocal areas of the CNS, with a polysymptomatic clinical presentation, and neuroimaging exams showing multifocal lesions, predominantly involving white matter, fulfilling the diagnostic criteria of ADEM [3].

The diagnosis of neurotoxocariasis was supported by the presence of clinical and laboratory features with high levels of eosinophils in both the serum and CSF, and in particular

the positive immunological reaction against *Toxocara canis*. The diagnosis was further supported by clinical improvement in response to the institution of treatment specific for toxocariasis.

MRI evidence of several aberrations resulting from *Toxocara* infection of the CNS has been reported, including a vasculitic pattern of abnormalities, focal lesions and nonspecific T2-weighted areas of increased signal corresponding to granulomas, microhemorrhages and cortical necrosis due to infarction [9]. We were not able to identify any specific imaging features that suggest neurotoxocariasis. However, similar to the first reported case, our patient also presented neuroimaging findings compatible with ADEM [6].

Toxocariasis is a highly prevalent condition in Brazil. In 2006, Damian et al. reported a positive serology for Toxocara canis in more than 50% of individuals in a community sample in the state of Amazonas [2]. In 2007, Paludo et al. [8] reported a positive serology of more than 30% in a pediatric sample from a large city in southern Brazil.

Although it is considered exceedingly rare and often only anecdotally reported, this study represents the second case of ADEM associated with toxocariasis of the CNS in less than a two-year period in the city of São Paulo, Brazil.

This fact has prompted us to recommend that more attention be given to investigating toxocariasis infection in children that fulfill the criteria for the diagnosis of ADEM, especially if associated with eosinophilia, high CSF eosinophil levels, hepatomegaly, and prolonged fever or cough. Our assertion supports the notion that specific treatments should be promptly authorized when this scenario is recognized. In our opinion, this recommendation should also be extended to other countries, where the prevalence of *Toxocara canis* infection is as high as in Brazil.

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