

Acute disseminated encephalomyelitis following intrauterine infected device

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ABSTRACT

Acute disseminated encephalomyelitis is an inflammatory, immune-mediated disease of the central nervous system (CNS) that usually appears in the first nine years of life, commonly following an infection or vaccination. We report the case of a middle-aged female, with history of recent perpetual infections, with neurologic symptoms masked by a severe septic shock and subsequent multiple organ failure. Although in adults the prognosis is more severe, and there are various reported cases with unfavorable evolution, following corticosteroid and physical therapy, our patient was able to recover an important part of her neurological deficits.

Keywords: encephalomyelitis, demyelination, white matter, infection, corticosteroids

INTRODUCTION

Acute disseminated encephalomyelitis (ADEM) is an inflammatory, immune-mediated disease of the central nervous system (CNS), associating demyelinating lesions of the white matter, frequently triggered by viral and bacterial infections or recent vaccination. It is usually monophasic, more specific to children (fifth to ninth years of life) and young adults, affecting predominantly male gender (male : female ratio \approx 1-2.3:0.8-1) [1-3].

Encephalopathy and multifocal neurological symptoms are commonly evident several days to several weeks after an initial illness, and the neurologic decline is rapid, succeeding the disease onset [4]. Various studies report favorable disease evolution and prognosis in

children, but appearance in middle-aged and elderly patients have an uncertain clinical course with poor prognostic [1,4].

Nowadays, this entity is used as a diagnosis of exclusion, with clinical and radiological findings that can vary over the first 3 month after the disease onset [2,5]. More than 80% of cases are preceded by an infection [6]. Symptoms start from headache and malaise, to pyramidal signs, brainstem symptoms and ataxia after few days, seizures, fever and meningism being present in some cases. Clinical presentation is more severe in adults [7,8].

Considering that clinical presentation of ADEM may mimic other demyelinating diseases, such as multiple sclerosis (MS) (the main differential diagnosis), neuromyelitis optica (NMO) or transverse myelitis (TM), over

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the years there have been established some criteria for ADEM diagnosis [9-11]: a multifocal clinical CNS manifestation caused by an inflammatory demyelinating disease; encephalopathy, manifesting through consciousness and behavior changes unexplained by an obvious cause (i.e. fever, critical illness, systemic disease, seizures); during the acute phase, brain magnetic resonance imaging (MRI) shows demyelinating lesions; after 3 or more months after ADEM onset, there are no new clinical or MRI findings.

Therefore, we report a case of ADEM in a middle-aged female patient, who was referred to our hospital for severe septic shock.

CASE PRESENTATION

A 49-year-old female, with history of 16-year-old infected intrauterine device (IDU) removed for 5 days, was admitted to the Intensive Care Unit (ICU) for multiple organ dysfunction syndrome (MODS) secondary to severe septic shock and extreme inflammatory response. She had a history of different infections during the previous year, like bacterial pneumonia, clostridium difficile pseudomembranous colitis, right leg infectious cellulite and mycotic stomatitis. Upon admission, culture of vaginal secretions revealed infection with multidrug-resistant Klebsiella and Enterococcus species, with subsequent positive haemocultures for Enterobacter species. The initial management focused on the control of the septic shock. From the time of admission and due to the progression of her pathologies over the first week, invasive ventilatory and vasopressor

support were needed for respiratory and cardio-circulatory failure. Extensive broad-spectrum antimicrobial therapy was used for the above-mentioned detected infections, associated with high value of serum procalcitonin (PCT) (29.6 ng/l), moderate leukocytosis $12.10 \times 10^3/\mu\text{l}$ with neutrophilia 89.70%, and C-reactive protein (CRP) 181.18 mg/l. In face of severe inflammatory response, associated with persistent anuria and continuous increasing values of serum creatinine and urea (2.53 mg/dl, respectively 182 mg/dL at admission), continuous renal replacement therapy with cytokine filter removal (CytoSorb® cartridge) was initiated. The multiple organ failure syndrome began to resolve, with the persistence of neurological dysfunction, encephalopathy and quadriplegia, with normal brain computer tomography (CT) appearance. Therefore, lumbar puncture was done and cerebrospinal fluid was collected for polymerase chain reaction (PCR) and cultures, a full bacterial, viral and parasitic screening were performed, all with negative results. The biochemical study of the cerebrospinal fluid (CSF) noted glucose = 41 mg/dl, proteins = 59 mg/dl, leucocytes = 40/cmm, red blood cells = 250 /cmm. Under these circumstances, a brain MRI was performed showing multiple bilateral demyelinating lesions of the profound white matter, basal nuclei and the cerebellar hemispheres, consistent with the diagnosis of acute disseminated encephalomyelitis (**Figure 1**). Thus, high dosed systemic intravenous corticosteroids were initiated, using methylprednisolone 1 g/day for three days, followed by subsequent tapering for the next nine days. Along with gradual and sustained physical therapy, the clinical and neurological

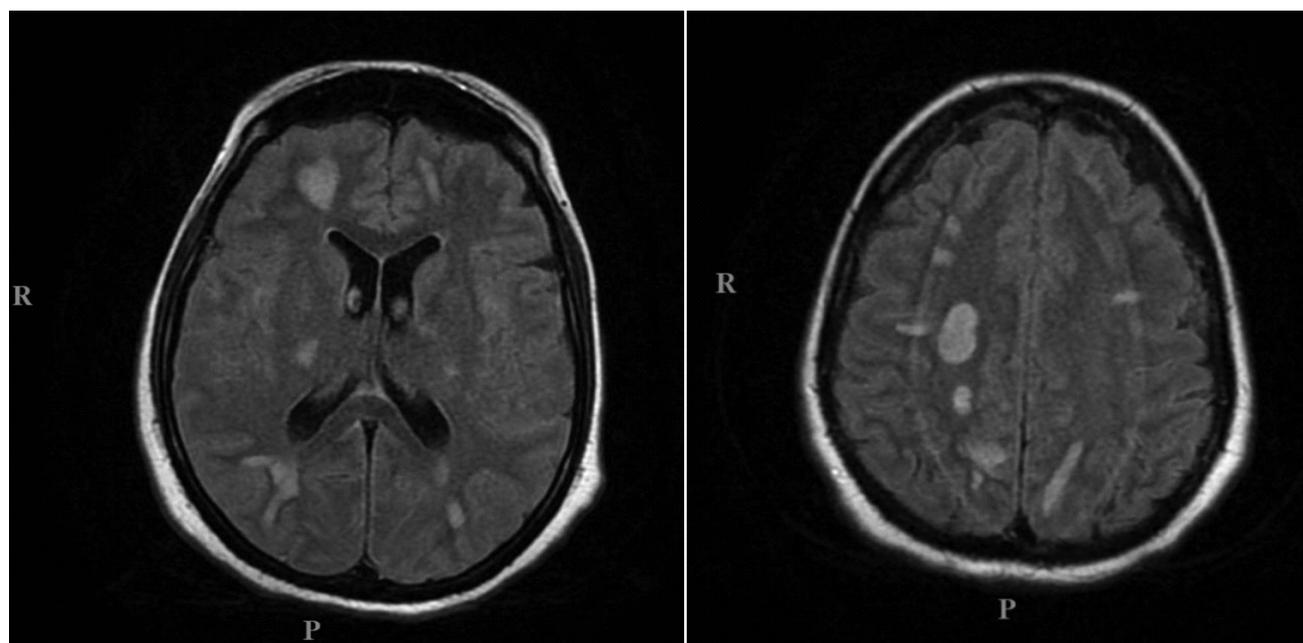


FIGURE 1. T2 FLAIR MRI sections of brain imaging showing bilateral oval-shaped, small or confluent high-signal intensity demyelinating lesions (part marked with white arrows) of the profound white matter, basal nuclei and the cerebellar hemispheres (day five after ICU admission)

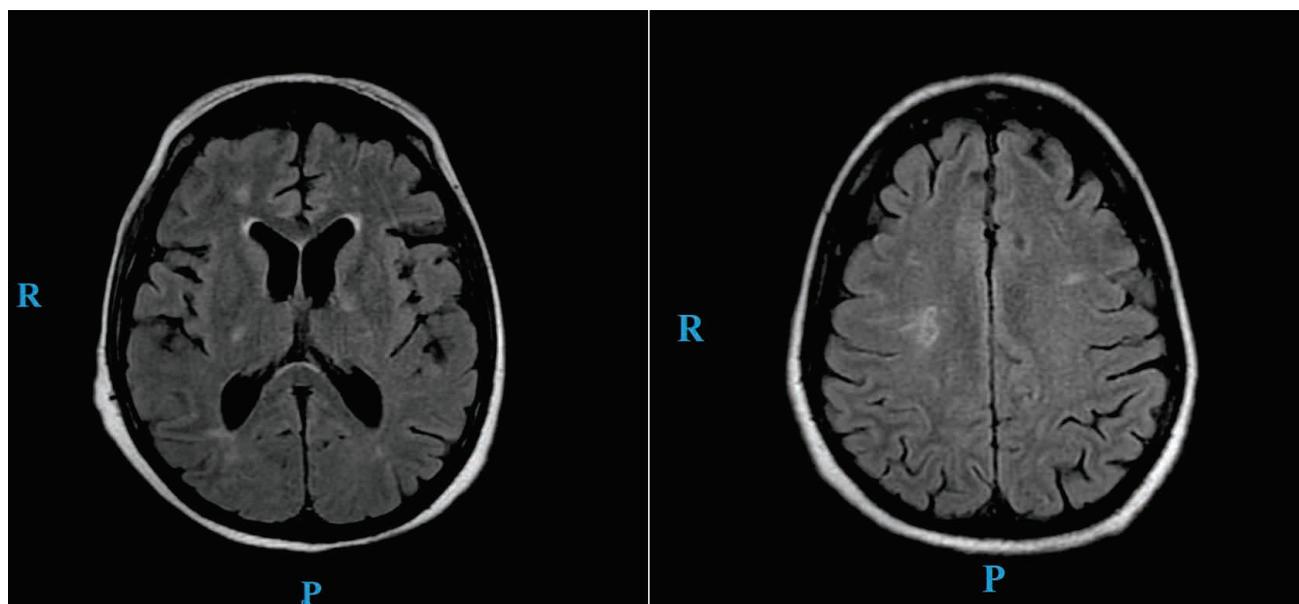


FIGURE 2. T2 FLAIR MRI sections of brain imaging showing reduction in size of the bilateral oval-shaped demyelinating lesions (part marked with white arrows) of the profound white matter, basal nuclei and the cerebellar hemispheres (60 days after the ADEM onset)

course improved, and after 30 days, she was discharged to a recovery center with persistent left hemiplegia. A brain MRI performed after 60 days (**Figure 2**), showed clear reduction in number and size of the initial lesions.

DISCUSSIONS

Over the years, a pathological course of ADEM has been shaped. The lesions of this demyelinating disease occurs perivascular, mainly in the perivenous space, leading to a sleeve-like aspect, with local accumulation of various inflammatory cells, such as macrophages, lymphocytes and microglia. In these cases, inflammatory cytokines, like interleukin 6 (IL-6), are commonly increased in correlation with the presence of oligoclonal IgG and myelin oligodendrocyte glycoprotein antibody (MOG-Ab), thus raising questions about the existence of a connection between IL-6 and plasmocytes [1,12]. Therefore, various studies have shown the importance of CSF analysis, especially through oligoclonal IgG band (OCB) patterns, in differentiating between MS and ADEM [12]. In contrast, in other CNS diseases, such as MS, the process succeeds a confluent pattern [1].

Regarding the ADEM pathophysiology, the molecular mimicry seems to be involved, with the measles infection and rabies vaccine being the classical models for disease induction. Furthermore, resemblances between the pathogen and the host may induce a T-cell activation, without tolerance occurrence [13]. Experimental studies have shown that acute, chronic, or relapsing-remitting encephalomyelitis can be induced by infecting the healthy subjects with protein components of myelin [14]. In this report, the patient's disease trig-

ger appears to be the recently removed infected intra-uterine device.

The brain MRI is considered the main diagnosis tool, and our case support this aspect. The brain CT investigation is usually unable to reveal any abnormality [15]. Reported studies showed that the presence of diffuse white matter lesions, with symmetrical bilateral involvement, helps differentiate the ADEM from MS [16,17]. In our case, the MRI showed increased T2-weighted signal in multifocal areas in the CNS white matter and deep gray matter in the frontal, temporal, parietal and occipital lobes bilaterally. Furthermore, the latest MRI showed no evidence of new contrast enhancing lesions, but only a partial resolution of the demyelinating lesions, associated with clinical improvements of the initial neurological deficits.

Apart from MS, NMO and TM, other inflammatory disorders enter the spectrum of the differential diagnosis, such as secondary CNS vasculitis – systemic lupus erythematosus, Behçet syndrome, AAV (ANCA associated vasculitis), antiphospholipid syndrome, or myeloneuropathy in Sjögren's syndrome, neurosarcoidosis, Erdheim-Chester disease and antibody-mediated disorders [18,19].

Regarding ADEM therapeutic management, corticosteroids are considered the first-line therapy [2]. Intravenous methylprednisolone is apparently superior to intravenous dexamethasone, according to a retrospective, non-randomized study of 84 children with ADEM [20]. The standard dosing represented by methylprednisolone 20-30 mg/kg (maximum 1 g) per day intravenously for 3-5 days, followed by prednisolone 1-2 mg/kg/day orally for 1-2 weeks with subsequent

tapering over 6 weeks. Several observational and retrospective studies have shown that there is an increased risk of disease relapsing with steroid withdraw after three weeks or less [21]. Generally, any vaccine should be avoided six months after the disease rehabilitation [17].

In case of first-line treatment failure, plasma exchange (PE) have shown good results in patients with ADEM. 4-6 PE cycles led to good and sustained clinical improvement [21,22]. Some elements allow predicting a proper evolution, such as timely PE initiation, male gender and preserved reflexes [23]. The third-line of treatment is consider to be reserved to intravenous immunoglobulin therapy (0.4 mg/kg/day for 5 days), with clinical improvement seen after two to three days, but with controversial results [24,25]. Schwarz et al. showed favorable outcomes of Cyclophosphamide use in adult patients with ADEM [26].

Case particularity

ADEM usually appears in the first nine years of life, commonly following an infection or vaccination, predominately in males. Our case describes a middle-aged female, with history of recent perpetual infections, with neurologic symptoms masked by a severe septic shock with concomitant MODS. Although in adults the prognosis is more severe, and there are various reported cases with unfavorable evolution, following corti-

costeroid and physical therapy, our patient was able to recover an important part of her neurological deficits.

CONCLUSIONS

Acute disseminated encephalomyelitis development after a septic episode, in a female patient with an infected intrauterine device, is a rare case presentation. The clinical course followed the monophasic pattern of a demyelinating disease, with lesions affecting white matter and deep grey matter, as identified on the brain MRI. Rapid management led to a more favorable outcome, with neurological and imagistic improvement at hospital discharge, allowing us to emphasize the fact that for such cases, clinical suspicion is important, followed by rapid exclusion of the main differential diagnosis, especially through brain imaging test, and afterwards ensuring a proper therapeutic management.

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