Acute Disseminated Encephalomyelitis: a Case Report

Merel Kwakernaat [a], Elisabeth Elst [a], Thomas Mangodt [b]

[a] AZ Voorkempen, department of paediatrics, Malle, Belgium
[b] University of Antwerp, Antwerp University Hospital, department of paediatrics, Edegem, Belgium

merelkwakernaat@hotmail.com

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Abstract

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated inflammatory and demyelinating disorder of the central nervous system. In this case report, we describe a ten-year-old-boy who presented with weakness in the legs. After work-up, a post-viral ADEM was diagnosed, possibly caused by Bocavirus. This case illustrated how mild signs of encephalopathy as part of the presenting symptoms of ADEM can easily be missed. When treating ADEM, beyond initial therapy, early initiation of physical, occupational and speech rehabilitation can help facilitate more timely and complete recovery.

Introduction

Acute disseminated encephalomyelitis (ADEM) is an immune-mediated inflammatory demyelinating disorder of the central nervous system (CNS) (1-5). Diagnosis requires both multifocal involvement of the CNS and encephalopathy (1, 3-8). ADEM is commonly preceded by a viral infection, but can be seen after vaccination (1-6, 8, 9). Corticosteroids are considered the first-line treatment. Other treatments include intravenous immunoglobulins (IVIg) and plasmapheresis (1, 3-6, 8). ADEM has a favourable prognosis, with low mortality (1, 3, 4, 6). However, reports have shown that most patients suffer from a variety of cognitive deficits post-ADEM (1-4). To reduce these deficits rehabilitation therapy should be initiated early on (3, 4).

Case Report

A ten-year-old boy, previously known with developmental dysphasia, presented with weakness in his legs and inability to sit independently. Two days prior he suffered from back pain and pain and stiffness in his legs. There was no urinary or faecal incontinence. There were no signs of concurrent infection. Three weeks prior he suffered a common cold. At clinical examination he was alert, yet quiet, and showed minimal interaction. Apart from minimal movements of the toes of his right foot, he was unable to move his legs and feet, nor could he stand. He had no motor response in his left leg and had minimal response in his right quadriceps, being unable to move against gravity. Patellar and Achilles reflexes were absent bilaterally. Plantar reflexes were normal. Sensibility of the legs was preserved, as were strength and sensibility of the arms. There were no meningeal signs. There was no photophobia, pupils were equal and reactive to light. Examination of the cranial nerves was normal. Examination of the heart, lungs and ENT-region was normal. During hospitalisation he attained urinary- and faecal retention, with need of bladder catheterisation, laxatives and rectal enema's.

Based on this, the differential diagnosis included acute infection of the central nervous system (CNS), an acute demyelinating syndrome, auto-immune encephalitis and malignancies of the CNS (1-3). Therefore, lab-work up, a lumbar puncture and brain/spinal MRI were performed. Laboratory findings showed C-Reactive Protein <5mg/L, sedimentation 5 mm/h, leukocytes 13.22x10E9/L. Serology was negative for Cytomegalovirus, Borrelia, Treponema, Herpes simplex virus, Mumps virus, Rubella virus, Coxsackievirus, Parvovirus, Mycoplasma pneumoniae and SARS-CoV-2. Serology for Epstein-Barr virus and Measles virus was IgG positive, indicating immunity or old infection. PCR for Bocavirus was positive on nasopharyngeal swab, but PCR of the liquor came back negative. The lumbar puncture showed 5 white blood cells/microliter, < 100 red blood cells/microliter, total protein 48 mg/dL, CSF-serum glucose ratio of 0.62 and absence of oligoclonal bands. Liquor cultures were negative for Herpes simplex virus, Varicella zoster virus, Enterovirus and Mycoplasma pneumoniae. Auto-immune work-up showed borderline antinuclear antibody positivity, with a titre of 1:80, which was considered irrelevant. Antibodies for myelin oligodendrocyte glycoprotein (MOG) and aquaporin-4 were negative. An MRI of the spinal cord showed longitudinal central inflammation of the thoracic part (figure 1a and b), and was considered most likely to be due to longitudinally extensive transverse myelitis. In further work-up of the extent of CNS lesions, MRI of the brain was performed, showing multiple diffuse nodular white matter lesions, mostly located subcortically (figure 2). This, combined with the longitudinal inflammation at the thoracic spinal cord, confirmed the diagnosis of ADEM.

Initially, a five day cycle of high-dose intravenous corticosteroids; methylprednisolone 30 mg/kg/day, was started. This showed an unsatisfactory response with only slight improvement of the symptoms, i.e. improvement in strength of the right leg, yet inability to move the left leg, unchanged urinary- or faecal incontinence and persistent minimal interaction. Therefore, plasmapheresis was started. In total five cycles were performed, showing good clinical response, with the boy regaining strength of the legs, a significant improvement in interaction and some improvement of urinary- and faecal incontinence. Aetiology was deemed post-viral, potentially due to a Bocavirus infection, considering an otherwise negative work-up. No EEG was performed in this case as his quiet behaviour was initially considered to be part of his personality. After the plasmapheresis it was noticed that this represented a mild sign of encephalopathy, which had thus been misinterpreted at first.

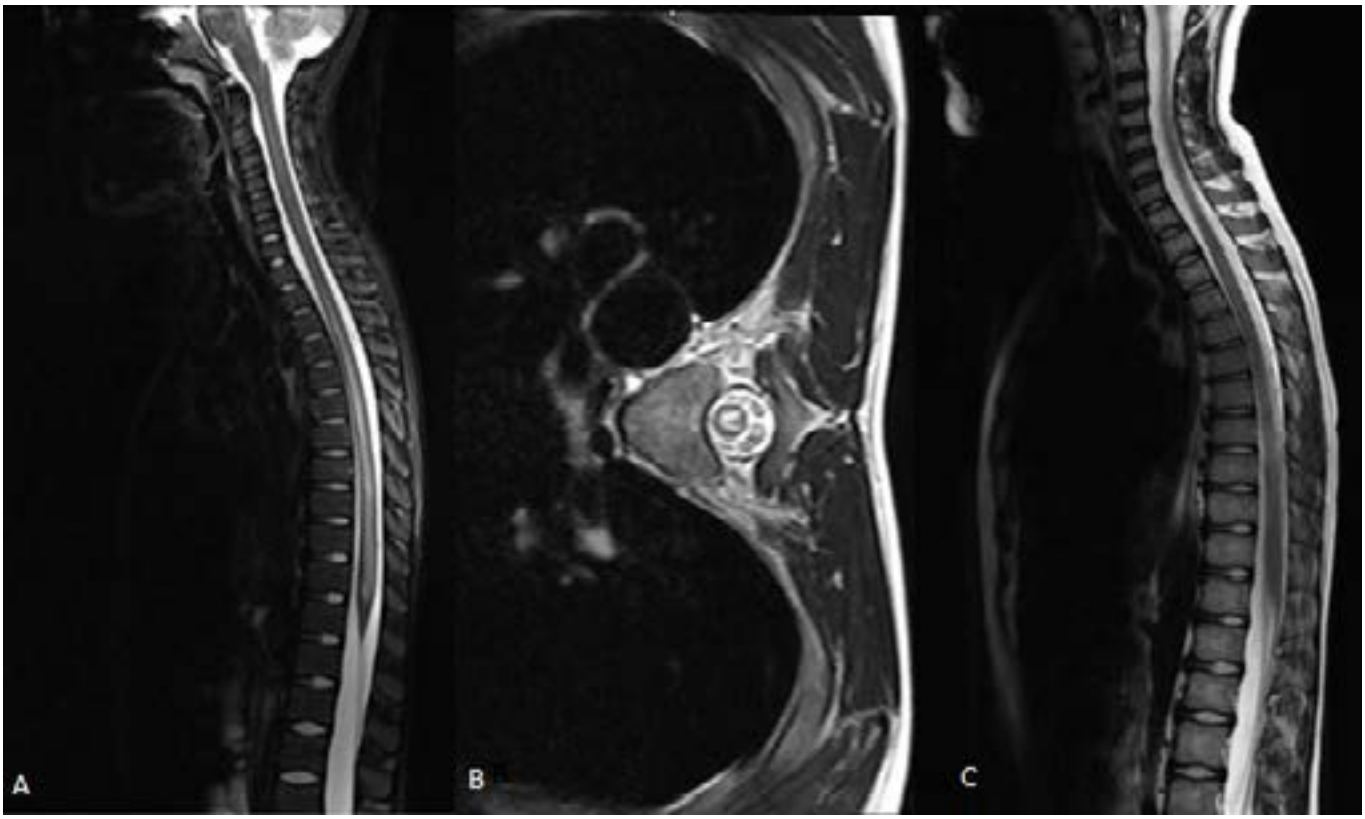
Two weeks after onset of the symptoms he was discharged from the hospital and started clinical rehabilitation in a specialised centre, which focussed on somatic, motor, urological and communicative rehabilitation. He was discharged after eight weeks. He fully regained strength in his legs. At discharge no lasting cognitive defects had been observed. There are however, residual complaints of a neurogenic bladder. Six-month follow-up showed a normal neurological examination. The MRI showed disappearance of the white matter lesions of the brain and considerable regression, yet no resolution, of the inflammation of the spinal cord (figure 1c).

Discussion

Definition and pathogenesis

ADEM is an immune-mediated inflammatory demyelinating disorder that mainly affects children, with a reported incidence of 0.23-0.6/100.000

Figure 1 A-C: Figure 1a and b: MRI of the spinal cord. It shows longitudinal central myelopathy from T2 to T12-L1.Figure 1c: MRI of the spinal cord. It shows regression of the inflammation from T2 to T12-L1. Images obtained with STIR which is a technique most sensitive for inflammatory spinal cord lesions.



per year (1-6). Mean age at presentation is between five to eight years (5, 7). It is commonly preceded by a viral infection, but can be seen after vaccination (1-7).

The precise aetiology of ADEM is unknown. Evidence suggests that it results from a transient autoimmune response triggered by an environmental event toward myelin or other self-antigens through activation of T-cell clones in genetically susceptible individuals (1-4). One protein known to play a role in ADEM is myelin oligodendrocyte glycoprotein (MOG), a protein exclusively expressed in the CNS, that is part of the myelin sheath. Expression of MOG antibodies are associated with different inflammatory diseases of the CNS such as ADEM, optic neuritis and transverse myelitis. In ADEM, 64% of children have positive MOG-antibodies. Ninety-six percent of those children turn out to have relapsing ADEM. A decline in MOG-antibodies to undetectable levels after treatment is associated with a smaller chance of future relapse and thus a better long-term prognosis (1, 2, 6, 8).

In our patient, the preceding viral infection could have well been a Bocavirus infection considering the positive nasopharyngeal PCR. Bocavirus has been associated with neurological sequalae such as encephalitis and epileptic convulsions (9). However, we found no previous literature describing association of Bocavirus with ADEM.

Clinical and biochemical findings

As ADEM is a polyfocal disease, initial presentation is highly variable. It typically has a monophasic course, but a multiphasic course is described (1, 4). Clinical presentation of ADEM may resemble other demyelinating diseases. Mortality is rare, with most studies reporting no deaths, and some with a maximum of 3% (1, 2) . However, up to 25% of children require admission to the paediatric intensive care unit due to respiratory failure (1-4, 7). Encephalopathy is a required criterion for the disease, varying from altered behaviour such as irritability, sleepiness or confusion, to altered consciousness such as lethargy, stupor or coma (1, 2, 4-8). Patients with polyfocal onset of symptoms without encephalopathy are categorised under 'Clinically isolated syndrome' (CIS). Multiple studies have shown that these patients are at higher risk of developing Multiple sclerosis (MS) (1, 7).

ADEM is diagnosed on clinical grounds and MRI, which shows demyelinating lesions. The abnormalities found are large, asymmetric patchy, poorly marginated areas of increased signal intensity in the white matter tracts of the cerebral hemispheres, brainstem, optic nerves and spinal cord (1-7).

Other investigations in the work-up of ADEM are to exclude other diagnoses such as infectious, neoplastic and metabolic disorders (4-6). Cerebrospinal fluid may be normal or show a mild pleocytosis with, or without, elevated protein levels (1-3, 6, 7). In the acute phase, the majority of EEG's are abnormal, with nonspecific findings. Most commonly, diffuse slowing of the background pattern is found (2).

Treatment

There are no randomized controlled trials regarding the treatment of ADEM. Therefore, advice is based on case reports and expert opinions (1-3, 6). High dose intravenous methylprednisolone is widely accepted as the first line treatment of choice. A 3 to 5-day course of 30mg/kg/day is started, followed by oral tapering during 4-6-weeks. Other treatments with beneficial effects include IVIg and plasmapheresis. They are considered when corticosteroids are contra-indicated or ineffective (1-7). As ADEM is not associated with the development of new lesions on follow-up, it is important to have long-term clinical and radiological follow-up to exclude a multi-phasic disorder, such as MS, and to mitigate any potential neurological of psychosocial sequelae of the condition. The international Study Group suggested reassessing the patient with at least two additional MRI's after the first normal MRI, over a period of 5 years from the initial episode (1, 2, 4).

Prognosis

ADEM has a favourable prognosis, as complete recovery is reached in most cases and mortality is rare (1-4, 7). Recovery is typically seen between 26-34-days after onset (2, 3, 6). However, few reports are available on

the cognitive outcomes of ADEM. Several studies have shown that patients frequently suffer from a variety of mild cognitive deficits: up to half of the children may have mild deficits, and moderate-severe deficits can be seen in up to 18% (2-4). Early initiation of physical, occupational and speech therapy might prevent this and can help facilitate more timely and complete recovery (3, 4).

As mentioned above, encephalopathy is a main criterion for the diagnosis of ADEM. In this case, as there were minimal symptoms, it could be argued that the correct diagnosis would have been CIS. CIS constitutes a polyfocal onset, but no encephalopathy. It has a less favourable outcome, with a high risk of developing MS (1, 7). However, during the initial days the boy was notably quieter and more withdrawn, showing minimal interaction with other people, which improved significantly after treatment.

Conclusion

We report the case of a ten-year-old boy with ADEM, provoked by a preceding viral infection, possibly due to Bocavirus, treated with corticosteroids and plasmapheresis. Because signs of encephalopathy as a presenting symptom of ADEM may be mild, they can easily be missed. For good clinical outcome early initiation of physical, occupational and speech therapy is important.

Conflict of interest: The authors declare no conflict of interest.

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Figure 2: MRI of the brain. Diffuse white matter lesions, mostly sub- and juxtacortical and in the basal ganglia, corpus callosum and brainstem. Images obtained with FLAIR which is a technique most sensitive for white matter lesions in the brain.