Encephalopathy/Encephalitis with a Reversible Splenial of the Corpus Callosum Due to the Influenza a Virus: A Case Report

Y. EL Badri1*, D. Basraoui2, H. Jala1

1,2 Department of Radiology, Mother and Child Hospital, Mohammed VI University Hospital, Cadi Ayyad University, Marrakech, Morocco

Abstract

The encephalopathy/encephalitis syndrome with reversible lesion of the splenium of the corpus callosum (MERS) is a clinical-radiological syndrome, associating encephalopathy and a specific radiological image. This syndrome is more frequently described in the Asian population and has been associated with certain viral and bacterial infections, including influenza. In this case, patients usually present general symptoms before the onset of neurological symptoms. We report the case of a 06-year-old child who presented a flu-like syndrome associated with dysarthria and ataxia then a disorder of consciousness. The cerebral CT scan showed a hypodensity of the splenium of the corpus callosum and the cerebral MRI showed an increased diffusion with restriction of the ADC of the same region. The influenza A virus was isolated in the nasopharyngeal swab. The neurological symptoms of MERS can be highly variable, mainly in the paediatric population. Clinicians should be aware of this disorder and include it in the differential diagnosis of encephalopathic patients, especially during the flu season. The prognosis is generally good with complete neurological and radiological resolution within few days or weeks, as observed in our patient.

Keywords: Encephalopathy, reversible splenic lesion of the corpus callosum, Influenza A, Pediatrics.

INTRODUCTION

The encephalopathy/encephalitis syndrome with reversible lesion of the splenium of the corpus callosum (MERS) is a clinical-radiological syndrome, associating non-specific clinical signs and a characteristic radiological presentation in magnetic resonance imaging (MRI). Clinically, it manifests as an encephalopathy combining - in varying degrees - confusion, disturbances of consciousness, or epileptic seizures. The prodromal phase includes a febrile syndrome, headaches, cough or digestive symptoms. In MRI, the lesions appear hyperintense in fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted sequence (DWI), hypointense in apparent diffusion coefficient (ADC), and hyper- or isointense in T1-weighted sequence, without enhancement after injection of contrast (gadolinium-based contrast material). Lesions are seen in the centre of the splenium of the corpus callosum and can extend to the entire corpus callosum or the adjacent hemispherical white matter and disappear in less than a month. [1]

The syndrome was first described in 2004 by Tada et al. in Japan, and the vast majority of reported cases involved East Asian children and young adults, suggesting a strong genetic predisposition in this population, although there are some cases described in European countries and Australia.[3-6] The etiologies are varied, often infectious, but similar lesions are found in acute mountain sickness or with the use of antiepileptic drugs (the main ones being: vigabatrin, phenytoin, lamotrigine, carbamazepine and oxcarbazepine). Takanashi evaluated 54 Japanese paediatric patients with MERS and concluded that seasonal influenza viruses A and B were the most naturally pathogenic viruses[7].

CASE REPORT

We report the case of a 06-year-old girl without any particular pathological history or recent medication. She was admitted in the emergency department for a fever (39°) and headache associated with dysarthria and ataxia evolving for 4 days complicated 24h later by a consciousness disorder. The neurological examination found the same day ataxia on finger-nose maneuver, jerky eye movements and dysarthria, all regressive within a few hours. The cerebral CT scan performed without contrast showed
hypodensity of the splenium of the corpus callosum (Fig. 1). The MRI scan performed later showed a lesion in the center of the splenium of the corpus callosum hyper intense in diffusion with low ADC signal, hyper intense in FLAIR and in T2 weighted sequence and isointense in T1 weighted sequence (Fig. 2). The T2* sequence and the 3DTOF were normal. An electroencephalogram (EEG) performed the same day the patient was admitted was normal. A biological assessment revealed an inflammatory syndrome with a C-reactive protein (CRP) at 11 mg/L, lymphopenia at 630/mm3. The ionogram, particularly the natremia, was normal. A hepatic cytolysis was noted with transaminases twice normal and no cholestasis. The prothrombin time (PT) was lowered to 55%. The liver ultrasound and the cerebrospinal fluid (CSF) analysis were normal (1/mm3 element, 1/mm3 hematite, proteinorachy at 0.12 g/L, glycorachy at 0.86 g/L). Influenza A virus was found on a nasopharyngeal swab after viral and bacterial PCR amplification. The neurological signs completely disappeared on day 3. Biological abnormalities were normalized within 5 days. A follow-up MRI scan performed one month later noted the complete disappearance of the lesion (Fig. 3). Magnetic resonance angiography of the supra aortic trunks with contrast was normal with no pathological enhancement. Given the initial presence of encephalopathy, the reversible splenic lesion of the corpus callosum and the detection of the influenza A virus, the diagnosis of MERS due to the influenza A virus had been made.

Fig-1: Brain scan without injection of contrast medium (A) axial section and (B) coronal section at day 0 showing hypodensity of the splenium of the corpus callosum.

Fig-2: Cerebral MRI without contrast injection at D0 (A: diffusion sequence; B: ADC sequence C:T2, D: FLAIR and E: T1) showing a lesion in the centre of the splenium of the corpus callosum, in hypersignal in diffusion sequence, in hyposignal in ADC, in hypersignal in FLAIR and in isosignal in T2 weighted sequence and in isosignal in T1 weighted sequence.

Fig-3: Cerebral MRI without contrast injection at D30 (A: diffusion sequence; B: ADC sequence C:T2, D: FLAIR and E: T1) showing the total regression of the splenium lesion of the corpus callosum.
**DISCUSSION**

MERS is a syndrome characterised by an acute encephalopathy state generally with a moderate clinical course and excellent prognosis, where MRI is the key in establishing the diagnosis. [3]

Transient cerebral oedema is due either to the release of specific myelin neurotoxins with intramyelinated oedema or to a transient inflammatory infiltrate with release of cytokines and activation of T-lymphocytes. [3] The different arterial vascularisation and water content in the corpus callosum may be related to the distribution of lesions in MERS. [4] Compared to other areas of the brain, neurons, astrocytes and oligodendrocytes of the corpus callosum have a higher density of receptors, including cytokine receptors, glutamate and other excitatory amino acid receptors, toxin receptors and drug receptors. [9] The corpus callosum is the largest bundle of brain fibre with projections in the prefrontal, premotor, primary motor, and primary sensory areas and oedema of this structure can cause a disturbance of motor control and disruption of technical functions such as spatial orientation, vision, hearing and language-related behaviour, as observed in our case report (ataxia, dysarthria). [5] Different cohorts present a wide spectrum of MERS symptoms. The most commonly described are delusional behaviours (Takanashi J. 29/54 patients), consciousness disorders (Tada et al. 12/15 patients; Takanashi J. 19/54 patients) and seizures (Tada et al. 8/15 patients; Takanashi J. 18/54 patients; Yildiz A. et al. 4/8 patients). Others, such as muscle weakness, ataxia, tremors, abnormal speech, blindness, pseudobulbar paralysis, facial nerve paralysis, ophthalmoplegia, visual hallucinations, drowsiness and headaches are also described in the case reports. Most cases recover completely in 1-7 days [3, 5, 7, 10]. Despite different infectious causative agents, the clinical and radiological features found in the literature are almost identical. [3]

The differential diagnosis of Mild Encephalopathy is broad including infection, electrolyte abnormalities, use of certain medications, non convulsive epileptic seizure disorder, cerebral ischemia or hemorrhage, intracranial masses and acute dissemination encephalomyelitis (ADEM). [2] Although ADEM usually occurs in paediatric age and after infection, it can be easily differentiated from MERS, as it is maintained by autoimmune-mediated demyelination of the brain and spinal cord, with multifocal white and grey matter lesions that may be bilateral but asymmetrical, without selectivity for the corpus callosum and may have some improvement without restricted dissemination; complete recovery is less common and more delayed. [3, 4] Pourable corpus callosum lesions occur in a wide group of physical entities and are, in fact, an epiphenomenon. The term cytotoxic corpus callosum lesions have recently been expanded to include these multiple entities. [9]

The presence of reversible lesions involving CTS has been directly associated with convulsions, antiepileptic withdrawal, high altitude oedema, metabolic disorders (mainly hyponatremia), in addition to infectious triggers (especially viruses) which were the most common etiologies of abnormalities identified in childhood. [4, 5]

Acute Necrotizing Encephalitis of Childhood (ANEC) is another encephalopathy associated with influenza, which has different lesions on MRI and poor results compared to MERS. [8] The MRI results in our patient were not compatible with inflammatory diseases or malignancies, the history of the disease, the physical examination and clinical course, the CSF and the conclusive laboratory results, allowed to exclude these hypotheses. The MRI results in our case are similar to those reported in the other studies. Lesions generally are hyperintense in T2-weighted sequence, iso-intense to slight hypo-intense in T1-weighted sequence, and reduced diffusion (low ADC values) and are not enhanced after the injection of contrast [5]. The CSF is usually normal, sometimes showing pleocytosis, supporting the idea that MERS is an infection associated with encephalopathy syndrome, rather than encephalitis. [3,5] There is no evidence or consensus on the treatment of MERS. There are case reports of patients treated with antiviral drugs, antibiotics, corticosteroids, intravenous immunoglobulins and a major proportion of non-treated patients [3,7] There are no available data concerning the clinical efficacy of oseltamivir and influenza-associated central nervous system damage [2]. The prognosis is generally good, even in delayed cases where no treatment has been administrated, with full clinical recovery regardless of treatment [2, 7]. Despite this, some patients need several days to recover. This is why the treatment be must considered in patients with severe pathological conditions, such as severe neurological manifestations [2].

**CONCLUSION**

The presence of an asymmetric lesion in the The splenium of the corpus callosum on MRI, associated with previous viral infection, in a patient with neurological symptoms suggests the diagnosis of MERS. Although this entity is more frequently described in Asiatic population, it can be seen worldwide. Children may present a wide spectrum of neurological symptoms including aphasia and behavioural changes. The prognosis of MERS is good in the majority of patients with a full recovery. We report this case as a reminder so that clinicians should be aware of this disorder and make it included as a differential diagnosis in encephalopathic patients, particularly during Influenza season.

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