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OPEN ACCESS Case Report

Clinically mild encephalitis/ encephalopathy with a reversible splenial lesion (MERS) in a child with ataxia and diplopia.

Erim van Os[1], Malou Nijhuis[2] and Stephan Malm[3]
[1]Department of Pediatrics
[2] Emergency Department
[3] Department of Neurology, Rode Kruis Ziekenhuis, Beverwijk, The Netherlands
Corresponding author: Erim van Os; evanos@rkz.nl

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Abstract

We report the case of a 15-year-old boy with clinically mild encephalitis/encephalopathy with a reversible splenial lesion (MERS). He presented with diplopia and ataxia, and his cerebrospinal fluid (CSF) showed mild pleocytosis and elevated protein. MRI demonstrated a reversible splenial lesion in the corpus callosum. He did not receive any treatment and recovered quickly within two weeks. The results of a neurological examination after three months were completely normal. MERS is relatively unknown in Europe, and most patients are reported in East Asia. This post-infectious encephalitis/encephalopathy arises soon after the onset of symptoms. The prognosis is excellent, and most patients recover completely without neurological sequelae. MRI typically shows a reversible splenial lesion with diffusion restriction and without contrast enhancement, sometimes with adjacent symmetrical lesions extending into the subcortical white matter. The pathogenesis is still unknown. Recognition of the condition and its clinical radiological discrimination from acute disseminated encephalomyelitis (ADEM) may prevent unnecessary treatment.

Keywords: Splenium; corpus callosum; diffusion restriction; MERS type 1; MERS type 2; ADEM

Background

Mild encephalitis/encephalopathy with reversible splenial lesions (MERS) in children is a rather unknown disease entity in Europe. In 2002, Kobata et al. was the first to describe a reversible lesion in the splenium of the corpus callosum (SCC) on magnetic resonance imaging (MRI) in a child with rotavirus encephalopathy [1]. MERS is described most often in patients with influenza-associated encephalitis/encephalopathy and the incidence is much higher in patients of East Asian origin [2, 3, 4]. Neurological symptoms include features of acute encephalopathy, such as altered state of consciousness, delirium behaviour, speech difficulties, and seizures [3, 4, 5, 6]. A striking feature is that the encephalitis/encephalopathy is clinically mild and almost all patients recover completely without sequelae [6]. Characteristic MRI findings show a reversible lesion in the SCC, sometimes extending bilaterally into the adjacent white matter. The lesions are symmetrical and demonstrate T2 hyperintensity with transiently decreased diffusion and no contrast enhancement [3, 4, 6]. To our knowledge, MERS was only described in 15 children outside East Asia, one of them of Indian origin [3, 5, 7, 8, 9, 10, 11, 12].

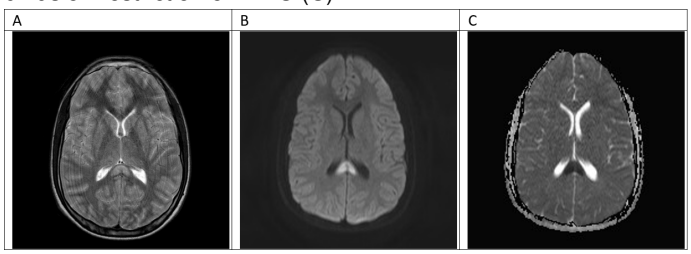
We report the case of a 15-year-old Caucasian boy with MERS presenting with ataxia and diplopia. The purpose of this article is to increase awareness of the MERS disease entity in children presenting with encephalitis/encephalopathy. We therefore review the literature and point out the difference between MERS and acute disseminated encephalomyelitis (ADEM), an important disease in the differential diagnosis.

Case Report

A previously healthy 15-year-old boy developed high-grade fever, headache, and vomiting 10 days before presentation. On the day of admission to our hospital, he had presented with diplopia and dysarthria for two days. Physical examination revealed no fever, and a normal pulse rate and blood pressure. Neurological examination revealed binocular diplopia, worse on right lateral gaze, without evident eye movement disorders, suggesting a possible nervus abducens palsy. He also suffered from a cerebellar syndrome characterized by dysarthria, disturbed tandem gait, and dysmetria while performing the finger-to-nose test. There were no signs of meningism. His blood count and biochemical examinations were normal except for decreased sodium (133 mmol/L). Cerebrospinal fluid (CSF) demonstrated an increased cell count (110 cells/mm^3, polymorphonuclear/mononuclear 3/107), and increased protein (1,34 g/L), but a normal glucose level. Oligoclonal bands were not detectable. MRI revealed a hyperintense lesion in the SCC on

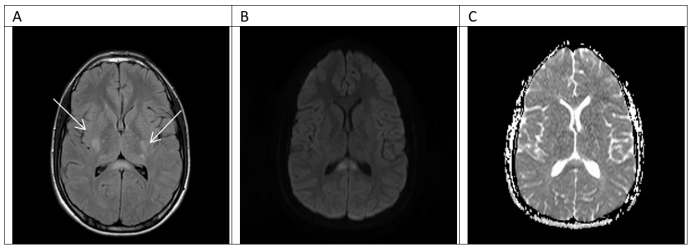
T2-weighted images, and a reduced apparent diffusion coefficient (ADC) on diffusion-weighted images (DWI), reflecting restricted diffusion without any contrast enhancement (Figure 1).

Figure 1. MRI on day of presentation. Axial MRI taken on the day of presentation demonstrates a lesion in the SCC, which is hyperintense on T2-weighted (A) and DWI (B) with corresponding diffusion restriction on ADC (C).



The described clinical radiological features were best explained by MERS. Intravenous acyclovir was empirically administered until herpes simplex virus infection was ruled out; corticosteroids were not administered. No pathogen was detected in his stool, blood, nasopharyngeal swab, or CSF samples. Follow-up MRI at day 10 still showed the splenial lesion on T2-weighted images, but a decreased restriction on DWI. However, T2-weighted images revealed new lesions at the location of the basal ganglia and thalamus region, slightly more prominent on the right side than on the left (Figure 2). At follow-up, our patient had improved clinically. Two weeks after admission he had no diplopia or dysarthria, and he showed a normal tandem gait. On performing tasks, he revealed only a mild dysdiadochokinesia in the right hand. The follow-up three months later showed a complete recovery without neurological sequelae. All described lesions on MRI were completely resolved after three months (Figure 3).

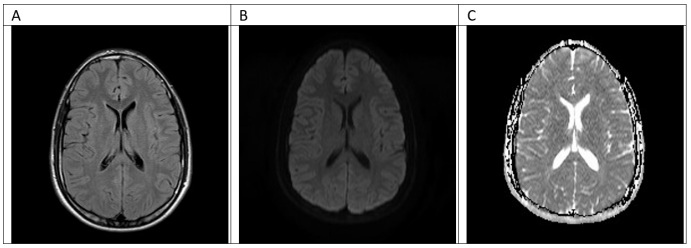
Figure 2. MRI on day 10 after presentation. Axial MRI taken on day 10 after presentation. T2-FLAIR imaging still showed some hyperintensity in the SCC, but also new hyperintense lesions in the basal ganglia and thalamus region (A) (see arrows). Signal intensity at the splenium on DWI is diminished (B), as well as diffusion restriction (C).



Discussion

MERS is defined as a syndrome of mild encephalitis/encephalopathy associated with characteristic reversible abnormalities in the SCC, and sometimes in the adjacent white matter on MRI. After nonspecific prodromal symptoms, the most described neurological symptoms at presentation are delirium behaviour, decreased consciousness, and seizures [4, 6]. Ataxia has been described previously in case reports [9, 13]. Notebaert et al. described a patient with ataxia without a cerebellar lesion on MRI [5]. Our patient suffered from ataxia as well, but MRI did not reveal lesions in the cerebellum. Evaluation of CSF shows normal parameters in most patients. Sometimes a mild pleocytosis can be found [4, 9], although an infectious pathogen has not yet been demonstrated in CSF.

Figure 3. MRI on day 73 after presentation. Axial MRI taken on day 73 after presentation. Signal intensities in the basal ganglia and thalamus region as well as the splenium completely disappeared on T2-FLAIR imaging (A). There is no longer any signal intensity on DWI (B) and no diffusion restriction on ADC (C).



Various causative agents have been associated with a splenial lesion, such as influenza virus A and B, mumps virus, adenovirus, rotavirus, parainfluenza virus, human herpes virus 6, *Escherichia coli* and *Salmonella enteritidis*. However, as in the case of our patient, an infectious trigger is not always found [2, 4, 5, 9, 10, 13]. MRI typically shows a symmetrical hyperintense lesion in the SCC on T2-weighted images and decreased diffusion with low ADC values on DWI. No contrast enhancement is seen [3, 4, 6]. These lesions are called MERS type 1 lesions [3]. Sometimes the lesions extend into other parts of the corpus callosum or other brain areas in a symmetrical pattern, so-called MERS type 2 lesions [3]. They show the same radiological characteristics as the isolated splenial lesions [3, 4].

After one week, most of these abnormalities had completely disappeared, although some lesions were still visible on MRI after three months [4]. Hashimoto et al. described a patient showing clinical full recovery within two weeks with a persistent splenial lesion for more than five months [14]. Ka et al. also described three patients with MERS type 2 lesions with persisting but reduced T2 hyperintensity with no associated diffusion restriction [3]. In our patient, the first MRI showed an isolated lesion in the SCC (Figure 1). His follow-up MRI on day 10 still showed the lesion in the splenium, although restriction was diminished. T2-weighted images also showed symmetrical lesions without diffusion restriction at the location of the basal ganglia and thalamus region (Figure 2). MRI results after three months showed no abnormalities (Figure 3).

A more variable presentation of radiological findings is seen in patients with MERS type 2. Authors have reported cases presenting initially with MERS type 2 lesions, showing MERS type 1 lesions at follow-up, before disappearance of all abnormalities

on MRI [15]. Notebaert et al. have also described patients with residual MERS type 2 lesions after disappearance of the MERS type 1 lesion [5]. Our patient first showed a lesion confined to the SCC (MERS type 1), followed by symmetrical lesions at the location of the basal ganglia and thalamus on the second MRI (MERS type 2 lesions). As in our case, a remarkable feature is that there seems to be no relation between the neurological deficits and the location of the lesions found on MRI [3].

MERS is generally self-limiting and has a good to excellent prognosis. Although one case has been described with neurological sequelae [16], all other authors report complete neurological recovery. A large number of these patients did not receive corticosteroids [1, 4, 6, 9, 13, 14, 15, 17]. Therefore, it seems unnecessary to treat patients with corticosteroids [3].

The exact pathophysiology of MERS is still unknown [3, 10]. Cytotoxic cerebral edema seems to play an important role and leads to a transitory restricted ADC. Cytotoxic cerebral edema is seen in MERS, antiepileptic drug (AED) administration or withdrawal, and high-altitude cerebral edema; all characterized by a reversible SCC lesion. Many AEDs can influence water balance by targeting cation channels [4]. In MERS, hyponatremia is often seen, as in our patient, and this could potentiate cerebral edema [4, 18]. Other possible causes include intramyelinic edema, interstitial edema in tightly packed fibres, or a transient inflammatory infiltrate with related cytotoxic edema [6, 17, 19].

ADEM is also an important disease in the differential diagnosis of MERS. Both may present with a disturbance of consciousness, seizures and focal neurological signs. The CSF examination in our patient revealed a mild pleocytosis. Although an elevated protein does not rule out ADEM, it is usual that the pleocytosis is no more than 100/mm^3 in ADEM [20]. In contrast with MERS, the MRI characteristically shows multifocal bilateral and asymmetrical lesions in the deep cortical gray (basal ganglia) and subcortical white matter, with often poorly defined margins. Most of these ADEM lesions enhance with gadolinium in the acute phase. If the corpus callosum is involved, the lesions are usually asymmetrical and are contrast-enhanced, as opposed to MERS. Corticosteroids are considered the standard treatment of ADEM. Clinical recovery takes weeks to months and resolution of the lesions lasts the same amount of time [3, 4, 5, 6, 17, 21]. Some children will be left with neurological sequelae. In our patient, (1) the clinical course resulted in fast and almost complete recovery within two weeks without corticosteroids, and (2) the MRI findings at presentation showed an isolated symmetrical SCC lesion without any contrast enhancement, which agrees with the described development of MERS. It seems very unlikely that our patient suffered from ADEM.

Conclusion

Recognizing MERS as a rare condition in children is very important, as this may prevent unnecessary treatment and provide assurance about the excellent prognosis of the disease.

Competing interests

The authors declare that they have no competing interests.

Author contributions

Dr. Van Os drafted the initial manuscript and approved the final manuscript as submitted. Dr. Nijhuis and Dr. Malm reviewed and revised the manuscript and approved the final manuscript as submitted.

Abbreviations

ADC	apparent diffusion coefficient
ADEM	acute disseminated encephalomyelitis
AED	antiepileptic drug
CSF	cerebrospinal fluid
DWI	diffusion-weighted images
MERS	mild encephalitis/encephalopathy with a reversible lesion of the splenium
MRI	magnetic resonance imaging
SCC	splenium of the corpus callosum

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