Imaging findings of reversible lesions in the splenium of the corpus callosum associated with mild encephalitis (MERS).
What's new about it?

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Learning objectives

• Illustrate the imaging findings of our case series of MERS.
• Discuss the possible etiologies and physiopathological mechanisms.
• Display differential diagnosis of lesions of the splenium of the corpus callosum.
Images for this section:

![MRI of a 22-year-old man showing an oval lesion in the splenium of the corpus callosum, hyperintense on DWI.](image)

**Fig. 1:** MERS in a 22-year-old man. MRI display oval lesion in the splenium of corpus callosum, hyperintense on DWI.

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Background

MERS is a clinical-radiological entity, characterized by mild encephalitis or encephalopathy associated with reversible lesion of the corpus callosum, which commonly involves the splenium.

Epidemiology

Affects mainly young patients and children, being reported mostly in oriental population, with more than 50 published cases. Its precise frequency is unknown, but it is likely underreported, since magnetic resonance imaging examination is not routinely performed in the responsible disorders. [1]

Clinical presentation

Clinically its present with nonspecific prodromal symptoms including cough, rhinorrhea, vomiting, headache, and sore throat. Later symptoms are consistent with encephalopathy as speech difficulties, drowsiness, decreased consciousness, delirium, seizures, irritability, agitation, and disorientation. [2] A multi-center study performed in Japan showed that the most common neurological symptom is delirium behavior representing 54%. [3]

All reports refer present a mild clinical course, with complete resolution of symptoms in a short period of time generally does not exceed 30 days from the onset of symptoms.

Causes

The first description of this entity was by Chason et al. in 1996. Lately it has been described in patients with encephalitis/encephalopathy of varied etiology, including infections, high altitude cerebral edema, metabolic disturbances like hyponatremia and hypoglycemia, and antiepileptic drug therapy. It also occurs in nonepileptic patients who are on antiepileptic drugs for other reasons.

During the last years several studies have been reported related to other causes such as measles, rotavirus, hemorrhagic fever, neuroleptospirosis. Also associated to hemolytic uremic syndrome, malnutrition during chemotherapy, anorexia nervosa and use of corticosteroids.

There are few reports of reversible splenium lesion in neonates. (Fig 1-2). Some authors postulated that the timing of the MRI or the severity of brain damage influenced the results. Barkovich described differences in the pattern of injury in neonates cases during the first two weeks after the clinical onset.[4]
Pathophysiology

Reversible brain lesions have been attributed to the transient development of intramyelinic edema due to the separation of myelin layers, which is a possible mechanism for the transiently decreased diffusion of the splenium lesion.[5] It has to be remembered that during the neonatal period myelination of the corpus callosum is not completed and then, the hypothesis of intramyelinic edema cant be the cause of the diffusion weighted imaging signal. The reduced diffusivity might be the result of interstitial edema in the extracellular space between tightly packed axons. Reversible diffusion changes in the corpus callosum are also observed in patients with epilepsy receiving antiepileptic drugs, in which the involvement of focal cytotoxic edema occurring at the glial level is speculated by the absence of fiber interruption on diffusion tensor imaging. [6] Kim et al. attributed it to possible anti-epileptic drug (AED) toxicity induced reversible demyelination. Others postulated that sudden cessation of AED could lead to alteration of the arginine-vasopressin (AVP) system, resulting into hydric imbalance. [7]

Another possible explanation is the development of an inflammatory infiltrate. The influx of inflammatory cells and molecules, possibly combined with related cytotoxic edema, might have decreased the ADC. Some authors have examined oxidative stress markers in cerebrospinal fluid (CSF) in MERS patients demonstrating that the values of tau protein in the CSF were not increased, indicating less possible involvement of axonal injury. This is in good accordance with the absence of fiber interruption on diffusion tensor imaging in the aforementioned epileptic patients with a similar SCC lesion. The symmetry and absence of contrast enhancement makes an inflammatory etiology less likely.

Others authors suggests that the difference in arterial vascularization and/or water content in the corpus callosum may lead to the frequent occurrence of SCC lesion. The reversibility of the lesion of the splenium of the corpus callosum within a brief period also suggests that this entity is distinct from the cytotoxic edema seen in cellular energy failure, such as an acute infarction, which is nearly always irreversible.

Some genetic factors might predispose to reversible lesion in the splenium. Familial cases of clinically mild encephalitis/encephalopathy with transient splenial lesions have been reported, and an autosomal recessive model of inheritance, if any, was suspected. [8]
Fig. 2: Neonatal MERS. MR DWI of a 12 days old patient after seizures. After 10 days the patient showed complete clinical improvement.

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**Fig. 3:** Neonatal MERS. MR DWI of a 12 days old patient after seizures. After 10 days the patient showed complete clinical improvement.

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Imaging findings OR Procedure details

Classification

Recently, reversible lesions with transiently reduced DWI have also been reported with lateral extension from the splenium into the frontoparietal subcortical white matter, and with anterior extension to involve the entire corpus callosum.

Then, MERS is classified into types 1 which exhibits only splenial corpus callosum lesions, and type 2 that shows white matter lesions in addition to lesions of the entire corpus callosum; however, the splenial lesion is always the last to disappear. In general, patients with MERS type 2 lesions have also good prognosis with complete resolution within two weeks.

MERS type 1 lesions are detected more frequently in patients with encephalitis/encephalopathy than type 2 lesions. Lesions on MRI corresponding to the so-called MERS type 2 lesions are not always given this name in the literature. (Fig. 3-7, 9-10)

The splenium involvement appears hyperintense on T2WI and FLAIR image and iso- or hypointense on T1WI. The changes in DWI appear earlier than the changes in T2WI and FLAIR.

Involvement of the splenium, based on signal changes, can be divided into two types according to its shape and extent: Oval, circumscribed, with well-defined borders usually located in the middle; or wider, with less regular borders and involving the entire splenium ("Boomerang sign"). (Fig 8).

While MRI detected abnormality only in the splenium, SPECT indicated hypoperfusion in areas with normal MRI findings, some of which overlap with lesions involving MERS type 2. It is possible that such hypoperfusion generally occurs in other MERS cases.

Magnetic resonance spectroscopy (MRS) revealed normal NAA/Cr and Cho/Cr ratios, reflecting that there isn´t neuroaxonal damage and demyelination, respectively. Diffusion tensor MRI shows normal FA values reflecting indemnity of the fibrous structures. [9]

Differential diagnosis

Among the differential diagnoses include posterior reversible encephalopathy syndrome (PRES), diffuse axonal injury, multiple sclerosis, lymphoma and pontine myelinolysis.

In any encephalitis/encephalopathy patient with lesions in the white matter, acute disseminated encephalomyelitis (ADEM) should be considered in the differential diagnosis. However, in ADEM, recovery occurs within weeks, and in our case the symptoms recovered within 7 days without specific treatment. MRI in ADEM usually
shows multiple foci of T1 and T2 prolongation in the subcortical white matter that typically is bilateral and asymmetric. The lesions usually evolve over weeks to months and disappear only after several months. After contrast-agent infusion, ADEM lesions will show variable enhancement depending on their acuity.
**Fig. 4:** MERS type 1 in a 5-year-old child. MRI shows hyperintense oval lesion in the SCC on DWI (4) and FLAIR (5). This lesion has true diffusion restriction in the ADC map (6).

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**Fig. 5:** MERS type 1 in a 5-year-old child. MRI shows hyperintense oval lesion in the SCC on DWI (4) and FLAIR (5). This lesion has true diffusion restriction in the ADC map (6).

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Fig. 6: MERS type 1 in a 5-year-old child. MRI shows hyperintense oval lesion in the SCC on DWI (4) and FLAIR (5). This lesion has true diffusion restriction in the ADC map (6).

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**Fig. 7:** MERS type 1. MRI of control at 2 months of the same patient, shows complete resolution of lesion in the SCC on DWI (7) and ADC (8).

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**Fig. 8:** MERS type 1. MRI of control at 2 months of the same patient, shows complete resolution of lesion in the SCC on DWI (7) and ADC (8).

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**Fig. 9:** MERS type 2 in a 3-year-old patient. MRI DWI shows diffusion restriction lesion in the SCC (boomerang sign).

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Fig. 10: MERS type 2 in a 3-year-old patient. MRI shows also diffusion restriction of the frontoparietal white matter.

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Conclusion

This lesion itself seems to be a nonspecific phenomenon. Per definition, all patients had symptoms suggestive for encephalitis/encephalopathy and showed the typical lesions on MRI the corpus callosum and/or on the center semiovale bilaterally.

The more frequent use of MRI allows more patients to be examined, resulting in detection of the lesion. It is important to consider this entity and be differentiated from other diseases affecting the corpus callosum. Moreover, it is expected that the variety of pathogens in patients with MERS type 2 lesions will expand in the future.
References


