

# Transient Elevation of Cerebrospinal Fluid Protein in a Patient of Mild Encephalitis with Reversible Lesion in the Splenium: A Case Report

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## Abstract

Mild encephalitis with reversible lesion in the splenium (MERS) is a clinoradiological syndrome presenting as a solitary lesion in the central portion of the splenium of the corpus callosum (SCC) with a radiological finding of restricted diffusion and low apparent diffusion coefficient (ADC) values. Complete resolution of the lesion on follow-up imaging and full clinical recovery are the hallmarks of this syndrome, even with only supportive therapy. MERS is usually associated with normal Cerebrospinal fluid (CSF) findings and an excellent prognosis, even without corticosteroid therapy. Magnetic resonance imaging (MRI) is the ideal modality for initial diagnosis and follow-up. Not many cases of this uncommon clinoradiological syndrome with transient elevation of CSF proteins have been reported. In the subsequent sections, we present a case report of this unusual clinoradiological entity with raised CSF protein. We also elaborate on possible differential diagnoses and the syndrome's proposed pathophysiology.

**Keywords:** encephalitis, corpus callosum, reversible lesion, splenium, cerebrospinal fluid protein, diffusion magnetic resonance imaging

## Introduction

Mild encephalitis with reversible lesion in the splenium (MERS) is a clinoradiological syndrome presenting as a solitary lesion in the central portion of the splenium of the corpus callosum (SCC) with a radiological finding of restricted diffusion and low apparent diffusion coefficient (ADC) values. Complete resolution of the lesion on follow-up imaging and full clinical recovery are the hallmarks of this syndrome, even with only supportive therapy. Encephalitis has been defined as an acute onset of brain dysfunction in association with inflammatory changes in the cerebrospinal fluid (CSF). When there is no evidence of inflammatory changes in the CSF, it is called as encephalopathy. MERS is usually associated with normal CSF findings (1). We present a case report of this unusual clinoradiological entity with raised CSF protein and will elaborate on possible differential diagnoses and the syndrome's proposed pathophysiology in the subsequent sections.

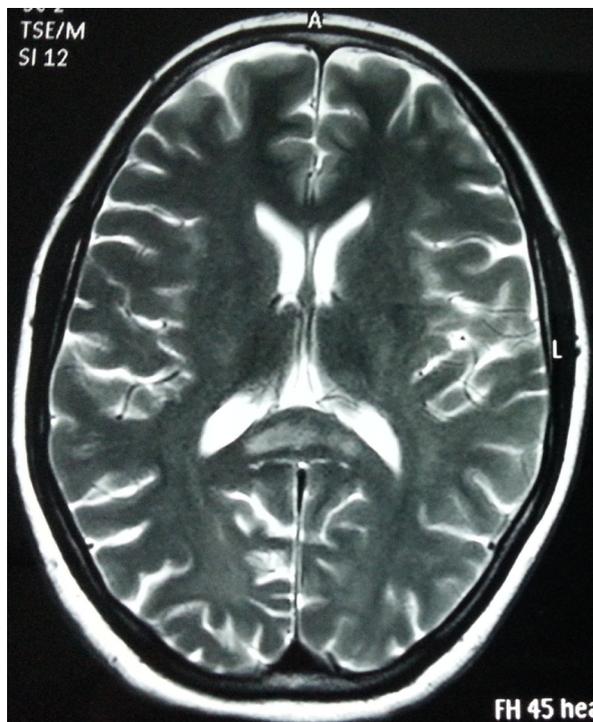
## Case Report

A 27-year-old female who was not a known case of chronic illness presented with a one-day history of fever with irrelevant speech and altered sensorium. The patient did not have a recent history suggestive of infectious disease(s). The patient was not on antiepileptics or any other chronic medications, and she had no family history of epilepsy. On examination, she was afebrile and conscious but drowsy with Glasgow coma scale as E3V4M5. Physical and neurological examinations were otherwise unremarkable with no focal neurological deficits. Routine blood investigations were normal. Contrast magnetic resonance imaging (MRI) of her brain showed a hyperintense lesion in the splenium of corpus callosum along with diffusion restriction (Boomerang sign). The lesion did not show contrast enhancement (Figures 1 and 2). CSF fluid examination showed elevated protein (85 mg/dL) with normal cells and sugar but was negative for Gram, acid-fast bacilli, and India

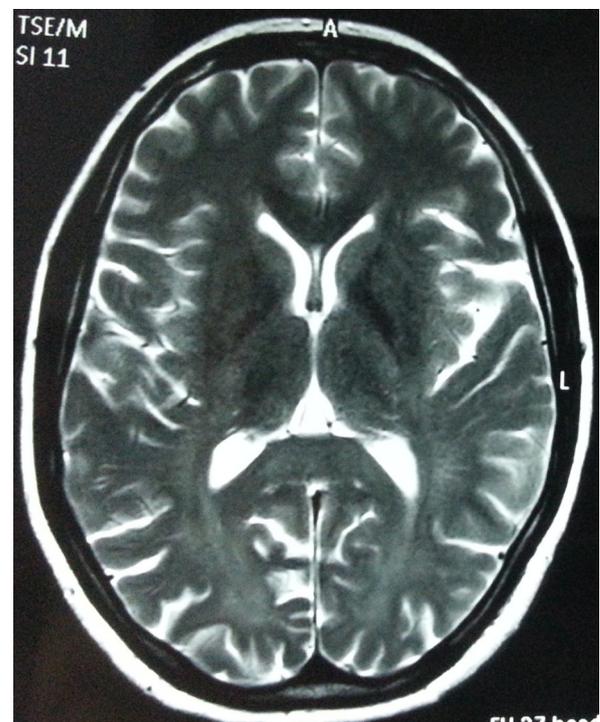
ink stains. CSF polymerase chain reaction (PCR) assays for Herpes simplex virus, *Escherichia coli*, *Neisseria meningitidis*, *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Streptococcus agalactiae* were negative. CSF IgM antibodies for Epstein-Barr virus and Japanese encephalitis virus were also negative. Stool culture was negative for enterovirus and adenovirus, and no rotavirus antigen was found by enzyme immunoassay in rectal swab. No titer of antibody-to-influenza virus was seen in the serum, and the blood culture was sterile. The patient was managed conservatively and showed significant clinical improvement over a period of 2–3 days. Repeat MRI and CSF examinations conducted five days later showed a complete recovery (a complete radiological recovery and CSF protein of 40 mg/dL) (Figure 3). Thus, diagnosis of MERS was established. The clinical and radiological courses in our patient were similar to previously reported reversible lesions isolated to SCC in MERS, except for transient elevation of CSF protein, which normalised in concordance with radiological recovery within a period of five days. Very few cases of reversible SCC lesions have been reported from India.



**Figure 2:** MRI Brain DWI showing diffusion restriction in the splenium of corpus callosum.



**Figure 1:** MRI Brain T2WI showing hyperintense lesion in the splenium of corpus callosum.



**Figure 3:** Follow up MRI Brain T2WI (done five days after the first MRI) showing resolution of lesion.

## Pathophysiology

There are various theories postulating the pathophysiology of MERS and its radiological findings of transient reduced diffusion and decreased ADC values, but the exact mechanism remains unclear. Separation of myelin layers leading to intramyelinic edema and inflammation and inflammatory infiltrate are two proposed hypotheses (1,2). As per the second hypothesis, the influx of inflammatory cells and molecules and cytotoxic edema could be the cause of reversible SCC lesion and decreased ADC values (3). However, with either intramyelinic edema or inflammation, ADC values usually return to normal with early resolution of the underlying cause (1). In our opinion, the latter theory partially defines the associated elevated CSF protein in our patient. Inflammatory etiologies are usually asymmetric and show contrast enhancement on radioimaging, which were not seen in our case. Thus, the reason for the callosal involvement in MERS remains purely speculative.

## Discussion

Various transient abnormalities of corpus callosum on MRI have been described with or without involvement of the SCC. Transient signal abnormality involving exclusively the splenium of the corpus callosum on MRI is not frequently encountered in clinical practice.

Reversible MRI lesions in the SCC have been reported earlier in epileptic patients on antiepileptic therapy. Reversible demyelination in these patients was probably related to antiepileptic drug toxicity (1). Various infectious organisms, including the influenza A, mumps, measles and varicella zoster viruses, adenovirus, rotavirus, O-157 *Escherichia coli* and *Salmonella enteritidis* have been suggested as infectious causative factors of MERS (3).

Our patient was not on antiepileptic drugs, and her medical history did not suggest recent infection. The CSF and stool investigations were negative for common pathogens. Thus, the etiology of MERS in our patient remains unknown.

Radiologically, all the described cases of SCC lesion have demonstrated T1 and T2 signal prolongation, restricted diffusion (Boomerang sign) and ADC values, non-contrast enhancing, and showed complete resolution on repeat imaging performed three days to two months following the initial abnormal study (3). Our patient had a similar radiological presentation with a hyperintense lesion in the splenium of the

corpus callosum along with diffusion restriction, did not show any contrast enhancement and repeat MRI conducted five days later showed a complete recovery.

There are various case reports on MERS by different authors, but CSF abnormality has rarely been presented. Takanashi et al. presented a case in which CSF cell count was elevated, however, none of the patients reported by these authors had elevated CSF protein (1,2). Recently, Man and Fu reported a case of MERS with raised CSF proteins in a patient with Japanese encephalitis (4). Thus elevated CSF protein, although uncommon, can be seen in a patient of MERS.

The clinical courses in the reported patients of MERS have been mild, with a complete recovery occurring within one week to one month after the onset of neurological symptoms (most commonly presents with headache, drowsiness or seizures). Clinical recovery is achieved with or without the administration of corticosteroids, and none of the patients has been reported to suffer any permanent neurological impairment/sequelae (1). Our patient also showed complete clinical and radiological recovery without any sequelae within five days and with only supportive care.

Possible differential diagnoses of splenial lesions include ischaemia, reversible posterior leukoencephalopathy syndrome, diffuse axonal injury, multiple sclerosis, Marchiafava-Bignami disease, lymphoma, extrapontine myelinolysis, and acute disseminated encephalomyelitis (ADEM) (5).

ADEM should be kept as the first differential for cases of MERS. ADEM is a monophasic post-infectious or post-vaccinal inflammatory disorder presenting with seizures, focal neurological signs, and alteration of consciousness, developing days to weeks after the onset of a presumed causative factor. In ADEM, CSF analysis usually shows mild pleocytosis, and MRI shows multiple foci of T1 and T2 signal prolongation in the subcortical white matter, typically bilateral, and asymmetrical. Callosal involvement in ADEM is nearly always asymmetrical and is rarely encountered without other white matter lesions. Depending on their acuity, the lesions in ADEM will show variable contrast enhancement. Improvement of the white matter lesions may take weeks to months, and part of the damage may be permanent. Imaging evolution of the disease also lags behind the clinical picture. Corticosteroids are accepted as useful in the treatment of ADEM, and recovery usually occurs within weeks. Absence of these MRI features, CSF pleocytosis, short disease course and complete clinicoradiological recovery within

five days differentiated our case from ADEM (3).

The absence of symptoms of hemispheric disconnection (apraxias of the left hand, pseudoneglect, alien left hand, agraphia, alexia, visual apraxias, etc.) and reversibility after the control of underlying disease, differentiates MERS from other differential diagnoses. Paramagnetic contrast enhancement, which is very rarely present with transient splenium involvement, is commonly associated with other differential diagnoses (6).

## Conclusion

In conclusion, a solitary, reversible lesion demonstrating restricted diffusion and reduced ADC values in the central SCC can be seen in association with clinically mild encephalitis/encephalopathy. Prognosis is excellent, even without corticosteroid therapy, and MRI is the ideal modality for initial diagnosis and follow-up. Although the exact pathogenesis is not yet known, recognition of this recently described clinicoradiological syndrome is important to avoid unnecessary invasive investigation and therapeutic intervention.

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Conception and design, analysis and interpretation of the data, drafting of the article, final approval of the article: BS, RH, KN, SP, AP

Critical revision of the article for the important intellectual content: BS

Provision of study materials or patient: RH

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