Received: 28 October 2023 | Revised: 12 January 2024 | Accepted: 20 January 2024

DOI: 10.1002/ccr3.8493

CASE REPORT

Clinical Case Reports Open Access WILEY

Transient blindness due to mild reversible encephalopathy in a 7-year-old boy

Shima Shekari[1] | **Farima Farsi**[2] | **Farah Ashrafzadeh**[1] | **Shima Imannezhad**[1] | **Ahmad Sohrab Niazi**[1] | **Samane Kamali**[1]

[1]Department of Pediatrics, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

[2]Student Research Committee, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

Correspondence
Farima Farsi, Student Research Committee, School of Medicine, Mashhad University of Medical Sciences, Azadi Square, Mashhad 9177899191, Iran.
Email: farima.farsi1999@yahoo.com

Key Clinical Message

Mild encephalopathy with a reversible splenial lesion (MERS) is a rare phenomenon, which shows transient lesion in corpus callosum and causes temporary encephalopathy features. A disturbance of consciousness and abnormal and delirious behavior are the most significant neurological symptoms. A seven-year-old child with a history of fever and cough was admitted to our hospital due to sudden bilateral blindness. His physical examination showed confusion, fever, and delirious behavior. No sign of meningeal irritation or focal neurological deficit was observed. The electroencephalogram showed diffuse slow waves representing mild encephalopathy. Brain MRI showed a signal alteration in the splenium of the corpus callosum, and magnetic resonance angiography (MRA) was normal. This finding was suggestive of a reversible cytotoxic lesion. Treatment with empiric antivirals was initiated, and the symptoms were completely resolved. In a few children, sudden blindness has been reported to be an initial symptom of MERS. There is currently no evidence of efficient treatment methods. However, to convince patients and their families about the good outcome of the disease, the diagnosis of MERS provides pediatricians with useful prognostic information.

KEYWORDS

bilateral blindness, corpus callosum, delirious behavior, magnetic resonance imaging, reversible encephalopathy

1 | INTRODUCTION

Tada et al. first defined the term mild encephalopathy with a reversible splenial lesion (MERS) in 2004 as a rare clinical-radiological syndrome[1,2] that occurs more frequently in East Asian populations.[3] It is usually found in children under the age of 16 and only occasionally in adults.[4] Infections are considered to be the main trigger of the disease; the main pathogens associated with MERS are viruses, such as influenza virus (A and B).[3] Noninfectious conditions associated with reversible splenial lesions include seizures, antiepileptic drug withdrawal, metabolic disorders, and renal or hepatic dysfunction.[5] A common pathophysiological mechanism explaining selective splenial involvement has not yet been identified. However, there are some hypotheses

This study was conducted in Ghaem Teaching Hospital, Mashhad, Iran.

regarding MERS pathogenesis such as intramyelinic edema, hyponatremia, axonal damage, and oxidative stress.[6] MERS is typically characterized by a prodromal illness consisting of fever, cough, and digestive tract symptoms; encephalopathy usually manifests 1–7 days later.[7,8] The neurological features of MERS include disturbance of consciousness, abnormal speech, delirious behavior, headache, agitation, disorientation, seizures, facial nerve paralysis, and nuchal rigidity; however, visual disturbances are rare symptoms of this syndrome. The neurological symptom most commonly described in the literature is delirious behavior with altered consciousness, which can manifest as akinetic mutism.[5,9] On MRI, MERS is almost always associated with a transient splenial lesion that is slightly hyperintense on T2-weighted images and isointense to slightly hypointense on T1-weighted images, showing reduced diffusion without enhancement of contrast during the acute period of the disease. Based on MRI findings, MERS is classified into two groups; In MERS type 1, the lesions are limited to the splenium (ovoid or band-shaped), as observed in our case report, whereas in MERS type 2 the lesions are not limited to the splenium.[10,11] The clinical and radiological prognosis is usually favorable, with clinical improvement occurring within 1 to 2 days and radiologic improvement occurring within 10 days to 4 months. Normally in children diagnosed with MERS, raised serum inflammatory markers (white cell count and C-reactive protein) in the absence of CSF inflammation can be found, supporting the hypothesis that this syndrome is an infection-associated encephalopathy rather than an encephalitis.[7] There is currently no reliable evidence on the therapeutic approaches. For patients with infectious encephalopathy, regardless of pathogen or clinical-radiological syndromes, methylprednisolone pulse therapy and intravenous immune globulin (IVIG) are recommended.[8] Here we describe a case of MERS in a seven-year-old Iranian male patient, presenting with a cytotoxic lesion in the SCC (Splenium corpus Callosum) detected by MRI and the unusual clinical presentation of acute bilateral blindness.

2 | CASE HISTORY AND EXAMINATION

A previously healthy seven-year-old child was admitted to our hospital due to sudden-onset bilateral blindness. One day before admission, he suddenly developed a fever of 39°C, cough, and loss of appetite. He was examined by his pediatrician, and azithromycin and intravenous fluid therapy was prescribed due to suspected streptococcal pharyngitis. Despite being treated with azithromycin and oral antipyretics, the patient still had a fever of 38°C. On the day of admission, he experienced all at once constant bilateral blindness and delirium. The symptoms were continuous, and therefore, he was admitted to the hospital emergency department. His family history was unremarkable. On physical examination, the patient was agitated associated with an encephalopathy feature and his general condition was not good. During the medical assessment, the child was collaborative, although his responsiveness was to some degree impaired. Neither focal neurological deficits nor meningeal irritation signs including nuchal rigidity, Kernig signs and Brudzinsky signs were observed.

3 | METHODS

The chemistry panel and urine analysis showed no abnormalities except for a highly elevated level of CPK (Creatine phosphokinase) (569 U/L), a slightly elevated level of AST (Aspartate aminotransferase) (47 U/L), and mild hyponatremia (134 mEq/L). The presence of blindness prompted an ophthalmologic evaluation, including a fundus oculi examination that was negative.

On the following day, the electroencephalogram (EEG) showed diffuse slowing waves approving of mild encephalopathy. A mild increase in deep tendon reflex (DTR) was reported by the child's neurologist, but no significant focal neurological deficit was found.

The child was then admitted to perform a brain MRI and a lumbar puncture (LP) to exclude acute cerebral vascular accident (CVA) and the presence of viral encephalitis, cerebral abscesses, or other cerebral inflammatory lesions, such as acute disseminated encephalomyelitis (ADEM).

Four hours after admission, an MRI of the brain was performed. Diffusion-weighted imaging (DWI) revealed restriction in the corpus callosum, and this was correlated with the apparent diffusion coefficient (ADC MAP), indicating an abnormal diffusion restriction and a reversible cytotoxic lesion (Figure 1). The results of additional views of brain MRI were negligible. An arachnoid cyst in the posterior fossa and abnormal signal intensity in the maxillary and ethmoid sinuses were found as collateral findings on MRI.

The following course of treatment against suspected meningitis was started while awaiting the results of the polymerase chain reaction (PCR) search for neurotropic viruses, bacteria, and fungi in the cerebral spinal fluid (CSF) and peripheral blood: intravenous ceftriaxone (100 mg/kg once a day), vancomycin (15 mg/kg every 6 h), acyclovir (10 mg/kg every 8 h), and dexamethasone (0.2 mg/kg every 8 h). Antibacterial therapy was suspended because the blood and CSF (Cerebrospinal fluid) culture had been

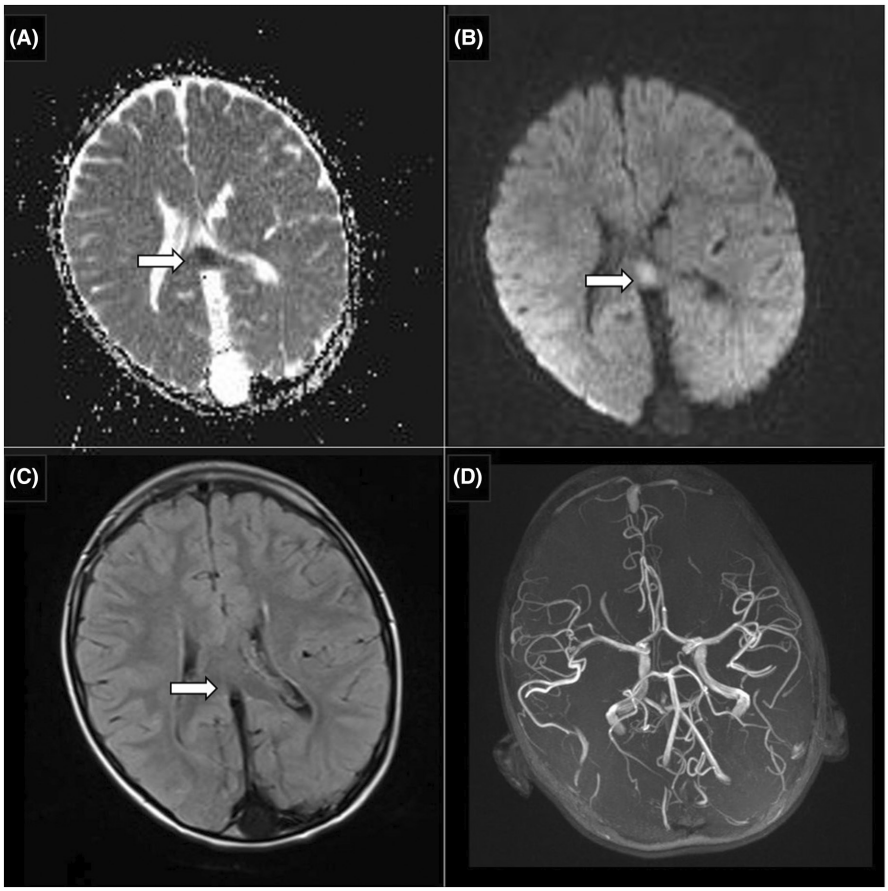

FIGURE 1 Initial cranial MRI of the patient. The lesion in the midspelenium of the corpus callosum had decreased ADC value (A), showed restriction on DWI (B), and had high signal intensity on Flair (C), MRA was normal (D). Date of MRI: March 11, 2023.

negative. Despite a positive nasal swab test for metapneumovirus virus, the patient's management remained unchanged. A summary of the patient's clinical data is presented in Table 1.

4 | OUTCOME AND FOLLOW-UP

A short-term follow-up MRI was performed after 4 days to confirm the transient nature of MERS. The results showed a complete normalization of the signal alteration in the SCC (Figure 2). The EEG was also repeated, and the pattern completely normalized. The child had no neurological impairments and was in good overall condition. He was thus discharged after 6 days of admission and treatment with acyclovir and dexamethasone.

5 | DISCUSSION

In our case, the unusual main neurological symptom was acute bilateral blindness, which appeared 1 day after the beginning of symptoms suggestive of viral infection (low-grade fever, nonproductive cough).

Concerning laboratory findings, our patient had a highly elevated level of CPK, a slightly elevated level of AST, and mild hyponatremia at hospital admission. Lately, numerous patients with MERS associated with hyponatremia have been stated.[12,13] Takanashi et al. estimated sodium levels in a series of cases with MERS. The sodium levels of patients with MERS were significantly lower than groups with other types of encephalopathy.[12] However, the mild hyponatremia of our patient only provides a limited contribution to the clinical presentation. The increased levels of CPK and AST can be explained because of stress to the brain tissue. In contrast to the study of Ka et al.,[7] the serum inflammatory markers were within the normal range in our patient; however, the CSF inflammation was similarly not detected.

The patient's clinical picture makes it difficult to interpret the slight metapneumovirus positivity found by PCR in the oropharynx and nasopharynx. The lack of emphasis placed on metapneumovirus in the etiology can be attributed to multiple factors. Even in patients without associated symptoms, a slight positive metapneumovirus PCR test can occasionally be detected. In the study of Peng D et al., it was also concluded that metapneumovirus load was not correlated with infection severity and its viral shedding occurs between 6 and 11 days after the onset of the symptoms.[14] The seven-year-old child presented with nonspecific symptoms, which could be attributed to a variety of viruses, and metapneumovirus disease usually

TABLE 1 Clinical information, paraclinical data, treatment, and follow-up of the patient in summary.

Medical history of the patient
• Chief complaint: Sudden-onset bilateral blindness • Recent respiratory illness • No response to the previous medications (antibiotic treatment and antipyretics)
Physical examination
• Agitation with encephalopathy features, not good general condition, and slightly impaired responsiveness • Fever of 38°C • Focal neurological signs and meningeal irritation signs including nuchal rigidity, Kernig signs and Brudzinsky signs were negative • Mild increase in DTR[a] • Fundus oculi examination was normal
Differential diagnosis
• Cerebral vascular lesions including CVA[b] • Cerebral inflammatory lesions such as viral encephalitis, meningitis, cerebral abscesses, ADEM[c], etc. • Encephalopathies including MERS[d]
Laboratory data
• Chemistry panel and urine analysis were normal except for a highly elevated level of CPK[e] (569 U/L), slightly elevated level of AST[f] (47 U/L), and mild hyponatremia (134 mEq/L) • LP[g] and blood culture: PCR[h] search for neurotropic viruses, bacteria, and fungi in both CSF[i] and blood was negative
Imaging
• EEG[j] findings: diffuse slowing waves in favor of mild encephalopathy • Brain MRI[k]: restriction in the corpus callosum was seen in diffusion-weighted imaging (DWI), with correlation in ADC map[l], suggesting an abnormal diffusion restriction and a reversible cytotoxic lesion
Treatment
• Intravenous ceftriaxone (100 mg/kg once a day) • Vancomycin (15 mg/kg every 6 h) • Acyclovir (10 mg/kg every 8 h) • Dexamethasone (0.2 mg/kg every 8 h)
Follow-up
• General condition: good without neurological deficits • Brain MRI: complete normalization of the signal alteration in the SCC • EEG: complete normalization of the pattern

[a]Deep tendon reflex.
[b]Cerebral vascular accident.
[c]Acute disseminated encephalomyelitis.
[d]Mild encephalopathy with reversible splenial lesion.
[e]Creatine phosphokinase.
[f]Aspartate aminotransferase.
[g]Lumbar puncture.
[h]Polymerase chain reaction.
[i]Cerebrospinal fluid.
[j]Electroencephalogram.
[k]Magnetic resonance imaging.
[l]Apparent diffusion coefficient.

occurs in winter and autumn. Furthermore, in this case, the PCR search for metapneumovirus in the CSF was not done, and therefore, its involvement was not confirmed.

EEG abnormality was diffuse slowing in favor of mild encephalopathy. In the previous studies, the EEG of the patients was either normal or showed slow waves in temporo-occiptal regions.[15–17] MRI imaging showed lesions limited to the splenium, which was restricted in DWI with correlation in ADC map (MERS type 1).

We considered ADEM to be the most important differential diagnosis. Lesions in MERS do not show contrast enhancement and usually disappear quickly,[7] whereas lesions in ADEM are often asymmetric and contrast-enhanced, extending into the white matter and spinal cord, and persist for weeks to up to several months.[18] The brain MRI of our patient showed also no finding in favor of CVA, encephalitis, cerebral abscesses, or other cerebral inflammatory lesions. Another differential diagnosis that should be always considered in patients presenting with neurological symptoms, a history of recent respiratory illness, and refractory fever is meningitis. However, in contrast to meningitis, the symptoms of our case resolved quickly independent from the antibiotic treatment. Nevertheless, we did perform LP to exclude this diagnosis and it was negative for meningitis.

Intravenous treatment for suspected meningitis and herpes virus was administered to our patient until the results of the PCR and culture tests for these agents in CSF and blood were negative. Furthermore, the patient underwent 5 days of corticosteroid therapy with low-dose dexamethasone. In the study of Masiello et al., isotonic fluids, empirical antibiotic treatment with ceftriaxone, intravenous acyclovir, and systemic corticosteroids were also used for patients with MERS. However, according to this study, it was concluded that MERS has an overall good prognosis regardless of treatment approach.[16] The following medications have been also used for the treatment of patients with suspected MERS: IVIG, acetaminophen, and diazepam.[1,11,19] To date, there is no evidence of an effective treatment for patients with MERS; however, the prognosis is regardless of treatment good.

In children, MERS shows a wide spectrum of clinical presentations; however, visual disturbances are rare symptoms of this syndrome. There are possible variations in the approach to treatment for MERS. It is still not known whether a specific treatment can change the clinical course of this disease. Multicenter studies have to be developed to clarify its cause and set guidelines for treatment, taking into account the limited number of MERS cases and various severity levels. Most of the MERS cases show a favorable outcome regardless of treatment. The early recognition of this condition in children with encephalopathy may limit unnecessary and potentially

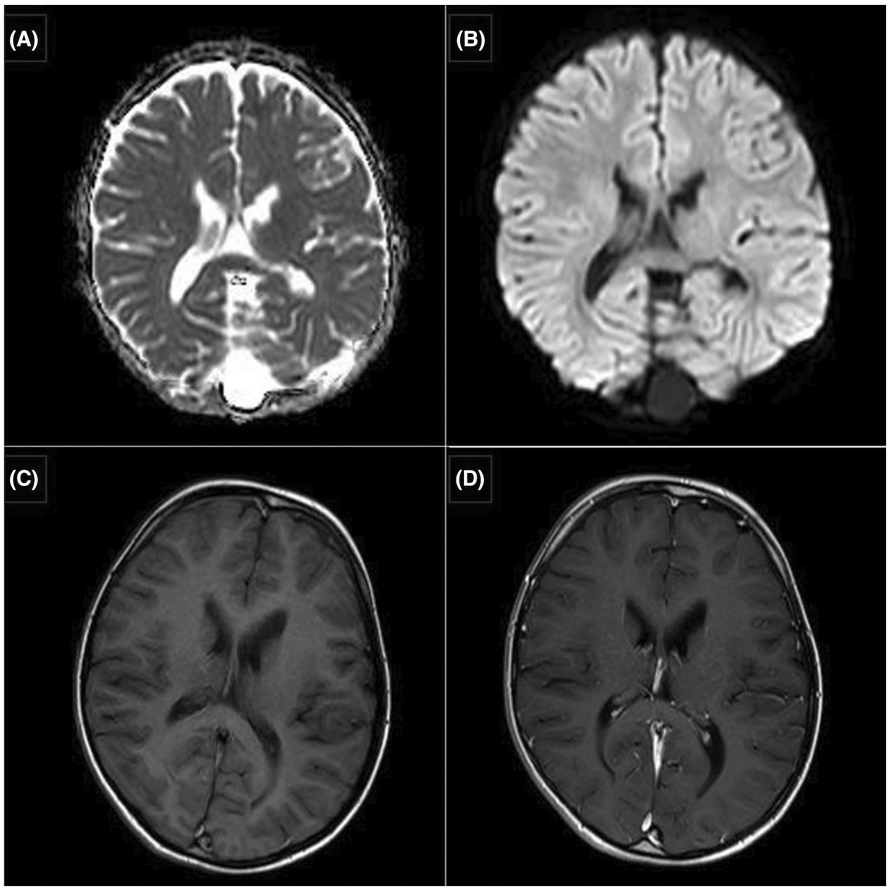

FIGURE 2 Follow-up cranial MRI. The follow-up cranial MRI showed no lesion on any sequence. ADC (A), DWI (B), T1-weighted imaging without contrast (C), and T1-weighted imaging with contrast (D). Date of MRI: March 15, 2023.

toxic treatments. Moreover, MERS diagnosis allows pediatricians to reassure patients' families about the good outcome of this disease.

AUTHOR CONTRIBUTIONS

Shima Shekari: Conceptualization; writing – original draft. **Farima Farsi:** Conceptualization; writing – original draft. **Farah Ashrafzadeh:** Supervision; writing – review and editing. **Shima Imannezhad:** Visualization; writing – review and editing. **Ahmad Sohrab Niazi:** Data curation; writing – review and editing. **Samane Kamali:** Data curation.

ACKNOWLEDGEMENTS

The authors would like to express their gratitude to Mashhad University of Medical Sciences.

FUNDING INFORMATION

The authors of this manuscript received no financial support for the research and authorship of this article.

CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

The data, supporting this study, are available upon reasonable request from the corresponding author.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Farima Farsi https://orcid.org/0000-0003-3715-4858

REFERENCES

1. Tada H, Takanashi J, Barkovich A, et al. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. *Neurology*. 2004;63:1854-1858.
2. Garcia-Monco JC, Cortina IE, Ferreira E, et al. Reversible splenial lesion syndrome (RESLES): what's in a name? *J Neuroimaging*. 2011;21:e1-e14.
3. Fang Q, Chen L, Chen Q, Lin Z, Yang F. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion of corpus callosum in Chinese children. *Brain and Development*. 2017;39(4):321-326.
4. Hoshino A, Saitoh M, Oka A, et al. Epidemiology of acute encephalopathy in Japan, with emphasis on the association of viruses and syndromes. *Brain and Development*. 2012;34(5):337-343.
5. Vanderschueren G, Schotsmans K, Maréchal E, Crols R. Mild encephalitis with reversible splenial (MERS) lesion syndrome due to influenza B virus. *Pract Neurol*. 2018;18(5):391-392.
6. Chen W-X, Liu H-S, Yang S-D, et al. Reversible splenial lesion syndrome in children: retrospective study and summary of case series. *Brain and Development*. 2016;38(10):915-927.

7. Ka A, Britton P, Troedson C, et al. Mild encephalopathy with reversible splenial lesion: an important differential of encephalitis. *Eur J Paediatr Neurol*. 2015;19(3):377-382.
8. Pan JJ, Zhao Y-Y, Lu C, Hu Y-H, Yang Y. Mild encephalitis/encephalopathy with a reversible splenial lesion: five cases and a literature review. *Neurol Sci*. 2015;36(11):2043-2051.
9. Ka A, Britton P, Troedson C, et al. Mild encephalitis/encephalopathy with a reversible splenial lesion in children. *Diagn Interv Radiol*. 2018;24(2):108-112.
10. Jea A, Vachhrajani S, Widjaja E, et al. Corpus callosotomy in children and the disconnection syndromes: a review. *Childs Nerv Syst*. 2008;24(6):685-692.
11. Takanashi J, Barkovich AJ, Shiihara T, et al. Widening spectrum of a reversible splenial lesion with transiently reduced diffusion. *AJNR Am J Neuroradiol*. 2006;27(4):836-838.
12. Takanashi JI, Tada H, Maeda M, Suzuki M, Terada H, Barkovich AJ. Encephalopathy with a reversible splenial lesion is associated with hyponatremia. *Brain and Development*. 2009;31(3):217-220.
13. Tokano M, Tarumoto N, Osawa I, et al. A case of COVID-related MERS (clinically mild encephalitis/encephalopathy with a reversible splenial lesion) with a typical imaging course and hyponatremia in adults—A case report and literature review. *COVID*. 2023;3(2):183-191. doi:10.3390/covid3020013
14. Peng D, Zhao X, Liu E, et al. Analysis of viral load in children infected with human metapneumovirus. *Iran J Pediatr*. 2010;20(4):393-400.
15. Grosset L, Hosseini H, Bapst B, et al. Mild encephalopathy with reversible splenial lesion: description of nine cases and review of the literature. *Seizure*. 2021;(88):83-86.
16. Masiello E, Gatto A, Lazzareschi I, Rigante D, Mariotti P, Valentini P. Mild encephalopathy with reversible splenial lesion associated with echovirus 6 infection: a case report and review of the literature. *Turk J Pediatr*. 2020;62(2):293.
17. Tuscano A, Zoppo M, Canavese C, Cogoni M, Scolfaro C. Transient blindness associated with mild encephalitis/encephalopathy with a reversible splenial lesion (MERS): a case report and review of literature. *Ital J Pediatr*. 2020;46:1-7.
18. Barkovich AJ. *Pediatric neuroimaging*. Lippincott Williams & Wilkins; 2005.
19. Kobata R, Tsukahara H, Nakai A, et al. Transient MR signal changes in the splenium of the corpus callosum in rotavirus encephalopathy: value of diffusion-weighted imaging. *J Comput Assist Tomogr*. 2002;26(5):825-828.

How to cite this article: Shekari S, Farsi F, Ashrafzadeh F, Imannezhad S, Niazi AS, Kamali S. Transient blindness due to mild reversible encephalopathy in a 7-year-old boy. *Clin Case Rep*. 2024;12:e8493. doi:10.1002/ccr3.8493