CASE REPORT

Successful management of severe paediatric influenza-associated encephalopathy with shock and a reversible splenial lesion using combined immunomodulation and early haemopurification: A case report

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Abstract

A rare case of influenza-associated encephalopathy with shock and a reversible splenial lesion is reported. A two-and-a-half-year-old Chinese girl presented with acute onset of fever, two brief seizures, and rapidly deteriorating consciousness (GCS E1V2M2) within 6 hours. Four hours after post-admission, high-dose methylprednisolone (30 mg/kg) and intravenous immunoglobulin (2 g/kg) were administered, along with three consecutive days of continuous blood purification (CBP). Clinical improvement followed, allowing extubation after 72 hours. MRI on day 4 confirmed MERS with a characteristic isolated splenial lesion. Cytokine levels normalized by day 12 (IL-6: 3.0 pg/mL, IL-10: 2.2 pg/mL), coinciding with complete radiological resolution of the lesion. The patient was discharged on day 14. At 1-month follow-up, she exhibited full neurological recovery with age-appropriate function.

Keywords: encephalopathy with a reversible splenial lesion, influenza, blood purification treatments, immunomodulatory, child.

DOI: https://doi.org/10.47391/JPMA.31854

Introduction

Influenza infection is prevalent and, although typically mild and self-limiting, recurrent epidemics impose a significant economic burden.[1] Mild encephalopathy with a reversible splenial lesion (MERS) associated with influenza is a rare condition predominantly reported in East Asia. Management of MERS is largely empirical and lacks robust evidence-based guidelines.[2] Herein, we report a young Chinese child with severe influenza-associated MERS who received prompt immunomodulatory and blood purification following the onset of impaired consciousness and subsequently achieved complete neurological recovery.

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Submission completed: 28-07-2025 **1st Revision received:** 09-12-2025

Acceptance: 06-06-2026 **Last Revision received:** 05-06-2026

Case Presentation

On 14 January 2025, a previously healthy two-and-a-half-year-old girl was urgently transferred from the emergency department of the northern campus of Women and Children's Hospital of Ningbo University to the paediatric intensive care unit (PICU) of the main campus. The transfer was prompted by a 6-hour history of persistent fever and altered consciousness. Prior to admission, she had been diagnosed with influenza - A by a local physician based on a rapid antigen-detection test using a nasal swab. At 08:30 AM on the day of admission, she experienced two distinct seizures at home, each lasting approximately 1-2 minutes, followed by a deterioration in consciousness. On examination upon arrival, her vital signs were as follows: body temperature of 41.5°C, respiratory rate of 30/min, a heart rate of 205/min, percutaneous SaO_2 of 92%, a blood pressure of 66/39 mmHg, capillary refill time of 4s and the Glasgow Coma Scale score of E1V2M2. Bilateral pupil size was 1.5 mm with preserved light, ocular, and corneal reflexes. She was intubated for airway protection.

On admission, laboratory investigations revealed the following values: leukocyte count 9.0×10^9/L, C-reactive protein 4.5 mg/L (normal < 8), procalcitonin 52.8 ng/mL (normal < 0.1), B-natriuretic peptide 290.5 pg/mL (normal < 100), sodium 138 mmol/L, potassium 4.0 mmol/L, chloride 102 mmol/L, AST 165 U/L (normal < 45), ALT 51 U/L (normal < 30), ammonia 11 µg/dL (normal < 30). Blood cytokine levels were markedly elevated: IL-6 4483.5 pg/mL (normal < 16.6), IL-10 2693.5 pg/mL (normal < 4.9), and TNF-α 10.2 pg/mL (normal < 5.2). Cerebrospinal fluid (CSF) IL-6 was 626.1 pg/mL (normal < 16.6) and IL-10 was 13.3 pg/mL (normal < 4.9), but CSF analysis and mNGS revealed no abnormalities. Serological tests for hepatitis A, B, and C antibodies, Epstein-Barr virus antibodies, cytomegalovirus antibodies, and ceruloplasmin levels were within normal limits. Additionally, electroencephalogram (EEG) showed diffuse slow waves, while computed tomography scans showed no evidence of masses or cerebral haemorrhage. Based on these clinical and laboratory findings, a diagnosis of influenza-associated encephalopathy was established.

Following admission to the PICU, the patient's condition deteriorated rapidly despite aggressive fluid resuscitation and continuous infusions of norepinephrine at 0.3μg/kg/min, epinephrine at 0.3μg/kg/min, and pituitrin at 0.0005U/kg/min, progressing uncompensated shock and worsening metabolic acidosis. Four hours post-admission, intravenous methylprednisolone (30mg/kg) and intravenous immunoglobulin (2g/kg) were administered. Additionally, the patient underwent three consecutive days of continuous blood purification (CBP) (Figure 2). CBP was performed using the continuous haemodiafiltration (CHDF) mode, with the following parameters: blood flow rate 3-5 mL/(kg·min), fluid exchange volume 35 mL/(kg·h), dialysate volume 35 mL/(kg·h), and ultrafiltration volume 0-5 mL/(kg·h).

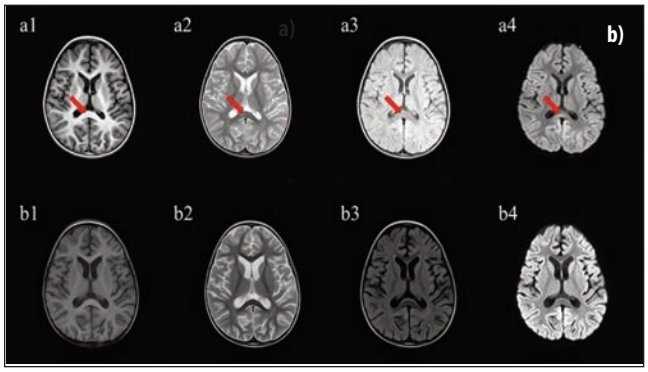

Figure-1: MRI results. a1-a4: T1-weighted image showed hypointensity; T2-weighted, fluid-attenuated inversion recovery and DWI imaging demonstrated hyperintensity in the splenium of the corpus callosum on day 4; b1-b4: T1-weighted image, T2-weighted image, fluid-attenuated inversion recovery and diffusion-weighted image demonstrated complete resolution demonstrated complete regression on day 12; Arrows indicate lesion on the splenium of the corpus callosum.

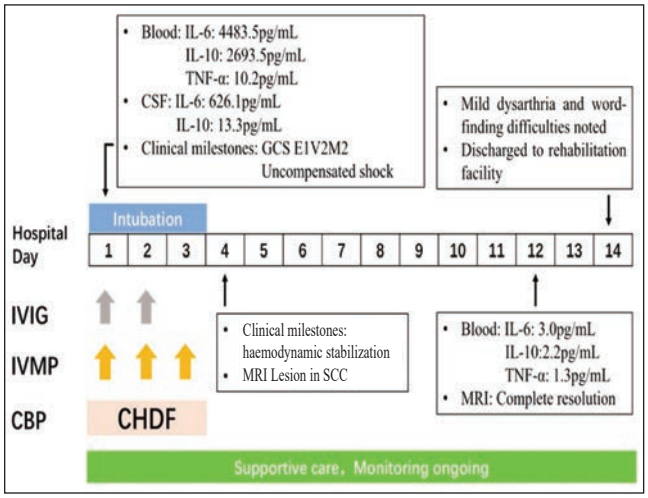

Figure-2: The interventions timeline and clinical response for the case. Abbreviations: IVIG, intravenous immunoglobulin; IVMP, intravenous methylprednisolone; CBP, continuous blood purification; CHDF, continuous haemodiafiltration; SCC, the splenium of the corpus callosum.

Her clinical status gradually improved thereafter. She was successfully extubated 72 hours after admission. A magnetic resonance imaging (MRI) performed on the fourth hospital day revealed a distinct lesion in the splenium of the corpus callosum (SCC), showing slight hyperintensity on T2-weighted images and hypointensity on T1-weighted images. Notably, diffusion-weighted images demonstrated prominent high-intensity signals in the SCC (Figure 1 a1-a4).

On day 12 of admission, cytokine levels had normalised: IL-6 levels of 3.0 pg/mL, IL-10 levels of 2.2 pg/mL, and TNF-α levels of 1.3 pg/mL. Follow-up MRI demonstrated complete resolution of the previous SCC lesion (Figure 1 b1-b4). Despite overall improvement, the patient experienced mild expressive speech impairment characterized by dysarthria and word-finding difficulties. She was discharged on the 14th hospital day and subsequently transferred to a rehabilitation centre for further management. At the 1-month follow-up, she was clinically stable without any neurological sequelae and had regained age-appropriate motor and language skills.

Discussion

During seasonal influenza epidemics, paediatric infection rates may reach as high as 50% of the childhood population. In recent decades, the incidence among Chinese children and adolescents has increased tenfold.[3] Influenza-associated encephalopathy is a major contributor to acute encephalopathy syndrome in children, primarily affecting young individuals and resulting in high rates of both mortality and neurological morbidity. MERS was the second most frequent syndrome.[4] Typically, MERS exhibits a benign clinical course, with full recovery occurring within approximately one week.[5] In contrast, we present a severe, life-threatening case of influenza-associated MERS complicated by rapid-onset shock, mental dysfunction, and a marked cytokine storm. Fortunately, following initial immunological support, blood purification therapy, and subsequent rehabilitation interventions, the patient achieved complete neurological recovery without sequelae. This case necessitated an aggressive, multimodal approach aimed at simultaneously stabilizing haemodynamics and mitigating cerebral inflammation.

MERS is classified as an infection-associated encephalopathy rather than encephalitis, as it results from a dysregulated host immune response instead of direct viral invasion.[6] Similar to our patient, there was no direct evidence of influenza virus in the CSF. The mechanism underlying this reversible brain lesion, particularly the selective splenial lesions in SCC, remains poorly understood. Shi BC et al.[7] reported that most MERS patients

exhibited mild hyponatraemia. Hypotonic hyponatraemia may lead to water influx into the brain, causing cerebral oedema. However, our patient had a normal serum sodium level and markedly elevated levels of cytokines (IL-6 and IL-10) in both blood and CSF, which shifted the focus to the inflammatory cascade as the predominant mechanism. The significantly elevated cytokine levels upon admission indicate a severe cytokine storm, which is strongly correlated with the clinical severity of influenza-related encephalopathy.[8] This storm likely contributed to increased vascular permeability, driving both encephalopathic oedema and distributive shock. This correlation may explain the rapid progression of symptoms in our patient. In addition, we observed that once the encephalopathic symptoms subsided, cerebellar symptoms, such as slow speech and dysarthria, became evident, despite no abnormality on later MRI. This observation contrasts with the findings of Fluss J et al.[9] It is plausible that an underlying immunological abnormality may contribute to this progression.

The management of MERS is challenging due to the broad differential diagnosis of encephalopathy and the frequent need for intensive supportive care.[2] This challenge is exacerbated by the occurrence of hypotension and shock in approximately 55% of critically ill influenza patients, which often serves as an initial sign of impaired perfusion.[10] Despite advancements in treatment, the mortality rate remains approximately 30%.[11] In this high-risk case, we implemented a therapeutic strategy based on established principles of critical care management. Joannes-Boyau O et al. demonstrated that CBP improves haemodynamic stability in refractory septic shock, thereby creating a therapeutic window for additional interventions.[12] Okajima K et al.[13] reported that in hyperinflammatory conditions like acute necrotizing encephalopathy, early and proactive immunomodulatory interventions combined with CBP were linked to improved outcomes.[13] In paediatric critical care, CBP has been employed to address haemodynamic instability associated with inflammatory storms.[14,15] thereby justifying its adjunctive use in our case. Accordingly, the rapid clinical stabilization observed in our patient may be attributed to the synergistic effects of the combined therapeutic approach. Early immunomodulation with IVMP and IVIG aimed to suppress the systemic inflammatory cascade. Simultaneously initiated CBP played a dual role: it provided crucial haemodynamic and metabolic support during shock and facilitated the removal of circulating inflammatory mediators, potentially preventing further endothelial injury and brain oedema. This integrated approach which combines targetted immunomodulation with extracorporeal supportive therapy may explain the rapid normalization of cytokines and the subsequent neurological recovery.

This integrated strategy of immunomodulation with CBP may explain the rapid cytokine normalization and subsequent neurological recovery. However, these favourable outcomes should be interpreted with caution due to significant limitations in the existing evidence supporting adjunctive CBP in this context. First, the therapeutic role of CBP in paediatric influenza-associated MERS remains unestablished, as robust clinical data are lacking. Second, extrapolation of evidence from adult septic shock to paediatric MERS is limited and may not be directly applicable. This concern is further emphasized by the absence of clear recommendations for cytokine removal via blood purification in current paediatric guidelines.[16] Third, as an invasive procedure requiring vascular access, CBP carries inherent risks, including bleeding, electrolyte disturbances, and circuit thrombosis. Therefore, this case should be considered hypothesis-generating, illustrating the exploratory use of CBP within a multimodal rescue strategy for a critically ill paediatric patient, rather than providing definitive evidence of efficacy.

Despite these limitations, our case supports the exploratory application of this combined strategy in severe influenza-associated MERS with shock, indicating it may serve as a viable rescue approach for this high-risk presentation. Nonetheless, several practical challenges persist. Early diagnosis of MERS is challenging, as initial imaging may appear normal, as observed in our case. Given the rapid progression of brain damage in MERS within hours, prompt and aggressive immunomodulatory therapy should be initiated upon strong clinical suspicion. Furthermore, only a limited number of centres have the capacity to promptly initiate continuous blood purification (CBP) in paediatric patients. Paediatricians must swiftly recognize the characteristic clinical features of MERS and commence aggressive neurocritical care and immunomodulatory therapy upon strong suspicion. Alternatively, patients should be securely transferred to a facility equipped to provide the necessary treatment.

Conclusion

This case report describes a life-threatening presentation of influenza-associated mild encephalitis/encephalopathy with a reversible splenial lesion (MERS), characterized by shock and a cytokine storm, thereby expanding the recognized clinical spectrum of this condition. In response to this critical presentation, the prompt initiation of combined immunomodulation (steroids + IVIG) alongside adjunctive CBP resulted in rapid clinical stabilization. Although short-term recovery was excellent at one month,

the duration of follow-up remains limited, necessitating longer-term surveillance to fully evaluate neurological permanence. Therefore, this therapeutic approach may warrant cautious consideration in similar critical scenarios; however, its generalizability requires validation through large-scale, multicentre prospective studies.

Disclaimer: None.

Conflict of Interest: None.

Funding disclosure: This work was supported by Ningbo Medical and Health Brand Discipline (PPXK2024-06), Medical and Health Technology Plan Projects of Zhejiang (2024KY1568 and 2025KY273), Zhejiang Provincial Health and Wellness Industry Science and Technology Plan (2025HY1022 and 2025HY1023), Ningbo Health Technology Plan Project (2024Y15), Zhejiang Province Traditional Chinese medicine science and technology project (2025ZL122), and Zhejiang Provincial Traditional Chinese Medicine Science and Technology Collaborative Development Project (GZY-KJS-ZJ-2026-094).

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Author Contribution:
JW: Concept, design, data acquisition, analysis, interpretation and drafting.
PR: Revision it critically for important intellectual content.
HC: Final approval and agreement to be accountable for all aspects of the work.