

An unusual presentation of infective endocarditis: Transient encephalopathy with reversible lesions in corpus callosum and white matter

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Abstract

Clinical mild encephalitis/encephalopathy with a reversible splenic lesion (MERS) is a clinic-radiological syndrome, which has been reported to be associated with many conditions and the most common pathogens are virus. However, bacteria are rare pathogens for MERS. We report a 20-year-old man diagnosed with definite infective endocarditis, who presented with transient encephalopathy with reversible lesions in the entire corpus callosum and bilateral white matter on magnetic resonance imaging (MRI). The blood culture indicated a *Staphylococcus aureus* infection. His neurological manifestation improved and imaging abnormalities faded after receiving a combination of intravenous immunoglobulin, methylprednisolone, and antibiotics. Clinicians should be aware of transient encephalopathy with reversible callosal lesions as a potential unusual presentation of infective endocarditis.

Keywords: Encephalopathy, reversible lesion, corpus callosum, MERS, infective endocarditis, *Staphylococcus aureus*

INTRODUCTION

Mild encephalitis/encephalopathy with a reversible splenic lesion (MERS) is a clinic-radiological syndrome, which is characterized by a mild clinical course with good prognosis and a reversible lesion in the splenium of the corpus callosum on magnetic resonance imaging (MRI).¹ Actually, lesions extending to other areas of corpus callosum or bilateral white matter have also been reported.^{2,3} Most cases are of infectious etiology, although other causes such as metabolic abnormalities, vaccination and intoxication can result in MERS. Various infections including influenza virus⁴, hantavirus⁵, hepatitis A virus⁶, Dengue fever⁷, Salmonella enteritis⁸ and Legionella pneumonia⁹ have been reported to be associated with MERS. We report a case of a 20-year-old man who had transient encephalopathy with reversible lesions in the entire corpus callosum and bilateral white matter associated with *Staphylococcus aureus* endocarditis.

CASE REPORT

A 20-year-old Chinese man was admitted to our hospital, after being found unresponsive

in bed early in the morning. The night before admission, he had developed mild diarrhea and lightheadedness. Physical examination showed a body temperature of 40.7, blood pressure of 169/66mmHg, and pulse rate of 149beats/min. Neurological examination showed loss of consciousness with absence of nuchal rigidity or Babinski signs. His past medical history was unremarkable.

His complete blood count demonstrated leukocytes at $9.26 \times 10^9/L$ with 90.5% neutrophils. Coagulation function tests showed mildly elevated activated partial thromboplastin time (43.1s, normal range: 20-40s) and prothrombin time (15.6s, normal range: 9-13s) with an international normalized ratio (INR) of 1.32. Blood glucose was 6.8mmol/L. Sodium was mildly decreased (133mmol/L, normal range: 135-145mmol/L), and potassium was mildly decreased (3.3mmol/L, normal range: 3.5-5.2mmol/L). Creatinine (60umol/L) and blood urea nitrogen (2.9mmol/L) were normal. Liver function tests demonstrated elevated levels of alanine transaminase (125U/L, normal range: 5-40U/L), aspartate transaminase (130U/L, normal range: 8-40U/L), alkaline phosphatase (140U/L, normal range: 35-129U/L), gamma-glutamyl transferase (98U/L, normal

range: 7-50U/L), total bilirubin (55umol/L, normal range: 3-22umol/L), and direct bilirubin (11umol/L, normal range: 0-6 umol/L). Blood ammonia (31umol/L) was normal. Serological tests revealed no acute infections of hepatitis A virus, hepatitis B virus, hepatitis C virus, rubella virus, cytomegalovirus, toxoplasma, herpes simplex virus-1 and -2, EBV, legionella, mycoplasma pneumoniae, Q fever, chlamydia pneumoniae, adenovirus, influenza A virus, influenza B virus, parainfluenza virus, respiratory syncytial virus, syphilis, or human immunodeficiency virus.

Lumbar puncture was performed on the day of admission, and it revealed an opening pressure of 270mmH₂O. Further cerebrospinal fluid (CSF) analysis revealed normal white blood cells (0x10⁶/L), normal glucose (4.1mmol/L), and mildly increased protein (0.6g/L, normal range:0.15-0.45g/L). Thoracic and abdominal computed tomography scan was normal. Brain MRI was performed on the day of admission. Diffusion-weighted imaging (DWI) revealed high-intensity signals in the entire corpus callosum and bilateral frontoparietal subcortical white matter (Figure 1A,1B). The lesion in the corpus callosum was slightly hyperintense on fluid-attenuated inversion recovery (FLAIR) images as well (Figure 1C).

The patient was suspected of having mild encephalitis/encephalopathy with a reversible splenic lesion (MERS). He was treated with a combination of intravenous immunoglobulin (0.4g/kg/day for 5 days) and methylprednisolone

(0.8g/day for 3days followed by 0.25g/day for 3days) on the day of admission. Ganciclovir and ceftriaxone were also administrated intravenously. On day 2 of admission, his temperature returned to normal and the neurological manifestation improved dramatically. He became alert with good orientation and was able to communicate normally. On day 10 of admission, the high-intensity signals on DWI completely resolved in the corpus callosum (Figure 1E) and were only faintly detected in bilateral frontoparietal subcortical white matter (Figure 1F). FLAIR images became normal (Figure 1G).

Interestingly, 3 days after admission a routine transthoracic echocardiogram showed vegetation on the mitral valve and mild regurgitation. A subsequent transesophageal echocardiogram confirmed the abnormality with a vegetation of 9mmx4mm on the anterior mitral valve (Figure 2A). Seven days after admission the patient had a high fever again and four sets of blood cultures exhibited the growth of *Staphylococcus aureus*, more specifically, methicillin sensitive *Staphylococcus aureus* (MSSA). He had continuous fever, splenic infarction, and embolism in the fingers (Figure 3), despite aggressive antibiotic treatment (including gentamicin, ampicillin/sulbactam, vancomycin, levofloxacin and phosphonomycin). He then underwent mitral valve replacement and made a complete recovery. Microscopic examination of the vegetation attached to the anterior mitral valve revealed large numbers of bacteria admixed with fibrin and blood cells.

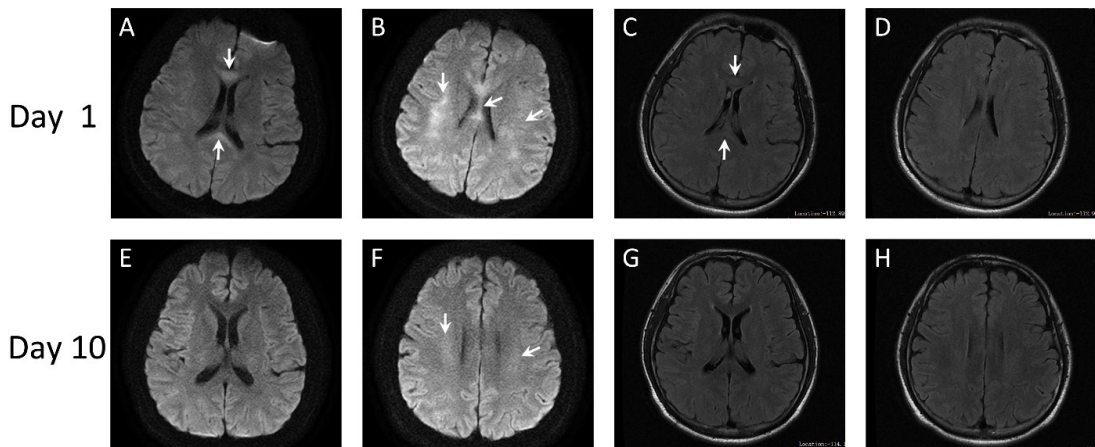


Figure 1. Diffusion-weighted imaging (DWI) (A, B) and fluid-attenuated inversion recovery (FLAIR) imaging (C, D) on day 1 of admission, and DWI (E, F) and FLAIR imaging (G, H) on day 10 of admission. On day 1 of admission, lesion in corpus callosum was hyperintense on DWI (A,B) and slightly hyperintense on FLAIR imaging (C), and lesions in the white matter were hyperintense on DWI (B) alone. On day 10 of admission, the abnormal signal in the corpus callosum had disappeared on DWI (E) and FLAIR imaging (G), and the high signals in the white matter were only faintly detected on DWI (F).

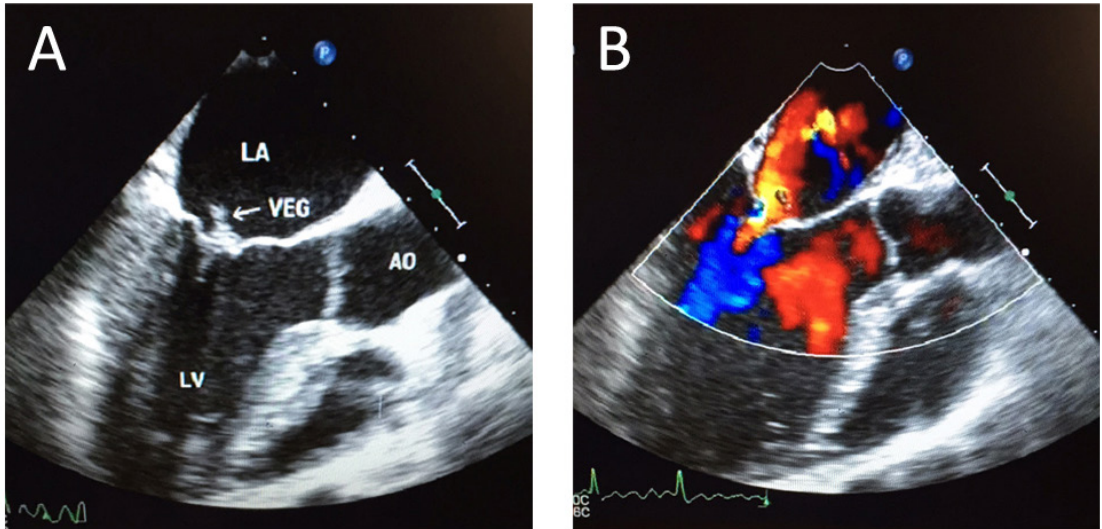


Figure 2. A transesophageal echocardiogram showed a vegetation of 9mm×4mm on the anterior mitral valve (A) and regurgitation (B).

DISCUSSION

In our case, the patient presented with transient encephalopathy as the first main clinical feature of an underlying cardiac disease. The lesion in corpus callosum resolved completely and the lesions in bilateral white matter were only faintly detected on follow-up diffusion imaging. The subsequent echocardiogram, positive blood culture

and microscopic examination led to a diagnosis of *Staphylococcus aureus* endocarditis. Thus, we diagnosed him with transient encephalopathy with reversible lesions in corpus callosum and bilateral white matter associated with infectious endocarditis.

To the best of our knowledge, there are only two case reports that described similar patients.^{10,11} Takanashi *et al.*, in 2006, reported a case of a

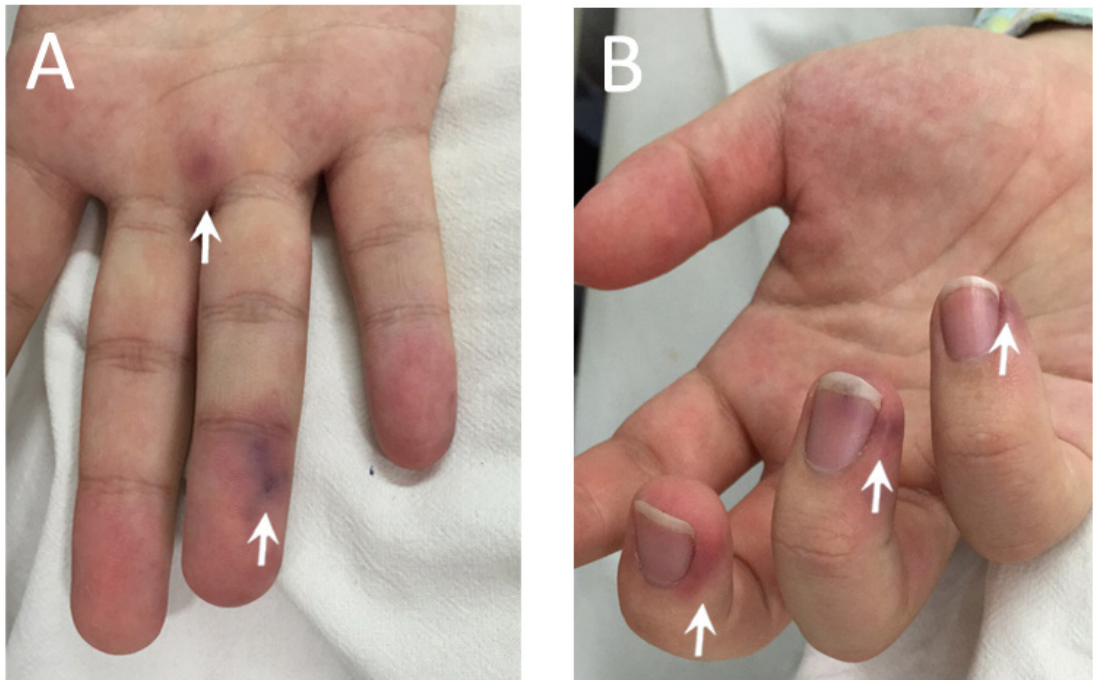


Figure 3: Embolism in fingers of the right hand.

31-year-old man who had transient meningo-encephalitis with reversible lesions involving the entire corpus callosum and bilateral cerebral hemispheric white matter associated with possible infectious endocarditis.¹⁰ No pathogen was found in his blood or CSF, but CSF showed an increased cell count ($253 \times 10^6/L$, polymorphonuclear/mononuclear=217:36) suggesting CSF invasion of bacteria. Fukagawa *et al.*, reported in 2013 a 36-year-old man who had mild encephalopathy with a reversible splenial lesion associated with definite infectious endocarditis caused by *Staphylococcus aureus*.¹¹ Unfortunately, many details such as CSF findings, treatment and outcome were not described in that short report.

In contrast with increased cell count in CSF in Takanashi *et al.*'s report¹⁰, the CSF analysis did not reveal any cellular components in our case. So, we speculated that the damage to the brain was not caused by the direct invasion of bacteria. In addition, the symmetric distribution and reversibility of lesions can also exclude microembolism from endocardial vegetation. The mechanism for reversible lesions in the brain might be infiltration of inflammatory cells or cytokines secondary to systemic bacterial infection, and the pathological process can be isolated to the splenium, or affect the entire corpus callosum and bilateral white matter. However, the exact mechanism by which MRI diffusion is transiently restricted decreased is not yet known.

Neurological manifestations account for 20-40% in infectious endocarditis, and include ischemic or hemorrhagic strokes, purulent or aseptic meningitis, headache and encephalopathy.¹² Our case suggests encephalopathy with a callosal lesion could present as the first sign of infectious endocarditis. *Staphylococcus aureus* endocarditis carries a high mortality rate of 20-40%, partly because of the variability in clinical presentation, which may delay the early diagnosis and treatment of this disease.¹³ Thus, we suggest echocardiographic evaluation should be carried out early for patients presenting with fever, encephalopathy and lesions affecting the corpus callosum with or without additional white matter involvement on MRI.

DISCLOSURE

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Conflicts of interest: None.

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