

Probable Bacterial Meningoencephalitis Presenting With Reversible White Matter Restricted Diffusion: A Case Report

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Abstract

Bacterial meningoencephalitis typically presents with fever and altered mental status, and neuroimaging is frequently normal. We report an 82-year-old man with diabetes mellitus and chronic kidney disease who was found unresponsive at home. He was febrile on arrival with a Glasgow Coma Scale (GCS) score of 3/15. Initial investigations showed acute kidney injury, raised inflammatory markers, and rhabdomyolysis, and a computed tomography (CT) scan of the brain was unremarkable. Subsequent magnetic resonance imaging (MRI) of the brain showed bilateral, symmetrical restricted diffusion in the centrum semiovale and periventricular deep white matter, an appearance that suggested toxic metabolic encephalopathy (TME). Thereafter, cerebrospinal fluid (CSF) analysis showed a neutrophil-predominant pleocytosis with raised protein, but Gram stain, cultures, and viral polymerase chain reaction (PCR) studies were negative. Hence, the diagnosis made was probable bacterial meningoencephalitis. He was then started on ceftriaxone, ampicillin, and acyclovir. A repeat MRI after one week showed complete resolution of the diffusion abnormality. Despite this, the patient's level of consciousness did not improve, and he developed recurrent hypotension and worsening renal function and subsequently demised.

This case demonstrates that reversible white matter diffusion restriction may be mistaken for a pure metabolic process and may mask an underlying meningoencephalitis. Therefore, in a febrile, encephalopathic patient, clinical judgement should take precedence, prompt early lumbar puncture (LP) should be performed where indicated, and imaging resolution should not be taken as a sign of clinical recovery.

Categories: Neurology, Radiology, Internal Medicine

Keywords: acute leukoencephalopathy with restricted diffusion, altered mental state, bacterial meningitis, diffusion-weighted imaging, meningoencephalitis, restricted diffusion, toxic metabolic encephalopathy

Introduction

Meningoencephalitis is an infection of the central nervous system (CNS) in which an intense inflammatory response can involve the meninges, subarachnoid space, and brain parenchyma [1]. The extent of CNS involvement accounts for the varied methods of presentation, from altered behavior to depressed consciousness [2]. CSF analysis remains the cornerstone of diagnosis, and neuroimaging is an adjunct that is usually normal or can show meningeal enhancement and complications such as infarction, empyema, and ventriculitis [3].

Bilateral, symmetrical restricted diffusion, where there is hyperintensity in diffusion-weighted imaging (DWI) that tracks the movement of water molecules in the brain, is a less common presentation of meningoencephalitis. On DWI, it overlaps with the appearances of toxic metabolic encephalopathy (TME) [4]; however, while meningoencephalitis frequently involves the cerebral white matter, TME usually involves the deep gray matter and cortex. Another differential is acute leukoencephalopathy with restricted diffusion (ALERD), a clinicoradiological syndrome that can be triggered by infections or toxins [5,6].

We report an elderly man with febrile encephalopathy, renal impairment, and rhabdomyolysis whose initial magnetic resonance imaging (MRI) showed this pattern of restricted diffusion, and lumbar puncture (LP) showed probable bacterial meningoencephalitis. Interestingly, the MRI findings resolved on repeat imaging one week later, in spite of the lack of clinical recovery. We discuss how such findings should be interpreted and that, despite an imaging pattern suggesting a metabolic cause, overall clinical correlation is crucial to ensure appropriate investigations such as an LP and treatment to cover for possible meningoencephalitis are carried out in a timely manner.

Case Presentation

Clinical presentation

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An 82-year-old man was brought to the hospital unresponsive after his family found him lying on a broken bed with urinary incontinence. He had last been seen well one day earlier. According to his family, he had had no preceding fever, neck pain, convulsions, or fecal incontinence, had not travelled recently, and had no exposure to alcohol or illicit drugs.

His medical history included diabetes mellitus, dyslipidemia, and chronic kidney disease secondary to diabetic nephropathy that did not require dialysis. At the time of admission, he was taking the following chronic medications: metformin, gliclazide, losartan, and atorvastatin. He had no prior hospital admissions and no significant history of alcohol use.

On examination, he was febrile (38.3 degrees Celsius), with a heart rate of 77 beats per minute and a blood pressure of 121/57 mm Hg. His Glasgow Coma Scale (GCS) score was 3/15, and both pupils were constricted at 1 mm but reactive. Doll’s and gag reflexes were still present. There was bruising over the left cheek and broken skin seen over the gluteal region, left elbow, left arm, and right thigh. There was no nuchal rigidity noted, and the patient was too drowsy for full neurological examination. Cardiovascular, respiratory, and abdominal examinations were unremarkable.

Investigations

Initial blood tests showed acute kidney injury, with a creatinine of 461 µmol/L (baseline: 250 µmol/L) and a urea of 34.6 mmol/L (baseline: 17 mmol/L). There was leukocytosis (white blood cells: 14.73 × 10⁹/L) with raised inflammatory markers (C-reactive protein: 58.5 mg/L, procalcitonin: 2 ng/mL), pointing toward infection. Creatine kinase was elevated at 4,200 U/L on admission and later peaked at 12,176 U/L. Aspartate aminotransferase was 177 U/L, and alanine aminotransferase was 43 U/L. The coagulation profile and cardiac enzymes were unremarkable, and the capillary glucose level was normal. The serum toxicology screen was also negative for paracetamol, salicylates, amphetamines, barbiturates, tricyclic antidepressants, phencyclidine, opiates, and benzodiazepines. The remaining results are shown in Table 1 and Table 2.

Test	Unit	Reference range	Day 1 (admission)	Day 3	Day 5	Day 9	Day 11	Day 13	Day 14
Total white cell count	×10 ⁹ /L	4-10	14.73	11.44	8.33	8.21	8.4	8.27	11.88
Hemoglobin	g/dL	13-17	11.9	11.9	11	10.6	10	8.9	8.9
Platelets	×10 ⁹ /L	150-450	171	152	129	112	105	87	76
C-reactive protein	mg/L	<3	58.5	43.8	-	-	75.9	-	-
Procalcitonin	ng/mL	<0.5	2	2.5	-	-	1.4	-	-
Lactate	mmol/L	0.5-2.2	1.6	2.4	-	-	-	-	-
Urea	mmol/L	2.8-7.7	34.6	37.6	40.7	38.2	29.5	28.3	24.8
Sodium	mmol/L	135-145	140	140	142	141	143	145	150
Potassium	mmol/L	3.5-5.0	5	4.4	4.3	4.1	3.9	3.9	4.1
Bicarbonate	mmol/L	19-31	17	14	17	16	19	21	20
Serum glucose	mmol/L	4-7	12.4	-	-	-	-	-	-
Creatinine	µmol/L	65-125	461	442	470	389	326	282	279
Creatine kinase	U/L	38-164	4,200	10,616	12,176	9,482	6,747	3,858	981

TABLE 1: Serial blood test results

Test	Result	Unit
Calcium	2.24	mmol/L
Magnesium	1.88	mmol/L
Phosphate	0.9	mmol/L
Free thyroxine	13.3	pmol/L
Thyroid-stimulating hormone	1.92	mIU/L
Aspartate aminotransferase	177	U/L
Alanine aminotransferase	43	U/L
Alkaline phosphatase	46	U/L
Albumin	33	g/L
Bilirubin	16	μmol/L
Prothrombin time (admission, repeat)	11.8, 11.1	Seconds
Activated partial thromboplastin time (admission, repeat)	24.5, 23.4	Seconds
International normalized ratio (admission, repeat)	1.07, 1.01	-
CSF white cell count	41, predominantly neutrophils	cells/μL
CSF red cell count	4	cells/μL
CSF protein	0.84	g/L
CSF glucose	4.2	mmol/L
Paired serum glucose	9.5	mmol/L
CSF opening and closing pressure	14 and 10	cm H2O
CSF Gram stain and aerobic culture	Negative	-
CSF HSV PCR, other viral studies, syphilis serology	Negative	-

TABLE 2: Other admission investigations and CSF results

CSF: cerebrospinal fluid

A chest radiograph on admission showed no focal consolidation. An initial computed tomography (CT) scan of the brain showed no acute intracranial abnormality.

Management and clinical course

The patient was treated empirically with intravenous amoxicillin-clavulanate for sepsis of unknown source and received a trial of intravenous thiamine. He was referred to Neurology, who suggested an electroencephalogram (EEG) and an MRI of the brain to exclude nonconvulsive seizures and posterior circulation stroke, respectively. The EEG showed slow diffuse encephalopathy with no seizure activity. MRI showed bilateral, symmetrical restricted diffusion in the centrum semiovale and periventricular deep white matter, suggestive of TME (Figure 1A and Figure 1B).

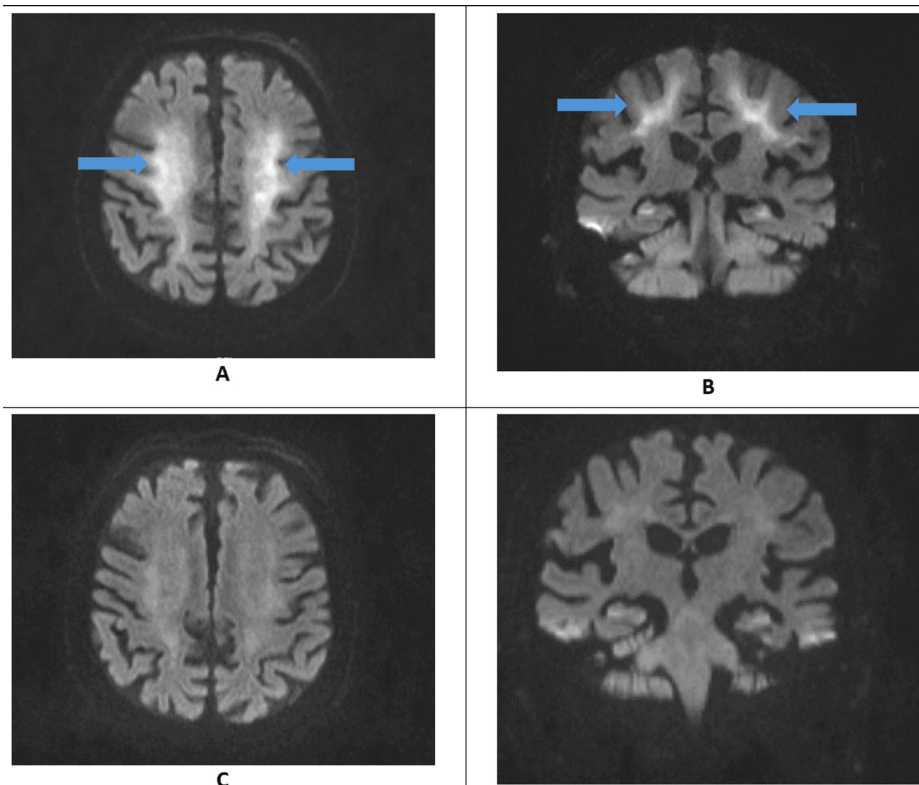


FIGURE 1: Diffusion-weighted MRI of the brain at days 3 and 10

Axial (A) and coronal (B) diffusion-weighted images at presentation show bilateral, symmetrical hyperintensity in the centrum semiovale and periventricular deep white matter at day 3 of admission. Axial (C) and coronal (D) images from the repeat examination one week later show resolution of the signal abnormality at day 10 of admission.

MRI: magnetic resonance imaging

The initial blood and urine cultures were negative, and there was no surrounding cellulitis at the areas of broken skin over the gluteal region and limbs.

A lumbar puncture was performed to exclude CNS infection on day 3 of admission, and amoxicillin-clavulanate was started. The CSF white cell count was 41 cells/ μ L (normal: 0-5 cells/ μ L), predominantly neutrophils, with a CSF glucose level of 4.2 mmol/L, compared to the serum glucose level of 9.5 mmol/L; the protein level was raised at 0.84 g/L (normal: 0-0.5 g/L). The opening pressure was 14 cm H₂O, and the closing pressure was 10 cm H₂O (Table 2). These findings were suggestive of probable bacterial meningoencephalitis. Antibiotic therapy was then escalated to intravenous ceftriaxone, ampicillin, and acyclovir. Gram stain and aerobic culture, herpes simplex virus (HSV) polymerase chain reaction (PCR), other viral studies, and syphilis serology subsequently returned negative.

During admission, his creatine kinase level rose initially and then improved gradually with intravenous hydration; this was attributed to rhabdomyolysis after an unwitnessed fall. A repeat MRI of the brain at day 10 of admission showed complete resolution of the diffusion abnormality (Figure 1C and Figure 1D).

Despite this, however, his condition deteriorated. He had several episodes of hypotension that responded to fluid resuscitation, and his renal function worsened. He was referred to the nephrology team for a trial of hemodialysis as uremia may have been a contributory cause of his drowsiness. His urea came down with hemodialysis, but his GCS did not improve. He continued to have fever spikes despite completing 14 days of antibiotic therapy. Repeat blood and urine cultures and non-contrast CT of the abdomen and pelvis were negative for other sources of sepsis. In light of medical futility, he was referred to the palliative team for comfort care and subsequently passed away. The timeline of key events is summarized in Table 3.

Event
Day 1
Found unresponsive, febrile, GCS: 3/15, brain CT unremarkable, empirical intravenous amoxicillin-clavulanate and thiamine started
Day 3
EEG unremarkable, first brain MRI: bilateral symmetrical restricted diffusion in the centrum semiovale and periventricular deep white matter
Day 4
Lumbar puncture: neutrophil-predominant pleocytosis, raised protein
Antibiotics escalated to ceftriaxone, ampicillin, and acyclovir
Creatine kinase peaks at 12,176 U/L, managed with intravenous hydration
Day 10
Patient remains drowsy
Repeat brain MRI: complete resolution of the diffusion abnormality
Day 11
Recurrent hypotension responsive to fluids, worsening renal function, trial of hemodialysis
Day 14 onward
Completes 14 days of antibiotics, persistent fever spikes
Urea improves, GCS unchanged
Referred to palliative care, demised

TABLE 3: Timeline of key events

CT: computed tomography, EEG: electroencephalogram, GCS: Glasgow Coma Scale, MRI: magnetic resonance imaging

Discussion

This patient presented with fever, profound depression of consciousness, and a neutrophil-predominant CSF pleocytosis. His initial MRI showed bilateral, symmetrical white matter restricted diffusion reported as TME, which resolved on the repeat MRI within one week. Nuchal rigidity was absent, which does not exclude meningitis, because it has been shown that classical meningeal signs have limited sensitivity [7].

The differential diagnosis of symmetrical restricted diffusion in a febrile, encephalopathic patient is very broad. TME is a nonspecific term for diffuse cerebral dysfunction caused by systemic illness, and it is often multifactorial, as in this patient. Regardless, the final common pathway is thought to be impaired function of the reticular activating system, in which disruption of the local milieu (pH, water balance, and metabolic substrates) upsets the balance between excitatory and inhibitory synaptic pathways [8,9]. Metabolic encephalopathies generally produce widespread, symmetrical injury that often involves the deep gray nuclei and cerebral cortex [4], whereas the abnormality in our patient was in the cerebral white matter.

We considered the main alternative explanations in turn.

Sepsis-associated encephalopathy is an important cause of TME [10] and probably contributed here; however, lumbar puncture should be performed in the absence of contraindications in a febrile patient with no other sources of sepsis, because CNS infection cannot be excluded on imaging alone.

Uremic encephalopathy was a strong consideration [11] given the creatinine of 461 μmol/L and urea of 34.6 mmol/L. However, his GCS score did not improve when the urea decreased with hemodialysis, which makes uremia unlikely to be the sole cause, although its contribution cannot be excluded because recovery of consciousness may lag behind biochemical correction.

Wernicke encephalopathy [12] was also considered. However, he had no significant alcohol intake history and had received thiamine during the admission.

Hepatic encephalopathy [13] was unlikely given the normal coagulation profile, and the mildly raised aspartate aminotransferase probably reflected muscle injury in the setting of rhabdomyolysis.

In addition, hypoglycemic encephalopathy [14] was another possible cause, but less likely given the normal serum glucose level on admission (Table 1).

The constricted pupils raised the possibility of opioid or sedative toxicity. However, the toxicology screen was negative, and the patient was not known to be on long-term painkillers or sleeping pills.

Another differential worth considering is delayed post-hypoxic leukoencephalopathy (DPHL) [15], given that the patient was found unresponsive after an unknown period, with urinary incontinence, rhabdomyolysis, and possible hypoperfusion. These features raise the possibility of occult hypoxic injury, which shows an overlap in characteristic MRI patterns. However, brainstem reflexes were still present, and there were no myoclonus or widespread infarcts noted, which are sometimes seen with DPHL.

The imaging pattern also resembles ALERD, in which acute encephalopathy is accompanied by diffusion restriction predominantly in the subcortical white matter, with infectious and toxic triggers [5,6]. Most published series involve children [5,16], and several other potentially reversible encephalopathic syndromes with diffusion restriction are recognized [17]. Ranjan et al. described a patient with *Staphylococcus aureus* meningoencephalitis whose MRI resembled ALERD [6], although the entity is more commonly seen in infectious and metabolic processes.

Although resolution of the diffusion abnormality followed treatment for meningoencephalitis, this temporal association may not be solely due to CNS infection. Restricted diffusion is a nonspecific marker of cytotoxic edema; in this case, sepsis, uremia, rhabdomyolysis, and hypotension could each have contributed, and correction of hydration and metabolic state over the same week could also explain the resolution on MRI. The diagnosis of bacterial meningoencephalitis is itself probable rather than definite: the CSF pleocytosis was modest (41 cells/ μ L), and Gram stain and cultures were negative, partially due to amoxicillin-clavulanate having been started three days before lumbar puncture, bearing in mind its limited CNS penetration.

It has been noted in previous studies that reduced diffusion was reversible in 12 out of 13 patients who had repeat MRIs done 21 days or later following an episode of acute TME [15]. However, in our patient, the MRI demonstrating resolution was repeated only after one week. Further studies would be useful to follow the temporal progression of TME on MRI scans. Management of TME is directed at the underlying cause [18], but in a febrile patient, empirical antimicrobial therapy should not be delayed while waiting for imaging or other causes to be excluded.

Notably, the resolution of the imaging abnormality was not accompanied by clinical recovery in our patient. Reversible DWI changes therefore did not indicate a favorable prognosis, and his persistent coma may reflect the other contributors described above or factors that cannot be detected on MRI. For example, he developed hyponatremia likely due to reduced water access and iatrogenic intravenous fluids. He also had falling hemoglobin and platelets, which led to the suspicion of a possible hemolytic uremic syndrome or thrombotic thrombocytopenic purpura. However, at that juncture, further extensive investigations were no longer in the patient's best interest.

As this case demonstrates, overall clinical judgment and correlation are paramount in managing a patient with several differential diagnoses. For a patient with unexplained fever and altered mental status, CNS infection should always be considered, and appropriate investigations and treatment commenced, as the absence of leptomeningeal enhancement on brain MRI does not confidently rule out meningoencephalitis.

This case report has several limitations. It describes a single patient whose CNS culture was negative and LP done after antibiotics had been started. Furthermore, no autopsy was performed to confirm the diagnosis, and several concurrent insults make attribution of the imaging finding uncertain. Further case reports on the causes of symmetrical restricted diffusion imaging on brain MRI will help clarify how often this pattern occurs in meningoencephalitis.

Conclusions

In summary, bilateral, symmetrical restricted diffusion in the cerebral white matter, commonly associated with a toxic metabolic process, may be present concurrently in febrile patients with CSF pleocytosis. In this case, given the clinical presentation, the patient was treated as having probable bacterial meningoencephalitis. Hence, in a septic patient with unexplained encephalopathy, clinical correlation and judgement are key, and such imaging findings should not delay lumbar puncture or empirical antimicrobial treatment.

Reversibility on follow-up imaging does not establish the cause of the abnormality and, as in this patient, does not guarantee clinical recovery. Close collaboration between the primary team, neurology, nephrology,

and radiology is thus recommended to interpret such findings in critically ill patients with altered mental status.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Acquisition, analysis, or interpretation of data: Li Fang Yeo

Drafting of the manuscript: Li Fang Yeo

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Critical review of the manuscript for important intellectual content: Veeraraghavan Meyyur Aravamudan

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