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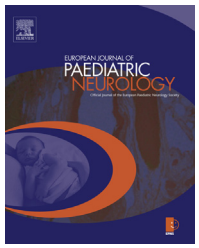

Case study

Mild encephalopathy with reversible splenial lesion: An important differential of encephalitis

Amy Ka [a,b], *Philip Britton* [c], *Christopher Troedson* [a], *Richard Webster* [a], *Peter Procopis* [a,d], *Joanne Ging* [b], *Yew Wee Chua* [b], *Adam Buckmaster* [e], *Nicholas Wood* [b,d], *Cheryl Jones* [c,d], *Russell C. Dale* [a,d,*]

[a] *TY Nelson Department of Neurology and Neurosurgery, The Children's Hospital, Westmead, Australia*
[b] *Department of Paediatrics, The Children's Hospital, Westmead, Australia*
[c] *Department of Infectious Disease, The Children's Hospital, Westmead, Australia*
[d] *Discipline of Paediatrics and Child Health, University of Sydney, Australia*
[e] *Department of Paediatrics, Gosford Hospital, NSW, Australia*

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ABSTRACT

Mild encephalopathy with a reversible splenial lesion (MERS) is a clinico-radiological syndrome characterized by a transient mild encephalopathy and a reversible lesion in the splenium of the corpus callosum on MRI. This syndrome has almost universally been described in children from Japan and East Asia. Here we describe seven cases of MERS occurring in Caucasian Australian children from one centre seen over a 3 year period. All patients had a fever-associated encephalopathy (n = 7), which presented with confusion (n = 4), irritability (n = 3), lethargy (n = 3), slurred speech (n = 3), drowsiness (n = 2) and hallucinations (n = 2). Other neurological symptoms included ataxia (n = 5) and seizures (n = 1). These symptoms resolved rapidly over 4–6 days followed by complete neurological recovery. In all patients, MRI performed within 1–3 days of onset of encephalopathy demonstrated a symmetrical diffusion-restricted lesion in the splenium of the corpus callosum. Three patients had additional lesions involving other parts of the corpus callosum and adjacent periventricular white matter. These same three patients had mild persisting white matter changes evident at followup MRI, while the other patients had complete resolution of radiological changes. A potential trigger was present in five of the seven cases: Kawasaki disease, Salmonella, cytomegalovirus, influenza B and adenovirus (all n = 1). Elevated white cell count (n = 4), elevated C reactive protein (n = 5) and hyponatremia (n = 6) were commonly observed. CSF was performed in four patients, which showed no pleocytosis. This case series of MERS demonstrates this condition occurs outside of East Asia and is an important differential to consider in children presenting with acute encephalopathy.

* *Corresponding author*. Clinical School, Children's hospital at Westmead, Locked Bag 4001, NSW 2145, Australia. Tel.: +61 298450000; fax: +61 298453389.
E-mail address: Russell.dale@health.nsw.gov.au (R.C. Dale).
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1. Introduction

Mild encephalopathy with a reversible splenial lesion (MERS) is a clinico-radiological syndrome which was first proposed by Tada et al.[1] in 2004 and further expanded by Takanashi et al.[2] It is typically characterized by a prodromal illness consisting of fever, cough, vomiting or diarrhoea, followed 1–7 days later by encephalopathy. Common neurological symptoms include behavioural change, altered consciousness and seizures.[2] These symptoms resolve rapidly over days without treatment and there is typically complete neurological recovery. Magnetic resonance imaging (MRI) during the acute episode reveals a lesion in the splenium of the corpus callosum, sometimes also extending to other areas of the corpus callosum and adjacent parenchymal white matter. The lesions are typically symmetrical and show T2 hyperintensity with corresponding diffusion restriction and no contrast enhancement. These changes resolve completely or near completely on follow up imaging within days to weeks.[1,2]

The underlying pathogenesis of MERS is unknown. Takanashi et al. proposed an infectious trigger in their case series of 54 Japanese patients with MERS.[2] A recent systematic review by Garcia-Monco et al. revealed multiple other potential causes of reversible splenial lesions, however infectious related MERS remains the most common cause of reversible splenial lesions in childhood.[3]

MERS is a condition that has largely been described in case reports and case series from East Asia and Japan. To our knowledge, there have been less than 10 published cases of MERS occurring children outside of Japan and East Asia.[4–8] In this study, we describe the findings of seven Caucasian Australian children who presented with MERS over a 3 year time period, demonstrating this to be an important clinical entity outside of East Asia.

2. Methods

Patients with possible MERS were identified by reviewing the neurology departmental database of inpatient consultations and by directly contacting the neurologists at the Children's hospital at Westmead. We performed a full retrospective chart review of the patients referred for the study. We collected information about ethnicity, past medical history, clinical features, medications, treatment, investigations and outcome. We reviewed all neuro-imaging in conjunction with the paediatric neuroradiology formal reports. All patients had acute transient encephalopathy and MRI showing a diffusion-restricted lesion in the splenium of the corpus callosum with or without lesions in other areas. The families provided written consent for publication.

3. Results

Seven patients presenting over a 3-year period (2010–2013) were included. All patients were Caucasian with median age of five years (range 3–9). Three patients had a pre-existing medical problems (Table 1). The other children were previously well with normal neurodevelopment.

All seven patients had non-specific symptoms of acute infection prior to encephalopathy onset: fever (n = 7), vomiting (n = 5), cough/coryza (n = 4), abdominal pain (n = 2), headache (n = 2) and diarrhoea (n = 1). One child had features consistent with a diagnosis of Kawasaki disease and was treated with intravenous immunoglobulin and aspirin one day prior to the onset of neurological symptoms. All patients had features of acute encephalopathy (n = 7), which was manifest as confusion (n=4), irritability (n = 3), lethargy (n = 3), slurred speech (n = 3), drowsiness (n = 2) and hallucinations (n = 2). 5 patients were ataxic. Only one patient had seizures during the encephalopathic phase. Initial empiric management included intravenous antibiotics (n=6), intravenous antivirals (n = 3) and intravenous steroids (n = 3).

Six patients had one or more raised inflammatory marker (white cell count $>11 \times 10^9$ (n = 4), C reactive protein >0.8 mg/L or both (n = 5)). Six of the seven patients were hyponatremic (Na < 135 mmol/L) (median 130 mmol/L; range 127–132 mmol/L). Five patients underwent lumbar puncture; four had normal cerebro-spinal fluid (CSF) cell counts, glucose, protein, lactate, and absence of growth on CSF culture. The fifth patient had CSF taken two days after intravenous immunoglobulin treatment for Kawasaki disease, and was the only patient with CSF pleocytosis. In total, five patients had a suspected aetiological trigger: Kawasaki disease, Salmonella (stool culture), cytomegalovirus (positive IgM serology), influenza B (nasopharyngeal aspirate, NPA) and adenovirus (NPA) (all n = 1).

Initial MRI was performed within 1–3 days of onset of neurological symptoms (Table 2 and Fig. 1). All patients had the characteristic symmetric lesion involving the splenium of the corpus callosum. Three patients had lesions which extended beyond the splenium of the corpus callosum to involve the genu of the corpus callosum (n = 2), the entire corpus callosum (n = 1) and the periventricular white matter (n = 3). All of these lesions were symmetrical and showed T2 hyperintensity with corresponding diffusion restriction. There was no contrast enhancement evident in those patients who had administered gadolinium (n = 4).

Average duration of hospital stay was 5.6 days (range 4–6). At the time of discharge from hospital, clinical features had resolved in five patients, and two patients had residual ataxia manifest as difficulty with tandem gait. However, all children had complete neurological recovery at further clinical follow-up, which was documented 1–4 weeks after discharge from hospital.

Follow-up MRI was done 1–8 months following the initial presentation in six patients (one patient lost to follow-up). All acute lesions involving the corpus callosum had completely resolved except in one patient who had mild persisting white matter change in the genu of the corpus callosum. In those patients who initially had white matter lesions outside of the corpus callosum, these changes had reduced in size and degree of T2 hyperintensity with absent or minimal corresponding diffusion restriction (Table 2).