

A 3-year old child with fever and disturbance of consciousness

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PART A

A 3-year old girl presented to the emergency department with high fever, irritability and moderate disturbance of consciousness. Laboratory tests did not show abnormal serum chemistry or inflammatory markers. Analysis of cerebrospinal fluid (CSF) showed a normal cell count and slightly elevated protein. Acute encephalopathy was suspected and a brain-MRI

was performed (**Fig. 1, 2**). Polymerase chain reaction (PCR) test for herpes was negative, while PCR analysis of nasopharyngeal secretions confirmed the presence of influenza-A, H1N1. The child was treated with oseltamivir for 10 days. Her conscious level gradually improved. A follow-up MRI was performed after six months (**Fig. 3, 4**).



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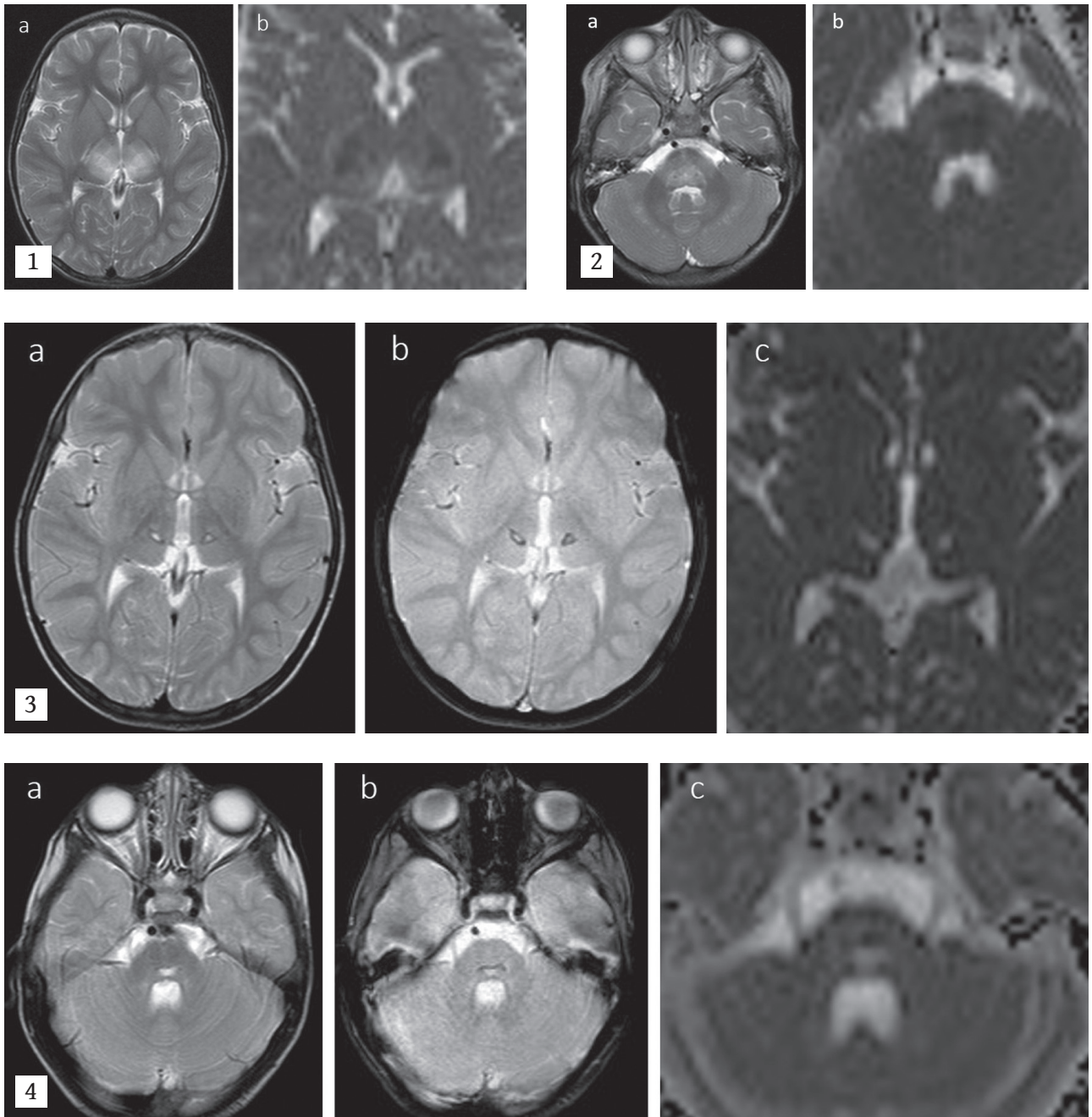


Fig.1. T2-weighted (a), Diffusion-ADC map (b)

Fig.2. T2-weighted (a), Diffusion-ADC map (b)

Fig.3. T2-weighted (a), T2*-weighted gradient-echo (b), Diffusion-ADC map (c)

Fig.4. T2-weighted (a), T2*-weighted gradient-echo (b), Diffusion-ADC map (c)

PART B

Diagnosis: Acute necrotising encephalopathy of childhood

Acute necrotising encephalopathy of childhood (ANEC) is a rare monophasic acute encephalopathy with devastating neurologic sequelae. Seventy percent of the affected children die a few days after the initiation of symptoms. ANEC occurs after viral respiratory tract infection mostly with Influenza A and B or novel influenza A (H1N1) [1, 2]. It is a sporadic disorder although some familial cases have been reported associated with a mutation of the RANBP2 gene [2]. Clinical presentation is characterised by high fever, convulsions, irritability, hyperreflexia, positive Babinski's sign, disturbance of consciousness and coma. CSF examination is characterised by elevated protein without pleocytosis. Neuropathology shows neuronal and glial cell necrosis in the center and perivascular petechial haemorrhage and swollen oligodendrocytes at the periphery of the lesions [3]. ANEC shows minimal brain inflammation and the most prevalent mechanism for its pathogenesis is hypercytokinaemia. "Cytokine storm" causes proteolytic disruption of blood brain barrier by increasing vascular permeability and leading to brain oedema, petechial haemorrhage and necrosis [4, 5].

Imaging shows multifocal, symmetric brain lesions involving both gray and white matter. MRI shows bilateral involvement of the thalamus, the posterior limb of the internal capsule, the posterior part of the lenticular nucleus, the putamen, the periventricular white matter, the cerebellar medullary substance around the dentate nucleus and the tegmentum of the pons or midbrain. The lesions are initially characterised by oedema evolving to petechial haemorrhage and necrosis. A low signal

intensity on T1 and a high signal intensity on T2 weighted images is initially observed followed by petechial haemorrhage and peripheral enhancement of the lesion. Restricted diffusion in the thalami and the pons has been associated with the presence of swollen oligodendrocytes and acute petechial haemorrhage [4]. At later stages cavitation, atrophy and haemosiderin deposits are observed [1, 4, 6-8]. MR spectroscopy shows reduction of N-acetyl aspartate and elevation of myoinositol and choline, but no lactate peak. ANEC should be differentiated from other entities associated with bilateral brain lesions. Differential diagnosis with acute haemorrhagic leukoencephalitis is based on meningeal and perivascular inflammation observed in the latter. An asymmetric lesion distribution is a differential finding from a acute disseminated encephalomyelitis. Reyes syndrome and Leigh syndrome present with hypoglycaemia, hyperammonemia and lactic acidosis that are not found in ANEC. Differential diagnosis from viral encephalitis is based on increased protein, lack of pleocytosis in the CSF of patients with ANEC [1, 5, 8, 9].

At the acute setting our patient's brain MRI revealed bilateral, symmetric oedema of the thalami, the posterior limb of the internal capsules, the putamen, the pontine and mesencephalic tegmentum and the cerebellar white matter. Restricted diffusion was observed in the thalamic and pontine lesions (**Fig. 1, 2**). Follow up MRI six months later showed cavitation of the lesions with peripheral haemosiderin deposition. A degree of thalamic and pontine atrophy was also observed (**Fig. 3, 4**). **R**

Conflict of interest:

The authors declared no conflicts of interest.



KEY WORDS

child; H1N1 infection; MRI, brain

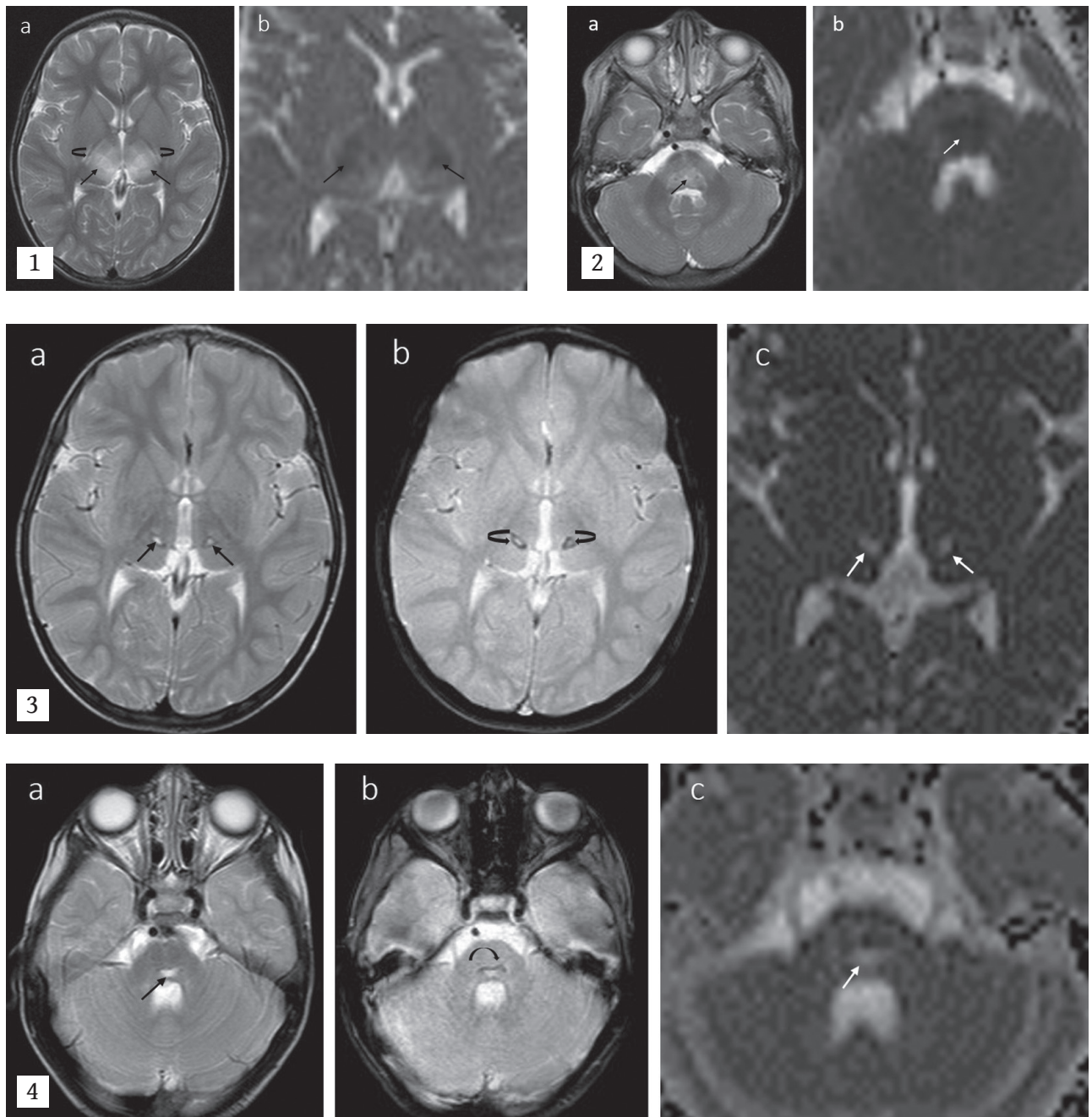


Fig.1. T2-weighted (a) image reveals bilateral, symmetric oedematous thalami with high signal (arrows) and bilateral involvement of the posterior limb of the internal capsule (curved arrows). Diffusion-ADC map (b) shows restricted diffusion of the thalami (arrows)

Fig.2. T2-weighted (a) image reveals high signal in the pons (black arrow) and restricted diffusion on diffusion-ADC map (b) (white arrow)

Fig.3. T2-weighted (a), T2*-weighted gradient-echo (b), Diffusion-ADC map (c) shows cavitation of the thalamic lesions (black arrows) with haemosiderin deposition at the periphery (curved arrows) and increased diffusion (white arrows)

Fig.4. T2-weighted (a), T2*-weighted gradient-echo (b), Diffusion-ADC map (c) shows cavitation of the pontine lesions (black arrow) with haemosiderin deposition at the periphery (curved arrow) and increased diffusion (white arrow)

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