Acute necrotising encephalopathy of childhood after exanthema subitum outside Japan or Taiwan

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Abstract Acute necrotising encephalopathy of childhood (ANE) is an uncommon disease which predominantly affects infants and young children living in Japan and Taiwan. A multifocal encephalopathy with symmetrical lesions in the thalamus, tegmentum of the brain stem, cerebral periventricular white matter and cerebellar medulla is characteristic. We present the imaging features in a 4-year-old Japanese boy who had been living in Germany for 2 1/2 years before presentation.

Key words Encephalopathy · Magnetic resonance imaging · Human herpes virus-6

Introduction

Acute necrotising encephalopathy is a rare disease that affects young children in Japan or Taiwan, without sexual predilection. In the acute phase, fever and upper respiratory symptoms precede neurological involvement. Multifocal neurological signs are often the sequelae. The prognosis is generally poor. It has been suggested that this encephalopathy might be a postviral disorder, although biochemical studies have not so far clarified the pathogenesis and the brain pathology is not compatible with an inflammatory disorder. Descriptions of the imaging features have focused on MRI findings, including symmetrical prolonged T1 and T2 relaxation times in the thalamus, tegmentum of the brain stem, cerebral periventricular white matter and cerebellar medulla. Contrast enhancement was described at the margin of the thalamus during the acute phase. In follow-up MRI the sulci and ventricles can enlarge, indicating volume loss, and the lesions in the thalamus became smaller. CT shows low-density areas in the same regions as the lesions on MRI.

We describe strikingly similar MRI and CT findings in a 4-year-old Japanese boy and discuss the role of MR spectroscopy (MRS) in making the distinction between this entity and other pathologically related conditions such as Leigh’s syndrome.

Case report

A 4-year-old Japanese boy who had been living in Germany for 2 1/2 years presented with generalised seizures followed by an acute febrile illness. He lapsed into coma with no response to pain; the pupils were equal with a sluggish reaction to light. The child had no perinatal complications, and no family history of acute encephalopathy or recent immunisation was obtained. At the age of 10 months he was diagnosed in Japan as having meningoencephalitis due to the exanthema subitum virus (HHV6). After that he developed recurrent partial, generalised and secondary generalised seizures. His blood showed a slight elevation of serum transaminases secondary to drug therapy; no hyperammonaemia, hyperglycaemia, haemostatic disorder, acidosis or elevated carnitine levels were seen, and lactate was normal. The cerebrospinal fluid profile showed normal glucose, elevated total protein and no
pleocytosis; electrophoresis showed increased levels of alpha-1-protease, suggestive of an acute-phase reaction. No intrathecal immunoglobulin was detected.

MRI revealed symmetrically bilateral longer T1 and T2 in the thalamus and on T2-weighted images, bilateral high signal in the external capsule, pontine and midbrain tegmenta and occipital periventricular white matter. No contrast enhancement was seen. Two years previously MRI had show bilateral changes in the thalamus, but to a smaller extent. Brain metabolism was measured by localised $^1$H MRS (STEAM sequence, TR/TE 1500/20 ms) in volumes of interest (voxels) of 8 cm$^3$ in the parieto-occipital white matter. In comparison with age-matched $^1$H MRS, it revealed increased choline (Cho) [Cho : creatine (Cr) ratio was 1.15; healthy controls 0.88 ± 0.098] and myo-inositol (mI) (mI : Cr ratio 0.76; controls 0.65 ± 0.063) with decreased N-acetyl aspartate (NAA) (NAA : Cr ratio 1.30; controls 1.66 ± 0.059). No lactate peak was seen. CT showed symmetrical low attenuation in the thalamus and brain stem.

The child was discharged from hospital after 10 days with right spasticity as a sequel.

**Discussion**

ANE was reported first in Japan and later in Taiwan. This prevalence in the Far East suggests genetic or environmental factors. The clinical course and imaging in this patient are strikingly similar to those in previous reports [1, 2]. The encephalopathy in this child followed Exanthema subitum [3] as did one of the cases described by Mizuguchi et al. [1].

CT and MRI showed symmetrical lesions in the thalamus, brain stem and cerebral white matter. Since there is no morphopathological specificity to the diagnosis of ANE, we can only assume the cause of the CT, MRI and MRS findings. The bilaterally symmetric long T1 and T2 in the thalamus are likely to represent cavi
tation (Fig. 1), probably related to previous petechial haemorrhage. On T2-weighted images the bilateral high signal in the external capsule, pontine and midbrain tegmenta and periventricular white matter is believed to be related at least partly to loss of neurones and myelin sheaths. The absence of contrast enhancement favours a progressive disease without disruption of the blood-brain barrier. MRS showed significant reduction of the neuronal marker NAA, interpreted as neuronal loss or damage. Elevated mI, associated with the increased glial marker Cho may reflect demyelina-

![Fig. 1](image) T2-weighted (4465/120 ms) spin-echo image 2 years before current admission

![Fig. 2](image) a T2-weighted spin-echo image during second admission. There has been extension of the bilateral high-signal foci in the thalamus. b, c FLAIR (9000/110 ms) images also show symmetrical high signal in the pons and the tegmentum of the midbrain matter.