

LETTERS TO THE EDITOR

A case of reversible blindness in maple syrup urine disease

EDITOR.—Maple syrup urine disease (MSUD) is an autosomal recessive disease associated with defects in the branched chain α ketoacid dehydrogenase complex. It may be divided into four major categories of classic, intermediate, intermittent, and thiamine responsive which carry differing symptoms and prognostic factors.¹ Those patients diagnosed and managed early have an improved neurological outcome.² Known ophthalmic complications which occur in untreated or late diagnosed patients include bilateral ptosis, ophthalmoplegia, nystagmus, strabismus, and optic atrophy.³ Cortical blindness has also been mentioned in the literature³; however, we failed to find any case reports confirming this.

At times of metabolic decompensation, oedema involving the deep white matter can be demonstrated on computed tomographic (CT) and magnetic resonance imaging (MRI). These abnormalities regress under dietary treatment, with clinical and neurological improvement.⁴

This report describes an infant diagnosed with intermittent MSUD at 6 months of age who had cortical visual impairment (CVI), with absent visual evoked potentials, and who showed clinical and electrophysiological improvement following dietary therapy.

CASE REPORT

Since birth our patient had been floppy, fed poorly, and irritable. She had suffered recurrent infections, was developmentally delayed, and became acutely unwell during a fast before a CT scan at the age of 27 weeks, which led to transfer to our hospital.

On admission, the baby was pale, malnourished, encephalopathic, with a pyrexia and a chest infection. She did not respond to stimulation, had brisk reflexes, and marked truncal hypotonia with peripheral hypertonia. There were "roving eye movements". The pupils reacted to light and the discs and maculae were healthy. A CT scan on admission showed

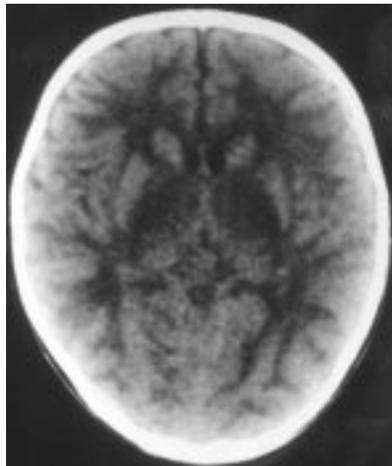


Figure 1 Computed tomogram showing swelling of white matter.

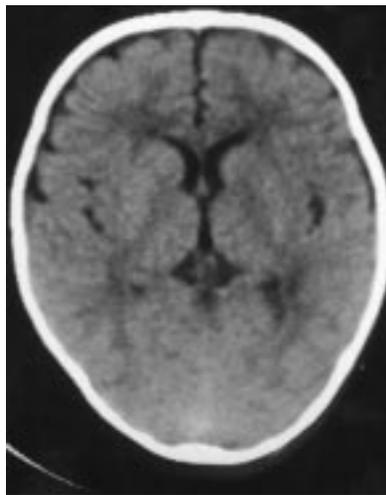


Figure 2 Computed tomogram showing changes in white matter appearances after acute presentation.

widespread low density change within the cerebral white matter which extended to involve the globus pallidus bilaterally (Fig 1). These changes had resolved on a subsequent scan (Fig 2).

Urinary organic analysis revealed increased excretion of branched chain keto acids. Plasma amino acid analysis showed marked elevation of leucine, isoleucine, valine and alloisoleucine. There were no reducing substances in the urine. A diagnosis of MSUD was made. On the fourth day of her admission visual electrophysiology gave a normal flash electroretinogram (ERG) but the flash visual evoked potential (VEP) was consistently not detectable, indicating severe postretinal dysfunction compatible with CVI (Fig 3).

Initially satisfactory control of branched chain amino acid levels in plasma were achieved by dietary restrictions; however, subsequent follow up revealed a need for oral thiamine which was instituted.

Three and a half months later, ERG/VEP tests were repeated with eye movement studies. Flash ERG results were again normal, but VEPs were now clearly detectable. Pattern VEPs to large and moderate check size were present, suggesting moderate acuity levels (Fig 4). Eye movement studies demonstrated asymmetric optokinetic nystagmus with poor gain to the left and absence of

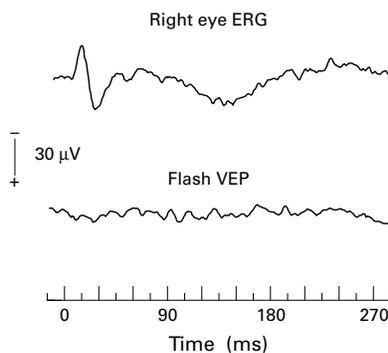


Figure 3 The right eye flash ERG and binocular flash VEP recorded at presentation. (Note, positivity is downwards). Averaged lower lid skin ERGs from the right and left eyes were of normal size and similar for each eye. No consistent flash VEP was discernible at the occipital midline.

quick phases which causes the eyes to remain in extreme lateral deviation, indicative of oculomotor apraxia. At the most recent follow up at age 2.5 years a Cardiff card acuity of 6/15 was recorded from each eye. There was no evidence of optic atrophy at this point.

COMMENT

In MSUD there is a defect in the branched chain ketoacid dehydrogenase complex. Four different genetic loci influencing this enzymatic pathway have been identified. A build up of branched chain amino acids and branched chain keto acids in the brain is neurotoxic and results in swelling of the white matter causing lethargy, reduced muscle tone, and convulsions.⁵ The classic form of MSUD is the most severe, usually presenting in the neonatal period. If it is not treated early, the patient may die or be severely brain damaged. The degree of psychomotor retardation generally correlates with the degree of residual enzymatic activity of the branched chain α ketoacid dehydrogenase complex. Children with milder forms may have an acute crisis precipitated by infection or starvation, which

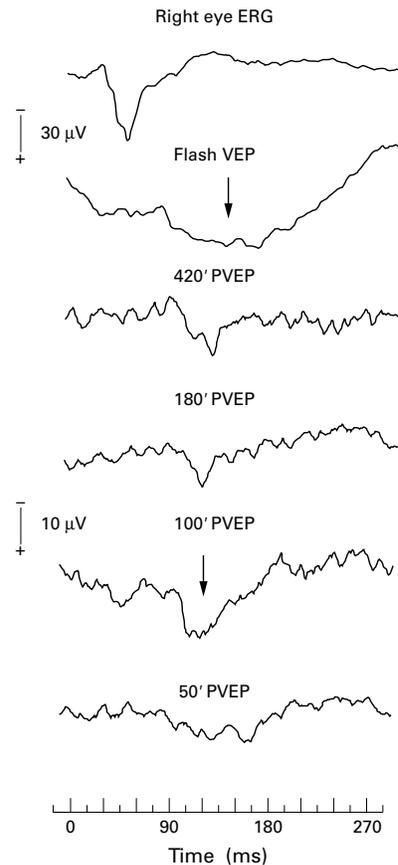


Figure 4 ERG and VEPs following treatment by dietary restriction. The top two traces show the flash ERG and flash VEP. A normal well defined retinal response was again recorded from both eyes (the right ERG is illustrated). On this occasion a broad positive flash VEP was consistently detected. Binocular pattern reversal stimulation with a range of check sizes also elicited consistent responses (P100 to 100 minute checks arrowed, note the higher display gain for the PVEPs compared with flash VEP and ERG). PVEPs were larger and better defined for the large and moderate check sizes, indicating moderate acuity levels.

leads to psychomotor retardation of varying severity. Thiamine responsive MSUD can show reversal of the biochemical changes on addition of dietary thiamine. Severe forms require the use of a branched chain free amino acid mixture.

A proportion of children thought to be cortically blind can make a partial recovery, and so CVI is a preferred term.⁶ Some reports show flash VEPs to be inaccurate in assessing the vision of children with CVI,⁷ while other reports have shown the presence of a VEP is a good indicator of subsequent recovery.⁸ Both in our experience and that of others⁹ VEPs are consistently reliable indicators of cortical visual activation in encephalopathies of varying aetiologies. In some metabolic conditions such as phenylketonuria there appears to be an association between metabolic state of the patient and changes in the VEP.^{9, 10}

The case we present had an absent VEP 4 days after admission but showed remarkable

clinical and VEP improvement over the next 3 months. Electrophysiological studies in this case show the reversibility of changes occurring within the brain associated with a crisis of MSUD.

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