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Glutaric aciduria and suspected child abuse

Subdural and retinal haemorrhages in young children without an appropriate history of trauma strongly suggest non-accidental injury. Similar features are occasionally found in patients with glutaric aciduria type 1 (GA1), a rare inborn error of metabolism, and have led to the misdiagnosis of non-accidental injury.[1–3] When and how should this condition be sought in cases of suspected child abuse?

GA1 is an autosomal recessive disorder caused by deficiency of the enzyme glutaryl-CoA dehydrogenase. Commonly it presents before age 18 months with a sudden onset of encephalopathy, following which the child has a severe and persistent movement disorder. Before this there may have been episodes of irritability or mild encephalopathy with no sequelae. Clinical examination at this stage often shows macrocephaly, and cerebral imaging may show bilateral frontotemporal atrophy or widening of the Sylvian fissure, with or without subdural effusions (fig 1). Following the catastrophic encephalopathic episodes, magnetic resonance imaging usually shows changes in the basal ganglia. Other patients present with a less acute deterioration and an unknown number remain asymptomatic.[2 4 5]

Subdural haematomas have been found in symptomatic and asymptomatic patients, even in the immediate postnatal period.[1–3 6 7] They can occur with minimal trauma, sometimes repeatedly, presumably because the bridging veins are elongated in the presence of cerebral atrophy and are easily ruptured. Retinal haemorrhages have also been reported.[1 2]

Investigation for GA1 is not entirely straightforward. Urine organic acid analysis by gas chromatography–mass spectrometry usually reveals glutaric and 3-hydroxyglutaric acids. Glutaric acid can, however, be

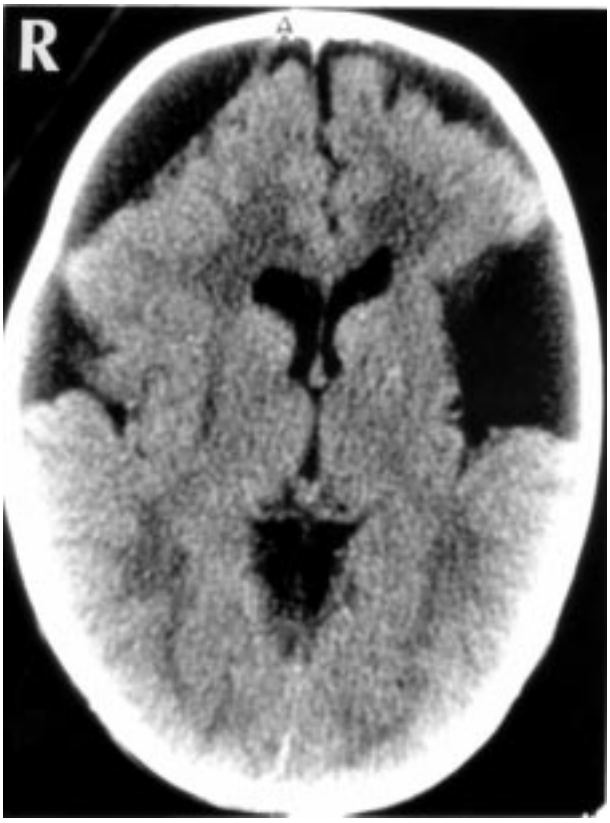

Figure 1 Axial computed tomogram at the level of the lateral ventricles in a child with GA1. There is a right frontal subdural collection, bilateral frontotemporal atrophy, and widening of the Sylvian fissures (reduced operculisation).

found in other conditions[5] and abnormalities are not always present in patients with GA1, particularly when the patient is clinically stable.[2 5 8] In the presence of normal total and free plasma carnitine concentrations, GA1 can be detected by measuring glutarylcarnitine in fresh blood spots, preferably using electrospray ionisation tandem mass spectrometry. Unfortunately, at the time of diagnosis, patients with GA1 usually have low plasma carnitine concentrations and glutarylcarnitine is then a less reliable diagnostic marker.[5] The definitive test for GA1 is measurement of glutaryl-CoA dehydrogenase activity in leukocytes or cultured fibroblasts[9] but this is expensive and may introduce a delay.

GA1 does not cause skeletal abnormalities. In particular, it does not predispose patients to fractures; if a subdural haematoma is accompanied by a fracture, exclusion of GA1 is probably unnecessary. Subdural haemorrhages have not been reported in cases of GA1 without frontotemporal atrophy and, given the proposed mechanism, they would not be expected. It is, therefore, not appropriate to look for GA1 if cerebral imaging shows subdural haematomas without any frontotemporal atrophy or widening of the Sylvian fissure. On the other hand, in the presence of bilateral frontotemporal atrophy, investigation for GA1 is essential. Under these circumstances, we recommend urinary organic acid analysis and the measurement of blood spot glutarylcarnitine, combined with total and free plasma carnitine concentrations. If the results suggest GA1, the diagnosis should be confirmed by measuring glutaryl-CoA dehydrogenase activity. The enzyme assay should also be undertaken if the initial tests show low plasma carnitine concentrations (free carnitine < 15 mmol/l) or equivocal findings (such as borderline blood spot glutarylcarnitine concentrations or raised urinary glutaric acid without 3-hydroxyglutarate).

All guidelines need to be interpreted in the light of individual circumstances. Even without the characteristic neuroimaging findings, biochemical investigations, including enzymology, should be considered if the history or examination reveals features typical of GA1, such as macrocephaly or an extrapyramidal movement disorder following an encephalopathic illness. It should also be remembered that the diagnosis of GA1 does not exclude non-accidental injury. Patients with GA1 tend to be irritable and many have severe problems, such as feeding difficulties that can cause parental frustration. We recommend performing a skeletal survey on all infants with unexplained subdural haematomas, even if they are known to have GA1.

Obviously, it is very important that potentially treatable metabolic defects should be detected and that parents should not be accused wrongly of injuring their children. It is equally important for children to receive protection when necessary. These recommendations should enable children with GA1 to be identified, without the need for extensive biochemical investigations in every patient with a subdural haematoma in whom non-accidental injury is suspected.

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