Fatty infiltration in the liver in medium chain acyl CoA dehydrogenase deficiency

H C Losty, P Lee, M Alfaham, O P Gray, J V Leonard

Abstract
Fatty infiltration of the liver at postmortem examination has been recommended as a criterion for selection of infants who have died suddenly and unexpectedly for further biochemical investigation for disorders of fatty acid oxidation. We describe a boy with medium chain acyl CoA dehydrogenase deficiency who died four months after diagnosis and in whom only minimal hepatic fatty infiltration was found.

Medium chain acyl CoA dehydrogenase (MCAD) deficiency is an inherited disorder of fatty acid metabolism in which the ability to oxidise fat is impaired. Patients often present within the first two years of life with hypoglycaemia, acute encephalopathy similar to Reye's syndrome and sudden, unexpected death. MCAD deficiency and the other rarer defects of fatty acid oxidation may be responsible for up to 5% of sudden, unexpected deaths in infancy (SIDS), but it is not feasible to investigate all SIDS for fatty acid oxidation defects. As affected infants have had pronounced fatty infiltration of liver and muscle at postmortem examination, it has been recommended that this be used as a selection criteria. We now report a patient with MCAD deficiency who died suddenly and unexpectedly four months after diagnosis. At postmortem examination only minimal fatty change in the liver was present.

Case report
This boy was the first child of unrelated parents, and he had been well until the age of 14 months when he presented with convulsions. For the previous 24 hours he had been febrile and had vomited several times. Several members of his family had diarrhoea and both Giardia lamblia and rotavirus were subsequently isolated from the patient's and the grandfather's stools. On admission he was unconscious with left sided focal seizures. He was hypoglycaemic (plasma glucose concentration 0·5 mmol/l) with a mild metabolic acidosis (pH 7·31, base deficit 10 mmol/l). Initially there was no hepatomegaly but during the next three days the liver became palpable 4 cm below the costal margin. His plasma ammonia concentration was 60 mmol/l. Although the aspartate transaminase activity was 204 IU/l (normal range up to 45 IU/l) and the alkaline phosphatase 1766 IU/l (normal range up to 340 IU/l), his alanine transaminase, γ-glutamyltransferase, bilirubin, and prothrombin time were normal. Electroencephalography demonstrated severe widespread abnormality with right sided focal features. He was treated with intravenous dextrose and diazepam but despite correction of the hypoglycaemia he had further convulsions over the next three days. He made a gradual recovery associated with a transient left sided weakness.

Analysis of organic acids in the urine collected on admission showed a hypoketotic
dicarboxylic aciduria, and the presence of hexanoylglycine and suberylglycine was confirmed by gas chromatography-mass spectrometry. He had appreciable reduction in free and total plasma carnitine concentrations (both less than 10 μmol/l) and excreted phenyl propionyl glycine after a phenyl propionate load. MCAD deficiency was confirmed by a reduced activity of 1-13C-octanoate oxidation (0.68 nmol carbon dioxide (CO₂)/hour/mg protein; controls 2-3.6 nmol CO₂/hour/mg protein) in cultured skin fibroblasts (G Besley, Royal Hospital for Sick Children, Edinburgh). He was discharged on treatment with phenobarbitone but despite therapeutic concentrations he continued to have fits of short duration. The family was given instructions about a high carbohydrate, low fat diet and a detailed plan about his management during any intercurrent illness.

At the age of 18 months he was found one morning convulsing in bed, no abnormality was found on admission, and he was allowed home. Two days later he became mildly unwell, vomited once, and was given several high carbohydrate drinks. He recovered during the day only to be found dead the next morning. On postmortem examination no abnormality was found. In particular frozen sections of the liver were stained for oil red 0 and showed only slight fatty change and not the panlobular steatosis that has been described.

Discussion
The poor outcome in this case emphasises the mortality associated with MCAD deficiency. However, most of the patients with MCAD deficiency who have died suddenly have a history of poor feeding during an intercurrent illness. This patient is unusual in that he received a high carbohydrate intake during his illness which, although it appeared to limit fat accumulation in the liver, did not prevent his death. It may therefore be necessary to give carnitine supplements and to continue a high carbohydrate intake during recovery from an acute illness.

An alternative explanation is that death may have been due to an epileptic fit but, although recognised as a cause of sudden, unexpected death, it is very rare in children. It seems more likely that this patient died as a result of a fatty acid oxidation defect.

The absence of significant fatty infiltration of the liver has important implications for investigation of SIDS as it suggests that fatty change cannot be used as a reliable screening test to identify a high risk group likely to have a defect of fatty acid oxidation.


General practitioner training needs for child health surveillance

L C Goodhart

Abstract
A postal questionnaire was sent to 136 Hackney general practitioners inquiring about their plans for child health surveillance. A total of 112 responded and detailed their training needs, both practical and theoretical. Ninety-one responders were providing or planning to provide surveillance. Responders were eager for further training particularly in premature baby follow up, mental handicap, speech and hearing assessment, and social and behavioural problems.

For some years there have been proposals to develop the role of general practitioners in child health surveillance. In 1976 the Court report proposed that there should be general practitioner paediatricians, but the General Medical Services Committee and the Royal College of General Practitioners felt unable to support this because it undermined the strength of the general practitioner as a generalist.

As the health and development of young children are so closely related to family circumstances, it is right that child health surveillance should be regarded as part of family medicine. General practitioners can bring together preventive and therapeutic care to provide a fully integrated child health service, a concept that is now firmly supported by general practitioners and paediatricians alike. However, the inclusion of paediatric surveillance in the new contract requires evidence of additional training if general practitioners are to be remunerated for this work.

In a 1985 survey of the qualifications of, and services provided by, general practitioners in the north of England, Marsh concluded that developmental screening, and even general paediatrics, was not yet safe with general practitioners. Similarly Wilmot, who ques...
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