Liver transplantation for neonatal haemochromatosis

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Abstract

Two cases of neonatal haemochromatosis, a rare and often fatal metabolic disorder, presenting with acute liver failure, are reported. Both presented in the first week of life with hypoglycaemia, jaundice, and coagulopathy, with rapid deterioration of liver function. Both received a transplantation using reduced liver grafts. One child was well 18 months later.

Few survivors have been reported and despite the difficult perioperative management, liver transplantation is the best treatment for neonatal haemochromatosis.


Keywords: liver transplantation, neonatal haemochromatosis, fulminant hepatic failure.

Neonatal haemochromatosis is a rare and frequently fatal disorder which causes either death in utero or acute liver failure in the neonate. The pathogenesis is uncertain: there may be more than one cause. It has been observed in siblings and in these cases seems to be inherited as an autosomal recessive gene.1,2 No infectious aetiology has been identified. Histologically, the condition is characterised by intense deposition of stainable iron in the liver, hepatocellular necrosis, and diffuse hepatic fibrosis with nodular regeneration. Other organs affected include the pancreas, heart, thyroid and salivary glands, with a characteristic sparing of the reticuloendothelial system. About 60 cases have been reported, with sporadic survivors described following supportive treatment. Liver transplantation is a definitive treatment but few successful cases have been reported.3,4 We report two cases born to parents with no consanguinity or familial history of death in early infancy.

Case reports

CASE 1

A full term baby girl weighing 2.32 kg at birth had an Apgar score of 9 at 1 and 5 minutes. She developed asymptomatic hypoglycaemia on day 2 and was admitted on day 9 because of lethargy, jaundice, and poor feeding. Laboratory findings (AST 74 IU/l, serum bilirubin 453 μmol/l, INR 2.3) were consistent with poor liver function. Further investigation revealed a patent ductus arteriosus with a left to right shunt on Doppler ultrasonography. Despite supportive treatment her liver function progressively deteriorated with an INR of 4.5 and she developed renal failure. She became increasingly jaundiced, hypoglycaemic, and acidotic, required ventilatory support and was referred to our centre. She received a transplantation on the 15th day of life with a reduced graft (segments II and III) from a 17 kg donor with a donor iliac conduit and Roux loop for arterial and biliary reconstruction, respectively. Ligation of the patent ductus arteriosus was undertaken.
Liver transplantation for neonatal haemochromatosis

Liver histology transformation.

Liver transplantation of neonatal haemochromatosis has been believed to be successful for cases of neonatal haemochromatosis, particularly in children with fulminant hepatic failure. Iron studies may support the diagnosis but are non-specific and may be misleading if performed after blood transfusions for concomitant anaemia. Liver biopsy is not usually possible because of the severe coagulopathy, but buccal mucosal biopsy, urinary cytology and magnetic resonance imaging (MRI) may assist in reaching a diagnosis. MRI is used as a method of defining the distribution of iron overload in haemochromatosis or haemosiderosis in children and adults. The presence of an increased amount of the ferric (Fe³⁺) ion shortens both T1 and T2 values of the affected organ, causing a reduction in signal intensity on the resultant image. T2 weighted sequences are proving the most sensitive and have been used in both antenatal and postnatal periods to investigate potential cases of neonatal haemochromatosis. A recent report describes the use of MRI at 34 weeks of gestation to diagnose neonatal haemochromatosis. Screening of 'at risk' families may be useful if MRI can give a reliable diagnosis before 24 weeks' gestation and would permit early antioxidant treatment and iron chelation, which has successfully been used in three infants with neonatal haemochromatosis.

Diagnosis of neonatal haemochromatosis is usually made at necropsy on the basis of the characteristic pattern of iron deposition in the liver and other parenchymal organs, sparing the reticulo-endothelial system. In neonates presenting with acute liver failure underlying viral and metabolic causes must be excluded, particularly haemophagocytosis. The diagnosis of neonatal haemochromatosis is usually made postoperatively and the criteria for transplantation are those used for children with fulminant hepatic failure. Iron studies may support the diagnosis but are non-specific and may be misleading if performed after blood transfusions for concomitant anaemia.

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The severity of acute liver failure was not outlined and the potential of this treatment remains unproved. Chelation treatment alone has been shown to be ineffective in altering the course of the disease.

Neonatal haemochromatosis is a complex condition requiring multidisciplinary management which includes neonatal intensive care and exchange transfusion therapy to keep the child stable while waiting for a suitable graft. Liver transplantation in neonates poses technical problems, including the use of reduced grafts to overcome extreme disparity in size, mismatch in vessel calibre, and the need for microsurgical techniques for vascular anastomoses. The postoperative care is demanding, but long term survival and normal development are possible.

A better understanding of neonatal haemochromatosis would lead to a classification of the disorder and assist in genetic counselling of affected families. To date effective medical treatment is not available and liver transplantation is presently the treatment of choice for neonates with acute liver failure as a result of neonatal haemochromatosis.


