Emergency liver transplantation after Kasai portoenterostomy

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Abstract

Three patients with stable liver function after Kasai portoenterostomy developed acute liver failure secondary to liver necrosis. Doppler ultrasound at presentation revealed reversed diastolic hepatic arterial blood flow. Two patients survived after urgent liver transplantation. Liver necrosis should be suspected in children with chronic liver disease presenting with fever and rapidly deteriorating liver function.

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Extrahepatic biliary atresia (EHBA) occurs in approximately one in 20 000 live births. Current 10 year survival after successful Kasai portoenterostomy approaches 50–70%,¹ whereas survival in the absence of surgical intervention is exceptional with the majority of children dying by the age of 2 years from liver failure and the complications of portal hypertension. Liver transplantation offers the prospect of survival for patients with progressive liver failure after unsuccessful portoenterostomy and is now the commonest indication for transplantation in children. The sudden onset of acute liver failure is uncommon in such cases and is usually seen only in the terminal stages. In the present report we describe three patients with stable liver function after Kasai portoenterostomy who developed acute deterioration of hepatic function due to extensive liver necrosis. Recognition of this unusual distinct clinicopathological entity and early referral for urgent transplantation offers the only prospect for survival.

Case reports

CASE 1

A 21 month old girl was admitted with a three day history of deepening jaundice, fever, and progressive encephalopathy. She had undergone a Kasai portoenterostomy at 7 weeks of age for EHBA and although satisfactory bile drainage was not established, her growth and development were normal. At 4 months of age her serum bilirubin concentration was 53 $\mu\text{mol/l}$ (normal <20 $\mu\text{mol/l}$) and aspartate transaminase 191 IU/l (normal <50 IU/l) with a normal serum albumin and international normalised ratio. Firm hepatosplenomegaly, palmar erythema, and cutaneous shunts were present. At 1 year her serum bilirubin was 39 $\mu\text{mol/l}$, but she had developed ascites and hard

hepatomegaly. A liver biopsy confirmed established cirrhosis with bile plugging and piecemeal necrosis.

After this admission broad spectrum antibiotics were started for suspected cholangitis, but she rapidly developed grade 4 encephalopathy with deteriorating liver function (international normalised ratio of 3.6 and serum aspartate transaminase greater than 10 000 IU/l) and was ventilated. A Doppler ultrasound showed a heterogenous liver with reversed portal venous and diastolic arterial flow. She died two days after admission from cerebral oedema. The liver at postmortem examination showed map-like areas of necrosis superimposed on a micronodular cirrhosis with a normal hepatic arterial tree (fig 1). Viral studies (including hepatitis A, B, C, E) were negative, but *Enterococcus faecium* was isolated from the spleen, liver, and lung.

CASE 2

A 9 month old boy was admitted with a three week history of fever and increasing jaundice and ascites. He had undergone a Kasai portoenterostomy at the age of 7 weeks for EHBA. At 7 months he was noted to have hepatosplenomegaly, palmar erythema, cutaneous shunts, and ascites with a serum bilirubin concentration of 45 $\mu\text{mol/l}$ and a normal aspartate transaminase and international normalised ratio.

On admission he was irritable and drowsy with a serum bilirubin of 689 $\mu\text{mol/l}$, aspartate transaminase of 333 IU/l, and an international normalised ratio of 2.1. He was treated for possible cholangitis, but the fever and liver decompensation were unresponsive to antibiotic therapy. A Doppler ultrasound showed a heterogenous liver with a patent portal vein but

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Figure 1 Explanted liver from case 1 showing map-like areas of necrosis superimposed on a micronodular cirrhosis. A large area of necrosis in the right lobe is clearly seen (N).

Figure 2 Photomicrograph of explanted liver from case 2 showing large areas of necrosis (N) separated from normal parenchyma (P) by bands of thick fibrous tissue.

a reduced arterial diastolic flow. He remained encephalopathic until he was transplanted. The explanted liver showed a 3 cm wide area of liver necrosis confined to the right lobe. Histologically there were wide areas of necrosis, separated from normal parenchyma by large areas of thick fibrous tissue (fig 2). There was no evidence of arterial thrombosis or other abnormality in the arterial tree or portal vein. No organism was identified from cultures of blood or tissue. Viral studies (including hepatitis A, B, C, E) were negative. Twelve months after transplantation he is anicteric and thriving.

CASE 3

A 1 year old girl was referred with fever, drowsiness, and deepening jaundice over four days. A Kasai portoenterostomy at 5 weeks of age had failed to produce satisfactory bile drainage. Although growing well with supplemental feeding, she developed signs of chronic liver disease with hepatosplenomegaly, jaundice (serum bilirubin concentration 130 $\mu\text{mol/l}$, serum aspartate transaminase 200 IU/l, albumin 32 g/l), portal hypertension, and ascites.

On admission she was treated for cholangitis as no extrahepatic site of sepsis could be identified. Doppler ultrasound showed a heterogeneous liver with a patent portal vein and reversed hepatic arterial flow in diastole. Rapid onset of grade 2–3 encephalopathy with an international normalised ratio of 2.3 and a serum aspartate transaminase of 8620 IU/l resulted in urgent liver transplantation eight days after the onset of her febrile illness.

The explanted liver showed necrosis of the entire right lobe, but no hepatic arterial or portal vein abnormality. The postoperative course was marked by rejection on day 5 and jejunal perforation on day 18. She remains well with normal liver function one year later.

Discussion

Episodes of liver necrosis as observed in these children with acute severe deterioration in liver function are not well described. To date only four cases have been reported in children with a fatal outcome in all.² The precise mechanism of liver infarction in these patients with biliary atresia and hepatic fibrosis is uncertain. Arterial hypotension in cirrhotic patients is poorly tolerated as they are abnormally dependent on

arterial rather than portal venous blood inflow.² Doppler studies in our patients demonstrated patent portal veins and reduced or reversed hepatic arterial diastolic blood flow. There were no episodes of hypotension documented in hospital to account for the necrosis. No arterial or portal vein abnormality was identified in the explanted liver. Reversed hepatic artery flow in diastole is an unusual and significant finding in these cirrhotic livers which may reflect decreased hepatic compliance and compromised flow without intervening thrombosis.

All three children were reasonably well, despite their chronic liver disease, before the onset of a febrile illness raising the possibility of an infective agent. No viral infections (hepatitis A, B, C, E, togaviruses) were identified in any of the children. *E. faecium* was isolated in case 1 within the necrotic segment, but may have been a secondary infection. Other explanations for ischaemic necrosis include compression of the lobar blood supply by regenerating nodules, reversed intrahepatic portal blood flow below threshold levels, and shunting via arteriovenous connections that has been noted in septicaemia.³ Whatever the mechanism, it is clear that liver necrosis is poorly tolerated in these children with reduced hepatic reserve.

The diagnosis should be considered in children with cirrhosis presenting with a febrile illness and rapidly deteriorating liver function. Cholangitis is common (50–80%) after portoenterostomy for EHBA and presents with fever, upper abdominal tenderness, and altered liver function.^{4,5} However, high transaminase activities, prolongation of the international normalised ratio, and progressive hepatic coma point to the diagnosis of liver necrosis. The recognition of the clinical presentation of liver necrosis in cases 1 and 2 resulted in the earlier diagnosis and transplantation of the third child. A high index of suspicion remains the most important diagnostic asset, but dynamic computed tomography perfusion scans may help. Liver biopsy is rarely possible because of the associated coagulopathy. Emergency transplantation has not been previously reported for hepatic necrosis complicating biliary atresia.⁶ This may reflect the difficulty in establishing the diagnosis and excluding infection as the cause of deterioration. Two patients reported by Gartner *et al* were listed for urgent transplantation, but both died before a suitable organ could be obtained.² Early recognition of this condition increases the time available to find a suitable graft.

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