Annotation

Extrahepatic biliary atresia

Recent developments in management

Conjugated hyperbilirubinaemia in infancy is always pathological and biliary atresia or choledochal cyst should be suspected if such jaundice persists for more than 2 weeks even if evidence of intrauterine infection, such as cytomegalovirus, has been found. Recent studies have suggested that a laparotomy to confirm or exclude a diagnosis of biliary atresia should be performed in all infants with conjugated hyperbilirubinaemia by 60 days of age providing (1) all known metabolic causes of neonatal hepatitis syndrome have been excluded (particularly α_1 -antitrypsin deficiency by Pi-typing¹); (2) percutaneous liver biopsy is consistent with extrahepatic biliary atresia; and (3) there is a faecal excretion in 72 hours of less than 10% of an injected dose of ¹³¹I-Rose Bengal. A prospective regional survey in south-east England indicates that 3 infants will develop idiopathic hepatitis for every case of biliary atresia². Laparotomy is not necessary to distinguish these two conditions.³

Atresia means 'without a hole'. In extrahepatic biliary atresia there is complete obstruction of bile flow due to obliteration or complete destruction of part or all of the extrahepatic bile ducts. This is associated with intrahepatic periductular fibrosis and marked proliferation of bile ducts leading ultimately to biliary cirrhosis with much dense fibrous tissue and scanty bile ducts. What initiates the bile duct obstruction and causes progression of the intrahepatic change is not known.

Infants with biliary atresia have normal birth-weights.³ The condition has occurred in one of identical twins.⁴ It is associated with an increased incidence of intra-abdominal vascular abnormalities⁵ and with the polysplenia syndrome.⁶ It has been found in infants who earlier in life had patent bile ducts.⁷ Where spontaneous perforation of the bile ducts occurs with low bile duct obstruction, the intrahepatic changes typical of biliary atresia do not occur.⁸

Extrahepatic biliary atresia is commonly divided into surgically correctable and noncorrectable types. The former implies that there is a segment of extrahepatic bile duct, patent up to the portahepatis,

available for direct biliary-intestinal anastomosis, whereas no such segment is identifiable in the non-correctable case. The term 'biliary hypoplasia' should not be confused with EHBA as it refers to the operative cholangiogram finding of a patent but narrow biliary tree with contrast medium flowing both into the duodenum and up into the liver. This finding is usually secondary to reduced bile flow in jaundiced infants with intrahepatic disease.

'Correctable' atresia accounts for approximately 15% of all cases but in individual series from 4% to 35% are in this category. Three types, all with occlusion of the distal common bile duct have been described.⁹ Type A may be confused with choledochal cyst, the common hepatic duct being dilated to 1.3-4.5 cm. In type B there is minimal dilatation of the common hepatic duct to 4-12 mm, while in type C the diameter is less than 4 mm. Retrospective analysis has shown satisfactory biliary drainage in types A and B.

The term 'correctable' is really a misnomer, for although a satisfactory anastomosis may be fashioned between bile duct and bowel, only a minority of cases drain bile satisfactorily and survive for an extended period. Kasai¹⁰ reported short-term survival in 25 out of 122 'correctable' cases in a collective series from Japanese hospitals. Arima *et al.*⁹ stress the importance of early surgery, satisfactory results being obtained in 7 of 12 operated on before 4 months of age, with failure in all 3 children operated on later.

'Noncorrectable' types of biliary atresia on routine microscopical examination and operative cholangiography of the extrahepatic ducts have no patent lumen available for the usual type of anastomosis. Attempts to treat this condition by partial hepatic resection, insertion of drainage tubes in the hepatic parenchyma, thoracic duct drainage to the oesophagus, and hepatic lymph drainage to the jejunum have all failed. Kasai and Suzuki¹¹ reported that transection of the remnants of the extrahepatic ducts in the region of the portahepatis frequently showed bile-containing channels of up to 300 μ m in diameter, an observation subsequently confirmed by Danks

*et al.*¹² at post-mortem dissection of the portahepatis in 4 out of 14 cases.

Kasai showed that removal of the extrahepatic bile ducts and anastomosis of a loop of bowel to the area of the portahepatis could result in bile drainage¹¹ and long-term survival.¹³ It was recommended that this procedure should be carried out before 4 months of age as delay would lead to increased intrahepatic fibrosis and cirrhosis. Bile flow occurred in 10 of the 52 cases reported.

Efforts to replicate Kasai's work were not universally successful.¹⁴ Kobayashi *et al.*¹⁵ reported bile drainage in 17 out of 55 cases, Miyata *et al.*¹⁶ in 15 out of 57 cases, and Lilley and Altman¹⁷ in 11 out of 21 cases. In these three series operation before 4 months of age was most frequently associated with satisfactory bile drainage. Odièvre *et al.*¹⁸ reported bile flow in 31 of 49 infants some of whom were successfully operated on at a later age. 5 of the 7 operated on at King's College Hospital in the last 3 years, who have had successful surgery, were operated on by 4 months of age. The most recent data from Kasai's unit⁴ suggest that if operation is carried out by 60 days of age, 80% will develop bile drainage, falling to 20% if delayed beyond 90 days.

The histological changes in the extrahepatic bile ducts at a level just below the portahepatis have been classified into three types by Gautier and her colleagues.¹⁹ Type 1 consists of connective tissue with only a few inflammatory cells, type 2 contains in addition to dense connective tissue several clusters of glands lined with cuboidal epithelium and many mononuclear and polymorphonuclear inflammatory cells, and type 3 shows narrow bile ducts with columnar epithelium and many inflammatory cells. Similar histological changes have been reported by Miyano *et al.*,²⁰ who suggest that the histological features in the extrahepatic bile ducts correlate with the degree of intrahepatic fibrosis at the time of surgery and with prognosis. Alagille²¹ reported bile drainage after portoenterostomy in 40% of cases of type 1, 60% of type 2, and 80% of type 3.

In spite of severe postoperative complications, satisfactory long-term survival does occur. Kasai⁴ reported that 17 of his patients are alive with normal physique 5 years after surgery, 5 of these patients being more than 10 years old, the eldest 22 years. A total of 48 Japanese infants have survived free from jaundice more than 5 years after surgery.

Three complications commonly occur after portoenterostomy: recurrent cholangitis, increased intrahepatic fibrosis, and portal hypertension. Liver cell carcinoma has also been described.²² Recurrent cholangitis frequently begins soon after operation. From blood cultures and liver biopsies many or-

ganisms have been identified including *E. coli*, *Klebsiella*, *Proteus*, and *Streptococcus faecalis*. The magnitude of the problem of cholangitis may be gauged from its incidence in a series of Kobayashi *et al.*¹⁵ of 50%, Miyata *et al.*¹⁶ 71%, and Valayer²³ 64%. Danks *et al.*¹² and Kasai *et al.*²⁴ related the severity of intrahepatic fibrosis to the frequency and severity of cholangitis. Repeated liver biopsies by Altman *et al.*²⁵ from children 1–2 years after the relief of jaundice showed progression of hepatic fibrosis in 8 out of 11 patients.

Portal hypertension occurs frequently in survivors, being found in 7 of 15¹⁶ and 20 of 33.²¹ 2 of these cases have already undergone portocaval shunt, but interestingly, varices assessed endoscopically have disappeared spontaneously in 5 of the anicteric patients.²¹ 7 of 36 children with extrahepatic biliary atresia treated by liver transplantation were alive 8 months to 5½ years after transplantation.²² A further 4 patients have survived for between 8 months and 3½ years. 29 died within 8 months of surgery. A number of the patients had had previous portoenterostomies. Considerable problems still exist in immunosuppression for these patients.

The introduction of portoenterostomy has clearly increased the chances of long-term survival in infants with extensive destruction of the extrahepatic bile ducts, but this is still only achieved in a minority of patients. The chances of apparent cure are increased when the operation is performed before 60 days of age. Suspected cases should be referred to centres with the necessary expertise to make an early presumptive diagnosis and to assess the condition of the bile ducts at laparotomy. We consider that the advice given by Dr. Gellis²⁶ in his influential *Year Book of Paediatrics*, 'to withhold surgery until it is certain by laboratory tests and clinical course that the case is not one of neonatal hepatitis', is not in the best interests of the patient with suspected biliary atresia, be it 'noncorrectable', 'correctable', or even choledochal cyst.

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