CASE REPORT

Pathology of common bile duct stenosis in cystic fibrosis

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Abstract

A case of cystic fibrosis complicated by common bile duct stenosis is described. Surgery successfully relieved the obstruction, but was complicated by *Candida* septicaemia. The previously unreported histological abnormalities of the common bile duct are discussed.

Patient history

A 17 year old man, presented with severe epigastric pain, radiating to the back, exacerbated by food and associated with nausea but no vomiting. Over the previous three months he had experienced intermittent bouts of pain in the same area.

Cystic fibrosis had been diagnosed at birth because of meconium ileus. A laparotomy was performed and he made an uneventful recovery. He had developed insulin dependent diabetes mellitus at the age of 14; and at 16 years, when he was transferred to the care of the adult cystic fibrosis unit, his sputum consistently grew *Pseudomonas aeruginosa*. At the time of his presentation with epigastric pain he had just reached puberty, his Swachmann Score was 75, and his Crispin Norman Score was 5.

On examination he had marked finger clubbing. He was not breathless and his chest was clear. Abdominal examination revealed mild distension, some tenderness in the epigastrium but no guarding or rebound and no masses. The bowel sounds were normal. A plain abdominal radiograph revealed only faecal loading. Haematological investigations were normal and the only abnormality of biochemical investigations was a raised alkaline phosphatase of 266 U/l. (Normal range up to 105 U/l.)

Further investigations included a normal gastroscopy and an ultrasound scan which showed a large gall bladder but no gall stones. The common bile duct and pancreas were not seen because of overlying bowel gas. An initial diagnosis of meconium ileus equivalent was suspected and the pain settled with conservative management. An oral cholecystogram as an outpatient confirmed that the gall bladder was distended. Further investigations were pre-empted when the patient was readmitted with a severe exacerbation of the same pain, associated with jaundice. On this occasion the liver function tests were markedly abnormal; bilirubin 29 mmol/l (normal up to 20 mmol/l), alkaline phosphatase 2335 U/l. Alanine aminotransferase

(ALT), 237 U/l (normal up to 40 U/l), and gamma glutamyl transpeptidase (GGT) 721 U/l (normal up to 65 U/l).

A Technecium HIDA scan showed prompt entry of isotope into the duodenum, and again showed the gall bladder to be distended. Endoscopic retrograde cholangiopancreatography (ERCP) was performed. A stricture of the intra-pancreatic portion of the bile duct was demonstrated. There was little proximal dilation and the intrahepatic ducts were normal (Fig 1).

Figure 1: Endoscopic retrograde cholangiogram showing stricture of the common bile duct.

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Figure 2: Common bile duct showing loss of surface epithelium (left) with prominent fibrosis of wall in which numerous accessory ducts are visible. (Masson Trichrome.)

In view of the radiological findings and the continued pain and jaundice it was felt that cholecystojejunostomy should be performed. The patient was judged fit for anaesthetic (FEV₁ 1.75 l FVC 3 l) and was treated perioperatively with intravenous Ceftazidime and Tobramycin to prevent exacerbations of respiratory infection.

At operation the bile duct was not easily defined because of multiple adhesions in the right upper quadrant but a cholecystojejunostomy was performed. The liver did not appear cirrhotic but a wedge biopsy was taken.

His postoperative course was complicated by an episode of meconium ileus equivalent (with classical clinical and radiographic signs), necessitating institution of parenteral nutrition through a subclavian line. Good diabetic control was achieved with continuous intravenous insulin infusion. By the 12th postoperative day the patient felt well and was pain free. The jaundice had resolved and there was improvement in the hepatic enzymes. (Alkaline phosphatase had returned to 377 U/l, ALT 14 U/l, and GGT 90 U/l).

On the 16th postoperative day he developed a swinging fever, which failed to settle after removal of the central line. Culture of both the line tip and blood grew *Candida albicans* and he was started on parenteral Fluconazole. Despite this his condition deteriorated with evidence of central nervous system infection and he died on the 36th postoperative day.

PATHOLOGY

At necropsy the clinical diagnosis of widespread candidal infection was confirmed. The cholecystojejunal anastomosis was intact. The distal common bile duct was embedded in dense fibrous tissue. Histology of the bile duct showed loss of the surface epithelium and marked mural fibrosis in which accessory ducts were prominent (Fig 2). These changes were evident from the junction of the cystic duct with the common bile duct down to the ampulla where inspissated calcified secretions were found in the lumen.

The hepatic architecture was preserved but there was mild fatty change. Most portal areas were normal; however, some showed slight

fibrosis with mild cholangiolar proliferation with inspissated concretions and a mild associated acute cholangiolitic reaction.

The latter features were felt to represent an early focal biliary cirrhosis.

Discussion

Distal common bile duct stenosis in cystic fibrosis has previously been reported,¹⁻³ but the histological abnormalities of the entire common bile duct that were found in this case have not. In one report¹ histology of the common bile duct was said to be normal, the stenosis being simply a result of pancreatic fibrosis. Despite the ERCP findings of a distal stricture in our case, it is noteworthy that the bile duct was abnormal from the origin of the cystic duct down to the ampulla, suggesting that the stricture was not simply a result of pancreatic fibrosis, but rather an intrinsic bile duct lesion.

A recent large series found a high (96%) incidence of common bile duct strictures in patients with cystic fibrosis and liver disease.⁴ Two patients were reported as having irregularly narrowed and beaded ducts resembling sclerosing cholangitis, but unfortunately histology was not available. In a Swedish centre,⁵ four patients who were specifically investigated with ERCP because of symptoms and signs suggestive of biliary tract disease were similarly found to have changes of sclerosing cholangitis.

Such findings should promote further investigation of the biliary system in cystic fibrosis and to the possible expression of 'the basic defect' of chloride impermeability in the biliary epithelium.

It has been suggested that common bile duct stenosis may play an important role in the pathogenesis of cirrhosis in cystic fibrosis.⁴ It is interesting, however, that in the four Swedish patients⁵ liver biopsy specimens revealed variable changes. Three patients showed portal abnormalities and one patient biliary cirrhosis. None had microscopic features of cholestasis, however, and in one patient, no changes were noticed over a two year observation period. As yet therefore, surgery has been recommended only on clinical rather than prognostic grounds. The former was true in this case and indeed despite grossly abnormal hepatic enzymes pre-operatively, the histological abnormalities in the liver were remarkably mild.

Two of the patients in the Swedish report,⁵ had suffered intermittent jaundice but the cause of this has not been discussed. Certainly, in our patient the second severe exacerbation of pain was associated with jaundice in the absence of any gall stone, and may have been related to cholangitis.

The fatal outcome in this case was undoubtedly the result of systemic candidiasis in a patient with the known predisposing factors of post-operative total parenteral nutrition through a central line, broad spectrum antibiotics, and diabetes mellitus.

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