Intraluminal biliary obstruction

N D Heaton, M Davenport, E R Howard

Abstract

Jaundice caused by intraluminal bile duct obstruction in infancy is rare but may occur in association with biliary sludge, inspissated bile plugs, or gall stones. Nine boys (age 2 weeks–6 months) with obstruction caused by inspissated bile (n=7) or gall stones (n=2) are presented. Haemolysis was not a factor in the patients' histories but an abnormal entry of the common bile duct into the third part of the duodenum was demonstrated in two and one had an asymptomatic haemangioma. Ultrasonography was the most useful investigation. Surgical removal of the bile duct obstruction was necessary in eight cases and included biliary tract drainage in six and cholecystectomy for changes of cholecystitis in four. Obstruction resolved spontaneously in one infant after percutaneous cholangiography. There were no postoperative complications.

Inspissated bile plug syndrome (IBPS) as a cause of neonatal obstructive jaundice is a well recognised complication of neonatal haemolysis caused by maternal rhesus and ABO blood group incompatibility.¹ The development of early exchange transfusion reduced the incidence.¹ An increase in the number of reported cases in recent years has been attributed to parenteral nutrition, diuretic treatment,² bowel dysfunction,³ and disseminated intravascular coagulation.⁴ The presence of an obstruction of the common bile duct in neonates and young infants caused by inspissated bile or gall stones in the absence of any of the above factors is unusual.⁵ Seven infants with obstruction caused by inspissated bile and two by gall stones are presented and the possible predisposing factors discussed.

Patients

Seven boys presented at a mean age of 6 weeks

(range 2 weeks–3 months) with jaundice, pale stool, and dark urine (see table 1 for patients' details). Another two boys presented at 4 and 6 months of age with obstructive jaundice secondary to stones in the common bile duct. Three of the nine had had significant obstetric complications: these included fetal distress, forceps delivery, and maternal eclampsia treated by caesarean section at 37 weeks' gestation. The mean birth weight was 3210 g (range 2400–3800 g) and the mean gestational age was 40 weeks (range 37–42 weeks). Four children developed neonatal problems including physiological jaundice that settled spontaneously, anaemia treated by blood transfusion, hypoglycaemia where there was a family history of consanguinity, and hepatic haemangiomas diagnosed on ultrasound. The hepatic haemangiomas were asymptomatic and no specific treatment was given.

All nine patients presented with a conjugated hyperbilirubinaemia. There was a wide variation in bilirubin concentration (mean 133 µmol/l, range 56–324 µmol/l), alkaline phosphatase activity (mean 917 IU/l, range 546–1963 IU/l), and aspartate aminotransferase activity (874 IU/l, range 157–179 IU/l). The haemoglobin concentration ranged from 91–122 g/l. The reticulocyte count as a percentage ranged from 1.8–4.2% and no significant haemolysis was identified.

DISIDA (technetium labelled diisopropyliminodiacetic acid) scans were performed in five patients, of whom four showed no excretion, suggesting a diagnosis of biliary atresia. One showed minimal excretion at six hours. Liver biopsy specimens taken from four patients (table 2) showed features of cholangitis and duct obstruction in two cases, cholestasis with mild portal fibrosis in one case, and bile duct proliferation in one.

Ultrasound scan results are shown in table 2. The extrahepatic biliary tree was dilated in eight cases. One child was incorrectly thought to have a choledochal cyst as the diameter of the

Table 1 Clinical details of patients with IBPS and gall stones

Patient No	Age	Symptoms	Neonatal history	Family history
			IBPS	
1	12 weeks	Jaundice	None	None
2	6 weeks	Jaundice	Forceps delivery, special care baby unit	None
3	4 weeks	Jaundice	None	None
4	2 weeks	Jaundice	Blood transfusion	Diabetes
5	10 weeks	Jaundice	Caesarean section, eclampsia, hypoglycaemia	Consanguinous
6	2 weeks	Jaundice	Capillary haemangiomas	None
7	8 weeks	Jaundice	None	None
			Gall stones	
8	6 months	Jaundice	Jaundice	None
9	4 months	Jaundice	None	None

Department of Surgery,
King's College Hospital,
Denmark Hill,
London SE5 8RX
N D Heaton
M Davenport
E R Howard

Correspondence to:
Mr Heaton.

Accepted 15 August 1991

Table 2 Findings on investigations performed

Patient No	DISIDA scan	Liver biopsy	Ultrasound scan	Percutaneous transhepatic cholangiography
1	No excretion	Cholangitis	Dilated common bile duct, dense bile	Free drainage, cystic duct into confluence of right and left hepatic duct
2	No excretion	—	Bile plug, ? Mirrizi's syndrome	—
3	—	—	Dilated common bile duct and gall bladder, inspissated bile	Obstructed lower common bile duct
4	No excretion	—	Dilated common bile duct (8 mm), ? choledochal cyst	—
5	? Excretion 6 hours	Cholestasis, bile duct proliferation	Normal	—
6	No excretion	—	Dilated common bile duct and gall bladder, haemangiomas	—
7	—	Cholangitis, features of duct obstruction	Dilated biliary tree	Obstructed lower common bile duct
8	—	Biliary cholestasis, mild portal fibrosis	Gall bladder stones, dilated common bile duct	Stones in cystic duct and common bile duct
9	—	—	Common bile duct stones	—

Table 3 Details of treatment and outcome

Patient No	Operation performed	Findings at operation	Results of operative cholangiogram	Procedure	Follow up (months)
1	No	(spontaneous resolution)	—	—	—
2	Yes	Dilated common bile duct, chronically inflamed gall bladder	Filling defect in cystic duct	Cholecystectomy, ECBD, T-tube	6, well
3	Yes	Tense common bile duct and gall bladder, bile plug removed	Bile plug, ? papillary stenosis	Cholecystectomy, ECBD, T-tube, sphincteroplasty	1, well
4	Yes	Dilated common bile duct and gall bladder, bile plug and debris	Dilated common bile duct, common bile duct into third part duodenum	ECBD, T-tube, dilatation of ampulla	1, well
5	Yes	Inspissated bile plug	Normal	Cholecystostomy, saline flush	1, well
6	Yes	Haemangiomas, two hepatic arteries, inspissated bile	Normal	Cholecystostomy, saline flush	1, well
7	Yes	Dilated biliary tree, inspissated bile	Common bile duct into third part duodenum	Choledochoduodenostomy, ECBD, sphincteroplasty	1, well
8	Yes	Stones in gall bladder and common bile duct	Stones in common bile duct	Cholecystectomy, sphincteroplasty	24, well
9	Yes	Stones in common bile duct	Stones in common bile duct	Cholecystectomy, ECBD, T-tube, sphincteroplasty	15, well

ECBD, exploration of the common bile duct.

common bile duct was 8 mm. Stones were correctly identified in the common bile duct and gall bladder in two patients. Percutaneous transhepatic cholangiograms were performed in four patients and one child settled spontaneously after this procedure. Evidence of distal obstruction of the common bile duct was present in the other three (see figure).

Eight of the nine patients were subsequently explored and the diagnosis of IBPS (n=6) and gall stones (n=2) confirmed. Operative cholangiograms via the gall bladder showed abnormal entry of the common bile duct into the third part of the duodenum in two patients with IBPS. Details of operative findings, treatment, and follow up are given in table 3. Four patients with thick walled or oedematous gall bladders underwent cholecystectomy (both patients with stones and two with IBPS). The common bile duct was explored in seven patients, four had sphincteroplasties, one had a choledochoduodenostomy, and one had dilatation of the ampulla. Interestingly a normal gall bladder was found in one child with stones in the common bile duct. T-tube or cholecystostomy drainage was used in six patients. Postoperative cholangiography was used to exclude residual obstruction before removal of the drainage catheter or T-tube 10–21 days after surgery.

Percutaneous transhepatic cholangiogram showing dilated extrahepatic bile ducts secondary to inspissated bile plug in the distal common bile duct.

Jaundice resolved in all nine patients and there were no postoperative complications. Patient follow up ranged from one month to two years with a mean of six months.

Discussion

Intraluminal biliary obstruction is a rare cause

of jaundice in early life,^{6,7} and the incidence may be estimated indirectly by a comparison with the 280 patients seen during the same time interval at this hospital with biliary atresia (incidence 1:15 000 live births).

Ladd described five patients with obstructive jaundice caused by a mechanical obstruction of the common bile duct by plugs of thickened bile.⁸ He believed that the condition was secondary to distal common bile duct stenosis. Hsia *et al* investigated 156 infants with obstructive jaundice of whom 60% had biliary atresia.⁹ Fifteen per cent had inspissated bile plug syndrome secondary to erythroblastosis fetalis and 19% had IBPS of unknown aetiology. It was thought that the syndrome was caused by a combination of factors that included small bile ducts, hepatic immaturity, dehydration, and thickened bile secretions. However, this group included patients with polycystic kidney disease and congenital hepatic fibrosis and this may have been a factor. Five patients of these patients with IBPS went on to develop cirrhosis.¹⁰

Haemolysis because of rhesus or ABO incompatibility was a significant factor in many of the early case reports,^{11,12} and the development of early exchange transfusion as an effective form of treatment led to a sharp reduction in numbers. More recently the use of prolonged parenteral nutrition has been associated with IBPS,¹³ cholestasis,^{14,15} biliary sludge,¹⁶ and gall stones.¹⁷ It has been proposed that a tenacious, viscid bile occurs either as a result of parenteral nutrition or secondary to enteral failure. Blood transfusion, dehydration, and diuretic treatment may cause an increase in the bilirubin/bile concentration leading to oversaturation.^{2,18} Many of these infants have other problems such as prematurity, respiratory distress syndrome, necrotising enterocolitis, or intra-abdominal sepsis and intravascular coagulopathy.^{4,13,14,19,20} Cystic fibrosis has also been implicated in the development of IBPS and cholelithiasis, particularly in small and premature infants.²¹

Lilly and Sokol considered that neonatal obstruction of the common bile duct in the absence of any of these factors was unusual.⁶ In our seven patients with intraluminal biliary obstruction possible contributory factors included forceps labour (n=1), neonatal jaundice (n=1), blood transfusion (n=1), consanguinity, hypoglycaemia, and caesarean section (n=1), and hepatic haemangioma (n=1). Bruising after forceps or caesarean delivery can produce hyperbilirubinaemia after breakdown of blood and immature hepatocyte function may be responsible for an impaired conjugation of bile acids. Undetected haemolysis associated with the hepatic haemangioma may have caused bilirubin saturation of bile in one of our cases. All nine infants were boys, but no sex difference has been reported in the predisposition to intraluminal biliary obstruction.

Abnormalities of the extrahepatic biliary tree²² and cholecystitis²³ have been associated with gall stone formation in children. Congenital anomalies of the lower common bile duct particularly anomalous pancreaticobiliary junc-

tions have recently been described in cases of IBPS.²⁴ An abnormal entry of the lower common bile duct into the third part of the duodenum was demonstrated in two of our patients. Abnormal entry of the lower common bile duct may be associated with abnormal sphincter formation and function, and at operation the common bile duct was dilated secondary to a distal functional obstruction. No predisposing factors were found in two children. It may be difficult to exclude biliary atresia in this group of patients. Clinical examination (and testing of stool) may not differentiate between the two groups. Liver function tests confirm an 'obstructive' picture, but the concentration of conjugated bilirubin and alkaline phosphatase and γ -glutamyltransferase activities can be higher than expected for infants with biliary atresia. Radionuclide scans pointed to the diagnosis of biliary atresia, but it has been suggested that a repeat examination will show excretion in IBPS.²⁵

Ultrasound scan was helpful in identifying a dilated extrahepatic biliary tree, biliary sludge/plugs and stones, although one patient with a common bile duct of 8 mm diameter was mistakenly diagnosed as having a choledochal cyst. Endoscopic retrograde cholangiopancreatography, although not performed in these patients, is now being assessed as a diagnostic test for biliary atresia.²⁶ In future it may identify patients with intraluminal biliary obstruction and anomalous junctions of the pancreaticobiliary ducts.

Liver biopsy specimens from infants in this series showed evidence of obstruction. The features (which included canalicular bile plugs, bile duct proliferation, and giant cell transformation) are non-specific, however, and represent a common type of response to bile duct obstruction in this age group. Other causes of conjugated hyperbilirubinaemia in the neonate include infection, metabolic disorders, or inflammatory disease of the liver.

A small number of patients with equivocal tests for biliary atresia come to laparotomy. At operation it is usually simple to differentiate between atresia and intraluminal biliary obstruction. Cholangiography is performed via the gall bladder to demonstrate the biliary tree. Brown has described successful irrigation of the common bile duct at surgery using a mucolytic agent, N-acetylcysteine, which has been used to reduce the viscosity of pulmonary mucus.²⁷ Endoscopic or percutaneous transhepatic cannulation and flushing of the common bile duct may therefore offer a satisfactory non-operative treatment for this condition. Cholecystectomy is recommended in children with thickened or inflamed gall bladders and gall stones within the gall bladder.

Gall stones are a rare cause of jaundice in infancy, but like IBPS the incidence appears to be increasing. The use of ultrasound to investigate children may account for some of this increase.²⁸ In a prospective ultrasound study of neonates receiving total parenteral nutrition, 44% were found to have biliary sludge and 5% developed stones.²⁹ Haemolytic anaemias are the commonest cause of gall stones in children,

and most are 10 to 13 years old at presentation.³⁰ Other causes include ileal resection, Crohn's disease,²⁰ biliary tract anomalies,⁵ and prolonged total parenteral nutrition and frusemide treatment.² The two patients reported in this paper were older (4 and 6 months) than our group with IBPS, but they were young in comparison to other reports of children with gall stones. Spontaneous resolution of both IBPS and gall stones has been reported.^{31 32}

There appears to be a range of clinical problems associated with increased breakdown of bilirubin, failure of secretion, and oversaturation of bile, which presents with obstructive jaundice in the young child. Canalicular bile plugs and cholestasis represent the commonest response and appear to be reversible. Inspissated bile plugs in the extrahepatic biliary tree may represent the next stage and occasionally the child will develop stones.

- 1 Lightwood R, Bodian M. Biliary obstruction associated with icterus gravis neonatorum. *Arch Dis Child* 1946;21:209-17.
- 2 Whittington PF, Black DD. Cholelithiasis in premature infants treated with parenteral nutrition and frusemide. *J Pediatr* 1980;97:647-9.
- 3 Benjamin DR. Cholelithiasis in infants. The role of total parenteral nutrition and gastrointestinal dysfunction. *J Pediatr Surg* 1982;17:386-9.
- 4 Gur I, Vinograd I, Dgani Y, Arad I. Jaundice due to inspissated bile following disseminated intravascular coagulation. *Isr J Med Sci* 1986;22:448-50.
- 5 Lilly JR. Common bile duct calculi in infants and children. *J Pediatr Surg* 1980;15:577-80.
- 6 Lilly JR, Sokol RJ. On the bile sludge syndrome or is total parenteral nutrition cholestasis a surgical disease? *Pediatrics* 1985;76:992-3.
- 7 Balistreri WF. Neonatal cholestasis. *J Pediatr* 1985;106:171-84.
- 8 Ladd WE. Congenital obstruction of the bile ducts. *Ann Surg* 1935;102:742-51.
- 9 Hsia DY, Patterson P, Allen FH, Diamond LK, Gellis SS. Prolonged obstructive jaundice in infancy. General survey of 156 cases. *Pediatrics* 1952;10:243-51.
- 10 Hsia YD, Gellis SS. Prolonged obstructive jaundice in infancy. *Am J Dis Child* 1963;85:13-9.
- 11 Oppe TE, Valaes T. Obstructive jaundice and haemolytic disease of the newborn. *Lancet* 1959;i:536-9.
- 12 Dunn PM. Obstructive jaundice and haemolytic disease of the newborn. *Arch Dis Child* 1963;38:54-61.
- 13 Enzenauer RW, Montrey JS, Barcia PJ, Woods J. Total parenteral nutrition cholestasis: a case of mechanical biliary obstruction. *Pediatrics* 1985;76:905-8.
- 14 Rodgers BM, Hollenbeck JJ, Donnelly WH, Talbert JJ. Intrahepatic cholestasis with parenteral alimentation. *Am J Surg* 1976;131:149-55.
- 15 Touloukian RJ, Seashore JH. Hepatic secretory obstruction with total parenteral nutrition in the infant. *J Pediatr Surg* 1975;10:353-60.
- 16 Bowen A. Ultrasound of the normal neonatal gallbladder. *Diagnostic Imaging in Clinical Medicine* 1984;53:231-6.
- 17 Roslyn JJ, Bergquist WE, Pitt HA, et al. Increased risk of gallstones in children receiving total parenteral nutrition. *Pediatrics* 1983;71:784-9.
- 18 Bernstein J, Braylan R, Brough AJ. Bile plug syndrome: a correctable cause of obstructive jaundice in infants. *Pediatrics* 1969;43:273-6.
- 19 Bernstein J, Chang CH, Brough AJ, Heidelberger M. Conjugated hyperbilirubinaemia associated with parenteral nutrition. *J Pediatr* 1977;90:361-7.
- 20 Pellerin D, Bertin P, Nihout-Fekete C, Riccour C. Cholelithiasis and ileal pathology in childhood. *J Pediatr Surg* 1979;10:35-41.
- 21 Davies C, Daneman A, Stringer DA. Inspissated bile in a neonate with cystic fibrosis. *J Ultrasound Med* 1986;5:335-7.
- 22 Moosa A. Cholelithiasis in childhood. *J R Coll Surg Edinb* 1973;18:42-6.
- 23 Morales L, Taboada E, Toledo L, Radrigan W. Cholecystitis and cholelithiasis in children. *J Pediatr Surg* 1967;2:565-8.
- 24 Kochhar R, Nagi B, Chawla S, et al. The clinical spectrum of anomalous pancreato-biliary junction. *Surg Endosc* 1989;3:83-6.
- 25 Spivak W, Sarkar S, Winter D, Glassman M, Donlan E, Tinker KJ. Diagnostic utility of hepatobiliary scanning with 99m Tc-DISIDA in neonatal cholestasis. *J Pediatr* 1987;110:855-61.
- 26 Wilkinson ML, Mieli-Vergani G, Ball C, Portmann B, Mowat AP. Endoscopic retrograde cholangiopancreatography in infantile cholestasis. *Arch Dis Child* 1991;66:121-3.
- 27 Brown DM. Bile plug syndrome: successful management with a mucolytic agent. *J Pediatr Surg* 1990;25:351-2.
- 28 Schirmer WJ, Grisoni ER, Ganderer MWL. The spectrum of cholelithiasis in the first year of life. *J Pediatr Surg* 1989;24:1064-7.
- 29 Avni EF, Matos C, Gansbeke D, et al. Atypical gallbladder content in neonates: ultrasound demonstration. *Ann Radiol (Paris)* 1986;29:267-73.
- 30 MacMillan RW, Schullinger JN, Santulli TV. Cholelithiasis in childhood. *Am J Surg* 1974;127:689-92.
- 31 Nabil NJ, Anderson KD, Eichelberger M, et al. Cholelithiasis in infancy: resolution of gallstones in three of four infants. *J Pediatr Surg* 1986;21:567-9.
- 32 Holgersen LO, Stolar C, Berdon WE, Hilfer C, Levy JS. Therapeutic and diagnostic implications of acquired choledochal obstruction in infancy: spontaneous resolution in three infants. *J Pediatr Surg* 1990;25:1027-9.