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Post-Surgical Abnormalities of the Duodenum Leading to Pancreaticobiliary Disease in Children

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Congenital duodenal obstruction is caused by duodenal atresia or stenosis, annular pancreas, and duodenal webs. It occurs as commonly as 1 per 5000–10,000 live births and is frequently associated with other congenital anomalies including pancreatic, intestinal, and biliary anomalies.[1,2] Long-term follow-up after surgical repair has demonstrated the development of morphological and functional changes, including megaduodenum, duodenal diverticula, and functional obstruction.[3] Duodenal diverticula leading to biliary disease is a well-established phenomenon in adults[4–6] but has not been well established in pediatric literature. We report 8 pediatric patients with congenital duodenal obstruction who later developed pancreaticobiliary disease.

METHODS

Pediatric patients (under 18 years) with history of duodenal obstruction who subsequently developed pancreaticobiliary disease were identified at 2 large pediatric hospitals between January 1994 and December 2018. One patient included in this series is also in the INSPPIRE cohort. Institutional review board approval was obtained at each participating institution.

PATIENTS

Patient 1

A 3-year-old female with trisomy 21, duodenal web status postduodenoplasty at 19 days of life (DOL) presented with abdominal pain and hepatomegaly. Her diagnostic evaluation included percutaneous cholangiogram, abdominal magnetic resonance imaging (MRI), and abdominal ultrasound, which showed marked dilation of the biliary tree with abundant sludge, as well as hepatic AV malformation. Laboratory evaluation demonstrated a peak aspartate transaminase 174 U/L (10–30 U/L), alanine transferase 190 U/L (10–30 U/L), conjugated bilirubin 0.9 mg/dL (<0.3 mg/dL), and gamma-glutamyl transferase 769 U/L (3–40 U/L) with normal amylase and lipase. Liver biopsy for persistent elevation of aminotransferase showed mild intralobular fibrosis on trichrome stain, as well as portal fibrosis with scattered neutrophils involving the bile duct epithelium, suggestive of cholangitis and biliary obstruction. Endoscopic retrograde cholangiopancreatography (ERCP) was performed at age 8, which demonstrated a normal common bile duct (CBD), normal gallbladder, and a beaded appearance of the intrahepatic ducts suggestive of recurrent cholangitis. A magnetic resonance cholangiopancreatography (MRCP) performed 4 years later for recurrent symptoms revealed a dilated proximal duodenum, beading of the intrahepatic biliary tree, and a new distal CBD stricture. She underwent an upper endoscopy for concern for upper gastrointestinal bleeding, during which eccentric duodenal dilatation, resulting in a diverticulum-like area, and a distorted ampulla were seen (Fig. 1). Over the following 3 years, patient developed symptoms and signs of portal hypertension, likely due to abnormal hepatic blood flow from hepatic vascular malformation. She had multiple life-threatening episodes of upper GI bleeding, and ultimately received a liver transplant. The explanted gallbladder was noted to have a normal morphology. Her posttransplant course was uncomplicated, and she has remained well 8 years posttransplant.

Patient 2

A 7-year-old male with trisomy 21, duodenal web s/p duodenostomy at 1 year of age, history of acute lymphoblastic leukemia in remission (treated with POG AALL0331 Regimen SR-High [mercaptopurine, cytarabine, daunorubicin, methotrexate, dexamethasone, vincristine, asparaginase, doxorubicin, cyclophosphamide, thioguanine]) who presented with a 4-week history of diarrhea and decreased oral intake. Abdominal ultrasound showed ascites, hepatomegaly, and a dilated CBD to 7 mm without cholelithiasis or a defect within the CBD. MRCP confirmed mild stenosis of the hepatic duct bifurcation with slightly greater involvement at the origin of the right hepatic duct and a markedly dilated duodenum (Fig. 2). He had no history of hepatic complications during acute lymphoblastic leukemia treatment. Due to persistent elevation in aminotransferases with peak aspartate transaminase of 360 U/L (15–40 U/L), alanine transferase 430 U/L (10–35 U/L), gamma-glutamyl transferase 73 U/L (13–25 U/L), and normal-conjugated bilirubin, patient underwent a liver biopsy that showed features consistent with extrahepatic biliary obstruction with biliary cirrhosis, extensive bile duct proliferation, and patchy portal inflammation seen on pathology. An ERCP was deferred due to severe cytopenias as well as subsequent improvement in clinical status. He subsequently developed portal hypertension, thought to be secondary to chronic biliary obstruction and prior chemotherapy. Three years later, a repeat MRCP demonstrated beading and dilatation of the hepatic duct bifurcation and intrahepatic bile ducts, worse on the right side. Repeat upper endoscopy demonstrated 1 grade IV and 2 grade III esophageal varices, marked portal gastropathy, and a duodenum with a slit-like ampulla. MRV abdomen showed chronic portal vein occlusion. He was transitioned to adult care for management of portal hypertension.

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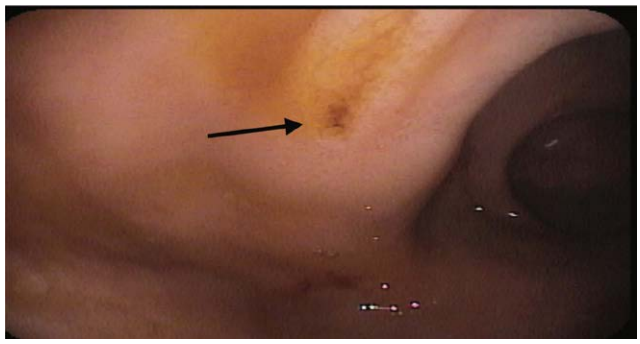

FIGURE 1. Duodenal dilation with distorted ampulla seen in patient 1.

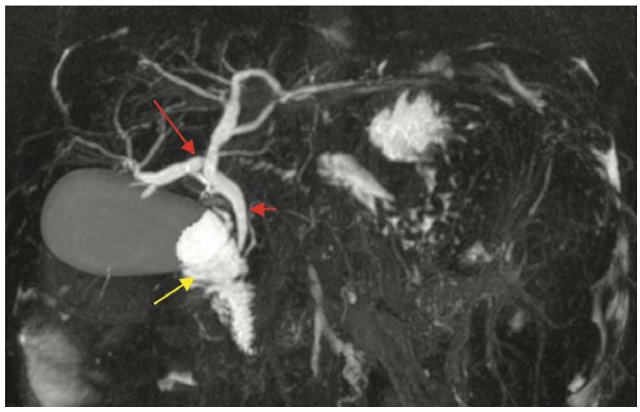

FIGURE 2. MRCP showing mild stenosis of the hepatic duct bifurcation with slightly greater involvement at the origin of the right hepatic duct (red arrows), and a markedly dilated duodenum (yellow arrow) in patient 2. MRCP, magnetic resonance cholangiopancreatography.

Data for patients 3–8 are presented in Table 1.
Selected results from all patients are presented in Table 2.

DISCUSSION

Duodenal atresia can result from the failure of the bowel to recannulate during weeks 8–10 of gestation, or from obstruction due to annular pancreas, in which a ring of pancreatic tissue surrounds the descending portion of the duodenum, thereby causing a mechanical obstruction.[2] Late complications after surgical repair of duodenal obstruction include duodenal dilation and altered motility.[7] In a review of 169 patients status post repair of duodenal obstruction over 30 years, Escobar et al found cases of megaduodenum occurring up to 18 years postoperatively.[8]

Pancreaticobiliary disease associated with duodenal obstruction or occurring late after surgical correction is sparsely documented in pediatric literature. Spigland et al followed 33 neonates who underwent repair for congenital intrinsic duodenal obstruction over 10 years, in which 1 patient had a liver biopsy suggestive of extrahepatic biliary obstruction and periportal fibrosis, but was lost to follow-up.[7] Various case reports have described pediatric patients who developed cholelithiasis or CBD stones up to 16 years after surgical repair for duodenal atresia.[9,10] Urushihara et al documented 6 children with annular pancreas s/p duodenoduodenostomy or gastrojejunostomy for duodenal obstruction who later developed complications such as recurrent pancreatitis, choledochal dilation, pancreatic duct stones, bile duct dilation, choledochocele.[11] In our case series, we describe 8 patients, 7 of whom underwent surgical correction of duodenal obstruction in infancy and 1 of whom was found to have complete annular pancreas resulting in duodenal obstruction.

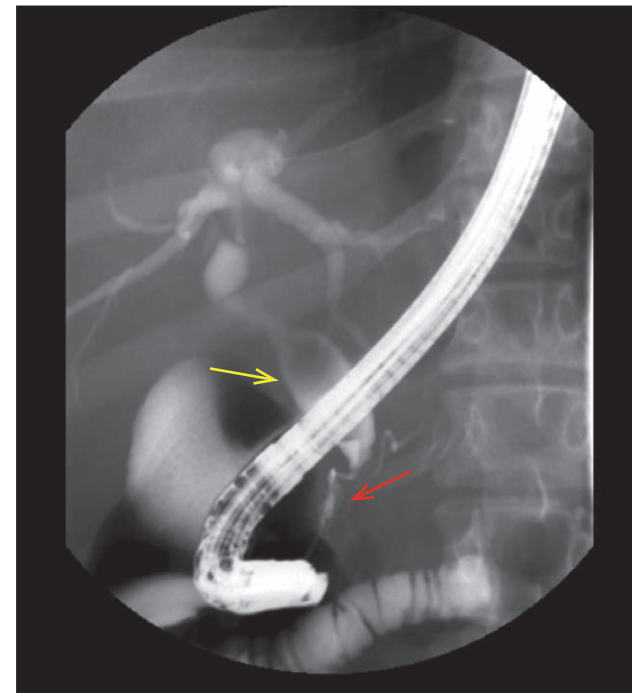

FIGURE 3. Cholangiogram from ERCP of patient 3 showing dilated CBD (yellow arrow) proximal to a long suprapapillary stricture (red arrow). CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography.

It is possible that pancreaticobiliary disease associated with duodenal obstruction is due to persistent duodenal dilation and altered anatomy after surgical repair. Although complete surgical records were not available for all patients, there were no known reports of vascular injury or postoperative leaks to suggest biliary injury, which lowers the suspicion of biliary or vascular injury leading to the pancreaticobiliary abnormalities seen in these patients. Duodenal dilation, which is seen in 4 patients, could result in hypomobility and stasis in the upper intestine. This could lead to intestinal bacterial overgrowth, resulting in calcium bilirubinate stones in the biliary tree.[12] Tenting and stretching of the ampulla from abnormal duodenal anatomy or injury during repair may have resulted in malfunction of the sphincter of Oddi, which can lead to the formation of bile duct stones.[13] On endoscopy, 5 patients were noted to have abnormal duodenal anatomy with distortion of the ampulla. While patient 6 did not undergo surgical repair, her ampulla was noted to be at the edge of the duodenal stenosis, which likely affected pancreaticobiliary flow. We hypothesize that these changes may lead to recurrent ascending cholangitis and stone formation, which consequently results in inflammation and stricturing in the CBD as seen in our case series. While this pattern of recurrent inflammation leading to stricture formation has characteristics similar to secondary sclerosing cholangitis,[14,15] this has not been well-characterized in pediatric patients.

Finally, 3 patients were treated for mild to moderate pancreatitis based on Atlanta criteria. Biliary obstruction can lead to pancreatitis, and functional pancreatic sphincter dysfunction has been associated with pancreatitis.[16,17] All 3 of these patients had duodenal obstruction caused by annular pancreas, which has been associated

TABLE 1. Data for patients 3–8

Patient	Age and Gender	Comorbid Conditions	Form of Duodenal Obstruction and Repair	Presentation	Peak Labs			Imaging Type	Imaging Results	Procedure	Procedure Results	Outcome
					Lab	Value	Ref					
3	12F	Trisomy 21	Duodenal atresia s/p duodenojejunostomy on DOL 3	Abdominal pain; jaundice	AST ALT GGT Cbili	161 U/L 252 U/L 1044 U/L 7.2 mg/dL	10–30 U/L 10–30 U/L 14–25 U/L < 0.35 mg/dL	AUS	Multiple dilated intrahepatic biliary ducts; CBD dilation to 1.5 cm with 2 impacted stones (1.5 cm and 1.0 cm)	ERCP	Dilatation of proximal second part of duodenum in diverticulum fashion; Distorted and stretched papilla with no overlying folds; Two large stones in dilated CBD proximal to long suprapapillary stricture (Fig. 3). Three black and yellow stones removed.	Cholecystectomy and end-to-side choledochoduodenostomy due to persistent obstruction
4	5M	Prematurity (27 weeks)	Annular pancreas s/p duodenojejunostomy on DOL 14	Pancreatitis	Lipase Amylase	17,560 U/L 2235 U/L	7–60 U/L 21–101 U/L	Abdominal CT MRCP (age 6)	2.4 mm stone at the head of the pancreatic duct; Cystic structure along anterior aspect of distal body of pancreas Prominence of the pancreatic duct with side branch dilatation throughout body and tail of pancreas Prominence of pancreatic duct with side branch dilatation throughout the pancreatic body and tail; stable appearance of cystic structure of anterior distal pancreas	ERCP (age 6)	Abnormal duodenal anatomy; Ampulla unable to be identified	Close monitoring with serial ultrasounds and annual MRCPs with imaging results stable at this time
5	0.6F	Prematurity (32 weeks) Heterotaxy AV canal defect	Annular pancreas s/p unspecified surgical repair on DOL 2	Incidental findings on pre-surgical ultrasound	GGT	32 U/L	3–22 U/L	AUS (age 0.6 years) MRCP (age 1.5) Hepatobiliary scan (age 6)	Cholelithiasis, choledocholithiasis with mild central and extrahepatic ductal dilatation; CBD 4.4 mm Cholelithiasis, choledocholithiasis, CBD dilation 11 mm, progressive intrahepatic and extrahepatic ductal dilatation. Normal pancreatic duct and parenchyma Normal	ERCP deferred due to cardiac status	N/A	Close monitoring with serial ultrasounds and annual MRCPs with imaging results stable at this time
6	11F	None	Annular pancreas; No surgical repair	Pancreatitis	Lipase	22,000 U/L	7–60 U/L	MRI (age 13)	Annular pancreas with narrowing at second portion of duodenum; no biliary or pancreatic ductal dilation	EGD (age 13)	Post-bulbar stenosis with superficial erosive changes in the bulb around stenosis; Ampulla at 9 o'clock at the back edge of stenosis	Close monitoring with serial ultrasounds and annual MRCPs with imaging results stable at this time
7	5F	Renal dysplasia s/p renal transplant	Annular pancreas s/p surgical repair (unspecified)	Recurrent pancreatitis	Lipase	>10,000 U/L	7–60 U/L	MRCP (age 8)	Stricture in ventral duct of Wirsung proximal to its orifice at the ampulla of vater. Distended 1st and second portions of the duodenum, possible short segment of mild ductal ectasia right of merging of CBD and pancreatic duct	Multiple ERCPs	N/A	Lost to follow-up
8	17M	None	Duodenal atresia s/p repair (unspecified) on DOL 30	Abdominal pain; Nausea; Vomiting	Lipase	987 U/L	7–160 U/L	MRI	Dilated pancreatic duct (6 mm), Area of calcification in the pancreatic head, altered duodenal anatomy with diverticulum	ERCP with pancreatic sphincterotomy	Distorted ampulla of vater; Removal of copious debris, two large, white pancreatic stones	Lost to follow-up

DOL, day of life; AST, aspartate transaminase; ALT, alanine transaminase; GGT, gamma-glutamyl transferase; Cbili, conjugated bilirubin; AUS, abdominal ultrasound; ERCP, endoscopic retrograde cholangiopancreatography; CBD, common bile duct.

TABLE 2. Selected results

Time to presentation with biliary complications (years)	Median	6
	Mean	7.6
Outcomes		
Endoscopic intervention	62.5%	(5/8 ERCP)
Surgical intervention	25.0%	(1/8 liver transplant) (1/8 choledochoduodenostomy)
Duration of follow-up following diagnosis (years)	Range	1–18
	Median	7
	Mean	8.13

with chronic pancreatitis in children; however, the cause of pancreatitis in annular pancreas remains obscure.[18]

In conclusion, altered duodenal anatomy seen in duodenal obstruction may lead to the obstruction of the pancreaticobiliary tree and subsequent development of pancreaticobiliary disease. More studies are needed to determine long-term risks of patients with altered duodenal anatomy in children.

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