Chronic obstructive pancreatitis due to a pancreatic cyst in a patient with autosomal dominant polycystic kidney disease

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Abstract

Background—Autosomal dominant polycystic kidney disease, the most frequent inherited polycystic disease, is a systemic disorder characterised by the development of numerous and bilateral kidney cysts leading to chronic renal failure. Extrarenal cysts are located mainly in the liver but also in various organs including the pancreas. To our knowledge, complications of pancreatic cysts in this disease have never been reported.

Patient—The first case of painful chronic obstructive pancreatitis due to a true pancreatic cyst in a patient with autosomal dominant polycystic kidney disease is reported. Abdominal transparietal and endoscopic ultrasonography, computed tomography, and endoscopic retrograde cholangiopancreatography showed a cystic lesion in the body of the pancreas associated with upstream dilatation of the main pancreatic duct. Intraoperative ultrasonography before and after cyst fluid aspiration, and pancreatography and pathological examination of the resected distal pancreas confirmed that both main pancreatic duct enlargement and chronic pancreatitis were caused by a benign cyst.

Conclusion—Chronic obstructive pancreatitis should be added to the extrarenal complications of autosomal dominant polycystic kidney disease.


Case report

A 36 year old white woman was admitted after three months of epigastric and left upper quadrant abdominal pain radiating to the back and the left shoulder. ADPKD with liver involvement had been diagnosed at the age of 24 on systematic familial screening. She had mild hypertension which was treated by perindopril. She was not taking any other drugs, and had no history of abdominal injury, gallstones, or chronic alcohol intake.

Physical examination showed abdominal left upper quadrant tenderness and palpable kidneys. High levels of serum amylase (ranging between 4 and 5 times the upper limit of normal values (N)), serum lipase (ranging between 3 N and 11 N), and urinary amylase (ranging between 2.5 N and 5 N) were found. Routine laboratory tests (including calcium, phosphorus, triglycerides, blood urea nitrogen, creatinine, and bilirubin, and amylase, γ-glutamyltransferase, alkaline phosphatase and lactate dehydrogenase levels) were repeatedly normal throughout the hospital stay. Carcinoembryonic antigen (CEA) and carbohydrate antigen 19–9 (CA19–9) levels were normal (<5 ng/ml and <37 U/ml respectively).

Abdominal ultrasonography showed enlarged polycystic kidneys and two cysts in the liver. In addition, it disclosed an irregular dilatation of the main pancreatic duct (6 mm in diameter) in the body and tail of the pancreas, which was considered to be due to compression by a corporeal cystic lesion measuring 14 mm in diameter. No gallstone or cholelithiasis was seen. Abdominal computed tomography (fig 1) and endoscopic ultrasonography (fig 2) confirmed the ultrasonographic data and ruled out pancreatic calcifications or biliary tract abnormalities. Endoscopic retrograde cholangiopancreatography showed a stop of the main pancreatic duct in the body. The cystic lesion was not opacified despite high pressure injection of contrast medium attested by acinarisation of the pancreas, suggesting a...
lack of communication with the pancreatic ducts. The main pancreatic duct was normal in the head and in the proximal portion of the body (fig 3). The common bile duct was normal. No calculi were seen in the biliary tree or gall bladder. Microscopic examination of the bile did not show calcium bilirubinate granules or cholesterol crystals.

The patient underwent a laparotomy to exclude the possibility of a pancreatic tumour. Surgical examination showed a cystic lesion of the pancreatic body measuring 15 mm in diameter. The head and proximal portion of the body of the pancreas appeared normal. By contrast, the remaining distal portion of the gland appeared firm and irregular, an aspect suggestive of chronic pancreatitis. Intraoperative ultrasound examination was performed and showed direct compression of the main pancreatic duct by the cyst, markedly decreasing after aspiration of the cyst fluid (fig 4). The cyst fluid was haemorrhagic. Cyst fluid analysis showed elevated levels of amylase (5819 U/l), lipase (37 650 U/l), CEA (36 ng/ml), and CA19–9 (5000 U/ml). Distal pancreatectomy with splenic conservation was performed. Pancreatography of the resected specimen showed a slightly enlarged main pancreatic duct without stenosis or morphological abnormalities (fig 5).

Histological examination of the resected pancreas showed a benign pancreatic cyst entirely lined by a cuboidal epithelium with no atypia. Mucin stains (Alcian blue and periodic acid-Schiff) were negative. Mild dilatation of the main pancreatic duct and mild fibrosis with foci of moderate inflammation were identified near the cyst and in the distal pancreatic parenchyma, a pattern consistent with chronic obstructive pancreatitis. By contrast, pancreatic parenchyma downstream of the dilatation was strictly normal. There were no pancreatic calcifications (fig 6).

The final diagnosis was chronic obstructive pancreatitis due to compression of the main pancreatic duct by a pancreatic cyst in a patient with ADPKD. Postoperative outcome was uneventful. After four years of follow up, the patient remained asymptomatic, and there has been no evidence of cyst recurrence in periodic ultrasonographic examinations.

**Discussion**

We report here the first case of complicated pancreatic cyst during the course of ADPKD. Pancreatic cysts represent the second extra-renal cystic manifestation of ADPKD after liver cysts, affecting about 10% of patients with this disease. 2 3 7 Pancreatic cysts are small (≤ 8 mm in diameter), and most of them are only
seen on microscopic examination. This fact may explain why they do not contribute to morbidity and mortality in large series of patients with ADPKD.

The occurrence of abdominal, flank, or back pain in about 60% of patients with ADPKD is usually considered to be a consequence of kidney or liver cysts. Chronic renal failure, which affects approximately 45% of patients with ADPKD by the age of 60, may result in a non-specific and usually mild increase in serum amylase levels. In the case reported here, repeatedly elevated amylase and lipase levels and normal renal function suggested that abdominal pain was caused by pancreatic disease.

The cyst did not communicate with the pancreatic ducts. Likewise, as ADPKD kidney or liver cysts enlarge, they lose their connection from renal tubules or the biliary tract. Acute severe pain in ADPKD is often due to haemorrhage or infection of kidney or liver cysts. In this patient, intracystic haemorrhage, suggested by the aspect of cyst fluid, may have led to rapid growth of the cyst which, secondary to main pancreatic duct compression, resulted in chronic obstructive pancreatitis.

Fibrosis and inflammation are common findings in ADPKD renal and extrarenal lesions, such as colonic diverticulosis or arterial aneurysms, and are thought to be related to extracellular matrix abnormalities and cytokine activation. In this case however, intraoperative ultrasonographic findings before and after aspiration of cyst fluid, pre- and post-operative pancreatographic findings, and pathological examination of the pre- and post-cyst resected pancreas clearly showed that both main pancreatic duct dilatation and chronic obstructive pancreatitis were caused by the cyst.

Although the clinical history did not support the diagnosis of a malignant lesion, neither imaging findings nor cyst fluid analysis were sufficiently accurate to exclude the possibility that this unilocular cyst was a cystic neoplasm or an intraductal neoplasm causing obstructive pancreatitis and pseudocyst. Whereas cholangiocarcinomas and adenomas of the ampulla of Vater have been described in ADPKD, benign or malignant pancreatic tumours have never been reported in this disease. By contrast, several cases of complicated cysts and malignant neoplasms have been reported in von Hippel-Lindau disease, another autosomal dominant polycystic disease involving the kidneys and the pancreas. Preoperative fine needle aspiration cytology or intraoperative biopsy with frozen section study of the cyst wall may help in the differential diagnosis between cystic neoplasms from pseudocysts if epithelial cells are found. In fact, an epithelial lining is also present in true cysts, and co-existence of benign and malignant appearing epithelia is the rule in cystadenocarcinomas; conversely, denudation of cystic neoplasms is a frequent event. Cyst fluid analysis of congenital true cysts has provided conflicting results and has never been reported in pancreatic ADPKD cysts.

Although distal pancreatectomy with splenic conservation appeared to be a relatively safe and eventually successful treatment in this
In conclusion, the case reported here suggests that pancreatic involvement should be considered as a possible cause of abdominal pain in ADPKD patients. Obstructive pancreatitis should be added to the list of extrarenal complications of ADPKD. Conversely, when cystic or polycystic disease of the pancreas is diagnosed, information about the personal and family history and the presence of cysts in other organs, particularly the liver or kidneys, should be obtained preoperatively.

Addendum
During the period of revision of this manuscript, Niv et al reported an association between pancreatic cystadenocarcinoma, malignant liver cysts, and ADPKD (Gastroenterology 1997; 112: 2104–7).

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