Ascites in a polycystic patient

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Case Report

Mrs G. F. had the first manifestation of polycystic kidney disease in 1973 when she was 37 years of age. Gross haematuria revealed the disease. Resection of several renal cysts was performed in California at that time. The inherited autosomal dominant nature of the disease was easily documented: the father and several members of the paternal family were affected.

In July 1990, umbilical hernia had to be operated on in Poitiers, France and ascites was discovered at surgery. Renal function was impaired at that time (serum creatinine concentration 174 mmol/l). Liver cysts had been documented 15 years before, and had so far been asymptomatic.

In October 1990, voluminous ascites and lower limb oedema required further investigation. Grade I oesophageal varices were found by endoscopy. Angiography showed that the portal and superior mesenteric veins were patent. Because of refractory ascites due to portal hypertension, side-to-side mesentericocaval shunting with Gore-Tex® graft prosthesis was surgically performed. Before surgery, the pressures were 18 mmHg and 27 mmHg, in the inferior vena cava and portal vein respectively (normal range: 7–12, and 10–15 mmHg respectively). After surgical anastomosis, the corresponding pressures were 22 and 28 mmHg. Thus surgery did not improve portal and caval hypertension. Not surprisingly, ascites recurred 8 days after surgery and thrombosis of the shunt was demonstrated.

In December 1990, the patient was referred to the Liver Transplant Unit. Ascites was still present. Liver and spleen were enlarged. No alcoholic intoxication was documented. Hepatitis B and C virus serologies were negative. Serum alkaline phosphatase and gamma-glutamyl transpeptidase activities were increased (X5N), whereas serum aminotransferases were normal. The protein content of the ascitic fluid was 22 g/l; this fluid contained 200–250 cells/mm³ including 76% lymphocytes, 15% polymorphonuclears, and 9% other cells. Echo Doppler imaging showed compression of the portal vein by liver cysts. On angiogram, the inferior vena cava was severely compressed in its suprahepatic segment. Injection of contrast into the hepatic vein showed no occlusion. Collateral circulation in the lower part of the inferior vena cava confirmed a functional obstruction (Figure 1). Magnetic resonance imaging showed that compression was mainly due to a voluminous liver cyst (Figure 2).

A second surgical operation was performed on 30 January 1991, with the aim of relieving obstruction. Voluminous ascites was evacuated, and several liver cysts were evacuated and resected. Despite this attempt,
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In June 1992 liver and kidney biopsies showed only minimal lesions. In April 1993 ascites had not recurred. Serum creatinine level was 115 \( \mu \text{mol/l} \). Liver tests were normal. The patient has been followed-up in California since that time.

Comment

Ascites is uncommon in polycystic kidney disease (ADPKD). Ascites was associated with portal hypertension in our patient, ruling out other causes of ascites in uraemia, such as tuberculous peritonitis. Basically, three disorders may lead to portal hypertension in ADPKD: liver cirrhosis, congenital hepatic fibrosis, and hepatic venous outflow obstruction. The possibility that innumerable hepatic cysts promote intrahepatic block, alone or in combination with outflow obstruction, has been suggested but not firmly established.

Liver cirrhosis was excluded on the basis of liver biopsy findings and on the lack of aetiologic factors: no alcoholism, no hepatitis B or C viral infection, and no evidence of haemochromatosis or primary biliary cirrhosis. Incidentally, liver cirrhosis due to chronic viral hepatitis was responsible for only two of 76 deaths among polycystic patients on regular dialysis in France in the 70s [1], and none in 242 patients from two series more recently published from North America [2,3].

Congenital hepatic fibrosis (CHF) has now been recognized in more than 20 patients with ADPKD [4], whereas it is a constant feature in autosomal recessive polycystic kidney disease [5]. Portal hypertension due to ADPKD-related CHF is recognized in early childhood, or before 25 years of age. It gives rise to splenomegaly and variceal bleeding. Ascites is rare and if present, transudative. Of note, liver cysts were detected in only two cases. ADPKD-related hepatic fibrosis has so far been only reported in PKD1 families. In these families several siblings may be affected but no vertical transmission of the liver involvement has been observed. Liver histopathological findings are characterized by enlargement of the portal spaces due to fibrosis, and bile-ductule proliferation. In addition, CHF may be associated with cystic dilatation of the segmental bile ducts (also called Caroli’s syndrome) which can be visualized by CT or US imaging. All these features were absent in this patient.

Hepatic venous outflow obstruction was therefore the most likely mechanism of portal hypertension. It develops mainly in ADPKD females, who are more prone than males to massive cystic liver. The huge size of the liver is responsible for mechanical problems concerning the gut, abdominal wall and elevation of the diaphragm, resulting in emesis and malnutrition, hernias, and respiratory compromise. Intractable ascites and tender hepatomegaly are the hallmark of hepatic venous outflow obstruction. Indolent presentation may lead to confusion with cirrhosis. However exudative ascites is suggestive. High protein content of ascitic fluid is ascribed to the high permeability of the
sinusoidal walls to proteins. In non-ADPKD patients, the site of flow disturbance causing hepatic venous outflow obstruction may be in the hepatic vein (thrombosis, also known as Budd–Chiari syndrome), in the inferior vena cava (thrombus or web) or downstream (constrictive pericarditis). Liver biopsy shows evidence of centrilobular congestion. If misdiagnosed, chronic obstruction may lead to liver cirrhosis. In polycystic patients, obstruction is due to compression of either hepatic vein or inferior vena cava, or both by one or multiple cysts.

At least three short series have firmly established the occurrence of hepatic venous outflow obstruction in polycystic liver disease [4,6,7] (the patient presented here was included in our own series). Including anecdotal case reports previously circulated, at least 30 patients with polycystic liver disease and ascites can be regarded as having proven or suspected hepatic venous outflow obstruction, 27 of them having also concurrent cystic kidneys. All had massive polycystic liver. In some cases thrombosis of hepatic veins was superimposed. This complication may also occur after nephrectomy or hepatic resection. Of interest, standard liver tests are usually normal or only minimally affected.

How to diagnose hepatic venous outflow obstruction? Imaging techniques (Doppler ultrasound and computed tomography) may demonstrate severe compression of hepatic veins and inferior vena cava by voluminous posterior cysts. When suspected, hepatic venous outflow obstruction may be demonstrated by direct measurement of the pressure above and below the site of obstruction; or by cavography showing compression and collateral circulation; or by showing occlusion of hepatic veins. Anatomic distortions often preclude an accurate study by Doppler ultrasound. Torres et al. [6] underlined the usefulness of magnetic resonance imaging for investigating patency and flow direction in the inferior vena cava, and hepatic and portal veins. Liver biopsy is hazardous in diffuse cystic disease and surgical biopsy is required, when needed.

Hepatic venous outflow obstruction is a severe condition, thrombosis being especially deleterious. Sodium and water depletion and anticoagulant treatment may relieve symptoms initially. To relieve obstruction, several approaches should be considered according to location and size of the compressive cysts, hepatic vein patency, and renal and liver function. Four main approaches can be discussed (in addition to mesocaval shunt, which should be restricted to cases with only hepatic-vein compression).

1. Cyst decompression. If few dominant cysts are causative, puncture and alcohol injection should be elected. Alternatively, laparoscopic fenestration may be of value to treat superficial cysts. As compared with surgical deroofing, this approach reduces the risk of subsequent adhesions.

2. Hepatic resection. In cases with diffuse cystic liver, this is often the only possibility [8] but entails a 10% mortality rate even in the hands of experienced liver surgeons [4].

3. Stent placement in the inferior vena cava: this technique has been successfully applied in a few well-selected patients with only inferior vena cava compression (Torres, personal communication).

4. In patients with poor liver function, or in those in whom the preceding approaches have failed or cannot be used, or who are at risk of developing cirrhosis, orthotopic liver transplantation is the only logical choice. Combined liver and kidney transplantation should be performed in those patients with moderate or advanced renal failure [7].

References