CASE REPORT

Liver Failure in Advanced Adult-onset Polycystic Kidney Disease

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SUMMARY

Polycystic liver disease is the most common extrarenal manifestation of autosomal dominant polycystic kidney disease (ADPKD). Hepatic cysts are typically incidental findings, with occasional complications including cyst haemorrhage, infection and rupture. In contrast to the typically benign course of polycystic liver disease, we present a rare case of fatal decompensated liver failure in a patient with ADPKD. This is a case of a 58-year-old man with end-stage renal disease on haemodialysis presenting with new-onset ascites and decompensated liver failure following bilateral nephrectomy. Cirrhosis in ADPKD is a late manifestation of the disease, but it should be considered in the perioperative risk of patients with ADPKD.

BACKGROUND

Polycystic liver disease is seen in 75%–90% of ADPKD cases.¹ Hepatic cyst formation is the most common extrarenal manifestation of cysts in patients with ADPKD.²

Hepatic cysts usually develop later than the renal cysts and have an annual growth rate of roughly 0.9%–3.2%. Research has shown that oestrogen exposure, insulin-like growth factor 1 (IGF-1) and dysfunction in cilia formation may influence cyst growth.^{2–4} Liver function tests may be mildly elevated with increased hepatic cysts but there is usually no significant liver disease.⁵ There is a strong correlation between advanced renal cysts or renal dysfunction and liver cysts.²

It is rare for polycystic liver disease to cause liver failure or decompensation causing death.² Cirrhosis is a late finding but can happen especially in the elderly. This is increasingly relevant as patients with ADPKD are living longer due to dialysis and transplantation.

We present a case of massive ascites and decompensated fatal liver failure in a patient with ADPKD. Our patient was on haemodialysis for years before he underwent a bilateral nephrectomy to alleviate discomfort and facilitate renal transplant. It is likely the hepatic cysts associated with his advanced polycystic Kidney disease (PKD) contributed to portal hypertension and the development of massive ascites postoperatively. It is possible that his kidney size and intra-abdominal pressure had obscured the presence of ascites on preoperative imaging. Ascites are not commonly seen in patients with chronic kidney disease.

Our case highlights an unusual manifestation of polycystic liver disease; in the postoperative period, our patient developed high-volume ascites production and decompensated liver failure in the absence of previously recognised liver disease. The case serves to emphasise the importance of evaluation for liver disease in patients with ADPKD undergoing elective surgery.

CASE PRESENTATION

A 58-year-old male patient with ESRD due to ADPKD on haemodialysis for 4 years presented for elective bilateral nephrectomy due to ongoing symptoms of abdominal discomfort. The patient did not have renal function and was told that he would require a nephrectomy in order to have sufficient space for potential renal transplant. The transplant surgeon and the urologist at our facility arranged for a bilateral nephrectomy. Risks were discussed with the patient and he agreed to undergo the procedure. The patient was admitted to the medicine service for haemodialysis and monitoring, until his surgery, with plans to follow postoperatively for potential adrenal insufficiency. Due to the extent of cystic enlargement, his adrenal glands were unlikely to be located and spared during the procedure.

At admission, the patient denied any haematuria, dysuria, worsening abdominal pain, scrotal pain or symptoms concerning bowel obstruction. His past medical history was remarkable only for hypertension, hyperlipidaemia, gastroesophageal reflux disease (GERD) and end-stage renal disease (ESRD) on dialysis (Tuesday, Thursday and Saturday) using left arm arteriovenous (AV) fistula. Surgical history was notable only for open prostatectomy. Family history included a son with polycystic kidney disease. The patient had quit smoking earlier in 2016, and was consuming about six cans of beer a day for 2 years. He took multiple antihypertensives including hydralazine, carvedilol, clonidine, amlodipine and furosemide as needed.

His vitals were stable and he was oxygenating well on room air. His physical exam revealed an extremely protuberant and distended abdomen that was non-tender to palpation without guarding or rigidity. There was no jaundice, scleral icterus, caput medusa or stigmata of liver disease. Extremities were thin.

Values of preoperative lab tests were notable for: haemoglobin 8.8 g/dL (13.9–6.3 g/dL), albumin 2.1 g/dL (3.4–5 g/dL), total bilirubin 0.8 mg/dL (0.2–1 mg/dL), aspartate aminotransferase (AST) 41 U/L (15–37 U/L), alanine aminotransferase

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Figure 1 Abdominal CT showing the patient's polycystic liver. There are innumerable hepatic cysts, which replace a significant portion of the hepatic parenchyma. Several of these cysts demonstrate progressive peripheral calcification.

(ALT) 39 U/L (12–78 U/L), INR 2 (<1.5). CT abdomen preoperatively showed innumerable hepatic and renal cystic lesions with dramatic hepatic enlargement, small-to-moderate ascites and subcutaneous infiltration suggestive of anasarca ([figure 1](#)). Previous brain magnetic resonance angiography (MRA) was negative for brain aneurysm, and prior coronary angiography showed no obstructive disease.

The patient's only surgical risk for a major cardiac event was ESRD. His significant hypoalbuminaemia was concerning for possible pulmonary complications. The patient received conventional haemodialysis a day prior to surgery and was given hydrocortisone 50 mg intravenous every 8 hours for potential adrenal insufficiency. He was typed and crossed for 4 units of blood prior to surgery. His hypertension was well controlled.

INVESTIGATIONS

Postoperative day 1: plasma albumin 2 g/dL (3.4–5 g), protein 4.4 g/dL (6.4–8.2 g/dL), bilirubin 2 mg/dL (0.2–1 mg/dL), alkaline phosphate 153 U/L (45–117 U/L), ALT 2163 U/L (12–78 U/L), AST 3032 U/L (15–37 U/L).

Day of transfer: albumin 2.4 g/dL, protein 5 g/dL, bilirubin 14.4 mg/dL, direct bilirubin 11.1 mg/dL, alkaline phosphatase 220 U/L, ALT 184 U/L, AST 213 U/L, ammonia 31.0 μ mol/L (11.2–31.7 μ mol).

Platelets were $160 \times 10^3/\mu$ L (150–450/ μ L) preoperatively, decreasing to as low as $50 \times 10^3/\mu$ L during admission. International normalized ratio (INR) was 2.02 preoperatively, increased to 7.9 postoperatively, and following fresh frozen plasma (FFP) was 2.66 on the day of transfer.

Paracentesis fluid had 75% neutrophils and total nucleated cells of $680/\text{mm}^3$. Total red blood cells in the fluid were 20×10^3 . Gram stain did not show any bacterial growth. Body fluid culture was negative after 5 days.

The model for end-stage liver disease (MELD) Score was 28 (19.6% mortality in 3 months) preoperatively, worsening to 41 (71.3% mortality in 3 months) by the time of transfer.

DIFFERENTIAL DIAGNOSIS

The patient had severe hypotension and fluid shifting intraoperatively after the removal of his massive kidneys (see [figure 2](#)).

Figure 2 One polycystic kidney of the patient.

His acute decompensated liver failure could be secondary to ischaemic hepatitis postoperatively. However, based on his preoperative lab results the patient had underlying liver disease given hypoalbuminaemia, coagulopathy, and innumerable cysts and ascites on abdominal CT.

One may argue that his liver disease preoperatively may be due to his alcoholism.

Despite the past history of alcohol use, he had discontinued use 2 years prior to presentation.

Principle causes of portal hypertension in ADPKD would be either congenital fibrosis, cirrhosis or hepatic venous outflow obstruction (HVOO).

Based on the pathology results of his liver postmortem, the patient did not appear to have bridging fibrosis, cirrhosis or portal vein thrombosis. In other words, there would be more severe histological changes in his liver if he had alcohol cirrhosis.

The patient likely had HVOO due to exclusion of other likely causes of portal hypertension including cirrhosis. The presence of small-to-moderate ascites on preoperative imaging could be due to HVOO, followed by dramatic worsening postoperatively. Although clinical course and pathology may point towards an additional diagnosis of shock liver in the postoperative period, this would not explain his immediate massive third spacing of fluid into the abdomen.

Our hypothesis is that his portal hypertension was related to HVOO. We do not have definitive imaging evidence to show that a dominant cyst or cysts were compressing the portal vein or hepatic vein, or both.

We believe that shock liver during the operation with his underlying polycystic hepatic disease led to decompensated liver failure.

TREATMENT

An open nephrectomy was performed due the size of the patient's kidneys. His right and left kidneys were 40 cm and 34 cm respectively, weighing a total of 12.7 kg.

Nephrectomy was complicated by serosal bowel injury with primary repair and splenic laceration resulting in emergency splenectomy. Massive transfusion for hypotension and coagulopathy was given postoperatively because of the large volume of ascites. The patient was transferred to the ICU with hypovolemic shock and acute lung injury on mechanical ventilation. He was on three high-dose vasopressors, diltiazem for atrial

fibrillation and steroids for suspected adrenal insufficiency. Random cortisol administered was 33 µg/dL.

He was maintained initially on continuous renal replacement therapy and later transitioned to daily intermittent haemodialysis for ultrafiltration. Volume overload was also managed with paracentesis on three occasions with removal of 4–10 L ascites. Multiple subspecialists were involved in his care including general surgery, urology, critical care, infectious disease, nephrology, internal medicine, cardiology and ophthalmology. Transaminases initially increased modestly from the previous level, but later to levels consistent with shock liver. FFP and cryoprecipitate were administered repeatedly for coagulopathy and low fibrinogen. He continued to require respiratory support via non-invasive positive pressure ventilation and the use of vasopressors.

He was given total parenteral nutrition (TPN) postoperatively. Unfortunately, blood cultures revealed fungaemia after the patient developed worsening leucocytosis. TPN was held and he was given anidulafungin. Extubation was eventually facilitated by ongoing ultrafiltration and paracentesis. He was transferred to a transplant centre for a liver transplant but was deemed to not be a fit candidate for transplant in the setting of ongoing critical illness with a decubitus ulcer and recent fungaemia.

OUTCOME AND FOLLOW-UP

The patient died due to complications of liver failure and fungaemia a few days after transfer to the transplant centre.

DISCUSSION

Hepatic cysts typically have a benign course in ADPKD, but may occasionally cause abdominal pain or result in complications such as malnutrition due to organ displacement. Cyst infection, rupture and haemorrhage may occur. As patients with ADPKD are living longer with dialysis and transplant, there have been rare reports of portal hypertension, hepatic venous thrombosis and fibrosis that may be caused by compression of the inferior vena cava (IVC) and other venous outflow by hepatic cysts.^{1,2}

Ascites is uncommon and is usually seen later in disease; the most common mechanism of ascites formation in PLD is thought to be HVOO caused by compression from cysts; this may lead to a thrombotic occlusion of small hepatic vein branches.^{1,6}

Uddin *et al* present a series of case reports in *Gut* showing ascites due to hepatic vein obstruction in patients with polycystic liver disease. All the four patients in the case reports had mildly elevated AST and ALT with increased bilirubin. Liver transplants were carried out in three patients, and the fourth underwent a successful mesocaval shunt that lowered the portal venous pressure. Transplant was successful in two of three patients with mild

reaccumulation of ascites controlled by diuretics.⁶ Liver transplant is the only known treatment for severe PLD.

Attention should be given to hepatic synthetic function at the time of nephrectomy for ADPKD, and risks of operative mortality due to liver disease should be carefully discussed. Liver-kidney transplantation should be considered. This case demonstrates a rare severe hepatic complication of ADPKD with production of new ascites and decompensated liver failure in the immediate postoperative period.

Learning Points

- Polycystic liver disease is the most common extrarenal manifestation of autosomal dominant polycystic kidney disease (ADPKD).
- Polycystic liver disease can rarely be a late cause of cirrhosis in patients with ADPKD due to hepatic venous outflow obstruction.
- Consider and discuss perioperative risk of patients with ADPKD with concomitant liver disease.
- Liver and kidney transplantation can be considered in select patients.

Contributors CA was a part of the team treating this discussed patient. She performed the necessary literature review, patient consent, the primary data collection and write-up of the case. GGG is the expert on the topic. He performed the literature review as well and provided the appropriate articles/references for the case and helped CA understand the topic. He proof-read and edited all CA's drafts, and assisted in drafting the discussion and the conclusion for this case.

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