Netherlands
The Journal of Medicine

CASE REPORT

Multiple cysts in the liver autosomal dominant polycystic liver disease

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ABSTRACT

A 45-year-old woman was admitted because of abdominal pain and a feeling of fullness. Ultrasound and CT scan of the abdomen showed a massively enlarged liver with hundreds of cysts and displacement of the right kidney. There were no cysts in the kidneys. Because several members of her family also had multiple cysts in the liver, the diagnosis of autosomal dominant polycystic liver disease (PCLD) was made. Genetic analysis demonstrated a protein kinase C substrate 80 K-H (PRKCSH) gene mutation (1338-2A>G) and confirmed the clinical diagnosis. A brief review of the genetics and possible treatments is given.

KEYWORDS

Autosomal dominant polycystic liver disease, liver cysts, polycystic liver disease

INTRODUCTION

Since the introduction of ultrasound investigation of the abdomen, cysts in the liver and kidney have become normal findings. The majority of diagnosed cysts are small and have no clinical consequences, nor do they cause symptoms. Adult polycystic kidney disease is a well-known disease entity and is characterised by hundreds of cysts in the kidneys and sometimes the liver and accompanying renal failure in most cases. Cysts in the liver may be part of this disease. If multiple cysts are seen solely in the liver, another diagnosis has to be considered. We describe a patient with a grossly enlarged liver due to hundreds of cysts, without involvement of the kidneys.

CASE REPORT

A 45-year-old woman was admitted because of progressive abdominal pain located mainly in the right upper quadrant. She had no relevant medical history and had always been healthy.

Her main complaint was pain in the right abdomen, with a feeling of fullness, her waistband had increased several sizes. She had no complaints of nausea, vomiting or fever. Her urine and stools showed no abnormalities. Her appetite was normal, her weight stable. Physical examination showed a normal body temperature, heart frequency and blood pressure. Heart and lungs showed no abnormalities. The abdomen revealed a very large painful mass in the right upper quadrant extending downwards for more than 10 cm. No signs of chronic liver disease were seen and there was no ascites. Blood tests showed no abnormalities; the transaminases were normal, there was a slight elevation of the alkaline phosphatase (137 U/l) and normal kidney function. Ultrasound examination of the abdomen showed a very large liver with hundreds of cysts varying from 0.7 to 6.5 cm in diameter. CT scan confirmed the ultrasound findings (*figure 1*).

Her family history was positive for the presence of multiple cysts in the liver. Her father had multiple cysts in the liver and one cyst in a kidney without signs of renal failure. Her father's brother underwent surgery because of large cysts in the liver, and her father's sister also had multiple liver cysts. A daughter of this aunt underwent drainage of liver cysts. *Figure 2* shows the family tree.

Genetic analysis was carried out, courtesy of the Department of Gastroenterology of the Radboud University Medical Centre. DNA from a control subject and the patient was amplified with primers surrounding the splice acceptor site of intron 15. Digestion of the wildtype polymerase chain reaction (PCR) product with the restriction enzyme Ban 1 produced fragments of 428 and 175 basepairs (left lane of *figure 3*). Digestion of the mutant 1338-2A>G

Figure 1. *CT scan of the enlarged liver, reaching the pelvi with diffuse cysts with a maximal diameter of 5 cm and displacement of adjacent organs*

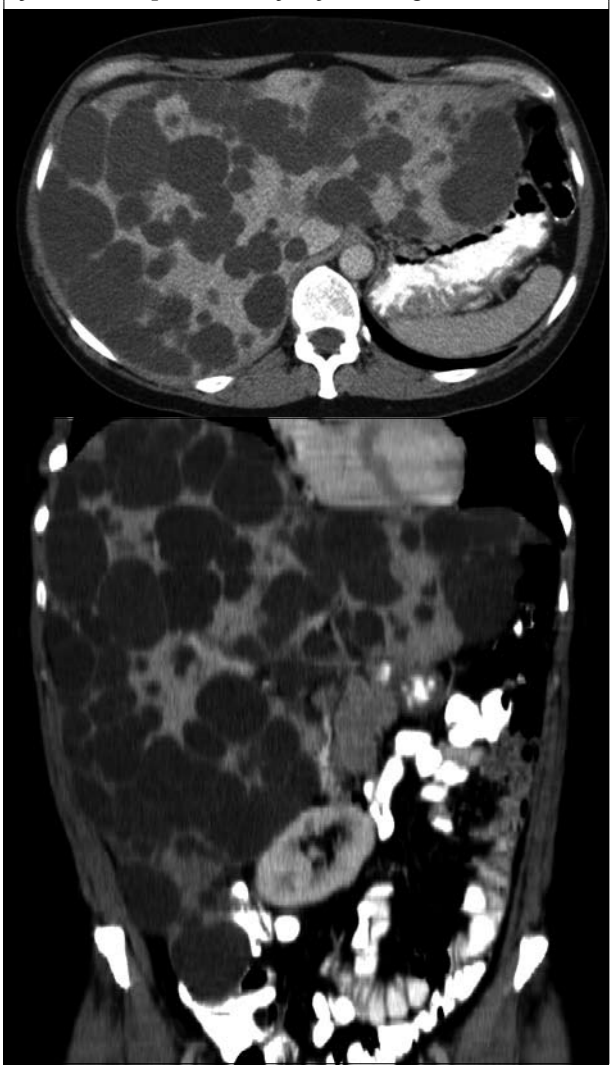
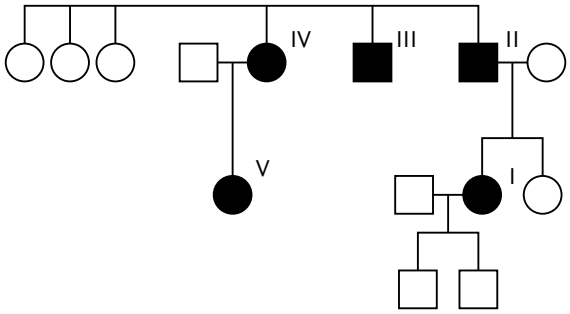
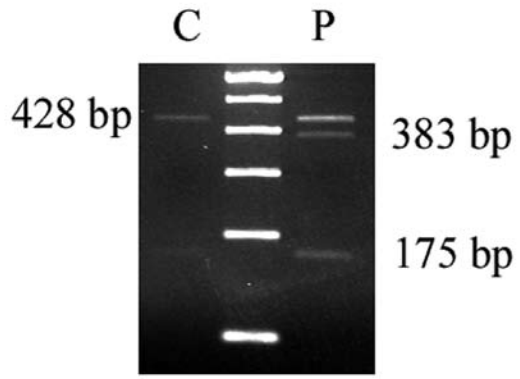


Figure 2. *Family tree*



I: patient; II: father; III: uncle; IV: aunt; V: niece.
○ = female; ● = female with polycystic liver desease;
□ = male; ■ = male with polycystic liver desease.

Figure 3. *Photograph of the gel depicting the genetic analys*



allele resulted in three additional bands at 383, 175, and 45 basepairs (right lane of *figure 3*). This confirms the presence of a 1338-2A>G mutation, hence confirming the clinical diagnosis polycystic liver disease (PCLD).

DISCUSSION

Given the family history and the absence of adult polycystic kidney disease (ADPKD), the diagnosis of polycystic liver disease (PCLD) was made. The diagnosis was confirmed via mutation analysis. PCLD is an autosomal dominant disorder. It usually runs an asymptomatic course. It is seldom diagnosed before puberty and is seen more often and more prominently in women. The cysts in PCLD can increase in size and number during pregnancy or simultaneously with the use of exogenous female steroid hormones.[1] Because of the increased volume of the liver, patients can have symptoms of abdominal distension, abdominal pain and early satiety. Other symptoms are nausea, vomiting, tiredness and shortness of breath.[2,3] Noncystic manifestation of the disease can be mitral valve leaflet abnormalities. True mitral valve prolapse is reported in 8% of patients.[4] Unlike ADPKD, PCLD is not associated with cerebral aneurysms.[4,5] However, in a large series of patients with PCLD one case of death due to subarachnoidal haemorrhage from an aneurysm was noted.[6] In a family with PCLD, two members had an intracranial aneurysm, while in one sibling without liver cysts an aneurysm was detected through screening.[7] Whether the prevalence of cerebral aneurysms is higher than in the general population is a matter of debate. Despite massive cysts, the synthetic capacity of the liver is almost always intact.

Two genes are known to be related to PCLD.[9,10] The first gene is PRKCSH, which encodes for the β-subunit of glucosidase II, an N-linked glycane processing enzyme in the endoplasmatic reticulum. It is located on 19p13.2-p13.1. The second is a SEC63 gene, which encodes a component of the protein translocation machinery in the endoplasmatic reticulum. It is located on 6q21-q23. These findings suggest a role for co-translational protein-processing pathways in maintaining epithelial luminal structure and implicate (noncilial) endoplasmatic reticulum proteins in PCLD. Mutations in these genes can be found in less than one third of the cases. This indicates the presence of at least one more locus associated with this disorder. Clinical genetic testing for PCLD is available and includes genetic sequencing of the coding portion of PRKCSH and/or SEC63.[8,9]

Less than 5% of patients have acute medical complications. These consist of cyst haemorrhage, rupture, infection, uterine prolapse due to displacement, obstructive jaundice, portal hypertension, transudative and exsudative ascites and Budd-Chiari syndrome.[2,3,6,10,11] Treatment should be considered in case of persistent symptoms and complications.

There are no medical therapies for PCLD. Use of somatostatin to block the secretin-induced secretion by hepatic cysts failed to demonstrate any significant effect on hepatic cyst growth size.[12] Cyst aspiration with sclerosis, open or laparoscopic cyst fenestration, combined hepatic resection and fenestration or liver transplantation,[2,3,6,10] are possible treatments. Aspiration combined with ethanol instillation to induce sclerosis of the cyst lining epithelium can be effective. Only small series with variable effect have been described, with variable effect. In the largest series, the symptoms returned after four years in 50% of the cases.[13] Recurrence of symptoms was due to growth of the untreated cysts and not to re-expansion of the treated cysts. This technique is limited by the number and accessibility of the cysts.

Cyst fenestration can be performed, but the peritoneum does not always have the capacity to absorb large amounts of fluids. Morbidity of laparoscopic fenestration was between 33 to 45% and recurrence of symptoms occurred in the majority of cases. Lower recurrence rates were seen in series of large dominant cysts in the anterior segment of the liver. Patients with small cysts throughout the liver have a greater risk of persistence and/or recurrence of symptoms.[6,10] Postoperative morbidity consists of temporary ascites, pleural effusion and rarely biliary leakage.[2] Combined hepatic resection and fenestration is more effective for reducing the hepatic mass and gastric compression. Patients are free of symptoms for a longer period of time than with fenestration alone. Recurrence rates are 0 to 50% and morbidity rates are 38 to 100%. This procedure has an advantage in the case of massive hepatomegaly and severe symptoms of gastric compression.[2] Liver transplantation has been performed in rare cases, especially when the above-mentioned interventions are not an option. One series reported that after a follow-up of 4.4 years, all patients were free of symptoms.[16] Transarterial catheter embolisation (TAE) can be effective.[17] After a follow-up of two years, a decrease in liver volume of 54% was seen. However, this technique can be dangerous; the outcome cannot be accurately predicted and a large area of necrosis can occur. It should be noted that most therapeutic interventions were done in small series and randomised controlled trials are not available.

A careful and thorough examination of the family history led to the final diagnosis of PCLD in this case. Patients should be treated in a specialised centre. Because of the very large liver in this patient she was referred to a centre specialising in both liver surgery and liver transplantation.

ACKNOWLEDGEMENT

Genetic analysis was preformed by E. Waanders at the Department of Gastroenterology and Hepatology, Radboud University Nijmegen Medical Centre.

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