

Massive liver involvement in autosomal dominant polycystic kidney disease

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ABSTRACT

Autosomal dominant polycystic kidney disease (ADPKD) is a common genetic disease with an estimated prevalence of between 1/400 and 1/1000 [1]. The PKD1 genetic mutation, encoding polycystin-1, is found in 80% of cases, while 20% of patients carry the PKD2 mutation, encoding polycystin-2. Liver involvement is the most common extrarenal manifestation, occurring in over 50% of cases of hepato-renal polycystosis the most frequent extrarenal manifestation in autosomal-dominant polycystic kidney disease (ADPKD). Liver cysts are responsible for most hepatic complications.

A 40-year-old female presented on 13st April 2013 to the Nephrology Unit of Fundeni Clinical Institute with abdominal distension and renal dysfunction.

ADPKD had been diagnosed 5 years previously and had progressed to end-stage renal disease, treated by haemodialysis, in May 2014. Her medical history included well controlled hypertension and hyperlipidemia. The family history included ADPKD affected relatives.

Conclusion. Because early complications and mortality after either procedure remain frequent, the hazards of surgery have to be balanced against benefits; therefore, selection of the optimum therapy still remains a challenge.

Keywords: polycystic kidney disease, hepatic fibrosis, cysts, transplantation

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is a common inherited disease prevalence 1 / 1,000 in the general population. It is the most common of hereditary nephropathies: it is the cause of 8 to 10% of kidney disease [1]. The disease is transmitted in the autosomal dominant mode. The risk that a parent reached transmits the disease is therefore 50% for each of his children, regardless of gender of this one. Within a family with PKRAD, an unaffected subject does not transmit the disease. ADPKD is genetically heterogeneous: two genes are involved in the vast majority of case, PKD1 and PKD2. The changes are "private". About 5% of patients have a *de novo* mutation, that is not transmitted by a parent [2-4].

Hepatic cysts are the most common extrarenal manifestation, occurring in over 50% of cases of hepato-renal polycystosis. They appear secondarily after renal involvement, which makes the prognosis of this pathology. Their management depends on the symptomatology, extent, distribution and anatomy of the cysts and may include percutaneous aspiration, alcoholic sclerosis or fenestration of the cysts; a partial hepatectomy or even a liver transplant is possible in the rare cases where the hepato-megaly is particularly debilitating [6-8].

CASE PRESENTATION

A 40-year-old female presented to the Nephrology Unit of Fundeni Clinical Institute with abdominal distension and renal dysfunction.

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ADPKD had been diagnosed 5 years previously and had progressed to end-stage renal disease, treated by haemodialysis. Her medical history included well controlled hypertension and hyperlipidemia. The family history included ADPKD affected relatives: her mother died of the same disease and her sister still suffers from the same disease.



FIGURE 1. Photos illustrating patient appearances at initial presentation

On admission she had a distended abdomen. The remaining physical examination did not reveal any notable findings. Blood analysis showed anaemia (Hb 10.9 g/dl). There was no leukocytosis.

There were no changes on chest X-ray. Screening for hepatitis B and C, cytomegalovirus and Epstein Barr virus was negative. No parasites were found.

An abdominal CT scan showed both liver cysts and bilateral kidney cysts consistent with ADPKD.

Six month later, she presented to our institution for a second opinion. She was asymptomatic and physical examination revealed increased abdominal mass. Her medication were unchanged.

We initiated haemodialysis programme with minor complications (dialysis hypotension) and she was on the waiting list of liver transplantation.

The last CT scan showed important hepatomegaly that completely occupies the upper and middle floor with an important effect on the mass of the stomach, spleen, as well as on the upper abdominal vascular axes. Herniation of the liver parenchyma at the level of the white line with dehiscence of the abdominal strains. The hepatic parenchyma appears to be completely replaced by numerous cystic formations, some with a tendency to confluence. Important bilateral nephromegaly with renal parenchyma replaced almost entirely by multiple cystic formations, some with spontaneous hyperdense content especially on the right side, tending to confluence.

During liver transplantation the patient died due to pulmonary embolism. Last patient weight was 122 kg, the patient being immobile.



FIGURE 3. Photos illustrating patient appearances before liver transplantation

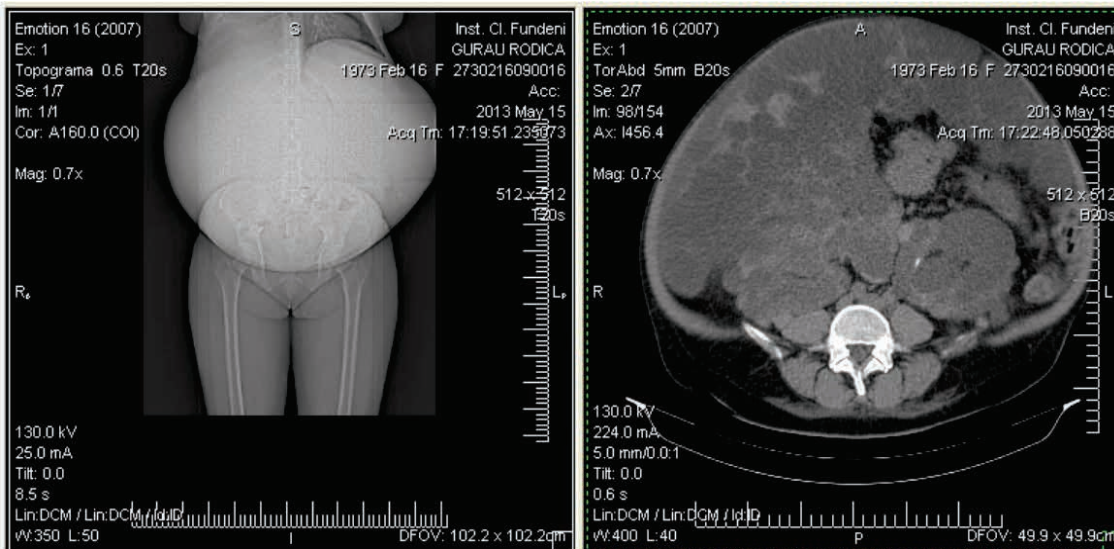


FIGURE 2. Contrast-enhanced computed tomography (CT) scan showing massive polycystic liver and kidney disease

DISCUSSION

Autosomal dominant polycystic kidney disease (ADPKD) is a common genetic disease with an estimated prevalence of between 1/400 and 1/1000 [1]. The PKD1 genetic mutation, encoding polycystin-1, is found in 80% of cases, while 20% of patients carry the PKD2 mutation, encoding polycystin-2 [2]. Hepatic cysts result from abnormal growth of the biliary epithelium (cholangiocytes) or dilation of the peribiliary glands, due to the persistence of embryonic bile structures. The cystic epithelium thus retains the characteristics of the biliary epithelium, but with increased secretory and proliferative activities. Another, much rarer form of polycystic hepato-renal disease, autosomal recessive polycystic kidney disease (PKRAR), is linked to the PKHD1 mutation. It is a severe pediatric form, occurring in 1 / 40,000 births, with an unfavorable renal prognosis with a high infant mortality rate [3,4].

Majority of the individuals with polycystic liver disease are asymptomatic and diagnosed accidentally. Transient pain in the right hypochondrium is common, but only a third of patients have chronic symptoms; symptoms depend on mass and therefore on the compressive effect, and include abdominal distension, early satiety, dyspnea, and back pain associated with hepatomegaly. Liver and renal function is often normal at the beginning of the disease, subsequently degrading during the disease. About 60% of the patients with ADPKD can develop hypertension before the onset of renal insufficiency [6-11].

Striking advances in liver surgery and transplantation have been made, but the selection of the appropriate approach remains a challenge [12]. The surgical technique differs depending on whether it is a symptomatic form of hepato-renal polycystosis with large cysts (> 5 cm), where the surgical technique of fenestration under laparoscopy is preferred, and a form with small cysts (< 5 cm) type Gigot III, where hepatectomy or even liver transplantation (HR) will be offered, most often combined with renal transplantation. Laparoscopic fenestration is an effective treatment when there are few large cysts (Gigot I and II), and which has the advantage of being able to be repeated in the event of recurrence [13-14]. However, the preoperative assessment tends to overestimate the size of large cysts which are in fact made up of several contiguous cysts, forcing fenestrations to be carried out step by step through the superficial cysts [15-17]. In 92% of cases, laparoscopic fenestration reduces symptoms but the cysts recur in 22% of cases [18]. In addition, complications are frequent (23%): ascites, pleural effusion, bleeding and bile leakage. It is important that kidney function is preserved oth-

erwise there is a risk of chronic postoperative ascites. Surgical fenestration is more complete than laparoscopic fenestration but it is not always effective if there are multiple small cysts. In the event of recurrence, reoperation is difficult. This is the reason why this treatment tends to be abandoned in favor of surgical resection of the most cystic part of the liver. Liver resection is indicated in severe Gigot II forms with at least one healthy liver segment; it is justified by the fact that the great majority of polycystosis consists of multiple cysts of small size, impossible or difficult to fenestrate. As the cysts are distributed inhomogeneously in the parenchyma with a permanently spared parenchyma zone, saving this zone will allow hepatic regeneration relatively free from cysts with a lasting result. This intervention is very effective on the symptoms (86%) but it remains difficult to achieve because the planes of anatomical fissures are repressed by the cysts. However, this technique experiences significant morbidity (51%) and mortality (3%) [18]. The consequences of these procedures are marked by sometimes significant ascites associated with a risk of postoperative hemorrhage and bile leaks due to the opening of bile ducts which were compressed in the wall of the cysts. These hepatectomies are poorly tolerated in malnourished patients and in those with impaired renal function.

Liver transplantation can be isolated, or associated with renal transplantation when there is symptomatic hepato-renal polycystosis associated with renal failure in a patient on dialysis. This treatment has the additional advantage of facilitating the immunological tolerance of the kidney transplant when both organs come from the same donor. The good results of renal transplantation tend to broaden the indications for double transplantation to patients at significant risk with the resection, especially in cases of malnutrition or when there is renal failure even without dialysis. Likewise, isolated HT is sometimes offered in cases of large hepatectomy with too little predictable residual liver volume (< 0.5% body weight). Polycystosis is considered an exception to Meld's score for HT. Survival in this indication is excellent (92%) at 5 years [19,20].

CONCLUSIONS

Transplantation is an excellent option for PLD with dramatic improvement in quality of life and acceptable morbidity. For combined liver and kidney transplantation one- and two-year patient survival rates were similar to combined transplantation for other indications. For patients with acceptable renal function at time of transplantation, solitary liver transplantation has an excellent outcome.

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