Case Report

Caroli’s disease and autosomal dominant polycystic kidney disease: a rare association?

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Key words: autosomal dominant polycystic kidney disease; Caroli’s disease; angiocholitis

Introduction

The visceral abnormalities most frequently associated with autosomal dominant polycystic kidney disease (ADPKD) are hepatic in origin. Liver cysts are the most common but by no means the sole manifestation: the extrahepatic biliary tract may also be involved [1,2] and rare cases of congenital hepatic fibrosis may be observed [3]. In a case of ADPKD associated with Caroli’s disease, we were confronted with diagnostic and therapeutic problems raising embryological and genetic issues.

Case report

Polycystic kidney disease was diagnosed in a 54-year-old man at the time of the rupture of an intracranial aneurysm. He had mild renal failure (serum creatinine level (SCL) 2.5 mg/dl) and several hepatic cysts. A study of his family suggested autosomal dominant type: the causes of death of his parents were unknown, but his three daughters, aged between 22 and 30 years, had bilateral renal enlargement due to cysts (more than 2 cysts in each kidney on renal ultrasonography) and one also had two hepatic cysts.

Three years later, the patient reached end-stage renal failure and maintenance haemodialysis was performed for 34 months. During this period, two episodes of E. coli septicemia occurred, presenting with fever and chills without any urinary or digestive symptoms. The patient then underwent a cadaveric kidney allograft. Immunosuppressive regimen successively associated antilymphocyte globulins, corticosteroids, mizoribine and cyclosporin A. The 4 years following transplantation were marked by four episodes of E. coli septicemia without urinary symptoms. CT scan and ultrasonography failed to identify abscesses or infected renal or hepatic cysts. During the fourth episode, gamma-GT increased for the first time to 545 UI/l (N<78 UI/l), and remained at this level 2 months later. A new abdominal CT scan without intravenous contrast showed hepatic cysts and also possible intrahepatic calcifications. The gallbladder appeared normal. Endoscopic retrograde cholangiography failed, but transparietal cholangiography showed diffuse cystic dilatations of intrahepatic biliary ducts with multiple calculi in the right lobe and led to the diagnosis of Caroli’s disease. We then concluded that previous E. coli septicemias were angiocholitis episodes.

Surgery was decided on, at first to explore the left lobe biliary system, and secondly to perform right lobe hepatectomy if Caroli’s disease was limited. In fact, because of diffuse dilatations (Figure 1) with lithiasis in both lobes, only a choledocoduodenal anastomosis was performed, with an enterostomy to permit endoscopic access to biliary ducts. The surgeon removed many calculi at the same time, but did not perform hepatic biopsy to look for hepatic fibrosis because of the risks of infected biliary leak after biopsy and the lack of portal hypertension in a 65-year-old patient. Moreover, it could be difficult to distinguish congenital fibrosis from fibrosis secondary to repeated cholangitis episodes.

Two months later, endoscopic biliary duct catheterization through enterostomy permitted right hepatic duct dilatation. Ursodeoxycholic acid treatment was undertaken in order to facilitate stone dissolution. Postsurgical follow-up has now lasted 18 months without septicemia. At the present time, gamma GT are 474 IU/l, ASAT 30 IU/l (N<45 IU/l), ALAT 17 IU/l (N<56 IU/l), bilirubin 9 mg/l (N<15). Immunosuppressive regimen consists of prednisone 10 mg/day, mizoribine 300 mg/day, cyclosporin A 150 mg/day. It was not possible to study DNA markers because the patient’s daughters refused.

Discussion

The diagnosis of ADPKD was reached on the following arguments: bilateral renal enlargement due to multiple cysts in the patient and his three daughters, hepatic...
case, postmortem intrahepatic cholangiogram might suggest Caroli’s disease because some cysts seem to communicate with the biliary tree (case 1). Clinical findings are not mentioned in this post-mortem study, biliary lithiasis is not reported in this case.

However, the association might be more common than supposed. Its ‘exceptional’ frequency is perhaps explained by diagnostic problems. Indeed, the diagnosis of Caroli’s disease can be difficult in patients with ADPKD. Like Jordon et al. [8], we encountered certain difficulties in confirming Caroli’s disease. Such problems in these patients are related to the existence of two types of cysts: hepatic cysts due to ADPKD and cystic dilatations of the intrahepatic biliary tree. Ultrasonography and CT Scan cannot easily distinguish between these two types of hepatic cysts [9]. Only the irregular aspect of the saccular dilatations, the communication of these structures with the biliary tree, and intraductal lithiasis can lead to the diagnosis. In some cases, CT Scan of the liver show tiny dots with strong contrast enhancement within dilated intrahepatic bile ducts (the central dot sign) [9]. CT cholangiography or MRI make it possible to pinpoint these facts. However, invasive methods such as percutaneous transhepatic cholangiography may be required to confirm dilatations of the biliary tree. So we must therefore keep the possibility of this association in mind, and perform CT cholangiography or MRI in ADPKD patients with repeated and unexplained fever episodes. Indeed, our patient’s biliary tract appears to be the probable portal of entry of five episodes of septicaemia without clinical or biological hepatic symptoms. The patient reported by Jordon et al. [8] also had ‘a 17-year history of recurrent fever of unknown origin’.

It may be important to make this diagnosis because it can modify management. When the lesions are limited to left or right liver lobes, a partial hepatectomy is the curative treatment. Conversely, when Caroli’s disease is extended to the whole liver, a liver transplant may be discussed in a young patient. Our 65-year-old patient also had a past history of myocardial infarction, and, at the time, liver transplantation seemed neither possible, nor necessary. We then decided to reduce the immunosuppressive regimen with a view to decreasing infectious complications. In order to reduce cholesterol crystal concentration in bile and cytotoxic bile acids, we used ursodeoxycholic acid as suggested by Ros et al. [10]. Indeed, these authors observed complete (in 3 patients) or partial (in 9 others) stone dissolution in Caroli’s disease.

This association raises questions about the relationship between the two diseases: coincidence, i.e. biliary dysgenesis independent of ADPKD, or genetic relation? For Desmet [5], Caroli’s disease and hepatic cysts in ADPKD could be considered as two expressions of ‘ductal plate malformation’. Moniliform or saccular dilated bile ducts of Caroli’s disease are in continuity with the biliary system. On the other hand, hepatic cysts of ADPKD are also considered as an expression of ductal plate malformation of the more peripheral branches of the intrahepatic biliary tree, but liver cysts...
do not communicate with the biliary system [11]. They result from progressive dilatation of bile duct micro-
hamartomas, the so-called von Meyenburg complexes. Von Meyenburg complexes are more often asympto-
tomatic embryonic remnants in normal liver. A von Meyenburg complex contains several more-or-less dilated bile ducts close to portal tracts with a fibrous stroma around [5]. The association of hepatic cysts of ADPKD and Caroli’s disease could therefore indicate an arrest in remodelling of the ductal plate both during the formation of the interlobular ducts and also earlier during the formation of segmental ducts [5]. The association might be summed up as an inadequate remodelling of ductal plates at all levels of the biliary system. Moreover, these biliary duct ectasias are mixed in many cases with various degrees of congenital hepatic fibrosis, where different forms have been observed: portal hypertensive, cholangitic or latent [5].

However, the mechanisms of ductal plate remodelling are complex and poorly understood. In addition, these embryological hypotheses are not at the present time correlated with genetic data. Several facts are established: Caroli’s disease is only considered as a hereditary recessive autosomal disorder in 25–50% of cases, the other 50–75% being sporadic [12]. Clinical observations have shown the preferential association of ARPKD with congenital hepatic fibrosis and, less often, Caroli’s disease [6,7], whereas these liver lesions are rarer in ADPKD patients. Nevertheless, Cobben et al. [3] have observed four families with autosomal dominant polycystic kidney disease and congenital hepatic fibrosis. Analysis in these families showed linkage with the PKD1 locus, but congenital hepatic fibrosis was not vertically transmitted. Genetic linkage between Caroli’s disease and ADPKD was not studied in the previous case [8]. On the strength of currently available data, it is therefore not possible to establish a genetic association.

Finally, various aspects of ductal plate malformations could be associated with ADPKD: liver cysts, congenital hepatic fibrosis, common bile duct dilata-
tion, or Caroli’s disease. We are unable, at the present time, to understand why Caroli’s disease and congenital hepatic fibrosis are more frequently associated with ARPKD than ADPKD. Liver evaluation by MRI or CT cholangiography is needed in presence of hepatic symptoms or cholangitis to study the biliary system and to adapt the therapeutic choice.

Acknowledgement. The surgical operation was performed by Prof. P. Rat.

References


Received for publication: 3.2.97
Accepted: 13.2.97