Congenital Hepatic Fibrosis in a Child with Autosomal Dominant Polycystic Kidney Disease

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SUMMARY

The association of congenital hepatic fibrosis (CHF) with autosomal recessive polycystic kidney disease (ARPKD) is well known and occurs in approximately 50% of cases. However the association of CHF with autosomal dominant polycystic kidney disease (ADPKD) is less well known and less well documented. We report a child with neonatal onset of hypertension due to ADPKD who later develops portal hypertension due to CHF in childhood. A review of this rare association follows.

KEY WORDS:
Polycystic kidney disease, Autosomal dominant, Children, Hepatic fibrosis, Portal hypertension

INTRODUCTION

Polycystic kidney disease is an inherited systemic disease characterised by the development of multiple cysts in the kidneys and other organs. There are two main forms: autosomal dominant polycystic kidney disease which occurs in 1 in 1,000 live births; and the much rarer autosomal recessive polycystic kidney disease which occurs in 1 in 20,000 live births[1].

The two renal conditions have been considered clinically different entities and the diagnosis is usually based on the family history, family studies, radiological and /or histological features[1]. The recessive form often causes foetal or neonatal death whilst renal failure and hepatic fibrosis develops in the majority of those who survive the neonatal period[1]. Milder forms of ARPKD have also been reported and in these cases the hepatic dysfunction resulting from congenital hepatic fibrosis overrides the milder or absent renal symptoms[1].

ADPKD generally manifests during the 3rd and 4th decades of life with symptoms of haematuria, pain or hypertension. Both kidneys are enlarged and contain numerous cysts of varying size. The disease progression is slow and often leads to end-stage renal disease after the fourth decade[1]. However, childhood cases of ADPKD have also been reported and may even present in neonatal life[1] as in the case illustrated here.

Congenital hepatic fibrosis is reported in approximately 50% of cases of ARPKD whilst polycystic liver is seen in 45% of ADPKD cases. The two hepatic conditions however are generally regarded as genetically, morphologically and clinically entirely different entities. The hepatic cysts in ADPKD are generally asymptomatic and portal hypertension and splenomegaly are not seen[2].

We describe a child with ADPKD presenting in the neonatal period and CHF which manifests with hypersplenism later in childhood.

CASE REPORT

Our patient was born at term via emergency Caesarean section. She had congenital pneumonia and required ventilatory support for one day. She developed Grade 1 necrotizing enterocolitis on Day 4 of life and was treated conservatively. She had an umbilical vein catheter in situ but no umbilical artery catheterisation. Oral feeding commenced at one week of life. At two weeks she was noted to be hypertensive and required therapy with prazosin and later captopril. Abdominal examination revealed a ballotable left kidney whilst an ultrasound of the abdomen ruled out aortic thrombus and revealed cystic lesions in the kidneys but none in the liver or pancreas. Echocardiogram ruled out coarctation of the aorta. Serum electrolytes, creatinine and urinalysis were all normal and her blood pressure remained stable on oral antihypertensive therapy.

At about the same time, her father, aged 36 years was diagnosed with hypertension. He gave a history of hypertension amongst his siblings and his mother had had renal failure for which the cause was not certain. His renal ultrasound revealed bilateral polycystic kidney disease. Ultrasound screening of the patient's mother and other siblings showed normal kidneys. The diagnosis of autosomal dominant polycystic kidney disease (ADPKD) was made, based on the three-generation family history and ultrasound findings (Figure 1).

Splenomegaly was detected in our patient from the age of four years. Haematological indices were normal and no further work-up was done at this point. At the age of six years, she presented with easy bruising over the lower limbs and was found to have thrombocytopenia (platelet count 67,000 x 10^9/L.) with a mild hypochromic microcytic anaemia (Hb 10 g/dL; MCV 73 fl, MCH 23 pg; TWBC 6,600 x 10^9/L). The peripheral blood picture showed giant form platelets (>30/hpf) and pencil-shaped red blood cells and she was diagnosed as having immune thrombocytopenic purpura. Her platelets however remained above 50,000 x 10^9 /L without any therapy.

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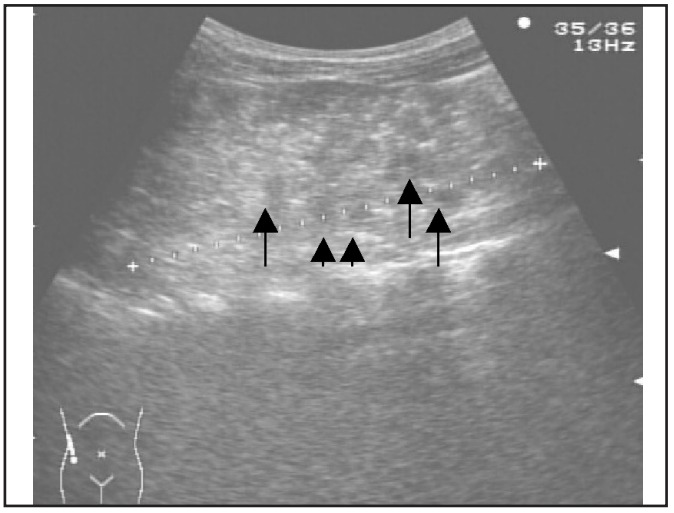

Fig. 1A

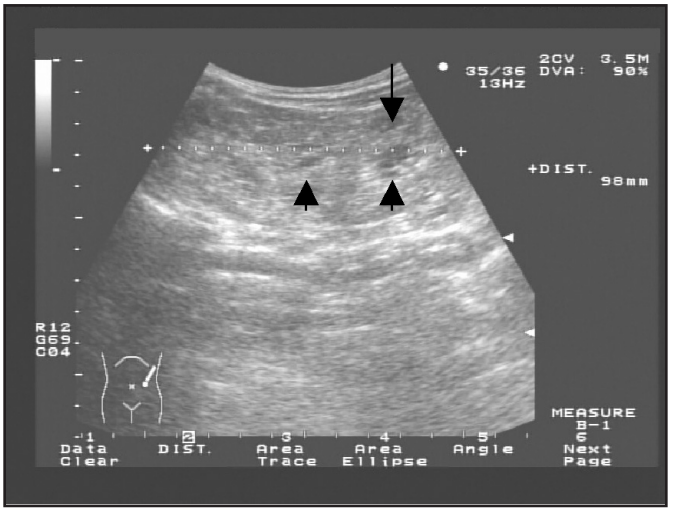

Fig. 1B

(A and B): Ultrasound of the right kidney (A) and left kidney (B) shows increased echogenicity of the both kidneys with multiple hypoechoic lesions (arrows) in keeping with multiple cysts in the kidneys.

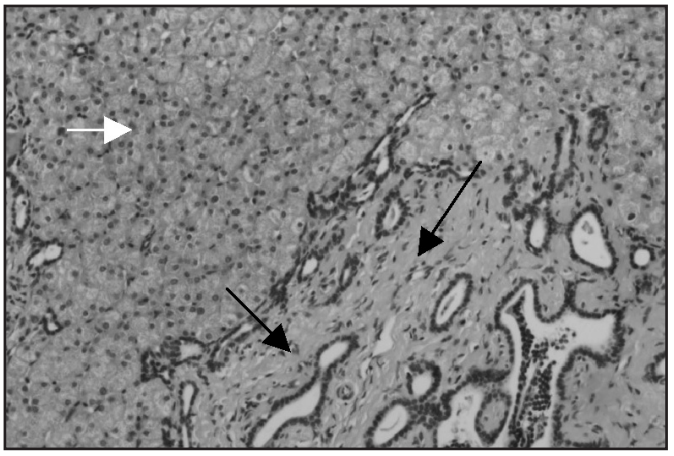

Fig. 2A

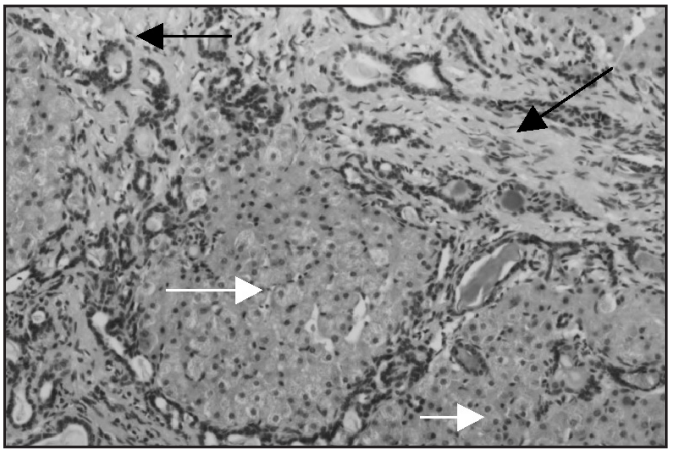

Fig. 2B

(A and B): The liver biopsy specimen under high magnification power (x100) shows the portal tracts are surrounded with fibrosis (black arrow). Normal looking hepatocytes (white arrows) are seen adjacent to the fibrosis.

After six months, her platelet count still remained low and her spleen had enlarged to 10cm below the subcostal margin, whilst the liver was not palpable. Bone marrow aspiration was performed and showed increased megakaryocytes, normal erythropoiesis and granulopoeisis and reduced iron stores. The trephine biopsy showed no blasts or malignant cells. Ultrasound of the liver showed increased echogenicity with multiple linear tubular hyperechogenecities outlining the portal veins. On colour Doppler, the portal vein demonstrated biphasic flow with dilated veins at the splenic hilum. These features were in keeping with periportal fibrosis and portal hypertension. A liver biopsy (Figure 2) showed normal hepatocytes with large portal tracts and portal-to-portal fibrous connections. The bile ducts were distorted and dilated but there was no evidence of inflammation, necrosis or parenchymal regeneration. Thus a diagnosis of congenital hepatic fibrosis was made.

She remains well and at the time of this report is aged eight years. Her height and weight are at the 3rd percentile. The renal and liver functions remain normal whilst the blood counts are on the lower limit of normal (TWBC 4,100x 10^9/L, Hb 10.4 g/dL) and her platelet count hovers at the 70,000 x 10^9/L mark. Thus this is a child with hypertension secondary to ADPKD associated with hypersplenism secondary to congenital hepatic fibrosis.

DISCUSSION

Congenital hepatic fibrosis is recognised as an important cause of portal hypertension in the pediatric age group. In half the cases of CHF, renal polycystic disease is of the autosomal recessive type and renal disease commonly precedes the development of liver disease[2,3]. Over the past two decades however, a small number of reports of adults with ADPKD associated with CHF have appeared in the

literature. In his review, Lipschitz *et al* concluded that most of these cases presented initially with portal hypertension and were only later found incidentally to have ADPKD, thus indicating that the renal disease was usually silent[3]. In our patient, however, the reverse is true; hypertension was noted prior to the development of symptomatic hypersplenism.

Hypertension in ADPKD is a frequent and early finding in adults, occurring in up to 75% of cases[4] and in up to 22% of childhood cases at the time of diagnosis[5]. This has an important impact on the morbidity and mortality as these patients have a more rapid loss of renal function and a higher risk for cardiovascular death[5]. Effective therapy is therefore crucial for this potentially treatable variable in ADPKD.

The more critical medical issues in our patient pertain to the CHF. The massive splenomegaly is a potential hazard for bleeding from trauma whilst the hypersplenism and portal hypertension are likely to lead to further morbidity and potential mortality from torrential oesophageal variceal haemorrhage as in other reported cases[2,3]. Options of therapy are being considered and have been discussed with the parents. These include prophylactic splenectomy and endoscopic screening and sclerotherapy for varices.

CONCLUSION

Congenital hepatic fibrosis and ADPKD do co-exist[3,4]. The few cases reported in the paediatric age group have severe portal hypertension. Thus children with ADPKD not only require close monitoring for the onset of hypertension but also for the potentially hazardous complications of portal hypertension associated with CHF. Further studies in children with both ADPKD and ARPKD who have associated CHF may enlighten clinicians on the best anticipatory therapy for those with early onset and severe liver disease.

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