

# Congenital Hepatic Fibrosis in a Case of Autosomal Dominant Polycystic Kidney Disease: A Case Report

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## Abstract

Ciliopathies are the newer group of human genetic disorders in which the ciliary structure or function is affected. Hepatorenal fibrocystic diseases (HRFCDs) are a part of ciliopathies and characterized by developmental abnormalities of the portobiliary system along with fibrocystic change in the kidneys. Polycystic kidney diseases (PKD) which is the largest subclass of HRFCDs had autosomal dominant and recessive forms. Autosomal dominant PKD (ADPKD) is characterized by multiple, bilateral renal cysts along with extra-renal manifestations. Liver is the most common extra-renal organ affected in ADPKD. Congenital hepatic fibrosis (CHF), is a rare, but well known forms of liver involvement in ADPKD. We report a case of a 26-year-old male was admitted to Lokmanya Tilak Municipal Hospital for the sudden loss of consciousness and one episode of convulsion in July 2012. Patient succumbed to his illness within 2 h, autopsy revealed bilaterally enlarged polycystic kidneys. Liver showed broad bands of portal to portal fibrosis. The portal tracts contained abundant irregularly shaped interlobular bile ducts. CHF is most commonly associated with ARPKD amongst the various renal ciliopathies. We present the rare association of ADPKD with CHF.

**Keywords:** Autosomal dominant, Congenital fibrosis liver, Polycystic kidney disease, Subarachnoid hemorrhage

## INTRODUCTION

Ciliopathies are the newer group of human genetic disorders in which the ciliary structure or function is affected. It can involve single or multiple systems and caused by a number of largely unrelated genes.<sup>1</sup> Hepatorenal fibrocystic diseases (HRFCDs) are a part of ciliopathies and characterized by developmental abnormalities of the portobiliary system along with fibrocystic change in the kidneys. Autosomal dominant polycystic disease (ADPKD) belongs to a group of inherited renal disorders called PKD which is the largest subclass of HRFCDs.<sup>2</sup> ADPKD is characterized by multiple, bilateral renal cysts along with extra-renal

manifestations which include polycystic liver disease and cysts in seminal vesicles, pancreas, and arachnoid membrane. In addition, patients may have a variety of other abnormalities, many of which are consistent with a generalized defect in epithelial cell differentiation and/or extracellular matrix function as a primary expression of the genetic abnormality in this disorder. These include vascular malformations like intracranial aneurysms, dolichoectasias, aortic root dilatation and aneurysms, dissection of the thoracic aorta and cervicocephalic artery, mitral valve prolapse, coronary artery aneurysms and abdominal wall and inguinal hernias and colonic diverticula.<sup>3-6</sup> Liver is the most common extra-renal organ affected in ADPKD. Although cystic liver is the most common form of liver involvement, congenital hepatic fibrosis (CHF), idiopathic dilation of the intra or extrahepatic biliary tract (Caroli syndrome), and cholangiocarcinoma are the rare but well known forms of liver involvement in ADPKD.<sup>7</sup> We report a case of ADPKD which presented with ruptured intracranial aneurysm along with CHF on examination of liver.

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## CASE REPORT

A 26-year-old man was admitted to Lokmanya Tilak Municipal Hospital for the sudden loss of consciousness and one episode of convulsion in July 2012. Patient had no similar history in the past or was not diagnosed with any major medical or surgical illness in the past. On admission, patient was unconscious with dilated pupils (8 mm), not reacting to light. His blood pressure recorded was 210/110 mm of Hg. Computerized tomography of the brain showed a large sized intracranial bleed measuring 5.2 cm × 4.9 cm × 4.4 cm in the right gangliocapsular region causing mass effect. Intra-ventricular hemorrhage noted in bilateral lateral ventricles and third and fourth ventricles. His hemoglobin, total white cell count and platelet count were within normal limits. Patient succumbed to his illness within 2 h of hospital stay despite all resuscitative measures taken. Autopsy revealed bilaterally enlarged kidneys (Figure 1) each measuring 480 g.



Figure 1: Gross appearance of bilateral polycystic kidneys



Figure 2: Gross appearance of liver showing vague nodularity

They had bosselated outer surface and cut surface revealed multiple cysts ranging in size from 0.5 cm to 2.5 cm involving both cortical and medullary areas. Histopathological examination of kidneys revealed the innumerable epithelial-lined cysts which were lined by simple cuboidal epithelium, and the cysts contained proteinaceous coagula. Areas of normal renal parenchyma showed interstitial fibrosis and infiltration by mixed mononuclear cells. Liver weighed 1200 g and was grossly firm, grayish brown in color and had vague nodular architecture on the cut surface (Figure 2). Histological examination of liver (Figure 3) confirmed the nodular architecture with broad bands of portal to portal fibrosis. The portal tracts contained abundant irregularly shaped interlobular bile ducts reminiscent of excess of embryonic bile structures lined by normal cuboidal epithelium (Figure 3). There were scarce portal vein branches in the fibrotic area. Inflammatory cells were absent in the periportal fibrotic area. The hepatic lobules as well as hepatic parenchyma were normal in morphology, unlike in cirrhosis. On examination of the cranial cavity, there was a large area of subarachnoid hemorrhage covering the right convexity of brain encompassing right frontal, temporal and parietal lobes. This was the cause of death in this case of ADPKD. Spleen weighted 160 g and was congested. Both the lungs had diffuse intrapulmonary hemorrhages.

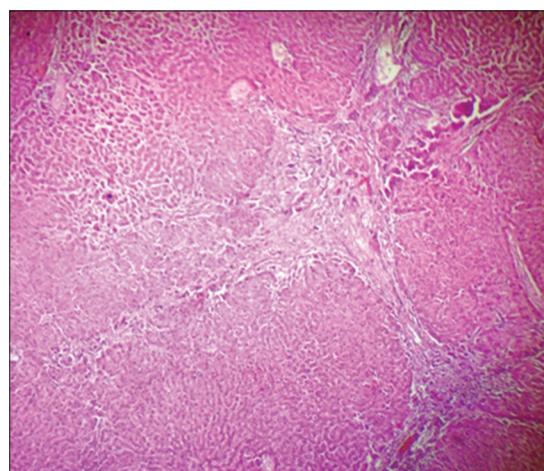


Figure 3: Liver-microscopy-low power-portal to portal fibrosis

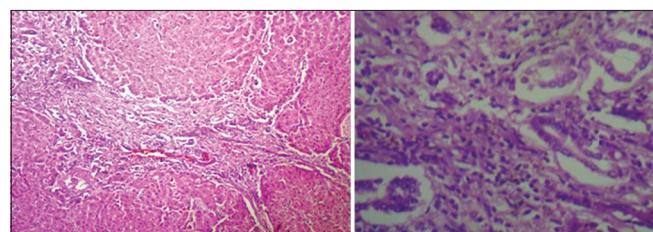


Figure 4: Liver-microscopy-portal tract fibrosis with (inset) increased number of bile ducts

## DISCUSSION

CHF, a developmental disorder of portobiliary system, rarely appears as an isolated finding and is often associated ciliopathies having associated renal disease like HRFCDs. The ciliopathy associated prevalence of CHF is 1 in 10,000 to 20,000.<sup>9</sup> It has ductal plate malformation (DPM) as the basic underlying pathology.<sup>8,10</sup> Histopathologically, it is characterized by defective remodeling of the ductal plate (DPM) in form of abnormal portal tracts with excess number of abnormally shaped embryonic bile ducts retained in their primitive ductal plate configuration, abnormal branching of the intrahepatic portal veins, and periportal fibrosis without inflammation. The bridging fibrotic bands extend from portal to portal tracts and not from portal tract to the central vein. The hepatocellular function is well preserved in CHF unlike hepatic cirrhosis.<sup>2,9</sup>

The most common fibrocystic renal disease that is associated with CHF is autosomal recessive PKD (ARPKD).<sup>2,9,11</sup> CHF is not so commonly associated with ADPKD but cases have been reported in the recent past.<sup>12-18</sup> ADPKD is genetically heterozygous disease caused by mutation of two genes viz. PKD1 (chromosome 16p13.3) and PKD2 (chromosome 4q21).<sup>3</sup> The inheritance pattern of CHF is autosomal recessive while ADPKD is transmitted by autosomal dominant pattern. It was proposed that there may be modification of ADPKD by an independent allele producing a phenocopy of the recessive form of PKD with CHF.<sup>13</sup> Now it is proved their concomitant association is found to be due to PKD1 mutation.<sup>9,15</sup> In most cases the renal lesions are usually silent clinically but few develop chronic kidney failure in adulthood.<sup>18</sup> Lipschitz *et al.* have found that many present with portal hypertension and only latter found incidentally to have ADPKD.<sup>14</sup>

The most frequent and early finding in ADPKD is hypertension seen commonly in adults up to 75% of cases. This causes the patients at an increased risk of cardiovascular death.<sup>19</sup> Also, pathologies involving other systems as mentioned earlier often lead to increased morbidity and mortality at an early age in these patients. In such events, asymptomatic CHF can be under-diagnosed<sup>2</sup> which is seen in our case.

## CONCLUSION

CHF is most commonly associated with ARPKD among the various renal ciliopathies. We present the rare association of ADPKD with CHF.

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