Dear Sir,

Autosomal dominant polycystic kidney disease (ADPKD) is a multi-systemic and progressive disorder characterized by formation of cysts in ductal organs particularly the kidneys, liver, pancreas, gastrointestinal tract, the central nervous system and the cardiovascular system.[1,2] The disease may occur anytime in life, including in utero in contrast with its previous name “adult polycystic kidney” which suggests affection of only adults.[3] ADPKD is the most frequent genetic cause of renal failure in adults and is slightly more severe in males than in females while symptoms generally increase with age.[1]

Dalgards in 1957 clarified the autosomal dominant pattern of inheritance of the disease,[4] while in 1985 the causative gene ADPKD1 was identified on the short arm of chromosome 16 that accounts for 85–90% of patients. A second gene ADPKD2 responsible for 5–15% of cases was later discovered on the long arm of chromosome 4 and a third gene probably exists.[3,5-7] Renal cystogenesis involves transepithelial transport of solutes in a process that involves an alteration in cell growth, fluid secretion, and extracellular matrix composition.[1,3,8] Despite the limited information on the pathogenesis of extra-renal abnormalities, a few reports on hepatic cystogenesis support a process in bile ducts similar to that in renal tubules and this is supported by the composition of hepatic cyst fluid.[1,2] Non-cystic extrarenal lesions include, cardiac valvular lesion (mitral, aortic), intra-cranial saccular (berry) aneurysm and colonic diverticular.[1,3,9]

A 56-year-old man presented with a 1-week history of a low-grade continuous fever and a dull pain in the epigastrium and right hypochondrium. It was associated with a progressive abdominal distention and easy satiety. He became jaundiced 3 days prior to presentation. The patient had no prior history of hematemesis or melena, alcohol ingestion or blood transfusion. On admission he was conscious but chronically ill looking, febrile (temperature 38°C) with a tinge of jaundice, flapping tremor, and a blood pressure of 110/70 mmHg. The liver was firm, mildly tender, and nodular with a span of 17 cm. There was no ascites or splenomegaly.

The kidneys were ballotable. Other aspects of the examination were not very remarkable. An initial assessment was made of hepatic encephalopathy secondary to chronic liver disease with probable malignant transformation and malaria. The patient was started on standard anti-failure regimen and cotecxin/fansidar. Results of investigations requested within the first 24 h of admission were as follows:

1. Liver function test (LFT)—ASAT 90 (up to 15) iu/l, ALAT 84 (up to 22) iu/l, total protein 65 (58-80) g/l, albumin 31 (35-50) g/l;
2. Renal function test (RFT)—Potassium 4.1 (3-5) mmol/l, sodium 122 (135-14) mmol/l, chloride 88 (95-110) mmol/l, bicarbonate 16 (20-30) mmol/l, creatinine 139 (44-132) mmol/l, urea 8 (2.5-2.7) mmol/l;
3. Urinalysis—proteinuria;
4. Serology—HBsAg, HC antibody, HIV and α-fetoprotein were all negative;
5. Full blood count—hemoglobin 9.8 g/dl, WBC 9 x 10^9 with neutrophilia of 76%. Malaria parasites were also present;
6. Urine microscopy showed numerous pus cells and grew E. coli sensitive to ciprofloxacin;
7. Blood culture—E. coli isolated, sensitive to ciprofloxacin, amoxicillin-clavulanic acid, ofloxacin and ceftriaxone;
8. Abdominal ultrasound—hepatomegaly with some decreases in echogenicity multiple cysts and dilated portal and biliary systems. The kidneys were also dilated with multiple cysts. The pancreas was enlarged with multiple cysts on the anterior--superior surface.

The diagnosis was reviewed for ADPKD with hepatic encephalopathy and septicemia secondary to urinary tract infection. The patient was then placed on intravenous ciprofloxacin, while the anti-failure regimen was continued. The patient’s clinical condition initially improved, but on the sixth day of admission, he became anuric with his creatinine and urea levels rising to 499 mmol/l and 21 mmol/l, respectively. Arrangements were initiated to transfer him to a center with dialysis facilities. The patient died during transfer to a center with dialysis facility. Post-mortem was not done.
The rarity of the case in our environment and the unusual presentation necessitated this report.

Although it has been suggested that ADPKD is rare in Africa and less common in American blacks than whites, the paucity of reports from this part of the world may be attributed to the low index of suspicion.[10] Moreover, most of the patients do not report a family history, coupled with poor documentation, making it difficult to establish the dominant pattern of inheritance from the history alone. In addition, since most patients are asymptomatic and are picked as incidental findings like the case being reported here, they can remain undetected for long. The most frequently used methods of diagnoses are ultrasonography, computed tomography, and magnetic resonance imaging (MRI). The high sensitivity of ultrasonography, lack of radiation exposure, low cost and availability makes it the preferred diagnostic imaging method particularly in resource poor settings like ours. The limited availability of the other methods may be barriers to the pursuit of other variants of fibropolycystic disease of the liver.

ADPKD has varying presentations but hepatic presentations are relatively uncommon. Nevertheless, liver cysts are still the most frequent extra-renal presentation.[8] The prevalence of liver involvement increases with age and affects both sexes.[11,12] Generally, massive liver cysts appear to be exclusive of females due to probable influence of female steroid hormone although the patient being reported is a male.[13,14]

Symptoms from the liver disease often result from complications of fibrosis or dilated ducts/cyst (sludge, lithiasis, infection).[13] The treatment is supportive with careful attention to associated renal disease. A portosystemic shunt by balloon-occluded retrograde transvenous obliteration and partial splenic embolization is an option.[16] In advanced disease, liver and or renal transplant may be offered.[17] All these options were not offered to our patient because of non-availability.

The development of renal insufficiency is highly variable in ADPKD, but the risk of ESRD increases with age, renal size, and earlier in patients with ADPKD1 gene mutation.[13] At 56 years, this patient has a relatively preserved renal function at the time of admission. The deteriorated renal function that developed in this patient is likely to be a complication of the hepatic encephalopathy and/ or septicemia. Dialysis has improved the outcome in a similar situation.[18]

Hypertension, which is found in about 60% of adults with ADPKD before the onset of renal insufficiency and 80% of those with ESRD has been linked to higher number and size of cysts.[1,10,20] Surgical removal of cyst has been shown to improve hypertension in a Chinese study.[21] Despite the multiplicity of and large sizes of the cysts, our patient had no hypertension. He may be among the minority that do not present with hypertension. The admitting clinical features presented by this patient of dull right hypochondrial pain, easy satiety, fever, hepatomegaly, and jaundice are consistent with the initial diagnosis of chronic liver disease with malignant transformation that has a high prevalence in the region.[23] On the other hand, the absence of positive family history and the paucity of reports for ADPKD make the index of suspicion very low. This is consistent with findings in some reports as up to 62% of parents with affected children were unaware because they were asymptomatic.[3] However, imaging of parents of index patients may reveal up to 30% of APKD cases.[3]

While in females, hepatic disease has been linked to earlier occurrence of renal insufficiency, in men it is urinary tract infection that appears to worsen the course of renal disease.[22] The case being reported appears to have followed this pattern with the isolation of E. coli in urine and blood. In a fairly similar report by Munemura et al, the renal failure was of gradual onset and precipitated the development of hepatic encephalopathy. The encephalopathy was reversed with dialysis and anti failure regimen.[23] In the present case, the development of renal failure during the admission appeared to have negatively affected the course of the illness. Moreover, dialysis was not available at the center and financial preparations have to be made before transfer and these must have contributed to the fatal outcome. The absence of a CT or MRI has inhibited further evaluation. Post-mortem was not done.

The case presented is a wake-up call on the possibility of ADPKD with hepatic encephalopathy in our environment and should be considered in all patients with similar presentation. A high index of suspicion and ultrasonography will lead to the detection of more cases. More qualified sonographers are needed in the country. There should be aggressive management and prompt referral to special care centers of all suspected cases with follow-up screening of family members.

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References