ISSN - 2250-1991 | IF : 5.215 | IC Value : 79.96

Original Research Paper General Surgery

An unusually long survival in a case of ARPKD - Polycystic Hepatorenal disease with Congenital Hepatic Fibrosis, presenting with variceal bleeding and hypersplenism due to portal hypertension, with review of literature.

Dr. Madhav D. Thatte	[Professor, Surgery] Faculty, Department of Surgery, Bharati Medical College and Research Centre, Pune.
Dr. Sunila Sewani	(Resident, General Surgery) Bharati Medical College and Research Centre, Pune.
Dr. Kshitij Raghuvanshi	(Resident, Urology) Bharati Medical College and Research Centre, Pune.

ABSTRACT

Autosomal recessive polycystic kidney disease[ARPKD] with long survival is not very common. Most of the patients succumb to the disease before the age of ten years. An adult case of ARPKD with congenital hepatic fibrosis leading to portal hypertension, hypersplenism and bleeding oesophageal varices, successfully controlled with a follow up of 4 years is reported.

KEYWORDS

ARPKD, ADPKD, Portal Hypertension [PH], bleeding oesophageal varices, Congenital Hepatic Fibrosis[CHF], End Stage Renal Disease [ESRD], hypersplenism, Thatte's modification of Tanner's operation with limited oesophagogastric devascularization.

Introduction:

Autosomal recessive polycystic kidney disease (ARPKD), a rare genetic disorder characterized by chronic, irreversible, progressive cystic degeneration of the kidneys [cystic dilatations of collecting ducts] and congenital hepatic fibrosis (CHF) [leading to biliary dysgenesis, periportal fibrosis], is the most common childhood onset ciliopathy, with an estimated frequency of 1 in 20,000 births [1:6,000 to 1:40,000 persons in the general population, depending on the source of reference]. It is caused by mutations in PKHD1. The carrier frequency for ARPKD in the general population is estimated at 1 in 70. [1]

It eventually leads to End Stage Renal Disease[ESRD] and effects of Congenital Hepatic Fibrosis (CHF) namely Portal Hypertension [PH], bleeding oesophageal varices and hypersplenism. The age spectrum for onset of symptoms is from birth to adolescence, seldom adulthood. We report a case of ARPKD, presenting at the age of 21 years, with the sequele of CHF.

Case report :

Presentation

21 yr old, married female was admitted to a community hospital in rural India, with a history of haematemesis and malaena for 2 days. She was a known case of bleeding oesophageal varices [FIG 1] who had repeated blood transfusions during past 3 years, had undergone variceal banding 3 months before, at a district place. Due to monetary constraints, she couldn't continue with further management and was on symptomatic treatment of some local doctor in her village. She presented to us with severe pallor, puffiness of face and features of cold shock - tachycardia, low BP, reduced urine output and cold clammy hands after a bout of haematemesis. Her blood investigations were as follows: Hb 3.5 gm %, total WBC count 2100, platelet count 60000 [pancytopaenia], blood urea 88 mg %, Serum creatinine 3.5 mg%. Urine routine showed plenty of pus cells and albumin. She had massive splenomegaly. She did not have ascites, icterus, clubbing and pedal oedema. Her routine liver function tests were fairly within normal limits except for marginally raised serum alkaline phosphatase.

Management:

She was resuscitated with blood transfusions, intravenous fluids, Octreotide and Ampicillin. A nasogastric tube was inserted, ice cold saline gastric lavage was given as an attempt to control variceal bleeding. She settled haemodynamically. CT scan of abdomen and pelvis revealed massive splenomegaly, gastrosplenic and splenic hilar varices, dilated extrahepatic portal vein [diameter 18mm], multiple dilated tortuous veins in periportal, peripancreatic area, in splenorenal ligament, perigastric area and lower oesophagus; Gall bladder stuffed with tiny calculi; enlarged kidneys with foetal lobulations, multiple cystic lesions and loss of corticomedullary differentiation; fibrosed right hepatic lobe with cystic lesions, compensatory hypertrophy of caudate and left hepatic lobe.[FIG 2]

After about 4 weeks of initial treatment, her haemoglobin was 7 gm%, total leukocyte count 2500, platelet count 40000, blood Urea 65 mg%, Serum Creatinine 3.1 mg%. Bone marrow biopsy revealed hyperplastic bone marrow. A clinical diagnosis of congenital hepatic fibrosis with polycystic kidney disease, portal hypertension, oesophageal varices, hypersplenism suggested ARPKD.

Surgical procedure : [Thatte's modification]

Instead of the classical Tanner's operation, author's modification [Thatte's modification] was carried out. Splenectomy [FIG 3] with limited Oesophago - gastric devascularizarion was performed. In this, paraoesophageal abdominal vessels were under-run at multiple places with a series of nonabsorbable sutures. Ascending divisions of Left gastric vessels were similarly under-run along the proximal half of lesser curvature of stomach. Further, left gastroepiploic vessels were dealt with in the same manner. Dilated, tortuous coronary vein was also cut between ligatures. [FIG 4] A running suture line along the entire gastric circumference including full thickness wall [locking every stitch] about 4 cm below oesophagogastric junction, ensured obliteration of vascular plexus in the wall of stomach – this completed the porto-azygus disconnection without transecting the stomach. [FIG 5] [Conventional Tanner's operation achieves the same by Gastric transaction reanastomosis]. Cholecystectomy was also performed in view of multiple tiny calculi within. [FIG 3]

Results:

The patient recovered well uneventfully, consuming full diet from 6th postoperative day. At four and half years follow up, her peripheral blood counts are fairly within normal limits, she never

had bleeding from varices, serum creatinine is around 2 mg% and she remains under Nephrologist's vigilance on regular basis.

Discussion:

Polycystic kidney disease [**PKD**], also known as polycystic kidney syndrome, is a genetic disorder. [2] PKD is characterized by presence of multiple cysts (hence, "polycystic") typically in both kidneys; however 17% of cases initially present with observable disease in one kidney, with most cases progressing to bilateral disease in adulthood. [3] PKD affects an estimated 12.5 million people worldwide.[4]

There are two major types of hereditary polycystic kidney disease, commoner autosomal dominant (ADPKD) and rare autosomal recessive (ARPKD). ADPKD is the most frequent hereditary renal disease [with an incidence of 1 to 2:1,000 live births] and is often encountered in the work up of renal patients. Incidence of ARPKD is 1: 6,000 to 1:50,000 live births. [3,5,6]

ADPKD exhibitss almost 100% penetrance, has three varieties, PKD 1 coded for on chromosome 16, PKD 2 on chromosome 4 and ADPKD 3 on an unknown chromosomal site. ARPKD is coded for on the short arm of chromosome 6. [7]

Characteristics of ADPKD and ARPKD [table 1] [7,8]

ARPKD is commonly diagnosed early in life or in utero and carries very high mortality postnatally or during infancy from pulmonary hypoplasia. The survivors develop progressive renal failure and ESRD requiring dialysis and renal transplant. The disease does not recur in transplanted kidneys. In addition to renal pathology, in ARPKD, one usually finds hepatic ductal plate malformations with cystic dilation of intra- and extra-hepatic bile ducts resulting in congenital hepatic fibrosis (CHF) and Caroli syndrome with PH [due to periportal fibrosis] or without PH. [8]

PKD can also damage pancreas and rarely, heart and brain. Mild renal failure may be accompanied by serious systemic hypertension in some patients. Over 2 to 20 years, almost all patients develop PH from CHF, a problem primarily noted in ARPKD as against ADPKD. The emergence of CHF and resultant PH in infants and children makes the clinical scenario still more complex. Many will eventually develop Oesophageal Varices, splenomegaly, hypersplenism, protein loosing enteropathy and gastrointestinal bleeding. Complications of hepatic involvement can include ascending cholangitis, cholestasis with malabsorption of fat soluble vitamins, and rarely benign or malignant liver tumors. [9,10,11]

Clinical Course of ARPKD

The classic presentation for ARPKD is systemic hypertension with progression to end-stage renal disease (ESRD) by the age of 15. In atypical presentation, a small number of ARPKD sufferers live to adulthood with some kidney function; but with significant deterioration in liver function [3] [as in our case].

The clinical presentation of ARPKD is highly variable.

a)antenatal form (most common)

90% of renal tubules show cystic changes with "in utero" onset of renal failure, oligohydramnios and dystocia (large abdominal masses - Enlarged kidneys) Prognosis: death from renal failure / respiratory insufficiency (pulmonary hypoplasia) within 24 hours in 75% cases, within 1 year in 93%; is uniformlyfatal.

b) neonatal form

60% of renal tubules show ectasia + minimal hepatic fibrosis + bile duct proliferation. Onset of renal failure is seen within 1st month of life. Impaired urinary concentrating ability and metabolic acidosis ensue as renal tubular function deteriorates. Prognosis: death from renal failure / hypertension / left ventricular failure within 1st year of life.

c) infantile form

20% of renal tubules are involved + mild / moderate periportal fibrosis. Disease appears by 3-6 months of age. Prognosis: death from chronic renal failure / systemic arterial hypertension / PH.

d) juvenile form

10% of renal tubules are involved + gross hepatic fibrosis + bile duct proliferation. Disease appears at 1-5 years of age. Prognosis: death from PH. The less severe the renal findings, the more severe the hepatic findings – is the working rule.

Lung - Severe pulmonary hypoplasia, Pneumothorax / pneumomediastinum

Liver - Portal venous hypertension, Tubular cystic dilatation of small intrahepatic bile ducts, increase in liver echogenicity [from congenital hepatic fibrosis]

Kidneys - unlike ADPKD the cysts rarely exceed 1 - 2 cm in diameter, kidneys appear enlarged and echogenic but usually retain their reniform shape.

Renal imaging : Bilateral gross renal enlargement, Faint nephrogram + blotchy opacification on initial images, Increasingly dense nephrogram, Poor visualization of collecting system, Loss of corticomedullary differentiation, "Sunburst nephrogram"[striated nephrogram with persistent radiating opaque streaks (collecting ducts) on delayed images], Prominent faetal lobulation

ADPKD-Specific: It is the 3rd most prevalent cause of chronic renal failure. It is a slowly progressive disease with mean age at diagnosis as 43 years. ADPKD is associated with pathologies in other body systems, in contrast to ARPKD. [10] In 50% of the cases cysts appear in other organs including the liver, pancreas, spleen, lung, seminal vesicles, and ovaries. 10 to 30% have saccular Berry aneurysms in the Circle of Willis [cerebral circulation]. The most common sites for cysts include coronary arteries; and abnormalities in cardiac valves especially Mitral valve prolapse, hernias, and diverticuli are all documented. Cysts in liver (25-50%), pancreas (9%), Hypertension (50-70%), Azotemia, Hematuria, proteinuria further complicate the clinical scenario.

Management of ARPKD:

No specific therapy exists for ARPKD. Improvements in mechanical ventilation, neonatal intensive care support, blood pressure management, dialysis, and kidney transplantation have led to survival well into adulthood. Complications of hepatic fibrosis may necessitate liver transplantation.

Management of PH may require endoscopic band ligation of oesophageal varices . PH may be decompressed surgically by proximal [in cases of hypersplenism] or distal [in cases without hypersplenism] lieno-renal or portocaval shunting. Prophylactic porta-caval shunting followed by renal transplantation is ideally suited to the sequence of events occurring clinically in the intermediate form of this condition, preventing complications of bleeding from oesophageal varices and hypersplenism.

Conclusion

Cases of ARPKD with hepatic fibrosis leading to PH with bleeding oesophageal varices are uncommon, and survival till adulthood is still rare. Though, ideally, renal and liver transplants are indicated, it remains a therapeutic illusion in the rural scenario of the developing world. Surgery / Author's procedure can control bleeding episodes.

Table 1:
Characteristics of ADPKD and ARPKD

ADPKD	ARPKD
*evidence of renal cyst in either parent	*absence of renal cyst in either parent
*Normal sized kidney	*Enlarged kidney
*Few or multiple usually larger cysts	*Multiple tiny cysts
*Cyst-free parenchyma exhibiting	*Diffuse increase of Parenchymal

Normal echogenicity	echogenicity
*Medulla clearly distinguishable from cortex	*Loss of corticomedullary distinction

Legends:

FIG 1: oesophageal varices
FIG 2: CT Scan of abdomen: R: right lobe of liver, L: left lobe of liver, C: caudate lobe, S: spleen, K: kidney
FIG 3: massive splenomegaly, specimen of spleen and gall bladder
FIG 4: black arrows point to dilated tortuous paraoesophageal veins
LTL : left triangular ligament of liver
White arrows point to ligation and division of dilated coronary vein
FIG 5: circumferential suture line on stomach [including all layers] achieves porto-azygus disconnection

FIG 1: oesophageal varices

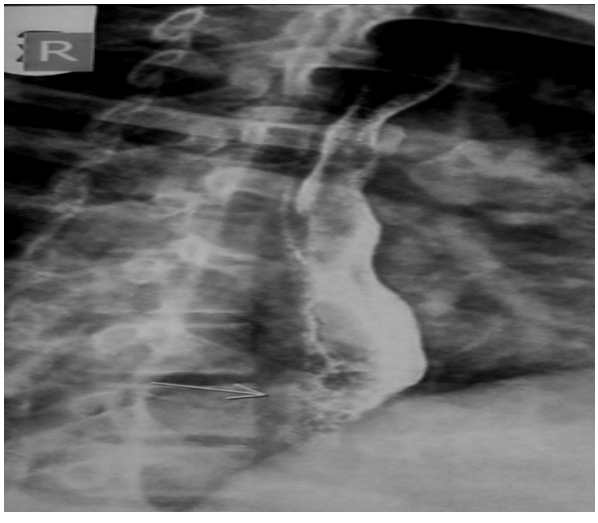


FIG 2: CT Scan of abdomen:
R: right lobe of liver, L: left lobe of liver, C: caudate lobe, S: spleen, K: kidney

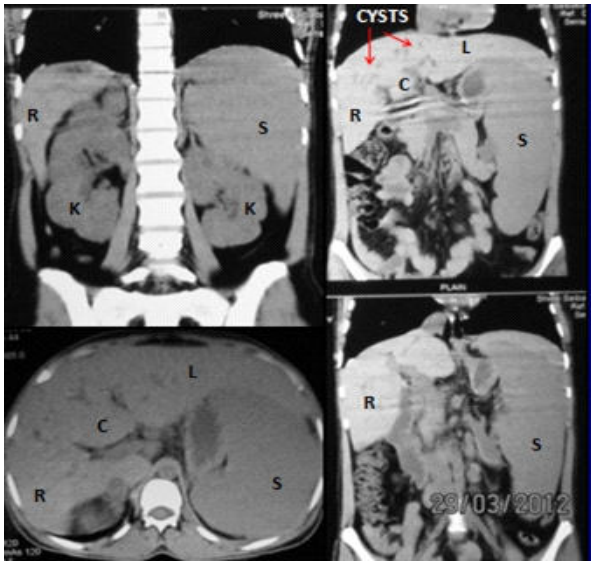


FIG 3: massive splenomegaly, specimen of spleen and gall bladder

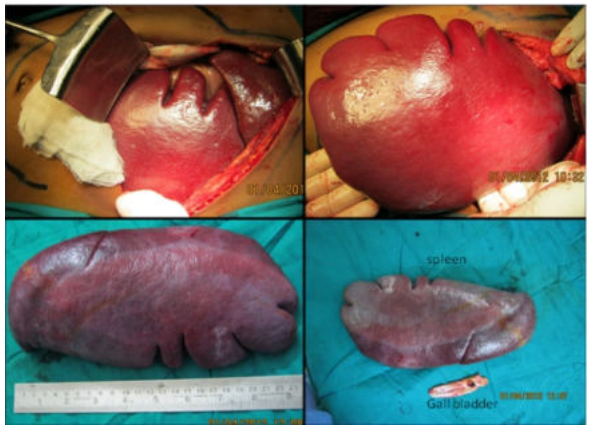


FIG 4: black arrows point to dilated tortuous paraoesophageal veins
LTL : left triangular ligament of liver
White arrows point to ligation and division of dilated coronary vein

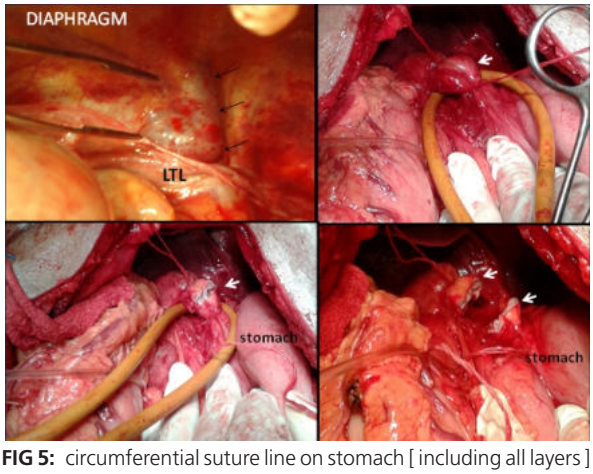
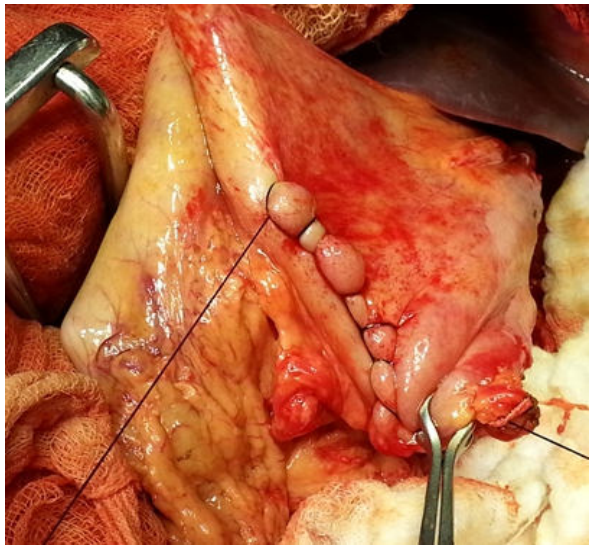


FIG 5: circumferential suture line on stomach [including all layers] achieves porto-azygus disconnection



References :

[1] Gunay-Aygun M, Turkbey BI, Bryant J, Daryanani KT, Gerstein MT, Piwnica-Worms K, Choyke P, Heller T, Gahl WA. Hepatorenal findings in obligate heterozygotes for autosomal recessive polycystic kidney disease. Source: Medical Genetics Branch, National Human Genome Research Institute, Bethesda, MD 20892, USA. mgaygun@mail.nih.gov: Published by Elsevier Inc.
[2] "polycystic kidney disease" at Dorland's Medical Dictionary
[3] Bisceglia, M; et al (2006). "Renal cystic diseases: a review". Advanced Anatomic Pathology (13): 26–56
[4] Wilson PD. Polycystic kidney disease. N Engl J Med 2004;350:151-164
[5] Torres, WE; Harris PC, Pirson Y (2007). "Autosomal dominant polycystic urology".

Lancet 369 (9569): 1287–301. doi:10.1016/S0140-6736(07)60601-1
[6] Simons, M; Walz G (2006). "Polycystic kidney disease: cell division with a c(l)ue?". Kidney International (70): 854–864.
[7] Chapman AB, Gabow PA. Hereditary and congenital renal cystic disease. In: Massry & Glassock's Textbook of Nephrology, Vol. 1, 3rd edn. Williams & Wilkins, Baltimore, 1995; 913–930
[8] Anna-Maria Nahm, Daniel Ernesto Henriquez and Eberhard Ritz. Renal cystic disease (ADPKD and ARPKD). Nephrol. Dial. Transplant. (2002) 17 (2): 311-314. doi: 10.1093/ndt/17.2.311
[9] ADEVA M, EL-YOUSSEF M, ROSETTI S, KAMATH PS, KUBLY V, CONSUGAR MB, MILLINER DM, KING BF, TORRES VE, HARRIS PC. Clinical and molecular characterisations defines a broadened spectrum of autosomal recessive polycystic disease (ARPKD). Medicine. 2006; 85:1–21. [PubMed: 16523049]
[10] BLYTH H, OCKENDEN BG. Polycystic disease of kidney and liver presenting in childhood. J Med Genet. 1971; 8:257–284. [PubMed: 5097134]
[11] TURKBEY B, OCAK I, DARYANANI K, FONT-MONTGOMERY E, LUKOSE L, BRYANT J, TUCHMAN M, MOHAN P, HELLER T, GAHL WA, CHOIKE PL, GUNAY-AYGUN M. Autosomal recessive polycystic kidney disease and congenital hepatic fibrosis (ARPKD/CHF). Pediatr Radiol. 2009; 39:100–111. [PubMed: 19089418]