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Case Report

Adult Polycystic Disease, a Cadaveric Case Report and Review of Literature

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Abstract

PKD is an inherited condition defined by the pathological development of fluid-filled cysts throughout the kidneys leading to organ enlargement and chronic kidney disease. Autosomal dominant polycystic kidney disease (ADPKD) is the fourth commonest cause of kidney failure worldwide. The main feature of ADPKD is the presence of cystic tubules, which are unable to perform their function properly, resulting in fluid retention, high blood pressure and kidney failure. Eventually, there is slow progression to End Stage Renal Disease (ESRD). During routine dissection for undergraduate students, we came across a case of adult polycystic kidney disease in a 60-year-old male cadaver, who died of complications of the disease which included accelerated hypertension, and renal failure. The kidneys showed bilateral multiple simple cysts of varying sizes. The kidneys were enlarged with an increase in weight. Patients with polycystic kidney disease may live a normal lifespan without knowing that they have the disease. More typically, however, ADPKD causes progressive renal dysfunction often necessitating dialysis or renal transplant for survival. Individuals with ADPKD may present with extra-renal disease like Hypertension, liver cysts, kidney stones, cardiac valvular abnormalities etc. Lately there have been many preclinical and clinical trials in mechanism based therapeutics for the control of cyst formation. Knowledge of the preventable or alterable aspects can help the clinician to delay the progression of renal failure to a great extent.

Keywords: Polycystic Kidney Disease; Autosomal Dominant; Cystic Tubules; Fluid Retention; High Blood Pressure; Kidney Failure; Dialysis; Renal Transplant; Clinician

Introduction

The kidneys are paired retroperitoneal structures that are normally located between the transverse processes of T12-L3 vertebrae, with the left kidney typically slightly superior in position than the right. The upper poles are normally oriented more medially and posteriorly than the lower poles. The average weight of a kidney is approximately 135 gm, measuring on average 10 × 6 × 4 cm [1].

The kidneys serve important functions, including filtration and excretion of metabolic waste products (urea and ammonium); regulation of necessary electrolytes, fluid, and acid-base balance; and stimulation of red blood cell production. They also serve to regulate blood pressure via the renin-angiotensin-aldosterone system, controlling reabsorption of water and maintaining intravascular volume. The kidneys also reabsorb glucose and amino acids and have hormonal functions via erythropoietin, calcitriol, and vitamin D activation [2].

The functional renal unit is the nephron, which is composed of the renal corpuscle: glomerulus and Bowman capsule, Proximal convoluted tubules (PCT, located in the renal cortex), Descending limb, loop of Henle, Thick Ascending limb (which resides in the renal medulla, Distal convoluted tubule, Collecting duct (which opens into the renal papilla) [3].

Polycystic kidney disease (PKD) is an important health care problem which is regarded as a group of diseases characterized by dilatation of the tubular units of the kidney. PKD is an inherited condition defined by the pathological development of fluid-filled cysts throughout the kidneys leading to organ

enlargement and chronic kidney disease. Autosomal dominant polycystic kidney disease (ADPKD) is the commonest inherited kidney disease and is the fourth commonest cause of kidney failure worldwide. It is a multisystemic and progressive disorder [4].

The main feature of ADPKD is a bilateral progressive increase in the number of cysts, resulting in end stage renal disease. The kidney tubules process 140 litres of fluid filtered by the glomerulus daily making the final urine volume of 0.5-2.0 litres. If tubules are cystic, they are unable to perform this function properly, resulting in fluid retention, high blood pressure and kidney failure. The characteristic finding of ADPKD is the development of fluid-filled sacs (cysts) in the kidneys which may vary in number, size, progression and severity of cyst development greatly from one person to another. In most cases, renal cysts continue to grow and multiply, and cause significant problems like pain, infection, haemorrhage or kidney stones. Also the shape, size, and weight of the kidney can be significantly abnormal, causing progressive renal failure, often necessitating dialysis or renal transplant for survival. Eventually, there is slow progression to End Stage Renal Disease (ESRD) in which there is impaired ability of the kidneys to perform their basic functions like filtering waste products, regulating hormones or electrolytes, or concentrating urine sufficiently to maintain life. Approximately 50 percent of individuals with the ADPKD type develop end stage renal disease by 53 years of age [5].

We report a case of adult polycystic kidney disease in a 60-year-old male cadaver, who died of complications of the disease which included accelerated hypertension, and renal failure.

Case Report

During routine undergraduate dissection, of 60 year old donated embalmed male cadaver in the Department of Anatomy, at K.J. Somaiya Medical College, Sion, Mumbai, India, multiple simple cysts of varying sizes were observed on both right and left kidneys slightly more on the left side.

The kidneys were carefully dissected and separated out from the posterior abdominal wall. They were measured and also weighed. The length, breadth and thickness was measured using scale and vernier callipers. The right kidney presented with a large cyst in the lower pole. The left kidney measured 18cm x 11cm x 7cm and weighed 1250 gm. The right kidney measured 15cm x 9cm x 6cm and weighed 1075 gm. The external surfaces of the kidneys were appeared deformed and bumped. The photograph of the cystic kidneys in situ was taken for proper documentation.

On section, the cortex and medulla present numerous spherical cysts, sized between 0.5-5 cm in diameter, containing a serous, hemorrhagic or gelatinous fluid. Between the cysts, the intervening parenchyma showed atrophy by compression.

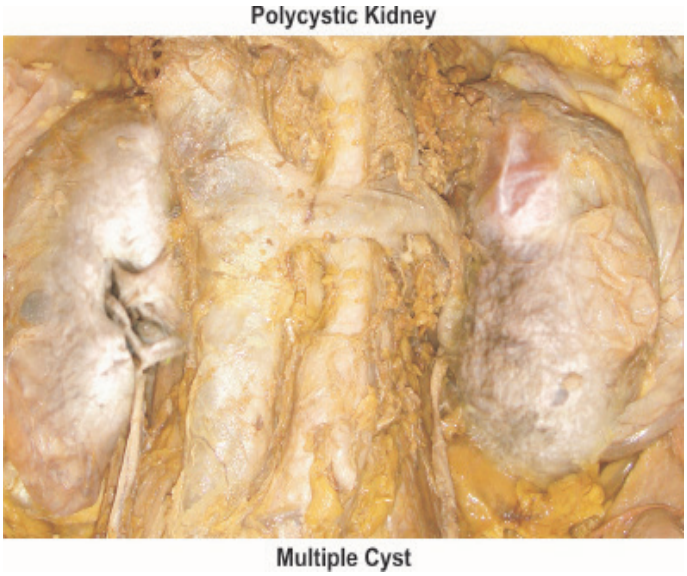

Figure 1: Showing bilaterally enlarged kidneys with multiple cysts

However, microscopically, this parenchyma was represented by functional nephrons.

The microscopic picture showed cysts (dilated tubules and collecting ducts) lined by cuboidal or flattened epithelium containing an eosinophilic fluid. The parenchyma between cysts was represented by few atrophic / compressed but still functional nephrons (glomeruli and tubules), with interstitial fibrosis and chronic inflammation. (HE, ob. 4x)

As per the medical records of the cadaver obtained from the next of kin, he was a known case of hypertension and renal failure.

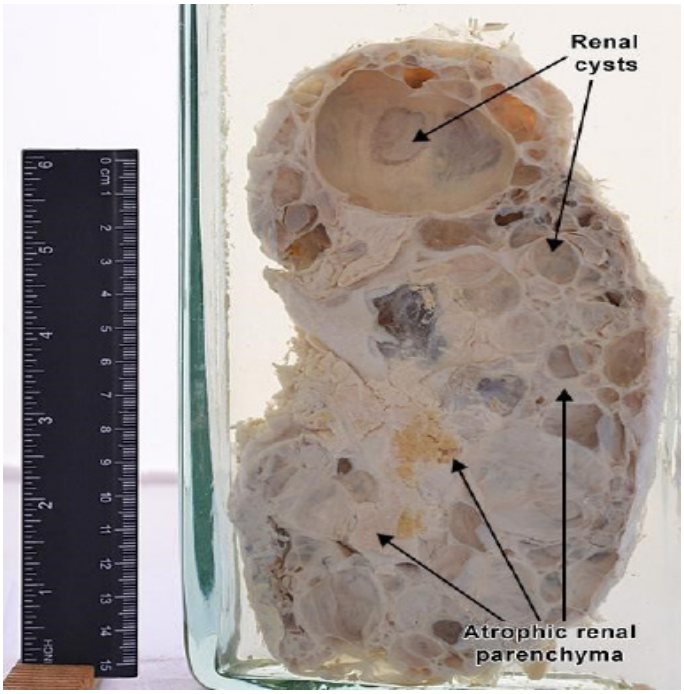

Figure 2: L.S. of Kidney showing cysts and atrophic parenchyma

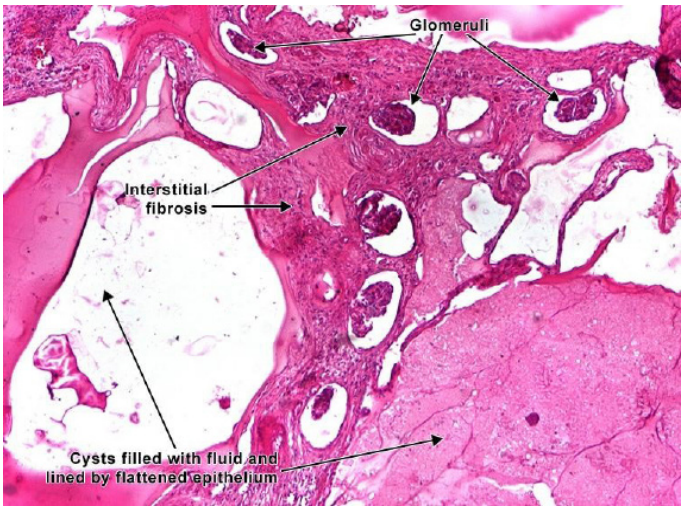

Figure 3: Microscopic picture showing cysts lined by flattened epithelium and filled with eosinophilic fluid

Discussion

Polycystic kidney disease affects 12.5 million people worldwide. It is found in all races and affects men and women equally. This disease affects people of all ages from neonates to adults, for adults usually it affects on their 50's. it is a life threatening condition to some individuals but to some it is asymptomatic.

Autosomal dominant polycystic kidney disease (ADPKD), is among the most common of all inherited diseases of humans, affecting between 1/500 and 1/2000 people. It is responsible for about 10% of the cases of End Stage Renal Disease (ESRD) [6].

Cysts are assumed to be formed by unusual cell differentiation leading to excessive proliferation and fluid secretion. There are defects in the extracellular matrix of renal tubules leading to dilatations or out-pocketing of the tubule wall, with the formation of a saccular cyst packed with glomerular filtrate that enters from the afferent tubule segment. This occurs in the early stages, due to the transformed polycystin. The immature and hyperplastic tubular epithelial cells, put across abnormal amounts of electrolyte transporters that are responsible for fluid accumulation and cyst growth in later stages. Progressive expansion leads the emerging cysts to separate from the parent tubule, leaving an isolated sac filled with fluid by transepithelial secretion Subsequently renal interstitium gets infiltrated with monocytes, macrophages, and fibroblasts, leading to fibrosis, and eventually loss of renal function. There is an inverse association between the size of polycystic kidneys and the level of glomerular filtration [7]. Though renal cysts look innocent when they occur alone, but in large numbers as in patients of ADPKD, they can lead to progressive renal parenchymal destruction and chronic renal failure. Each human kidney has about one million nephrons of which about 1% to 2% of nephrons only show cyst formation in ADPKD. It is fascinating that how such a small percentage of nephron involvement by cystic formation can lead to loss of renal function. Cellular proliferation and fluid secretion may be accelerated by cyclic adenosine monophosphate (cAMP) and growth factors, such as epidermal growth factor (EGF). In summary, cysts function as autonomous structures and are responsible for progressive kidney enlargement in ADPKD. Patients with polycystic kidney disease may live a normal lifespan without knowing that they have the disease. More typically, however, ADPKD causes progressive renal dysfunction, resulting in grossly enlarged kidneys and kidney failure by the fourth to sixth decade of life [8].

Currently most of the treatment of ADPKD is focused around the outcomes of the disease like blood pressure control. Lately there have been many preclinical and clinical trials in mechanism based therapeutics that look promising in the control of cyst formation [9].

Mammalian target of rapamycin (mTOR) is a serine/threonine kinase that regulates cell growth and cell cycle progression; It may minimize the increase in kidney volumes in patients but have limited impact on slowing down the decrease in GFR [10,11]. Somatostatin has been shown in clinical trials to slow renal and hepatic cyst progression and halt total liver and kidney volume increase, by reducing cyst fluid accumulation. It is similar to mTOR inhibitors as it has still not been shown to halt GFR [12]. Decreasing cAMP has been accomplished using vasopressor V2 receptor antagonists. They have been shown to inhibit cystogenesis and prevent renal enlargement and dysfunction in three different animal models with Phase II trials currently underway [13].

Genetic Factors

ADPKD is a hereditary autosomal dominant disorder occurring equally in males and females, each offspring having a 50% chance of inheriting the responsible mutation and hence the disease. Approximately 85-90% of patients with ADPKD have an abnormality on the short arm of chromosome 16 (ADPKD1). A second defect, termed ADPKD type 2 (ADPKD2), is responsible for 10-15% of ADPKD cases and is found on the long arm of chromosome 4.[14]

The proteins that are encoded by PKD1 and PKD2, polycystin 1 and polycystin 2, function together to regulate the morphologic constitution of epithelial cells. Polycystin 1 and polycystin 2 are highly conserved ubiquitous transmembrane protein located in the epithelial cells of the renal tubules—in particular, in the primary cilia at the luminal side of the tubules, as well as in other areas of the renal cell epithelium [15]. The primary cilium is a long, nonmotile tubular structure found on the apical surface of the epithelial cells in the renal tubules. It acts as a mechanoreceptor that senses changes in apical fluid flow. Polycystin 1 is a mechanical sensor of ciliary bending brought about by luminal fluid flow. Bending of the cilium would cause a conformational change in polycystin 1 that would, in turn, activate the polycystin 2–associated Ca2+

channel, increasing the intracellular Ca2+ concentration and triggering intracellular signaling pathways leading to normal kidney development [16].

In ADPKD, each epithelial cell within a renal tubule harbours a germ-line mutation, yet only a tiny fraction of the tubules develop renal cysts. It is currently held that the cells are protected by the allele inherited from the parent without ADPKD. When this allele is inactivated by a mutation (transformed polycystin) within a solitary renal tubule cell, the cell proliferates until a cyst develops. This abnormal growth program causes progressive expansion. The severity of ADPKD is thought to be a direct outcome of the rate at which this cystogenic process occurs within the kidneys [17].

Clinical Significance

Pain in the abdomen, flank, or back is the most common initial complaint of patients suffering from ADPKD, and it is almost universally present in patients with ADPKD. Dull aching and an uncomfortable sensation of heaviness may result from a large polycystic liver. pain may be severe (acute) due to bleeding (hemorrhaging) complications, the passage of kidney stones or chronic urinary tract infection. Patients may present with hematuria, poor function of the kidneys (renal insufficiency) and, potentially, kidney failure. Examination in patients reveals Hypertension with increased diastolic BP is the rule; Palpable, bilateral flank masses in advanced ADPKD and nodular hepatomegaly in severe polycystic liver disease [18]. 70% of patients with ADPKD would develop renal insufficiency if they survived to age 65 years. Currently, half of all patients with ADPKD require renal replacement therapy by age 60 years [19].

Individuals with ADPKD may have symptoms caused by problems outside the kidneys (extra-renal disease). Hypertension, liver cysts, kidney stones, cardiac valvular abnormalities like mitral valve prolapsed, thickening of the walls the heart, aortic root dilatation causing aortic insufficiency, Intracranial aneurysms, midline ventral hernia of abdominal wall, diverticula of the colon. Other organs that may be affected by the formation of cysts include the pancreas, arachnoid membrane and seminal vesicles [20].

An imaging study, such as an ultrasound, is recommended as the first diagnostic test and may reveal multiple cysts on both kidneys. Cysts may also be seen in the liver, pancreas, and spleen. For adults with a family history of ADPKD, criteria for diagnostic screening with ultrasound exist, although repeat screening may be required for younger adults if they had an initially negative scan [21].

In the early stages, the noncystic nephrons start adapting and gradually increasing their function, thus GFR increases to compensate the existing nephron loss, but in due course the compensatory mechanisms fail and renal function declines. Surgical decompression of the cysts eases pressure on the kidneys but does not prevent the diminishing GFR indicating that size, shape and number of cysts alone is not totally responsible for progression to renal failure. Thus there are alterable and unalterable factors playing a role in progression to renal failure in ADPKD [22,23].

However the knowledge of the preventable or alterable aspects like control of hypertension, management of urinary tract infection, haematuria, dietary modifications to reduce hyperfiltration, correction of hypokalemia and acidosis, prevention of complications, etc., can help the clinician to delay the progression of renal failure to a great extent [24].

Conclusion

Polycystic Kidney Disease (PKD) is an inherited condition in which cysts develop throughout the kidneys leading to its enlargement and later failure. Eventually, there is slow progression to End Stage Renal Disease.

Cysts cause significant problems like pain, infection, hemorrhage or kidney stones. Patient may present with Hypertension Currently most of the treatment is focused around the outcomes of the disease like blood pressurecontrol. The prevention of complications, etc., can delay the progression of renal failure to a great extent.

Competing Interests
The authors declare that they have no competing interests.

Authors' contributions
SPS drafted the manuscript, performed the literature review & SR assisted with writing the paper.

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