

Case Report

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Glomerulocystic Kidney Disease and its rare associations: an autopsy report of two unrelated cases

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Abstract

Background: Glomerulocystic kidney disease is an uncommon type of cystic renal disease. It is characterized by cortical microcysts, which are represented by cystic dilatation of Bowman's spaces.

Case presentation: We describe a case of glomerulocystic disease in a neonate and another in an abortus associated with tracheo-oesophageal fistula and megacystic-megaureter syndrome. The kidney on autopsy was sponge-like and revealed presence of cysts corresponding to dilatations of Bowman's space microscopically. In these two cases, the Glomerulocystic Kidney Disease in one case corresponded to a sporadic form and, in the other, to a syndromic, non-heritable form of glomerulocystic kidney disease.

Conclusion: The associated anomalies in Glomerulocystic Kidney disease are well described in the literature. Two more new unrelated associations are described in this article.

Background

Glomerulocystic kidney disease (GCKD) was characterized as a distinct histopathological entity in 1976 by Taxy and Filmer, who described this as a heterogeneous group of disorders with a common link being a variable degree of cystic dilatation of Bowman's spaces [1]. These cortical cysts seen grossly are mostly located in the subcapsular area of the renal cortex. It occurs in both sporadic and familial forms. Glomerular cysts have been observed in various renal cystic diseases such as autosomal dominant polycystic kidney disease (ADPKD), cystic renal dysplasia, autosomal recessive polycystic kidney disease (ADPKD), Zellweger's cerebral-renal-hepatic syndrome, and tuberosus sclerosis [2]. Familial GCKD can be associated either with hypoplastic or normal sized kidneys. Hence, GCKD

must be diagnosed by excluding other cystic renal disorders.

About one half of the examples of GCKD described in infants appear to be an expression of ADPKD with unusually early clinical onset, but not all cases of infantile-onset ADPKD have predominantly glomerular cysts. The exact significance of this morphologic expression in relation to ADPKD is yet not established. GCKD is also known to be encountered as sporadic condition in infants and young children who present in renal failure [3].

Case summary I

A male baby with gestational age of 41 weeks was born to a fourth gravida mother with three living issues. The mother had polyhydramnios. The baby was delivered by

vaginal delivery which was uneventful. At birth, the weight was 2.2 kg with APGAR score of 1, 1, 0. The baby developed resuscitation failure as the oro-gastric tube was not negotiable beyond 10–12 cm and he died within 3 hours after birth. With the clinical possibility of an airway malformation, the baby was sent for autopsy. A complete autopsy was performed after an informed consent. The weight at autopsy was 2.3 kg with crown-heel length measuring 50 cm, crown-rump length 32 cm, head circumference 33 cm, chest circumference 30 cm and foot length measured 7.5 cm. The newborn had 98th percentile of growth development according to crown-heel length. Externally, no congenital abnormalities were noted. The attached umbilical cord measured 10 cm and on transverse section showed presence of three vessels. Both the kidneys were normal sized with maintained reniform shape and a sponge-like appearance due to numerous, round, cystic spaces, which measured up to 2 mm (Fig 1a) and were evenly distributed all along the cortex on cut surface (Fig 1b). Medulla was devoid of these cystic lesions. Microscopically, there was uniform cystic dilatation of Bowman's space (Fig 2a). The glomerular tufts were reduced or rudimentary (Fig 2b). The cysts were lined by flattened epithelial cells. No dysplastic elements were observed. There was focal tubular dilatation. Interstitium and blood vessels were essentially normal. The ureter and urinary bladder were within normal limits. Examination of heart, lungs, liver, and pancreas was within normal limits. Neither cysts nor fibrosis were identified in any of these organs. Oesophageal atresia with tracheo-oesophageal fistula of type A was noted with a fistulous connection between the distal segment of oesophagus and the lower end of trachea (Fig 3). Brain weighed 446 gms and showed well developed gyri and sulci. There was meningeal congestion. Microscopic examination was essentially normal. Spleen, adrenals, thymus and undescended testes was within normal limits.

Case summary 2

A complete autopsy was performed after an informed consent on a 17 weeks male fetus aborted by a primigravida lady. Antepartum ultrasound had revealed presence of a cystic mass measuring 7 × 6 cm occupying whole of fetal abdomen and reaching upto sacrum posteriorly. Bilateral hydronephrosis was also noted. At autopsy, the baby weighed 310 gms with crown-heel length measuring 19 cm, crown-rump length 13 cm, head circumference 9 cm, chest circumference 11 cm and foot length measured 2 cm. The newborn had 90.4th percentile of growth development according to crown-heel length. Externally, the abdomen was distended. No dysmorphic facies or limb abnormalities were noted. The serous cavities were within normal limits. The right and left kidneys measured 1.5 × 1 × 0.8 cm and 2 × 1.7 × 1 cm, respectively. Fetal lobulations were present. On cut surface, the calyces were dilated

and renal parenchyma was seen as a peripheral rim (Fig 4a). Microscopically, there were features of GCKD with dilatation of Bowman's space in >50% of glomeruli. There was evidence of renal dysplasia with dysplastic tubules and circumferential cuffing of immature mesenchyme (Fig 4b). Megaureter with megacystic (megabladder) was noted. The distended bladder measured 5 × 6 cm and the wall was thinned out markedly measuring 0.1–0.2 cm. The rest of the organs including lungs, heart, thymus, liver, pancreas, spleen, GIT, testes, adrenals and brain were within normal limits. Neither cysts nor fibrosis were identified in any of these organs.

Discussion

Glomerulocystic kidney disease is an uncommon type of cystic renal disease. Roos first described it as an isolated abnormality in 1941 [4]. However, Taxy and Filmer proposed the term of GCKD in 1976 [1], which is widely used to describe the characteristic morphological features of dilatation of Bowman's space often without quantitative criteria. Bernstein defined glomerular cyst as dilatation of Bowman's space 2–3 times in the plane of section [2]. He also considered that the occurrence of glomerular tufts, within atleast 5 % of otherwise identifiable cysts, defines glomerulocystic kidney. However the definition does not exclude the presence of associated tubular dilatation. GCKD can be categorized into five major groups [3]:

1. Familial GCKD,
2. GCKD associated with heritable diseases such as ADPKD/ARPKD and tuberous sclerosis,
3. Syndromic, non-hereditary GCKD,

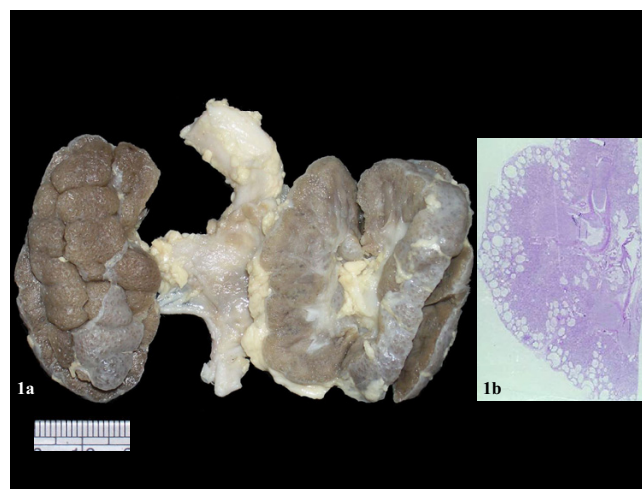


Figure 1
a. Bilateral sponge-like cystic kidneys, case 1. b. Scanner view of cystic kidney with microcysts in cortex, case 1.

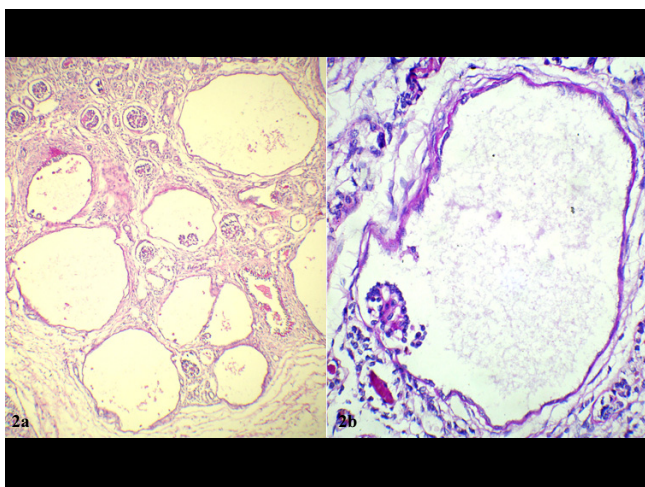


Figure 2
 a. Dilated Bowman's space with rudimentary glomerular capillary tufts, case 1 (Original magnification $\times 100$, H&E). b. Higher magnification showing the rudimentary capillary tuft at one end of dilated Bowman's space. Capsule is lined by flattened epithelial cells, case 1 (Original magnification $\times 400$, H&E).

4. Sporadic GCKD and

5. Acquired GCKD.

The first group includes autosomal dominantly transmitted GCKD (ADGCKD). The second group comprises of diffusely glomerulocystic kidneys in newborns and young children, many of whom have family histories positive for classical polycystic kidney disease. It also includes sporadic and familial disease in older children and adults. No differences between familial and sporadic cases have been

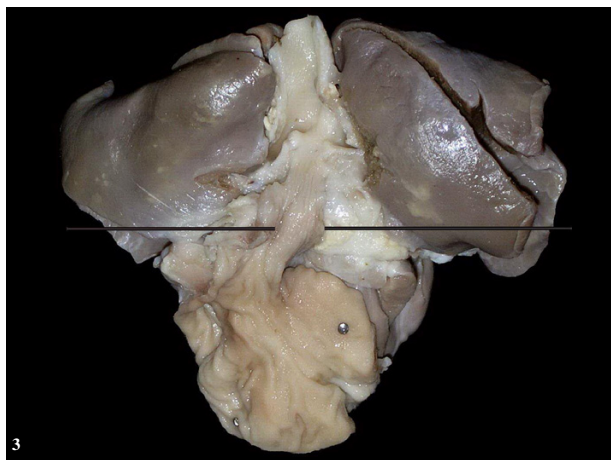


Figure 3
 Gross photo of tracheo-esophageal fistula, case 1.

identified, apart from the family histories. The sporadic cases conceivably represent new mutations of the same disease. It also includes glomerulocystic kidneys as major component of heritable syndromes such as tuberous sclerosis, trisomy 13 and others. The third group includes glomerulocystic kidneys as components of diffuse cystic dysplasia and renal-hepatic-pancreatic dysplasia syndrome. The fourth group comprises all the sporadically occurring GCKD. Acquired GCKD (group 5) has been described following hemolytic-uremic syndrome [5].

The mechanism of cyst formation in GCKD is poorly understood. Various factors that may be involved in the pathogenesis of GCKD include tubular obstruction due to renal medullary inflammation in neonates, increased intraglomerular pressure when the fetal glomeruli become functional and maternal intake of drugs such as phenacetin during pregnancy [6]. Baxter et al suggested that GCKD is produced late in gestation, by malformation in nephrogenic zone or tubular obstruction [7]. Ischemia, an acquired factor, may be involved in the genesis of glomerular cysts and explain sporadic forms observed in adults [8]. Evidence for the glomerular origin of the cysts was first provided by Baxter. Vernani et al in a study have shown that, the cysts showed negative staining with markers of proximal and distal tubular epithelium, thereby suggesting a glomerular origin of cysts [9]. Although no microdissection studies were performed in our cases, the morphometric findings also support glomerular origin of GCKD [10]. Recent studies have also suggested stenosis at glomerulo-tubular junction to be the main cause of

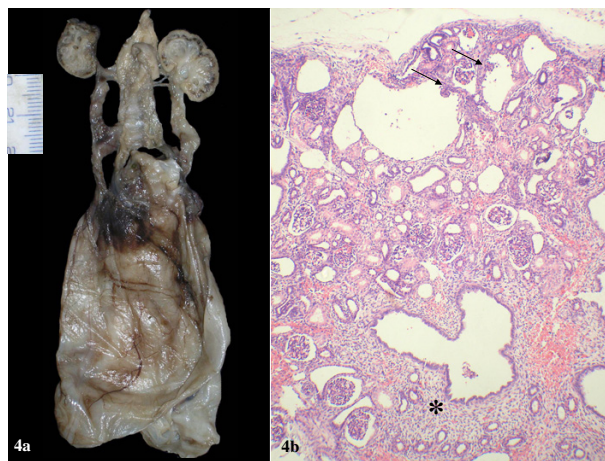


Figure 4
 a. Bilateral cystic kidneys with megacystic-megaureter syndrome, case 2. The bladder wall is thinned out and shows prominent vascular markings. b. Few dysplastic tubules with immature mesenchymal collar (asterix), case 2. The cystic glomeruli can also be seen (arrows) (Original magnification $\times 200$, H&E).

glomerular cyst development. However, three-dimensional imaging analysis has excluded stenosis or obstruction at the level of the glomerulo-tubular neck [11]. Recently, mutation in the hepatocyte nuclear factor-1beta (HNF-1 β) gene has been identified in hypoplastic GCKD variant [12]. The genetic studies could not be carried out in our cases. However there was no history of any cystic disease/or renal function derangement in the siblings in both the families.

Dilatation of the bladder and ureters can be seen with any obstructive lesion of lower urinary tract, but in the megacystic-megaureter syndrome, no anatomic obstruction is present [13]. Severe vesicoureteric reflux leads to the constant recycling of large volumes of refluxed urine, which in turn results in an enlarged bladder and massively dilated ureters [14]. There was no evidence of posterior urethral valves, thus the plausible explanation for megacystic-megaureter in abortus appears to be a functional defect, which must also have contributed partly to development of dysplasia and glomerular cysts. Evidence for such a mechanism derives from experimental ureteral ligation in neonatal animals [15].

The above two cases illustrates the sporadic form of GCKD (group 4) occurring in term baby and syndromic, non-heritable GCKD (group 3) in a 17-week abortus according to the above classification. A recent literature review failed to show a link between this rare association of GCKD with TEF, and megacystic-megaureter syndrome. Glomerular cysts are considered to be the basic and predominant lesions of GCKD. No dilatation of tubules is present; the absence of tubular dilatation excludes the diagnosis of ADPKD. Dysplastic elements were noted in the kidney sections of abortus, however were absent in term baby.

In conclusion, the above two cases highlight the rare associations with which this heterogeneous entity is associated.

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