J Ped Nephrol
Journal of Pediatric Nephrology
Spring 2023. Volume 11. Number 2

Case Report

Glomerulocystic Kidney Disease and End-stage Renal Disease in a Child: A Rare Case Report and Literature Review

Shanjida Sharmim[1*], Syed Saimul Huque[1], Golam Muin Uddin[1], Afroza Begum[1], Romana Akbar[1], Delwar Hossain[1]

1. Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh.41961

Use your device to scan and read the article online

Citation Sharmim Sh, Huque SS, Uddin GM, Begum A, Akbar R, Hossain D. Glomerulocystic Kidney Disease and End-stage Renal Disease in a Child: A Rare Case Report and Literature Review. Journal of Pediatric Nephrology. 2023; 11(2):97-101. https://doi.org/10.22037/jpn.v12i2.41961

https://doi.org/10.22037/jpn.v12i2.41961

Article info:
Received: 29 Apr 2022
Accepted: 20 Feb 2023
Publish: 01 Apr 2023

Corresponding Author:
Shanjida Sharmim
Address: Department of Pediatric Nephrology, (BSMMU), Dhaka, Bangladesh.
E-mail: shanjidasharmim@gmail.com

ABSTRACT

Glomerulocystic kidney disease (GCKD) is characterized by cystic dilatation of the Bowman's capsule and adjacent tubules. It is a rare form of cystic kidney disease and can occur at any age. Sometimes GCKD may not be differentiated from other cystic kidney diseases. It usually presents with renal failure. Here, we reported a case of a four-year-old girl presented with end-stage renal disease who had glomerulocystic kidney disease in renal histopathology.

Keywords: Renal cyst, Glomerulocystic kidney disease, ESRD, Child

Introduction

Dilatation of Bowman space greater than 2 to 3 times of normal size is defined as the glomerular cyst [1, 2]. Roos claimed that glomerular cysts were first recognized and described by him in 1941 [3]. It was termed glomerulocystic kidney disease (GCKD) by Taxy and Filmer after 35 years [3, 4]. A kidney with more than 5% cystic glomeruli is referred to as glomerulocystic kidney (GCK) [2]. There are different forms of cystic diseases and most diseases may present in childhood. Autosomal dominant polycystic kidney disease (ADPKD), cystic renal dysplasia, and autosomal recessive polycystic kidney disease (ARPKD) present with variable renal dysfunction from neonatal to adolescence [1, 5]. GCKD is a different entity characterized by glomerular cysts and associated renal dysfunction [4]. The cortical distribution of cysts in GCKD differs from infantile polycystic renal disease (IPCD), where dilata-

J Ped Nephrol
Journal of Pediatric Nephrology

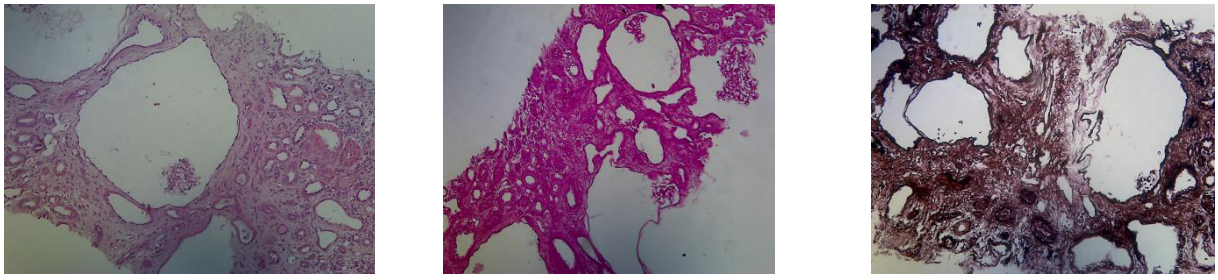
tion of the collecting tubules results in numerous cysts in the cortex and medulla [6]. GCKD is a rare condition with diverse etiology and has variable clinical manifestations. Although the disease usually occurs at a young age, GCK also occurs in adults [7]. GCKD has both sporadic and familial occurrences. GCKD can be classified further based on presentation, size of the kidneys, and associated multisystem disorders [5]. Although the diagnosis of renal cystic diseases may be different, ultrasonographic appearance may be similar. Cystic kidney may be normal, small, or larger with increased echogenicity in ultrasonogram (USG). Small renal volumes have typically been reported in cases of hereditary GCKD. However, sometimes cysts will not be detected by USG, especially in the case of small cysts [8]. Some forms of cystic kidney disease may show cortical hyperechogenicity instead of the typical anechoic appearance of simple cysts. Magnetic resonance imaging (MRI) is a more reliable diagnostic test and demonstrates small kidney cysts with a predominant cortical and subcapsular distribution. Thus, the diagnosis of GCKD is based on strong clinical suspicion, with US images showing echogenic kidneys with or without glomerular cysts [9]. Bowman space may be dilated 2-3 times greater than normal size in the cystic glomerulus [10]. The treatment of GCKD is symptomatic and supportive. Prognosis is variable according to the underlying cause and rate of deterioration of kidney function [11]. Here, we reported a rare case presented with ESRD and was finally diagnosed as a case of GCKD.

Case Presentation

A four-year-old girl, the first child born to consanguineous parents, had incidentally elevated serum creatinine and serum parathyroid hormone (PTH) three months ago when she presented to the physician because of her slow growth compared to her peers. Then, she was referred to the Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh. On admission, she was presented with complaints of anorexia, nausea, and vomiting for the last three months and a lack of good growth for the last year. She had no episodes of fever, dysuria, polyuria or polydipsia, hematuria, proteinuria or feature of obstructive uropathy, and vasculitis. Her birth history was uneventful. No renal disease was found in her family and ultrasonographic screening of the parents failed to reveal cysts in the kidneys. On examination, she was found mildly pale, hypertensive (blood pressure: 120/75 mm of Hg, systolic blood pressure (SBP) >99th centile, and diastolic blood pressure: DBP 95th -99th centile), severely underweight and stunted, with no edema, and urine color was straw and bedside urine albumin was nil. She had no organomegaly or ascites. Laboratory workup showed moderate microcytic hypochromic anemia, and high erythrocyte sedimentation rate (ESR). A urine routine examination showed only pyuria (10-15/HPF), but red blood cells (RBC) and protein were nil, with no growth in urine culture. Serum creatinine was raised (3.64 mg/dL) with an epidermal growth factor receptor (eGFR) of 10.55 mL/min/1.73 m^2, indicating stage 5 chronic kidney disease (CKD) or end-stage renal disease (ESRD). Serum urea was markedly raised along with hyponatremia, hyperchloremia, and metabolic acidosis. Inorganic phosphate was also raised along with marked secondary hyperparathyroidism (728 pg/mL) indicating CKD, and a high urinary albumin creatinine ratio (ACR) (74 mg/g) revealed significant proteinuria. USG of the kidney ureter and bladder (KUB) showed that both kidneys were mildly enlarged, the right kidney was 13.2 cm long and the left kidney was 12 cm. Cortical echogenicity was increased and cortico-medullary differentiation was poor with no echogenic structure suggesting bilateral acute renal parenchymal disease. Her eye evaluation and hearing assessment were normal. The histopathological report of the kidney showed reduced glomerular size, normal cellularity, no increased matrix, no thickening of the glomerular basement membrane (GBM), markedly dilated bowman's spaces containing rudimentary tufts of the glomerulus, and tubules were moderately atrophied with a few irregularly dilated tubule lined by flattened epithelium. Hyaline and RBC casts, moderate diffuse chronic interstitial inflammation with moderate fibrosis, and thick-walled blood vessels with hyaline atherosclerosis were present. Direct immunofluorescence (DIF) examination revealed no deposition of any antibody. All the biopsy features were consistent with glomerulocystic disease (Figure 1). A genetic study revealed no genetic mutation. The patient received antihypertensive treatment with amlodipine and prazosin. Immediately renal replacement therapy (RRT) was started in the form of intermittent peritoneal dialysis (IPD) and later on by continuous ambulatory peritoneal dialysis (CAPD) (Figure 2). As her pallor increased (Hb% 6.1 g/dL), one unit packed cell transfusion was given along with other supportive measures. After eight months of medical management and renal replacement therapy by CAPD, she is surviving without any further complications.

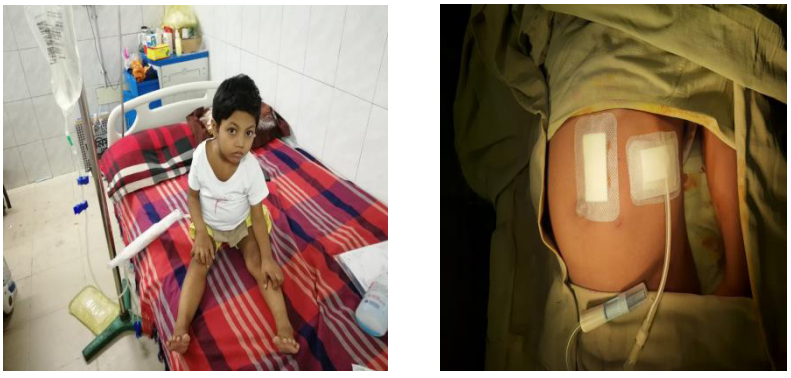
Discussion

GCKD is a rare disease that is most often seen in infants and young children but can also occur in adoles-



a b c

Figure 1. Photographs of renal biopsy, a) Bowman's capsule, b) Tuft of capillary, c) Glomerular cyst



a b

Figure 2. a) CAPD catheter inserted in the abdomen, b) Performing CAPD at the bedside

cents and adults [1, 12]. With recent advancement, its pathophysiological process is significantly understandable. Some syndromic genetic diseases are associated with GCKD due to their respective proteins localized to primary cilia or centrosomes. The transcription pathway of renal development is dysregulated in some forms of renal disease, which describes its importance in the pathogenesis of GCKD [10]. The disease can be divided into five major categories: 1) An early manifestation of ADPKD (PKD1 mutations); 2) Hereditary GCKD associated with other single-gene defects (e.g. hepatocyte nuclear factor-1 beta [HNF1B] and UMOD); 3) GCKD associated with syndromic disorders (e.g. Bardet Biedl syndrome, orofacial digital syndrome, and tuberous sclerosis complex [TSC]); 4) Obstructive GCKD with or without kidney dysplasia; and 5) Isolated, sporadic cases [7, 10]. According to the presentation, GCKD can also be divided into two types. Early-onset GCKD is common in neonates, and renal insufficiency is a more common feature [13, 14], whereas late-onset type is more common in adults and renal impairment will be less severe [12, 15]. Sometimes early-onset GCKD may follow a stable course for several years [13, 16] or progress to ESRD in a short period of three years [16-18]. Our reported case was a four-year-old girl presented with not growing well for one year along with nausea, vomiting, and raised serum creatinine for the last three months. The case had no family history of such type of illness and was diagnosed as a case of ESRD at the age of four. In the sporadic form of GCKD, there may be no discernible inheritance pattern, no distinct features of renal dysplasia, obstruction, or syndromic associations [7]. Our reported case may be an early-onset isolated sporadic type of GCKD.

Ultrasonography can be useful in the diagnosis of GCKD, where kidneys are usually bilaterally enlarged but sometimes normal or hypoplastic kidneys may be observed and renal contour is preserved. The cortex is hyperechoic with a distinct hypoechoic rim and loss of corticomedullary differentiation. A small cyst is usually present in the renal cortex that escapes the renal medulla, which is the main feature differentiating GCKD from ADPKD. In ADPKD, multiple cysts are varying in size present in the renal cortex as well as the medulla, which are larger than the size of GCKD and abnormal medullary pyramids [5, 19]. Because glomerular cysts are smaller, below the threshold of ultrasound or computed tomography, their diagnosis is often overlooked. In this

J Ped Nephrol
Journal of Pediatric Nephrology

case, an MRI is superior to a USG or CT scan [20]. USG of the KUB region of our reported case had bilaterally enlarged kidneys with increased cortical echogenicity and poor cortico-medullary differentiation. No cyst or echogenic structure was found.

In histopathological analysis, glomerular cysts are considered to be the basic and predominant lesions of GCKD. There may be multiple cysts in the renal cortex with dilated Bowman's spaces. The epithelium of Bowman's capsule is flat, and the glomerular tufts attached to the capillary wall may be significantly reduced, rudimentary, or collapsed. Periglomerular fibrosis and diffuse mild interstitial fibrosis may be present [4, 21]. Vascular tufts are not identifiable in all cysts and a few cysts may contain more than one tuft of capillaries and some cysts may be very large [22, 23]. Tubular cysts may rarely be present in GCKD but usually lack dysplastic elements in early GCKD [1, 21].

Renal histopathological study of our case had markedly dilated bowman's spaces containing rudimentary tufts of glomerulus, few irregularly dilated tubules lined by flattened epithelium, and hyaline and RBC casts and showed no deposition of antibody, which was associated with the GCKD.

Genes responsible for protein expression in primary renal tubule cilia or centrosomes may be mutated in inherited forms of GCKD [10]. Autosomal dominant GCKD may present with isolated renal involvement or familial hypoplastic disease or may present sporadically. The familial dominant variant of GCKD may be confused with ADPKD, but the genetic locus mutation in the GCKD phenotype is distinct from the ADPKD genetic locus mutation [24]. Some familial cases have been reported with distinct entity of hypoplastic GCKD, which is often inherited [17, 25]. In this case, kidneys may be small with abnormal pyelocalyceal system. Some genetic mutations may have renal and extra-renal manifestations. Mutations in the hepatic nuclear factor-1 beta (HNF-1β) gene may present with hypoplastic variants of GCKD with hepatic manifestations [26]. GCKD may be associated with specific syndromes, such as oral digital syndrome type 1, renal brachyromelia syndrome, trisomy 13 syndrome, short-rib polydactyly syndrome, Majewski type, and nephroptosis [1]. It is difficult to distinguish GCKD from other cystic diseases. Genetic testing could be helpful in these cases, but in our reported case, genetic testing failed to find any pathogenic or potentially pathogenic mutation. This may be due to a sporadic genetic mutation that has not been identified so far.

Treatment of GCKD is usually symptomatic and according to the clinical presentation. A case was reported, that got no definite treatment, and only the patient was followed up [11, 27]. Our reported case presented with ESRD, which was managed with CAPD and other supportive measures of chronic kidney disease.

Conclusion

Although glomerulocystic disease is a rare cause of CKD in children, it should be considered an important differential, especially when renal enlargement is present clinically or on imaging in a child with CKD.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

References

[1] Bernstein J. Glomerulocystic Kidney disease--nosological considerations. Pediatr Nephrol. 1993; 7(4):464-70. [DOI:10.1007/BF00857576] [PMID]

[2] Bernstein J, Landing BH. Glomerulocystic Kidney diseases. Prog Clin Biol Res. 1989; 305:27-43. [PMID]

[3] ROOS A. Polycystic kidney: Report of a case studied by reconstruction. Am J Dis Child. 1941; 61(1):116–27. [DOI:10.1001/archpedi.1941.02000070125011]

[4] Taxy JB, Filmer RB. Glomerulocystic kidney. Report of a case. Arch Pathol Lab Med. 1976; 100(4):186-8. [PMID]

[5] Vijayakumar M, Prahlad N, Nammalwar BR. Glomerulocystic disease. Indian Pediatrics. 2006; 43:434-7. [Link]

[6] Fredericks BJ, de Campo M, Chow CW, Powell HR. Glomerulocystic Renal disease: Ultrasound appearances. Pediatr Radiol. 1989; 19(3):184-6. [DOI:10.1007/BF02388653] [PMID]

[7] Lennerz JK, Spence DC, Iskandar SS, Dehner LP, Liapis H. Glomerulocystic kidney: One hundred-year perspective. Arch Pathol Lab Med. 2010; 134(4):583-605. [DOI:10.5858/134.4.583] [PMID]

[8] Cramer MT, Guay-Woodford LM. Cystic Kidney disease: A primer. Adv Chronic Kidney Dis. 2015; 22(4):297-305. [DOI:10.1053/j.ackd.2015.04.001] [PMID]

[9] Wood CG 3rd, Stromberg LJ 3rd, Harmath CB, Horowitz JM, Feng C, Hammond NA, et al. CT and MR imaging for evaluation of Cystic Renal lesions and diseases. Radiographics. 2015; 35(1):125-41. [DOI:10.1148/rg.351130016] [PMID]

[10] Bissler JJ, Siroky BJ, Yin H. Glomerulocystic Kidney disease. Pediatr Nephrol. 2010; 25(10):2049-56; quiz 2056-9. [DOI:10.1007/s00467-009-1416-2] [PMID]

[11] Loftus H, Ong AC. Cystic Kidney diseases: Many ways to form a cyst. Pediatr Nephrol. 2013; 28(1):33-49. [DOI:10.1007/s00467-012-2221-x] [PMID]

[12] Alvelos MI, Rodrigues M, Lobo L, Medeira A, Sousa AB, Simão C, et al. A novel mutation of the HNF1B gene associated with Hypoplastic Glomerulocystic Kidney disease and neonatal renal failure: A case report and mutation update. Medicine (Baltimore). 2015; 94(7):e469. [DOI:10.1097/MD.0000000000000469] [PMID]

[13] Landau D, Shalev H, Shulman H, Barki Y, Maor E, Zmora E. Oligohydramnion, renal failure and no pulmonary hypoplasia in Glomerulocystic Kidney disease. Pediatr Nephrol. 2000; 14(4):319-211. [DOI:10.1007/s004670050767] [PMID]

[14] Gupta K, Vankalakunti M, Sachdeva MU. Glomerulocystic Kidney disease and its rare associations: An autopsy report of two unrelated cases. Diagn Pathol. 2007; 2:12. [DOI:10.1186/1746-1596-2-12] [PMID]

[15] Dosa S, Thompson AM, Abraham A. Glomerulocystic Kidney disease. Report of an adult case. Am J Clin Pathol. 1984; 82(5):619-21. [DOI:10.1093/ajcp/82.5.619] [PMID]

[16] Reznik VM, Griswold WT, Mendoza SA. Glomerulocystic disease - A case report with 10 year follow-up. Int J Pediatr Nephrol. 1982; 3(4):321-3. [PMID]

[17] Rizzoni G, Loirat C, Levy M, Milanesi C, Zachello G, Mathieu H. Familial hypoplastic glomerulocystic kidney. A new entity? Clin Nephrol. 1982; 18(5):263-8. [PMID]

[18] McAlister WH, Siegel MJ, Shackelford G, Askin F, Kissane JM. Glomerulocystic kidney. AJR Am J Roentgenol. 1979; 133(3):536-8. [DOI:10.2214/ajr.133.3.536] [PMID]

[19] Jain M, LeQuesne GW, Bourne AJ, Henning P. High-resolution ultrasonography in the differential diagnosis of Cystic diseases of the kidney in infancy and childhood: Preliminary experience. J Ultrasound Med. 1997; 16(4):235-40. [DOI:10.7863/jum.1997.16.4.235] [PMID]

[20] Oliva MR, Hsing J, Rybicki FJ, Fennessy F, Mortelé KJ, Ros PR. Glomerulocystic Kidney disease: MRI findings. Abdom Imaging. 2003; 28(6):889-92. [DOI:10.1007/s00261-003-0024-z] [PMID]

[21] Gusmano R, Caridi G, Marini M, Perfumo F, Ghiggeri GM, Piaggio G, et al. Glomerulocystic Kidney disease in a family. Nephrol Dial Transplant. 2002; 17(5):813-8. [DOI:10.1093/ndt/17.5.813] [PMID]

[22] Hossain Z, Ali SM, Ko HL, Xu J, Ng CP, Guo K, et al. Glomerulocystic Kidney disease in mice with a targeted inactivation of Wwtr1. Proc Natl Acad Sci USA. 2007; 104(5):1631-6. [DOI:10.1073/pnas.0605266104] [PMID]

[23] Welling LW, Grantham JJ. Cystic and developmental diseases of the kidney. The Kidney. BM Brenner and FC Rector, Jr., editors. Philadelphia: Saunders Co; 1986.

[24] Sharp CK, Bergman SM, Stockwin JM, Robbin ML, Galliani C, Guay-Woodford LM. Dominantly transmitted glomerulocystic Kidney disease: A distinct genetic entity. J Am Soc Nephrol. 1997; 8(1):77-84. [DOI:10.1681/ASN.V8177] [PMID]

[25] Mache CJ, Preisegger KH, Kopp S, Ratschek M, Ring E. De novo HNF-1 beta gene mutation in familial hypoplastic glomerulocystic Kidney disease. Pediatr Nephrol. 2002; 17(12):1021-6. [DOI:10.1007/s00467-002-0975-2] [PMID]

[26] Bingham C, Bulman MP, Ellard S, Allen LI, Lipkin GW, Hoff WG, et al. Mutations in the hepatocyte nuclear factor-1beta gene are associated with Familial Hypoplastic Glomerulocystic Kidney disease. Am J Hum Genet. 2001; 68(1):219-24. [DOI:10.1086/316945] [PMID]

[27] Bolar NA, Golzio C, Živná M, Hayot G, Van Hemelrijk C, Schepers D, et al. Heterozygous Loss-of-Function SEC61A1 Mutations Cause Autosomal-Dominant Tubulo-Interstitial and Glomerulocystic Kidney Disease with Anemia. Am J Hum Genet. 2016; 99(1):174-87. [DOI:10.1016/j.ajhg.2016.05.028] [PMID]