Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/20005
DOI URL: http://dx.doi.org/10.21474/IJAR01/20005

RESEARCH ARTICLE

A CASE OF CYSTIC SISTERS

Dr. Bhavya Khattri and Dr. Manoj Prabhakaran

Manuscript Info

Manuscript History
Received: 05 October 2024
Final Accepted: 07 November 2024
Published: December 2024

Abstract

Autosomal Dominant Polycystic Kidney Disease or ADPKD is a common cause of renal cysts, which many a times can compromise renal function thus leading to chronic renal failure. It can occur in adjunct with cysts in other organs like liver, which have a sexual predilection for females. Positive family history is a key in making diagnosis of such inherited cystic disorders, especially in low economy settings in a country like India.

Introduction:-

Cystic lesions involving kidneys are not very uncommon. The most likely differentials of renal cysts presenting in adults are some inherited disorders, including Autosomal Dominant Polycystic Kidney Disease (ADPKD), Autosomal Recessive Polycystic Kidney Disease (ARPKD), medullary sponge kidney, medullary cystic disease, and multicystic renal dysplasia. Some other causes are simple cortical cysts, and some can also be attributed to neoplastic causes like renal cell carcinoma, and mesenchymal tumours including sarcomas and angiomyolipoma. Some cysts can also arise from the calyx or renal pelvis (calyceal diverticulum, pyelogenic cyst, or pyelocalyceal cyst) or within the hilum, such as lymphangitic cysts.

ADPKD is a clinically significant entity, as it is a common cause of developing renal failure later in life. Prevalence is reported as high as 1 in 400 to 1 in 1000, but often not diagnosed until the fifth decade of life and accounts for 8 to 10% of cases of end-stage renal disease (1, 2). It occurs due to an inherited single gene mutation involving PKD1 (85% of cases) or PKD2 genes. The mutation is present in all cells of the body. Formation of cysts in multiple areas of kidneys with ADPKD occurs when cells lose their second copy of the respective gene, as explained by Knudson's "two-hit" hypothesis, first described in retinoblastoma patients (3, 4).

Here we present a case of two sisters, divided by familial feuds but joined by cysts.

Case Report 1: Patient (A)

A 67-year-old female presented to the emergency department (E.D.) with acute, continuous, and progressive shortness of breath. The patient was severely dyspneic, but maintaining oxygen saturation on room air with blood pressure of 172/ 96 mmHg and a regular pulse of 112/min.The general physical examination revealed bilateral wheeze on chest auscultation and abdominal tenderness on palpation. Arterial Blood Gas (ABG) analysis in the E.D. revealed severe metabolic acidosis (arterial pH = 7.04, bicarbonate levels [HCO3-] = 6.8 mEq/L) and hyperkalemia (potassium levels = 6.7 mEq/L). The patient was given immediate treatment with intravenous calcium gluconate and sodium bicarbonate injections.Bedside ultrasonography revealed bilateral bulky kidneys with multiple anechoic cysts. A CT scan confirmed multiple cysts distorting renal architecture and involvement of the liver parenchyma. Haemodialysis to correct the metabolic acidosis provided significant relief to the subject.

Corresponding Author:- Dr. Bhavya Khattri

The likelihood of ADPKD was suspected. Patient was managed conservatively with intravenous antibiotics, fluids, and other supportive treatment and discharged with a working diagnosis of polycystic kidney disease leading to chronic kidney disease with metabolic acidosis and hyperkalemia, likely due to renal dysfunction.

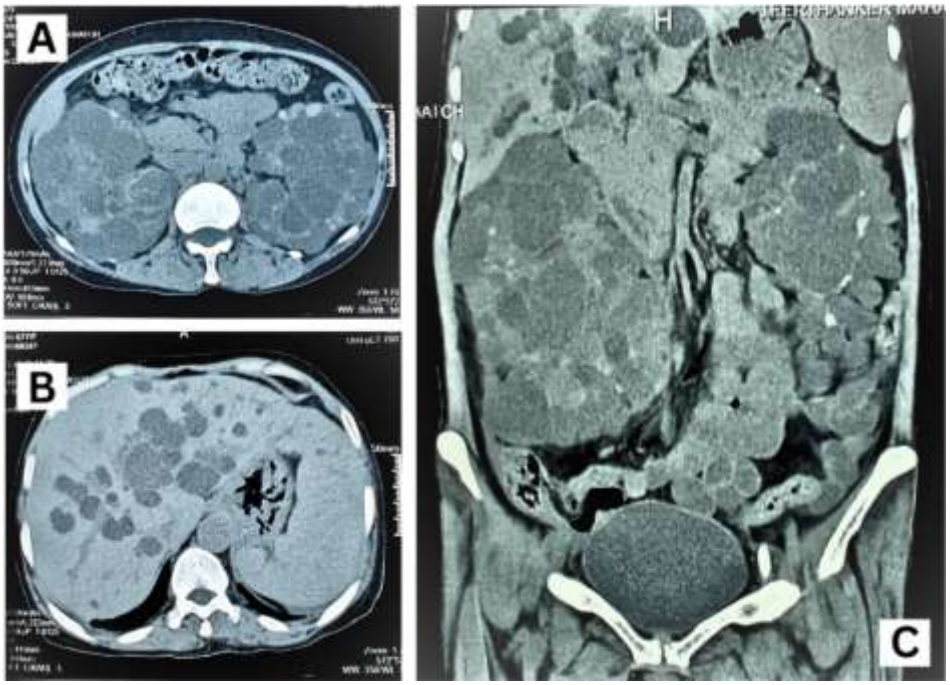

Figure 1:- NCCT KUB of patient A. (A)- Transverse section, showing bilateral bulky kidneys with multiple enlarged cysts distorting renal architecture. (B)- Transverse section, showing multiple cysts in liver parenchyma. (C)- Coronal section, showing multiple cysts in kidney and liver.

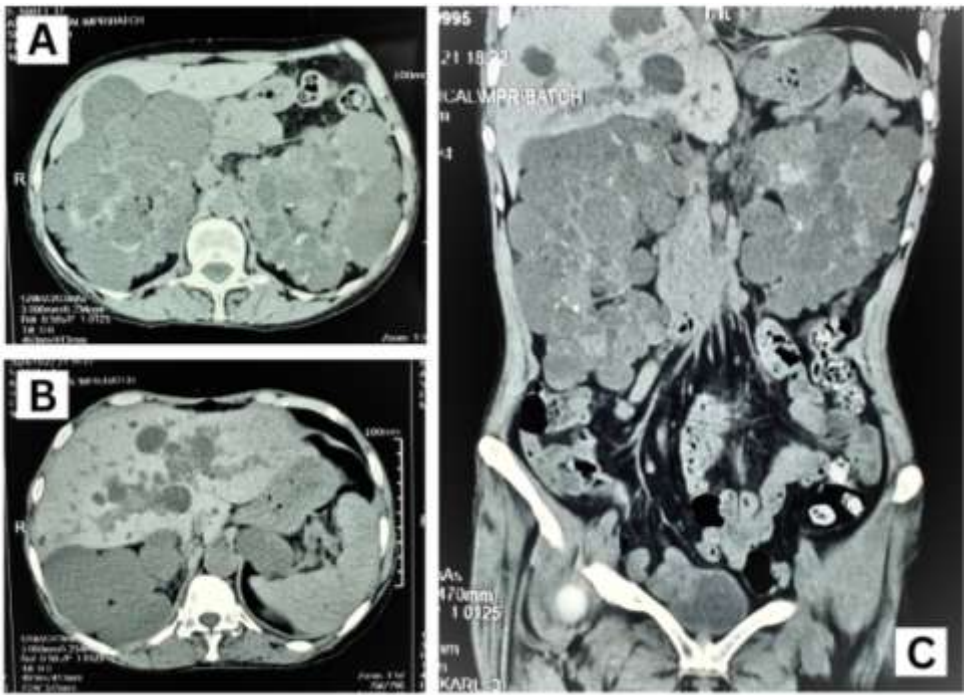

Figure 2:- NCCT KUB of patient B. (A)- Transverse section showing bilateral bulky kidneys with multiple enlarged cysts distorting renal architecture. (B)- Transverse section showing multiple cysts in liver parenchyma. (C)- Coronal section showing multiple cysts in kidney and liver.

Case Report 2: Patient (B)

A 69-year-old female presented to the outpatient department with generalized weakness persisting for three years. The general physical examination was unremarkable except for pallor and bilateral flank fullness. The patient had a history of multiple blood transfusions and was diagnosed with severe anaemia (Haemoglobin = 4.8 g/dL). Routine workup revealed multiple anechoic cysts in both kidneys on ultrasonography and deranged renal function tests. A possibility of polycystic kidney disease with chronic renal failure was considered. Non-contrast computed tomography scans revealed cysts in both kidneys and the liver. The patient was managed conservatively, given two packed red blood cell transfusions, and underwent a session of haemodialysis for advanced uraemia. After stabilization, she was discharged with advice for regular follow-ups and routine blood and renal function tests.

Table 1:- Routine Blood Investigations.

S. No.	Investigation	Patient (A)	Patient (B)	Reference values
1.	Haemoglobin	**8.2 g/dL**	4,8 g/dL	12 – 15 g/Dl
2.	Total Leucocyte Count	**11300 cells/mm^3**	7400 cells/mm^3	4000 – 11000 cells/mm^3
3.	Total Bilirubin	0.5 mg/dL	0.3 mg/dL	0.2 – 1 mg/dL
4.	Total Protein	**6.4 g/dL**	5,8 g/dL	6.6 – 8.3 g/dL
5.	Albumin	3.7 g/dL	3.0 g/dL	3.5 – 5.5 g/dL
6.	S. Urea	**276 mg/dL**	**330 mg/dL**	13 – 45 mg/dL
7.	S. Creatinine	**9.2 mg/dL**	**8.8 mg/dL**	0.5 – 1.2 mg/dL
8.	S. Uric acid	**8.6 mg/dL**	**7.8 mg/dL**	3.5 – 7.2 mg/dL
9.	Sodium	137 mEq/L	141 mEq/L	135 – 155 mEq/L
10.	Potassium	**7.4 mEq/L**	5.1 mEq/L	3.5 – 5.5 mEq/L
11.	Chloride	104 mEq/L	101 mEq/L	90 – 120 mEq/L

Both patients, (A) and (B) were admitted at a single point of time in the hospital. (Patient A in Intensive Care Unit, and patient B in general ward). On further probe in history, it was found that both the patients were real life siblings. This increased the likelihood of cysts in the two patients being inherited to multiple folds.

Discussion:-

The present study delineates two cases of ADPKD with different presentations. Clinically, ADPKD patients can go undetected, but symptoms like flank pain and fullness often occur. Compromised renal function in later stages can lead to complications such as uremia, metabolic acidosis, dyselectrolytemia (hyperkalemia), and anemia (1, 2).

The PKD1 gene produces a protein named polycystin-1, expressed on tubular epithelial cells (highly expressed in the distal nephron). Currently, its precise function is unknown; however, it contains domains that are putatively involved in cell-cell and cell-matrix interactions. The PKD2 gene produces polycystin-2, a calcium-permeable cation channel within the cell membrane of renal tubules as well as tissues outside the kidneys (5). PKD1 associated disease is more severe than PKD2 associated disease, due to more number of cysts development at an earlier age. Studies have reported that patients with PKD1 mutation often develop renal failure by their 50s, whereas those with PKD2 mutations may not develop renal failure until their 70s (6).

Altered polycystin-1 or polycystin-2 can affect membrane permeability and cell signaling pathways related to growth, apoptosis, and secretion, contributing to cyst formation through increased cell proliferation and fluid secretion, decreased cell differentiation, and abnormal extracellular matrix (7). However, not all patients have the same level of disease severity. ADPKD has 100% penetrance, but variable expressivity (i.e. difference in phenotypes). ADPKD can go undetected due to no symptoms and is often referred to as a clinically ‘silent genetic disorder,’ discovered incidentally on radiology studies (8). If symptomatic, flank pain is the most common presenting complaint, which can be due to infection or bleeding within cysts or kidney stones. Other presentations include hypertension, proteinuria, flank fullness, hematuria, or renal failure due to loss of renal parenchyma with increasing cyst number and size (1, 9). Large cysts press upon adjacent renal parenchyma and pelvicalyceal systems, compromising their function and at times making patients dependent on dialysis. Mass effects due to enlarged cysts can give rise to leg edema, gastrointestinal symptoms like abdominal fullness, dysphagia, emesis, early satiety, intestinal obstruction, and, in a few cases, heart failure or IVC compression. Cases have also been reported where blunt trauma leads to cyst rupture, complicating the clinical presentation and management (10).

Diagnosis can be made through routine screening of patients with a positive family history for ADPKD. For patients with a positive family history, the presence of at least two cysts in each kidney in adulthood is highly sensitive and specific for diagnosing ADPKD (11). The cysts vary in size, site, and number, and can also involve other organs, such as the liver. Cysts are often associated with berry aneurysms in the circle of Willis, which are prone to bleed (making control of renin-mediated hypertension a priority in ADPKD) (12). Liver cysts, the most common extrarenal manifestation of ADPKD, indicate a poor prognosis if present. Increasing renal dysfunction severity due to ADPKD is associated with an increasing incidence of liver cysts (13). However, most of the hepatic cysts are asymptomatic with preserved liver function. Similar cyst formation can occur in the seminal vesicles, arachnoid membrane, and pancreas. Other significant abnormalities reported include mitral valve prolapse and colonic diverticulosis (14). ADPKD patients may require renal transplantation later in life.

Cysts can concurrently form in multiple organs, such as the liver, as noted in both cases. Studies report that liver cysts in ADPKD are more common with increasing age, severity of renal dysfunction, and in females (6, 10).Liver cysts associated with ADPKD are different from the ones occurring in Adult Dominant Polycystic Liver Disease (ADPLD). ADPLD is in itself a manifestation of mutation in two genes (PRKSCH & SEC63), and does not progress to renal failure. Massive multiple liver cysts in adjunct with ADPKD is almost exclusively found in multiparous women, similar to the two cases being presented in the current text.Recent advances in molecular genetics of ADPKD include identifying loci—PKD1 on chromosome 16 and PKD2 on chromosome 4—and cloning the PKD1 and PKD2 genes, allowing for better prediction of protein products and pathways involved (3, 7). In low-income settings where genetic studies are not widely available, detailed family history can provide crucial diagnostic clues. The presented cases, siblings estranged due to family feuds but presenting simultaneously with the same diagnosis, highlight this approach.

Conclusion:-

ADPKD is a silent genetic disorder but can present in various ways. With increasing cyst size and age, and renal function compromise, ADPKD patients may progress to chronic renal failure. Cysts in other organs, particularly the liver, are common. Detailed history-taking, particularly in low-resource settings, remains vital for diagnosing inherited disorders. Screening individuals with positive family history can aid in early detection and intervention.

Ethical Committee Approval

Approval from the Health Research Ethics Committee of the institution was duly sought. Clinical data was obtained from patient records after obtaining written informed consent from the patients involved in the study, including permission for publishing relevant investigations.

References:-

1. Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. Lancet. 2007;369(9569):1287–301.
2. Grantham JJ, Torres VE, Chapman AB, et al. Volume progression in polycystic kidney disease. N Engl J Med. 2006;354(20):2122–30.
3. Chapman AB, Devuyst O, Eckardt KU, et al. Autosomal-dominant polycystic kidney disease (ADPKD): executive summary from a KDIGO Controversies Conference. Kidney Int. 2015;88(1):17–27.
4. Gabow PA. Autosomal dominant polycystic kidney disease. N Engl J Med. 1993;329(5):332–42.
5. Pei Y, Watnick T. Diagnosis and screening of autosomal dominant polycystic kidney disease. Adv Chronic Kidney Dis. 2010;17(2):140–52.
6. Harris PC, Torres VE. Genetic mechanisms and signaling pathways in autosomal dominant polycystic kidney disease. J Clin Invest. 2014;124(6):2315–24.
7. Ravine D, Gibson RN, Walker RG, et al. Evaluation of ultrasonographic diagnostic criteria for autosomal dominant polycystic kidney disease 1. Lancet. 1994;343(8901):824–7.
8. Chapman AB, Rubinstein D, Hughes R, et al. Intracranial aneurysms in autosomal dominant polycystic kidney disease. N Engl J Med. 1992;327(13):916–20.
9. Torres VE, Harris PC. Strategies targeting cAMP signaling in the treatment of polycystic kidney disease. J Am SocNephrol. 2014;25(1):18–32.
10. Reeders ST. Multilocus polycystic disease. Nat Genet. 1992;1(4):235–7.
11. Torres VE, Harris PC. Diagnosis and management of polycystic kidney disease. Nat Rev Nephrol. 2018;14(4):252–68.

12. Pei Y. Diagnostic approach in autosomal dominant polycystic kidney disease. Clin J Am SocNephrol. 2006;1(5):1108–14.
13. Qian Q. Clinical and genetic insights into ADPKD. Clin J Am SocNephrol. 2010;5(6):1021–9.
14. Harris PC, Bae KT, Rossetti S, et al. Cyst number but not the rate of cystic growth is associated with hypertension in ADPKD. J Am SocNephrol. 2008;19(4):820–7.