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Case report

A Bleeding Threat: Intracystic Hemorrhage in Autosomal Dominant Polycystic Kidney Disease Leading to Nephrectomy – A Case Report

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Abstract

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a common hereditary disorder characterrized by a progressive renal cyst formation, leading to chronic kidney disease (CKD) and end-stage renal disease (ESRD). A significant complication of ADPKD is intracystic hemorrhage, which can result in severe pain, hematuria, and anemia, often complicating disease management. We report the case of a 57-year-old female with a long-standing history of ADPKD and recurrent urinary infections. The patient initially presented with dysuria, fatigue, and fever, with a urine culture revealing Escherichia coli. Despite empirical antibiotic therapy, her condition deteriorated. She developed worsening kidney function, hematuria, and elevated inflammatory markers. Imaging studies, including ultrasound and CT urography, identified polycystic kidneys with suspected cyst infection and hemorrhage. Conservative treatment, including hydration, electrolyte supplementation, and parenteral antibiotics was initiated but failed to resolve symptoms. Due to persistent anemia, worsening renal function, and radiological evidence of intracystic hemorrhage, a left-sided nephrectomy was performed. After the surgery, clinical improvement was observed, with a decrease in CRP levels and stabilization of the hemoglobin. This case highlights the challenges in managing ADPKD-associated complications, particularly recurrent infections and hemorrhagic cysts. While conservative measures are the first-line approach, nephrectomy may be necessary in severe cases. Emerging therapies, such as vasopressin receptor antagonists, gene therapy, and regenerative medicine, have the potential to alter disease progression. An early diagnosis, close monitoring, and individualized treatment remain essential for optimizing outcomes in ADPKD patients.

Keywords: intracystic hemorrhage, nephrectomy, chronic kidney disease, polycystic kidney disease, cyst infection

Introduction

Adult Polycystic Kidney Disease also known as Autosomal Dominant Polycystic Kidney Disease (ADPKD), is a common hereditary disorder characterized by the progressive development of fluid-filled cysts in the kidneys. It is caused by mutations in the PKD1 or PKD2 genes, which encode proteins critical for maintaining normal tubular structure and function [1]. Over time, the expansion of these cysts leads to kidney enlargement, impairment of the renal function, and eventual chronic kidney disease (CKD) or end-stage renal disease (ESRD). ADPKD affects approximately 12.5 million individuals globally across all ethnicities. It accounts for up to 10% of cases of end-stage renal disease and poses a significant public health challenge [2]. A significant complication of APKD is hemorrhage into the renal cyst or the urinary tract. Cystic hemorrhage occurs due to the increased vascular fragility within the cyst walls, resulting from a pressure and vascular remodeling. Patients may present with gross hematuria, flank pain, or a sudden increase in abdominal or back pain, often accompanied by systemic symptoms like fever or anemia if the hemorrhage is extensive. Hemorrhagic complications can significantly impact the quality of life and may complicate disease management [3].

Case presentation

A 57-year-old female patient with a history of ADPKD has been regularly monitored for over 20 years at the University Clinic of Nephrology in Skopje. The patient reports recurrent urinary infections. She was hospitalized once in 2023 due to elevated inflammatory markers, positive urine sediment, and findings indicative of cyst infection,

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with a positive urine culture for Enterococcus. She was discharged from the hospital with a serum creatinine level of 222 µmol/L (normal 45-109 µmol/L), indicating chronic kidney disease stage 4.

Currently, for the past month, the patient has been experiencing dysuria, fatigue and fever. The urine culture ordered by her primary care physician revealed *Escherichia coli* (1, 000, 000 CFU/ml). Antibiotic treatment with Ceftriaxone and Azithromycin was initiated, followed by fosfomycin for three days. Two weeks after the treatment, her general condition deteriorated again, with reduced appetite, hematuria and fever when Azithromycin was restarted. At the third day of treatment, laboratory findings showed serum creatinine 299 µmol/L, serum urea 13 mmol/L (normal range: 2.7-7.8 mmol/l), leukocytes $11x10^9$/L (normal range: 4-9 x 10^9/l), CRP 87 mg/L (normal <6 mg/l), with a positive urine sediment and the patient was hospitalized.

On physical examination, palpable, volumetrically enlarged kidneys and varicose veins in both lower legs were noted.

Ultrasound findings of the urinary tract revealed bilaterally enlarged, polycystic altered kidneys extending into the small pelvis, with numerous cystic formations of varying sizes. Among the cysts, a few smaller calculi and calcification in the walls were observed, which did not obstruct urodynamic. A suspicious cloudy cyst was noted in the lower part of the right kidney. In the middle segment of the left kidney, a cyst measuring 3,5x3 cm was filled with a dense content. Multiple cysts were also present in the liver. The urinary bladder was empty and not available for evaluation (Figure 1).

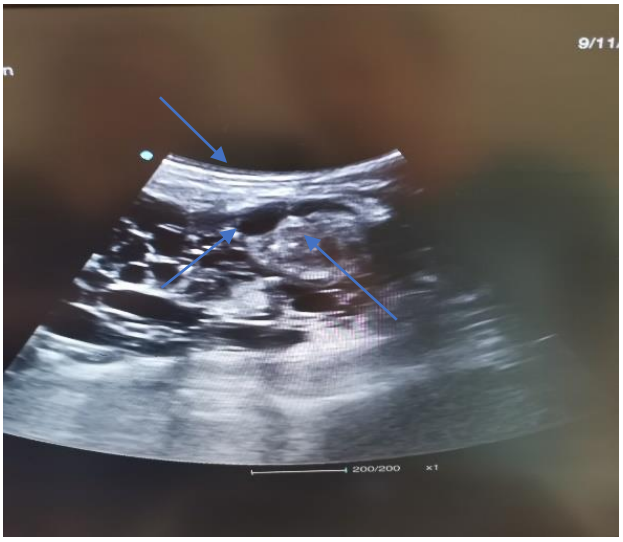

Fig. 1. Ultrasound imaging reveals a cystic formation containing echogenic material

The CT urography showed significantly enlarged kidneys with bilateral corticomedullary cysts, insufficient parenchyma and poor post-contrast imbibition and elimination of the administrated contrast. A small amount of fluid was noted in Douglas pouch (Figures 2A and 2B).

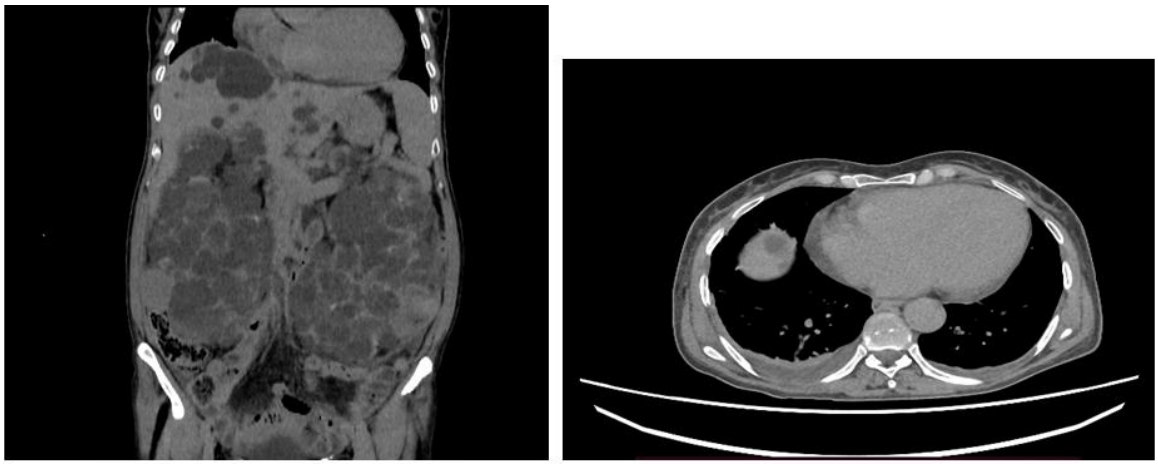

Fig. 2A and 2B. CT urography: Enlarged kidneys with cysts, poor contrast uptake and fluid in Douglas pouch

The patient was treated conservatively with hydration and electrolyte supplementation, achieving diuresis of up to 3400ml. The kidney function was stabilized without the need for hemodialysis. Throughout hospitalization, the patient experienced diffuse abdominal pain and high fever up to 38,2 °C, along with inflammatory markers and ultrasound findings suggestive of a left kidney cyst infection. Initial parenteral antibiotic therapy with ceftriaxone and amikacin was initiated and later switched to ciprofloxacin. Microbiological investigations (urine and blood culture) were sterile. The patient received pure blood transfusion. An urology consultation suggested infection or hemorrhage within the cyst. Due to persistent inflammatory markers despite the parenteral antibiotic therapy and worsening anemia with suspected cyst hemorrhage, further treatment continued at the Department of Urology.

Because of anemia, another CT urography was indicated, revealing significantly enlarged polycystic kidneys compressing adjacent abdominal and retroperitoneal structures. Hyperdense foci were detected within the cystic changes in the left kidney, with the largest

measuring 113x38 mm on axial scans and 163 mm on coronal scans. The density and lack of contrast enhancement changes were consistent with intracystic hemorrhage/hematoma. Both kidneys had minimal visible parenchyma with delayed and faint contrast enhancement. A small amount of low-density serous free fluid was observed in the Douglas pouch (Figures 3A and 3B).

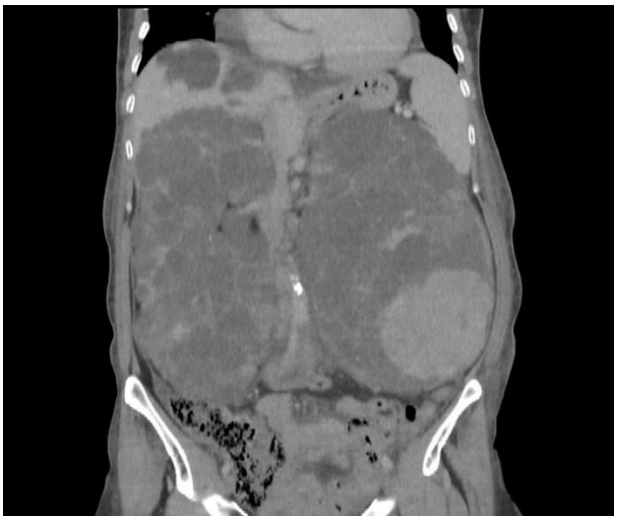

Fig. 3A. CT urography with enlarged polycystic kidneys and minimal visible parenchyma

The patient underwent a left-sided unilateral nephrectomy. Postoperative material sent to the pathology department showed the following macroscopic findings: the left kidney, encased in a scarce fibro-fatty capsule, weighed 2220 grams with dimensions 29x12x10 cm. Decapsulation was not possible. On sectioning, the renal parenchyma was replaced by numerous cysts, ranging in diameter from 0,2 to 4,5 cm. Some were filled

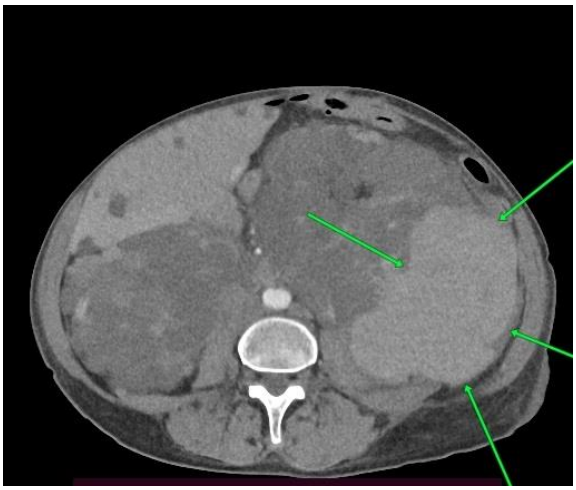

Fig. 3B. Hyperdense foci within the cystic changes in the left kidney

with clear yellow fluid, while others contained blood. Microscopic analysis revealed numerous cysts of varying size, lined with a cuboidal to flattened epithelium, with connective tissue septa in between. Some cysts contained hemorrhagic content, while others were empty or filled with proteinaceous material. Between the cysts, residual renal parenchyma was observed with pronounced fibrosis, areas of microcalcifications, chronic inflammatory infiltrate, regions of fresh hemorrhage, and single or grouped siderophages. Rare glomeruli were present, with some showing partial sclerotic changes. Eosinophilic protein casts were noted in the lumens of the tubules.

Six months after nephrectomy, the patient started with chronic hemodialysis via previous created arterio-venosus fistula. No new episodes of infection or bleeding in the cysts of the remaining kidney have been observed so far.

Table 1. Review of the dynamics of the most important laboratory parameters in the presented patient during hospitalization, five days after nephrectomy, and six months after the surgery when hemodialysis was initiated

Parameter	1st day	3rd day	7th day	5 days after operation	6 months after operation
Hemoglobin (120-180 g/l)	82	90	75	119	89
Erythrocytes (4.2-5.5x10^{12}/l)	3.1	3.3	2.7	4.3	3.4
Leucocytes (4-9 x 10^{9}/l)	8.7	9.5	8.1	6.1	4
CRP (< 6 mg/l)	135	221	128	29	2.3
Creatinine (45-109 µmol/l)	279	319	304	331	576
Urea (2.7-7.8 mmol/l)	12	12.8	11	15	26
Calcium (2.1-2.6 mmol/l)	1.97	1.9	1.9	2.1	2.1
Phosphate (0.8-1.4 mmol/l)	0.84	1.69	1.6	/	1.8
Potassium (3.8-5.5 mmol/l)	4	4.2	3.8	5	4.3
Sodium (137-145mmol/l)	134	135	136	138	144

Discussion

The APKD is a genetically inherited disorder that can lead to significant morbidity, primarily due to a progressive renal cyst formation and associated complications, including haemorrhage, infection and chronic kidney disease [3]. This case highlights a complex clinical scenario in which a 57-year-old female with APKD presented with recurrent urinary infections, dysuria, haematuria and elevated inflammatory markers, ultimately leading to a diagnosis of intracystic haemorrhage and the need for nephrectomy. The patient`s history of recurrent urinary tract infections (UTIs), elevated inflammatory markers and cyst infection, as evidenced by positive urine cultures, is a common complication in APKD [4]. CKD up to the stage IV CKD,

as seen in this case with a serum creatinine of 222 mmol/L, were also frequently observed in individuals with APKD, particularly as the disease progresses

Chapman A, *et al*., have reported that an infected cyst can become resistant to antibiotic treatment due to a thick cyst wall that impairs drug penetration [3]. One of the critical complications observed in APKD is haemorrhage into the cyst, due to increased vascular fragility within the cyst walls. The patient in this case exhibited elevated inflammatory markers, fever, haematuria and anaemia, suggesting an intracystic haemorrhage, as confirmed by CT urography. Intracystic haemorrhage is known to present with sudden onset of pain, hematuria and sometimes fever, reflecting the severe nature of the complication [5]. Sussman *et al*., reports of the presence of hyperdense foci in the cysts on CT scans that did not enhance with contrast, was indicative of a hemorrhagic event [6].

The management of APKD-associated complications often involves conservative measures, including hydration and electrolyte supplementation, as well as antibiotic therapy when infection is suspected [7]. However, as seen in this case, conservative treatment was insufficient, and the patient required surgical intervention. The decision to proceed with unilateral nephrectomy was based on the patient`s worsening kidney function and anaemia. Nephrectomy is considered in patients with end-stage disease, recurrent infections, or severe haemorrhage, and it can be a life-saving procedure [8]. A study by Torres *et al*., [9] demonstrated that the risk of haemorrhage increases with cyst size and underlying hypertension, both common features in APKD patients. A study by Chia-Ter Chao *et al*., [10] reported that the nephrectomy significantly improves quality of life in patients with recurrent cyst complications, particularly those requiring dialysis. Furthermore, a study by Chapman *et al*., [3] highlighted that the laparoscopic nephrectomy offers better postoperative recovery and reduced complications compared to an open surgery in APKD patients.

Comparing this case to previous studies, it is evident that while conservative treatment remains the first line of management, surgical intervention is often necessary when complications arise. Unlike the case reported by P. Duriseti *et al*., [11], where haemorrhagic cysts were managed successfully with supportive care, this patient required a nephrectomy due to a persistent anemia and worsening kidney function. Similarly, studies by Torres *et al*., [9] suggest that while tolvaptan has shown promise in slowing cyst growth, it does not mitigate the risk of hemorrhagic or severe infection, underscoring the importance of individualized treatment strategies.

While nephrectomy remains a critical intervention for severe cases of APKD, emerging therapies aim to slow disease progression and prevent complications such as cyst haemorrhage and infection. One of the most promising pharmacological treatments is tolvaptan, a vasopressin V2 receptor antagonist that has been shown to slow cyst growth and preserve kidney function. Clinical trials, such as the TEMPO 3:4 study, have demonstrated that tolvaptan reduces kidney volume expansion and delays the decline of renal function in APKD patients [3]. However, its role in preventing hemorrhagic complications remains under investigation.

Gene therapy and targeted molecular treatment are also emerging as potential strategies for APKD management. Research into PKD1 and PKD2 gene modulation has shown promise in preclinical studies, with RISPR-based genome editing being explored as a potential approach to correct pathogenic mutations [12]. Additionally, the use of mechanistic target of rapamycin (mTOR) inhibitors, such as sirolimus and everolimus, has been investigated due to their ability to inhibit cyst proliferation and reduce kidney volume [13,14].

In addition to pharmacological interventions regenerative medicine is being explored as a future option for APKD patients. Advances in stem cell therapy and kidney tissue engineering may eventually offer alternatives to nephrectomy and dialysis by promoting kidney regeneration and functional repair [15]. Although these approaches are still in the experimental phases, they hold a great potential for transforming the management of APKD in the future.

Another novel approach involves the use of somatostatin analogs, such as ocreotide and lanreotide, which have been found to reduce cyst growth and slow disease progression in some patients. These therapies work by reducing cyclic AMP levels, which play a crucial role in cyst expansion [16]. Recent studies have reported positive outcomes in patients treated with these analogs, though further research is needed to establish long-term efficacy and safety.

The management of APKD remains challenging due to its progressive nature and the multitude of complications that can arise. The impact of haemorrhagic complication, as seen in this case, underscores the importance of early recognition and intervention. While conservative measures such as hydration and antibiotics are essential, surgical intervention, such as nephrectomy, may be required in severe cases, particularly when patients experience substantial haemorrhage or infection.

Conclusion

This case illustrates the complexities of managing ADPKD, particularly in patients who develop complications such as intracystic hemorrhage, CKD, and infections. The need for an early diagnosis, prompt treatment of infections, and careful monitoring of renal function is critical in preventing further deterioration. In severe cases, nephrectomy remains a viable therapeutic option, although it is typically reserved for advanced disease stages. Further research should focus

on improved pharmacologic therapies to reduce the incidence of hemorrhagic and infectious complications.

Conflict of interest statement. None declared.

References

1. Torres VE, Harris PC, Prison Y. Autosomal dominant polycystic kidney disease. *The Lancet*, 2007; 369(9569): 1287-1301.
2. Spithoven E, Kramer A, Meijer E, *et al*. Renal replacement therapy for autosomal dominant polycystic kidney disease (ADPKD) in Europe: prevalence and survival-an analysis of data from the ERA-EDTA Registry. *Nephrol Dial Transplant* 2014; 29: 15-25.
3. Chapman AB, Devuyst O, Eckardt KU, *et al*. Autosomal dominant polycystic kidney disease (ADPKD): Executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) Controversies Conference. *Kidney International* 2015; 88(1): 17-27.
4. Alma Idrizi, *et al*. Urinary tract infections in polycystic kidney disease. *Med Arh* 2011; 65(4): 213-215.
5. Otto W, Psomiadis JS, Kirshner B. Management of suspected Renal Cyst Infection with intracystic Hemorrhage in a patient with Autosoman Dominant polycystic Kidney Disease. *Cureus* 2023; 15(5): e39319.
6. Sussman S, *et a*l. Hyperdense renal masses: a CT manifestation of hemorrhagic renal cysts. *Radiology* 1984. https://doi.org/10.1148/radiology.150.1.6689762.
7. Torres VE, Ahn C, Barten TRM, *et al*. KDIGO 2025 clinical practice guideline for the evaluation, management, and treatment of autosomal dominant polycystic kidney disease (ADPKD): executive summary. *Kidney International* 2025; 107(2): 234-254.
8. Dunn MD, Portis AJ, Elbahnasy AM, *et al.* Laparoscopic nephrectomy in patient with end-stage renal disease and autosomal dominant polycystic kidney disease. *American Journal of Kidney Disease* 2020; 35(4): 720-725.
9. Torres VE, *et al*. Tolvaptan in patients with autosomal dominant polycystic kidney disease. *N Engl J Med* 2012; 367: 2407-2418.
10. Chia-Ter Chao, *et al*. Bilateral Nephrectomy Significantly Improves Health-Related Quality of Life in a Hemodialysis Patient with Autosomal Dominant Polycystic Kidney Disease. *American Journal od Kidney Disease* 2013; 1221-1222.
11. Duriseti P, *et al*. Life-Treatening Retroperitoneal Hemorrhage Following Cyst Rupture in Autosomal Dominant Polycystic Kidney Disease (ADPKD): A case Report. *American Journal of Case Reports* 2023; 24: e938889.
12. Nguyen LT. Emerging therapies for autosomal dominant polycystic kidney disease-Current Perspectives. *Journal of Nephrology and Therapeutics* 2024.
13. Shillingford JM, Murcia NS, Larson CH, *et al*. The use of CRISPR/Cas9 PKD1 and PKD2 gene correction: Promising preclinical studies. *I Am Soc Nephrol* 2022; 33(7): 1284-1297.
14. Walz G, Budde K, Mannaa M, *et al*. Everolimus in patients with autosomal dominant polycystic kidney disease. *N Engl J Med* 2010; 363(9): 830-840.
15. Reiterova J, Tesar V. Autosomal Dominant Polycystic Kidney Disease: From Pathophysiology of Cystogenesis to Advances in the Treatment. *International Journal of Molecular Sciences* 2022; 23(6): 3317.
16. Suwabe T, Barrera FJ, Rodriguez-Gutierrez R, *et al*. Somatostatin analog therapy effectiveness on the progression of polycystic kidney and liver disease: A systematic review and meta-analysis of randomized clinical trials. *PLoS One* 2021; 16(9): e0257606.