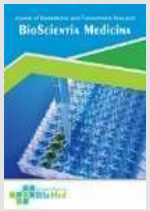
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Polycystic Kidney Disease with Breast Nodules in a Male: A Case Report

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ARTICLE INFO

Keywords:
Breast nodules
Hematuria
Polycystic kidney disease
Renal cysts

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v8i6.999

A B S T R A C T

Background: Polycystic kidney disease is a multisystem and progressive congenital kidney disorder characterized by kidney enlargement and the growth of cysts in the kidneys and other organs. Autosomal dominant polycystic kidney disease (ADPKD) is the most common type of inherited kidney disorder and is observed in 1/500 – 1/1000 people. The diagnosis is usually made by a positive family history , and the Ravine ultrasonographic criteria assess the age and number of cysts in both kidneys. **Case presentation:** A 37-year-old male was reported with complaints of intermittent hematuria and a painless lump in the right breast for the last 6 years. Patients routinely drink herbal medicine when symptoms appear. Abdominal physical examination revealed renal ballottement. The lump in the right breast is palpable as a lump ± 1 cm from the nipple. No abnormalities in kidney or liver function were found on laboratory examination. Ultrasound was performed, and polycystic kidney disease was obtained in both kidneys and liver, as well as a hypervascular solid nodule in the right breast. The patient was given antibiotics and antifibrinolytics. Healthy lifestyle education is also provided to patients. The patient was then referred for a biopsy of the nodule. **Conclusion:** Autosomal dominant polycystic kidney disease (ADPKD) is a common disease but only a few cases of ADPKD are accompanied by nodules in the breast, so a further approach is needed.

1. Introduction

Polycystic kidney disease is a congenital kidney disorder characterized by enlarged kidneys with extensive cyst growth. Cysts may enlarge with age, with a gradual decline in kidney function.[1] Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disorder. The incidence has been observed in 1/500 to 1/1,000 people. About 7 out of 10 ADPKD patients develop kidney failure.[2]

ADPKD is a multisystem disorder that presents with both renal and extra-renal manifestations. Manifestations in the kidneys can include low back pain, hematuria, urinary tract infections, kidney stones, hypertension, and even kidney failure.[2,3] Polycystic liver disease is the most common extra-renal manifestation of ADPKD and rarely causes liver function abnormalities. Cysts can also be found in the pancreas, spleen, and seminal vesicles. Apart from that, diverticular disease, vascular abnormalities, and abdominal hernias can also occur.[3]

The diagnosis of ADPKD is made by imaging based on ultrasound criteria.[2] Only a few cases of ADPKD are accompanied by nodules in the breast, so a structured history is needed to diagnose this disease, especially related to family history. Additional examinations are also an important factor in this disease. In this article, we will discuss a case of a 37-year-old male with autosomal dominant polycystic kidney disease with extrarenal manifestations accompanied by nodules in the breast.

2. Case Presentation

A 37-year-old male patient complained of hematuria for 2 days. Complaints are accompanied by lower abdominal pain that spreads to the right waist. Complaints are also accompanied by general weakness and shivering. The patient has experienced the same thing three times over the last 6 years, and it usually occurs when the patient feels tired due to work. Patients usually drink herbal medicine to relieve symptoms and usually recover on their own within 5-6 days. The patient also complained of a painless lump in the right breast that had appeared since 6 years ago. The lump was initially the size of the tip of a pin and grew to the size of a longan. The patient has no history of hypertension, diabetes mellitus or kidney stones. The patient's mother is deceased; has hypertension and stomach disease but the patient does not know his mother's disease. The patient routinely smokes approximately 1 pack per day.

On physical examination, the patient appeared mildly ill and fully conscious with blood pressure 130/80 mmHg, heart rate 88 times per minute, respiratory rate 16 times per minute, temperature 36.6°C, and oxygen saturation 99%. On examination of the chest wall, a lump ± 1 cm from the nipple of the right breast was palpable. The lump feels springy, well-defined with a smooth surface, moveable, and has no tenderness. On abdominal examination, the liver was not palpable, the kidney ballottement, the spleen was not enlarged, and there was no tenderness. Examination of the head, heart and lungs, and extremities showed no abnormalities.

Laboratory examination revealed urea levels of 24.3 mg/dl, creatinine 1.23 mg/dl, SGOT 16 U/L and SGPT 13 U/L. The results of an abdominal ultrasound examination showed complex cysts in both kidneys, with the largest size in the right kidney ± 3 x 3 cm, in the left kidney ± 1.5 x 2.2 cm (Figure 1A and B) and the liver with an average size of ± 14.2 cm (Figure 2), while an ultrasound examination of the right chest wall showed a hypervascular solid nodule with a size of ± 2.3 x 1.5 cm (Figure 3).

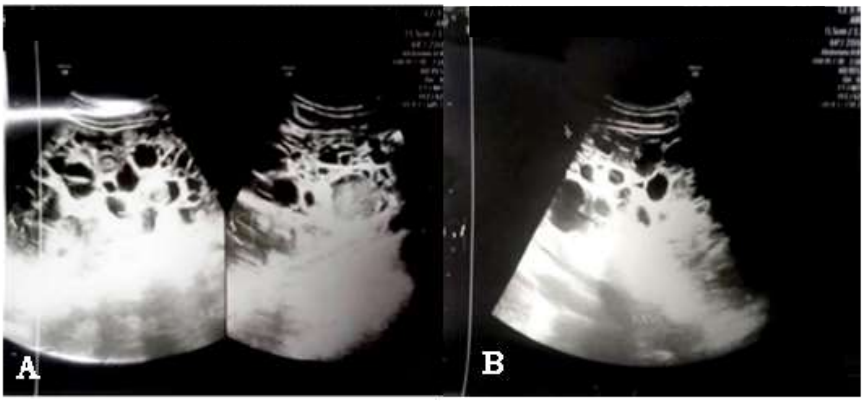

Figure 1. Kidney ultrasonography. (A) Right kidney (B) Left kidney.

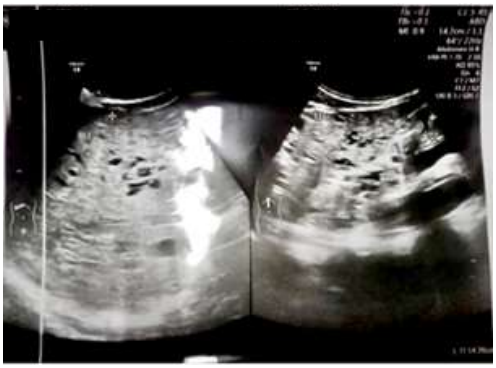

Figure 2. Liver ultrasonography.

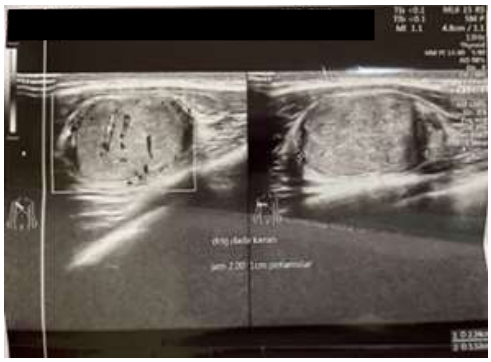

Figure 3. Right breast nodule ultrasonography.

Based on the data obtained, the patient was diagnosed with autosomal dominant polycystic kidney disease and right breast nodule. The patient was given therapy with cefixime 2 x 200 mg orally and tranexamic acid 2 x 500 mg orally for one week. When re-evaluated, complaints of hematuria decreased, and there were no complaints of lower back pain. Patients are educated to stop smoking and adopt a healthy lifestyle, such as increasing water intake and limiting sodium and protein intake, as well as maintaining optimal body weight and exercising regularly. The patient was then referred to an oncologist for a biopsy.

3. Discussion

Polycystic kidney disease is a multisystem and progressive disease with cyst formation and kidney enlargement as well as the involvement of other organs (e.g., liver, pancreas, spleen).[3] ADPKD can be found in men and women, and each generation has a 50% chance of developing the disease.[4] The pathogenesis of ADPKD is a mutation in two chromosomes. PKD1 on chromosome 16p13.3 encodes polycystin-1 (PC-1) in as many as 85% of cases and PKD2 on chromosome 4q22 encodes polycystin-2 (PC-2) in another 15% of cases. Polycystin is an integral membrane protein and located in the renal tubular epithelium. Research has found that abnormalities in polycystin-1 disrupt interactions between cells and the cell matrix in the renal tubular epithelium, while abnormalities in polystine-2 disrupt calcium signalling in cells.[2,5] Another mutation found in ADPKD patients recently is GANAB, which causes mild cystic disease that does not progress to kidney failure, and DNAJB11, which causes kidney failure without obvious kidney enlargement.[2] Additionally, ADPKD can be caused by mutations in genes associated with autosomal dominant polycystic liver disease (ADPLD), including SEC63 and PRKCSH.[4] This case found that the patient's mother had a history of hypertension and abdominal pain, but the patient did not know about her mother's illness.

The clinical features of ADPKD vary from patient to patient and can be divided into renal and extra-renal manifestations.[3,6] Pain is the most common manifestation. Low back pain may arise from large cysts due to compression of surrounding structures or stretching of the renal capsule. Enlarged cysts can cause compression symptoms such as rapid satiety and vomiting. Hematuria is usually gross and recurrent and is triggered by urinary tract infections, kidney stones, vigorous exercise, or minor trauma; or it can also be caused by a ruptured cyst and cyst bleeding.[2,3,6] Hypertension is a common sign that occurs in more than 50% of patients.[6] Complications of hypertension, such as left ventricular hypertrophy (LVH) and LV diastolic dysfunction, can occur earlier, possibly by renal ischemia caused by enlargement of the cyst which increases renin release. A history of kidney stones usually occurs in around 20% of patients.[3,6] The patient, in this case, experienced recurrent gross hematuria accompanied by low back pain and was usually triggered by work-related fatigue.

Extrarenal cysts often occur in ADPKD, with the most common being polycystic liver disease (PLD).[7] As many as 90% of patients over 35 years of age have liver

cysts, with the prevalence and total volume of cysts being higher in women than men. Usually, the liver parenchyma and function remain normal.[2,5,6] Cysts can also be found in various organs in ADPKD, including the pancreas, seminal vesicles in men, and ovaries in women.[2,3] An Iranian study found cysts in both breasts of women with ADPKD.[8] Other extra-renal manifestations include intracranial aneurysms (ICA), heart valve disease, colonic diverticula, and abdominal wall hernias.[2,6] The patient, in this case, had multiple cysts in the liver, and no other extra-renal manifestations were found.

Ultrasonography (USG) is the initial preferred approach for diagnosis due to its wide availability, non-invasiveness, and low cost. The diagnosis is usually made on the basis of a positive family history and the Ravine ultrasonography criteria (Table 1).[6,9] CT-scan and T2-MRI, with and without contrast, are more sensitive than ultrasonography and can detect smaller cysts. However, they may cause renal toxicity due to the use of contrast and should be used only if necessary. Genetic testing may be performed in ambiguous cases. Screening of asymptomatic patients with a positive family history is recommended after 18 years of age with ultrasound.[3,6] In a 37-year-old patient, ≥ 2 cysts in each kidney were found by ultrasonography.

Table 1. Ravine ultrasonography criteria (PKD1).[6,9]

Age (years)	Diagnostic criteria
15 – 29	≥ 2 cysts, unilateral or bilateral
30 – 59	≥ 2 cysts, in each kidney
≥ 60	≥ 4 cysts, in each kidney

Patients at risk or with ADPKD are recommended to maintain a healthy lifestyle by increasing hydration, limiting sodium and protein intake, maintaining optimal body weight, regular exercise, avoiding smoking and alcohol, and limiting the use of non-steroidal anti-inflammatory drugs.[4,5] High water intake (3-3.5 liters/day) and low sodium (2.3-3 g/day) are beneficial for preventing kidney stone formation and suppressing vasopressin, thereby reducing cyst formation and growth. Early detection and treatment of hypertension and dyslipidemia should be examined.[5,10] The HALT progression of polycystic kidney disease (HALT-PKD) study suggests a blood pressure target of < 110/75 mmHg in those less than 50 years of age with preserved estimated renal function rate (eLFG) (≥ 60 mL/min per 1.73 m²) and without significant cardiovascular comorbidities.[5,11] The patient in this case was not found to have hypertension, so no antihypertensives were given. The patient was also educated to quit smoking and adopt a healthy lifestyle.

Severe hematuria may be associated with cyst bleeding or infection, kidney stone discharge, and neoplasms of the kidney or urinary tract. Treatment of cyst bleeding is conservative, and most will resolve within 2-7 days. Administration of anticoagulant or antiplatelet, or antifibrinolytic drugs may be considered if conservative therapy fails. Treatment for cyst infections may include intravenous broad-spectrum antibiotics if systemic symptoms are present, followed by oral antibiotics that have excellent cyst penetration, such as ciprofloxacin or other quinolones, with a minimum treatment duration of 4 weeks. Cysts that are resistant to antibiotic therapy may require percutaneous or surgical drainage.[12] The management of nephrolithiasis in ADPKD patients is similar to that in the general population. Treatment for symptomatic cystitis and asymptomatic bacteriuria can be given trimethoprim-sulfamethoxazole and fluoroquinolones.[4] The management of hematuria given to the patient was cefixime 2 x 200 mg and tranexamic acid 2 x 500 then after re-evaluation, the symptoms had decreased.

Pre-clinical studies suggest a role for arginine vasopressin-mediated cyclic adenosine monophosphate (cAMP) as a trigger for cyst proliferation and fluid secretion in ADPKD.[5] Tolvaptan is a vasopressin receptor antagonist shown to slow eLFG decline compared to placebo over a one-year period in patients with end-stage chronic kidney disease. By blocking the reception of vasopressin signals, it decreases cAMP.[13,14] Currently, tolvaptan should be recommended for all ADPKD patients with the possibility of rapid disease progression. The criteria for tolvaptan use are proposed for those aged 18-55 years, with chronic kidney disease grade 1– 4 (eLFG 25 mL/minute per 1.73 m^2), those with high risk as measured by the risk score (longitudinal diameter > 17 cm by ultrasound, total kidney volume > 750 mL, Mayo imaging classification 1C, 1D, 1E or predicting renal outcomes in polycystic kidney disease (PROPKD) score > 6), and rapid decline in eLFG 3 mL/minute per > 1.73 m^2 over 5 years.[5,14]

Prophylactic nephrectomy in ADPKD patients is not routinely recommended as it is associated with increased morbidity and mortality. Nephrectomy before transplantation is only performed for specific indications (Table 2). Kidney transplantation is the best renal replacement therapy for ADPKD patients who have progressed to end-stage kidney failure.[2,3] This disease affects the biological, physical, and psychological aspects as well as the patient's quality of life; however, this is often missed by examiners.[4] ADPKD patients usually reach end-stage renal failure in the fifth or sixth decade of life, with 75% occurring by the age of 75 years.[3]

Table 2. Indications for Nephrectomy before Transplantation.[2,3]

Indications
Large kidney size causes a lack of space for graft placement
Recurrent cyst infection or bleeding
Symptomatic nephrolithiasis
Chronic pain (reduced quality of life or need for narcotics)
Compression symptoms (rapid satiety and recurrent vomiting)
Suspicion of malignancy

4. Conclusion

Autosomal dominant polycystic kidney disease is the most common inherited kidney disease. Clinical manifestations can be found in the renal and extra-renal. Diagnosis is based on ultrasound criteria and positive family history. Cysts are found in the kidneys as well as other organs such as the liver and pancreas. While cysts have been reported in both breasts of women with ADPKD, nodules have not been found in the breasts of men with ADPKD, so it is necessary to reassess the association with ADPKD. The main therapy is symptomatic according to what complaints arise in the patient. Tolvaptan, which is a vasopressin receptor antagonist, has been shown to slow the decline in eLFG. Patients with this disease usually develop kidney failure by the seventh decade of life. This disease can also affect biological, physical, and psychological aspects as well as the patient's quality of life. Therefore, early diagnosis and prompt management, including education, are recommended to avoid complications.

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