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Recurrent Hematuria in a Patient with Autosomal Dominant Polycystic Kidney Disease (ADPKD) and Renal Transplantation: A Case Report

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Abstract Hematuria occurrence in autosomal dominant polycystic kidney disease (ADPKD) is common and can be a manifestation of cyst bleeding. Patients with ADPKD who receive kidney transplantation can present with recurrent hematuria. Malignancy, urinary tract infections, calculus obstruction or any recent diagnostic or interventional procedures can all manifest with hematuria. Knowledge of the precipitating factors and clinical presentation in those patients will help practicing internists in performing an appropriate evaluation and management of these entities and their complications, as well as execute a timely referral to subspecialists for native kidney nephrectomies when indicated. We herein, present a case of 72-years-old female, with APKD who received kidney transplantation 14 years ago, presenting with repeated hospital admissions with flank pain and recurrent hematuria. She had experienced multiple admissions with hematuria, most likely caused by native kidney recurrent cyst bleedings.

Keywords: *hematuria, polycystic and renal transplantation*

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1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is one of the best-known and most common diagnosed genetic diseases that is defined by the presence of multiple kidney cysts, occasionally accompanied by hepatic cysts. Mutations in one of two genes, PKD1 (residing on chromosomes 16p13.3) or PKD2 (residing on chromosomes 4q21). Clinical manifestations are directly related to the cyst size and patients can present with dull aching flank pain due to increased cystic size, kidney stones, or complications related to cyst infection, hemorrhage, hematuria, or rupture. Extrarenal manifestations also include cardiac involvement (mitral valve prolapse, hypertension); other organ involvement (abdominal wall hernia, liver or pancreatic cysts, and brain aneurysm) [1]. Almost half of the patients with ADPKD will develop end-stage renal disease (ESRD), and the majority of patients are treated with renal transplantation and undergo immunosuppression, which may predispose them to comorbidities such as infections and malignancies. Macroscopic hematuria is a common presentation that is usually related to polycystic kidney disease, which could result in repeated hospital admissions and workups [2]. It should not be assumed that hematuria in those patients is of a benign origin, and it requires exclusion of urinary tract malignancy, infection, or obstruction. The main indications for native kidney nephrectomy in ADPKD include recurrent infection, hematuria, and pain [3]. The patient was informed that data concerning the case would be submitted for publication, and she provided an informed consent.

2. Case Report

72-years-old female, with past medical history of hypertension, type 2 diabetes mellitus, Alzheimer's, Saphenous and femoral vein deep venous thrombosis, polycystic kidney and liver disease, chronic kidney disease (CKD) stage 4, transplanted kidney (on the right side 14 years ago), holding a do not resuscitate (DNR) code, presented to the emergency department with a sudden one episode of hematuria that spontaneously subsided. History was obtained from the patient's proxy who also reported that the patient has recurrent admissions

with similar hematuria presentation in the past year. The patient denied having any fevers, chills, abdominal pain, flank pain, nausea or vomiting, or any other pertinent symptoms. Family history of polycystic kidney disease in the daughter and son was also reported. The patient home medications included acyclovir 400 mg daily, clonidine 0.1 mg daily, Apixaban 5 mg twice daily, losartan 100 mg daily, methylprednisolone 4 mg daily, metoprolol tartrate 100 mg twice daily, paricalcitol 1 mcg daily, tacrolimus 1 mg daily (which was increased from 0.5 mg recently), mycophenolate mofetil 250 mg four capsules once daily, memantine 28 mg once daily, rosuvastatin 20 mg daily, quetiapine 25 mg daily, Lantus insulin 10 units daily, and pantoprazole 40 mg daily. On physical examination, the patient had some conjunctival pallor, prominent abdominal distension and no costovertebral angle tenderness, heart and lung exams were normal and no edema in the lower limbs. The patient's vital signs were within normal limits. Laboratory testing was significant for mild anemia. Labs were as follows: WBC 10 (reference 4-11 10^3/uL); RBC 3.4 (reference 3.8-5.20 10^6/uL); Hgb 9.7 (references 12-15 g/dL); hematocrit 31% (reference 35-45%); and MCV 92(reference 80-100L). The levels of potassium, sodium, magnesium, calcium, phosphorus, and albumin were all within normal limits. Urinalysis showed moderate blood but was otherwise within normal limits with no evidence of infections. Additionally, the patient had borderline renal function with a creatinine of 1.33 (reference 0.52-1.04 mg/dL); BUN 20 (reference 7-17 mg/dL); estimated glomerular filtration rate (eGFR-CKD-EPI) of 53 ml/min/1.73^2. Tacrolimus drug trough was measured and was 5.7 (reference 2-20 ng/ml). The patient was on good adherence with immunosuppressive therapy. Abdominal ultrasonography (Figure 1, A-C) demonstrated no perinephric fluid collection around either kidney. The right native kidney measured 11.0 cm x 6.0 cm x 7.0 cm, while the left kidney measured 13.0 cm x 6.4 cm x 7.6 cm in its longitudinal, transverse, and anteroposterior diameters, respectively. There was evidence of decreased cortical thickness in both kidneys. Multiple anechoic/hypoechoic cystic lesions with variable size are seen but no evidence of hydronephrosis were seen in both kidneys. Additionally, a 3.0 mm non obstructive renal calculus was noted in the right kidney while 5.4 mm non obstructive renal calculus was noted in the left kidney. The transplanted kidney measured 11.0 cm x 5.0 cm x 5.2 cm and there was mild-to-moderate peri calyceal dilation but no evidence of nephrolithiasis. Additionally, no limited vascular flow stenosis was noted, and the urinary bladder was normally distended with non-thickened walls but exhibited intraluminal echogenicity likely clots in the setting of hematuria. Evident right-sided urinary bladder diverticula were also noted (measuring 4.6 mm. 1.7 cm x 1.5 cm). The postvoid test showed acute urine retention. Computed tomography (CT) of the abdomen and pelvis (Figure 2 A-C) was significant for the following: multiple fluid attenuation cystic lesions throughout the liver and bilaterally in both kidneys. On CT, many of the kidney cysts demonstrated peripheral rim of calcifications, as well as multiple parenchymal calcifications were seen bilaterally. Right iliac fossa transplanted kidney showed mildly dilated extrarenal pelvis, but no radiopaque calculi were visualized. Given the risk factors in the history and common cardiac complication in ADPKD, the patient also underwent an echocardiography which showed normal left ventricular (LV) function and ejection fraction of 55-60%, moderate LV hypertrophy, mildly dilated left atrium and mild diastolic dysfunction (Grade 1). The patient clinical course in the hospital was uneventful. No recurrence of hematuria occurred during hospital stay. The patient did not show any radiographic findings of chronic graft rejections and hence it was attributed that the hematuria source is from ADPKD cysts. The patient was referred for surgical consult regarding indication of native kidney nephrectomy. However, she and her proxy refused surgical options and opted for repeated medical follow up. The patient was discharged and scheduled for routine outpatient follow-up with her primary care physician.

3. Discussion

Cyst hemorrhage is a frequent cause of hematuria in ADPKD and can be self-limited while other differential diagnoses include cysts infection, urinary tract infection, renal stones, malignancy, or recent diagnostic or therapeutic procedures. Hence, recurrent hematuria in patients with APKD and kidney transplant, is a common presentation [4]. Awareness of such clinical presentations and precipitating factors is crucial for practicing internists to perform the appropriate evaluation and management of these complications, as well as the timely referral for surgery or other subspecialities. Indeed, Neef and colleagues [5] in their retrospective study of 100 consecutive renal transplantation simultaneously with unilateral nephrectomy in patients with polycystic kidney disease have demonstrated that it is a reasonable procedure for patients suffering from massively enlarged native kidneys with a reported overall patient and graft survival of 97% and 96% at 1 year, respectively and 93% and 80% at 5 years, respectively. Other studies have shown that 16–26% of renal transplanted patients who have polycystic kidney disease subsequently underwent successful native nephrectomy to treat complications including: recurrent hematuria, infection, or intractable pain from the large cysts. Hence the option of a combined surgery should be offered to patients prior to kidney transplantation [6,7].

In our case, the patient had experienced multiple admissions with hematuria, most likely caused by native kidney recurrent cyst bleeding. However, other causes for hematuria has been shown to occur in 12 % of post transplanted kidney patients. Hence, it is important to establish a differential diagnosis in respect to the preexisting states including urological procedures or immunosuppressants use for both induction and rejection therapies in these renal transplanted patients [8]. Clinical evaluation through a thorough history taking, a comprehensive physical exam and monitoring of the immunosuppression levels can all point towards nonadherence as a cause of chronic kidney graft rejections. Furthermore, kidney transplant function can be assessed by serum creatinine and estimated glomerular filtration rate [9]. ***In our case***, renal transplantation was performed 14 years a prior, and the patient has been in compliance

with immunosuppressant medications (achieving a therapeutic drug levels), renal function was stable across multiple outpatient and hospital admissions, and renal doppler ultrasound showed no evidence of graft vessels angiopathies. Native nephrectomy in ADPKD patients is a major operation with controversy related to its timing and indications [10]. Bellini and colleagues [11] performed a retrospective study showing that native bilateral nephrectomy for ADPKD can be performed safely and it is recommended for patients who either need space for a future kidney transplant, have significant refractory symptoms of cysts hemorrhages or if there is a suspicion of cancer. In conclusion, this case report underlines the importance of interdisciplinary, collaborative care management team in ADPKD patient presenting with recurrent hematuria with kidney transplant and on immunosuppression.

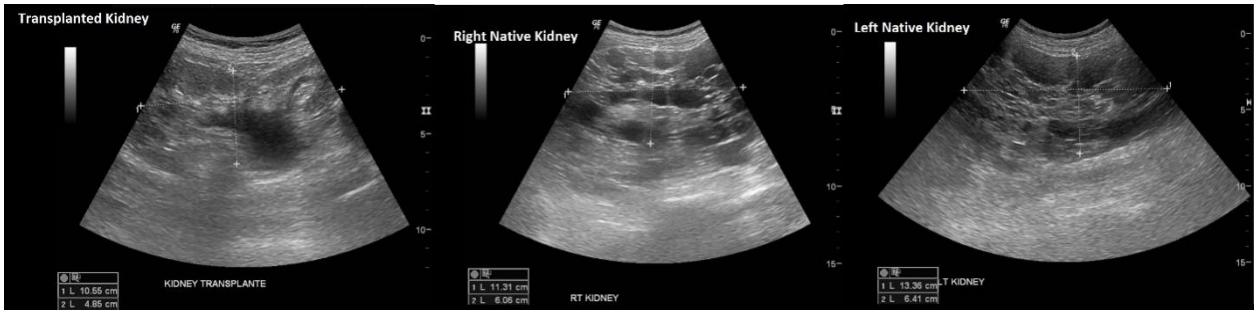

Figure 1. Kidney Ultrasound showing bilateral enlarged kidneys with several cysts of varying size, and multiple scattered echo-dense cysts

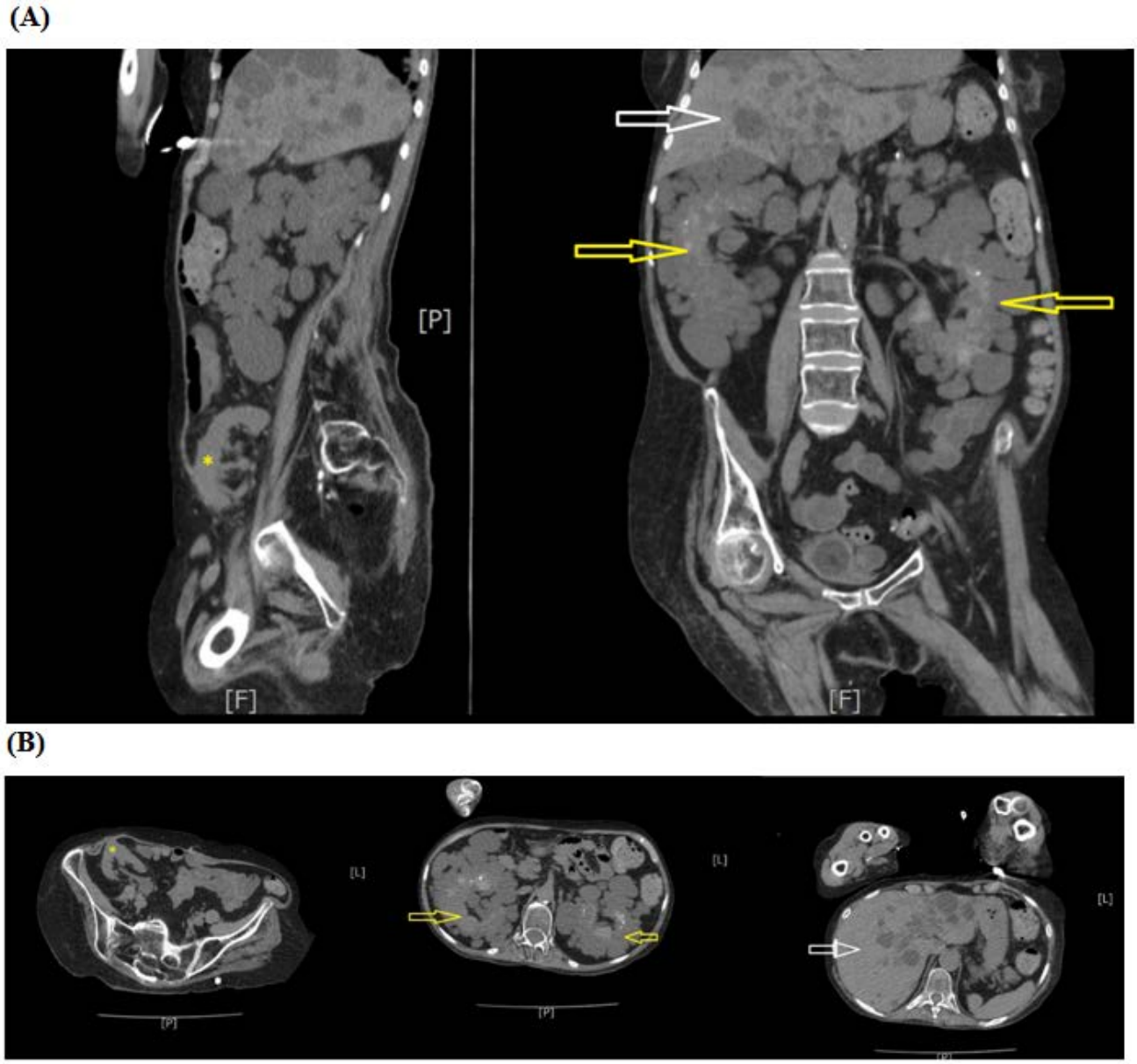

Figure 2. CT scan Abdomen and Pelvis without intravenous contrast (A and B) demonstrating bilateral polycystic kidneys (yellow arrows) and several cysts in the liver (white arrow). Transplanted kidney is also visualized (marked with *)

Movie Files

Movie file 1. Transverse section of CT Abdomen and Pelvis demonstrating Transplanted kidney in the right iliac fossa and moving upward to show the marked enlargement of both kidneys by innumerable cysts, along with visualized cysts in the liver.

Movie file 2. Coronal section of CT Abdomen and Pelvis demonstrating the marked enlargement of both kidneys by innumerable cysts, along with visualized cysts in the liver.

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