Case Reports in Nephrology and Dialysis

Case Rep Nephrol Dial 2024;14:116–121
DOI: 10.1159/000538951
Received: January 14, 2024
Accepted: April 4, 2024
Published online: July 15, 2024

Single Case

Unveiling Neglected Concerns: Possible Severe Hepatic Complications after Nephrectomy in Autosomal Dominant Polycystic Kidney Disease – A Case Report

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Keywords
Autosomal dominant polycystic kidney disease · Liver fibrosis · Nephrectomy · Pancytopenia

Abstract
Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is the most common genetic kidney disease and the 4th leading cause of renal replacement therapy in the world. ADPKD is a systemic disorder as cysts may develop in several organs. Liver cysts are the most common extrarenal manifestations and are often incidentally detected. Even though cysts do not influence liver function, they can grow to a very great size and can significantly enlarge liver volume, causing structural distortion of the biliary tree and patient discomfort due to the mass effect. Nephrectomy is frequently considered in preparation for renal transplantation in patients with remarkable kidneys' enlargement. There are currently no globally recognized clinical guidelines for nephrectomy. Although cysts do not normally affect liver function in ADPKD, after nephrectomy cases of liver fibrosis and Budd-Chiari have been reported. These are uncommon disorders due to the obstruction of the blood flow in the hepatic venous causing spleen and liver volume enlargement, portal hypertension, and hepatic cirrhosis. ***Case Presentation:*** We present a case of hepatic fibrosis with splenomegaly and severe pancytopenia as a tardive complication after bilateral nephrectomy in 47-year-old ADPKD patient. ***Conclusion:*** This finding underscores the critical significance of meticulously examining the anatomical relationship between polycystic kidneys and the liver before performing nephrectomy. Additionally,

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it highlights the importance of assessing liver involvement and associated complications. By integrating liver assessment into the criteria, we can significantly enhance patient care and improve the overall management of ADPKD before kidney transplantation.

Introduction

The CARE checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000538951). Around 12 million people worldwide suffer from autosomal dominant polycystic kidney disease (ADPKD), the most common genetic kidney nephropathy and the 4th leading cause of end-stage renal disease [1]. Renal cysts' enlargement process is accompanied by disorders such as hypertension, discomfort, pain, cyst bleeding kidney stones, and cyst infection. Despite the continuous destruction of renal parenchyma, glomerular hyperfiltration occurs in the residual glomeruli and preserves renal function for decades. Thus, a significant decline in renal function usually happens when patients' age is beyond 40 [2].

Liver cysts are common extrarenal manifestations of ADPKD, causing significant liver enlargement and structural changes in the biliary tree while maintaining liver function [3]. ADPKD is primarily caused by mutations in the PKD1 and PKD2 genes, which encode polycystin 1 and polycystin 2, respectively. The severity of ADPKD varies significantly, with PKD2 patients experiencing milder kidney disease and PKD1 patients experiencing more severe renal disease [4].

Research shows that AVP is crucial in ADPKD cystogenesis. Treatment with tolvaptan slows renal volume expansion and function decline [5], does not prevent dialysis and transplantation, and is totally ineffective on liver cysts.

Nephrectomy is often considered for renal transplantation due to risks of infection, nephrolithiasis, bleeding, pain, and mass effect. However, nephrectomy is associated with high morbidity and mortality, and there are no global clinical standards for it [6]. Late hepatic complications, such as liver fibrosis and Budd-Chiari syndrome, can occur after nephrectomy in patients with ADPKD [7, 8] These complications are related to the obstruction of hepatic venous blood flow, leading to spleen and liver enlargement, portal hypertension, and hepatic fibrosis. Endothelial cell lesions, intimal thickening, thrombotic obliterations, and scarring of the intrahepatic portal or hepatic venous circulation are the most common causes. Another possible explanation is that the polycystic liver moves downwards and narrows the inferior vena cava after nephrectomy. In this regard, Foresto et al. [9] reported a case of BCS after bilateral nephrectomy with significant clinical improvement after angioplasty and stenting of the inferior vena cava. While liver cysts in ADPKD patients typically do not impair liver function, nephrectomy seems to increase the risk of liver-related adverse effects. We present a case of a patient with ADPKD with late hepatic fibrosis, splenomegaly, and pancytopenia following bilateral nephrectomy.

Case Presentation

A 47-year-old male was hospitalized in our unit in August 2018 for high fever, malaise, nausea, and abdominal pain. The patient had a previous diagnosis of ADPKD with PKD1 truncating mutation. He was followed in our outpatient clinic where a progressive worsening of eGFR was observed with values up to stage IV of CKD in 2018.

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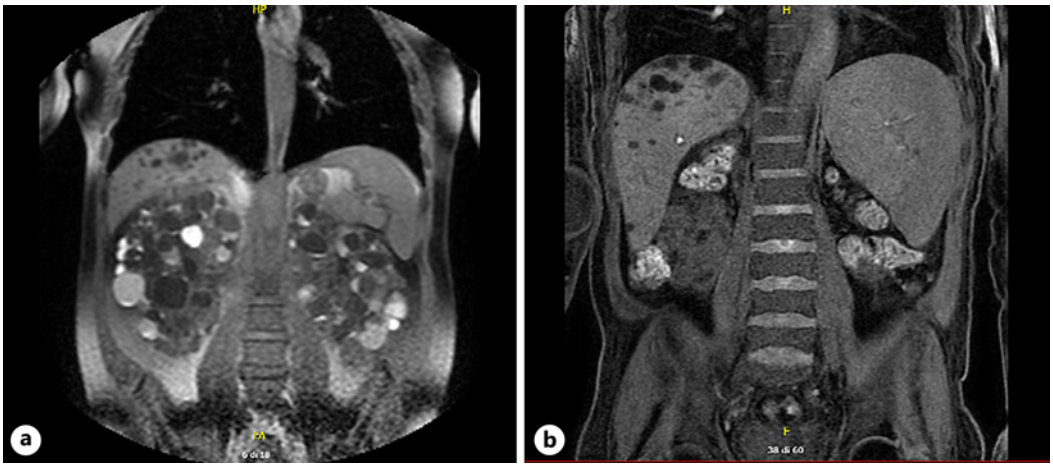

Fig. 1. a 2014 MRI (pre-nephrectomy): multiple liver cysts (maximum diameter: 3 cm). Parenchymal renal replacement by multiple cysts (maximum diameter: 5 cm). No spleen abnormality. **b** 2022 MRI (post-nephrectomy): multiple liver cysts (maximum diameter: 3 cm). Splenomegaly (bipolar diameter: 17 cm).

On admission to hospital, his renal function was severely impaired (creatinine 10 mg/dL). The other routine exams found no abnormalities, except for a significant increase in reactive C protein (156 mg/L; n.v. 0–6). A urine culture was found negative. Abdominal NMR revealed significant volumetric expansion of cysts in the kidney, with bipolar diameters of about 30 cm, as well as growth in the number and size of hepatic cysts. The spleen was found to be normal in size.

The patient, despite receiving multiple antibiotics for a month, experienced fever and pain, leading to ESKD. In September 2018, due to the ineffectiveness of the therapy and history of recurrent kidney cyst infections necessitating hospitalization and prolonged antibiotic treatments, the patient underwent a bilateral nephrectomy and began hemodialysis. After a nephrectomy, the patient resolved inflammatory symptoms and was discharged. Over the next 2 years, he continued hemodialysis three times a week and maintained satisfactory physical conditions.

An abdominal NMR was performed in November 2020 as part of an imaging study for inclusion on the transplantation list. Splenomegaly with a spleen bipolar diameter of 14 cm was reported for the first time. A further slight spleen expansion was observed in an NMR follow-up in January 2021, when its diameter increased to 14.5 cm. Afterward, the spleen achieved a 16 cm diameter at the NMR control in September 2022 (Fig. 1). During the follow-up in 2019–2022, immunologic parameters and viral hepatitis indicators tested negative as well as liver enzymes and bilirubin.

In November 2020, the patient began to present important trilinear pancytopenia that had been steadily getting worse with numerous concurrent infective and bleeding episodes (Table 1). We ruled out all hematologic causes. In September 2022, a FibroScan was carried out to identify the cause of the splenomegaly; 3 liver samples were taken at the level of the right hepatic lobe resulted with a median of 11.9 kPa IQR = 1.6 IQR ratio/median = 0.13 (n.v. <0.3) indicative of significant liver stiffness (Fig. 2). In light of these clinical findings, splenectomy was considered, but current clinical circumstances prevent it.

Discussion

Our report shows a patient with ADPKD with splenomegaly, pancytopenia, and an overall worsening of the general condition as complications of hepatic fibrosis raised after bilateral nephrectomy. After mono or bilateral nephrectomy, few incidences of Budd-

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Table 1. Evolution of blood count, bilirubin, and spleen size throughout time

	2015	Aug 2018	Nov 2020	Jan 2021	Sep 2022	Jul 2023
Hemoglobin (nv 14–18), g/dL	12.2	8.9	8.6	9	9	9.2
White blood cells (nv 4.8–10.8), $\times 10^9$/L	9	9	3.4	3.9	0.9	2.6
Platelets (nv 130–400), $\times 10^9$/L	190	148	196	90	87	67
ESA	NO	NO	NO	NO	YES	YES
AST/ALT (nv 5-35/6/59), U/L	14/14	8/7	18/13	20/19	27/26	13/14
Total bilirubin (nv 0.1–1), mg/dL	//	0.23	0.24	0.6	0.78	0.28
Spleen size, cm	//	//	14	14.5	16	17

Bilateral nephrectomy was conducted in 2018. ESA, erythropoiesis-stimulating agent.

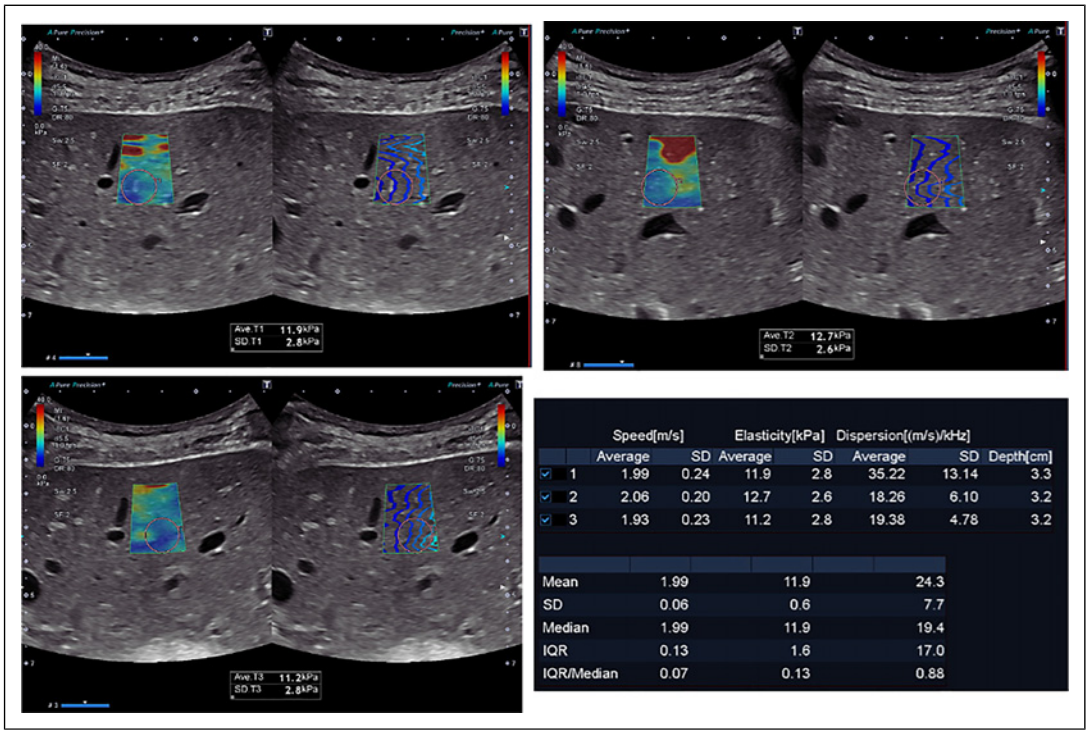

Fig. 2. FibroScan performed in September 2022.

Chiari syndrome (BCS) or hepatic fibrosis have been documented in patients with ADPKD [7–9]. All patients had significant hepatomegaly but apparently no specific risk factors for BCS or hepatic fibrosis. However, nephrectomy may become an additional risk since the removal of the kidneys can lead to liver cyst enlargement with obstruction of the hepatic veins.

In the literature, there are only few reports about hepatic effects after nephrectomy, likely because such complications occur late and often go unrecognized or ascribed to other causes, although they might occur more frequently than expected complicating the overall clinical condition over time. Given these potential consequences and the best-known high risk of morbidity and mortality related to this procedure, the crucial question is "when is nephrectomy truly required in ADPKD patients?"

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There are currently no globally recognized clinical practice guidelines, and there are significant variations in the approach. It may also be helpful to keep in mind that the size of the native kidney sometimes declines after transplantation probably due to the subsequent immunosuppressive therapy.

Liver involvement is still not sufficiently considered as a risk factor for late problems during the pre-kidney transplant examination. Some patients with severe hepatomegaly have mild portal hypertension, which is frequently undiagnosed, and, on rare occasions, a minor ascitic effusion. These patients are likely to be at a higher risk of complications following nephrectomy, and it would be prudent to assess this risk before proceeding.

Conclusions

Even though in the specific case described in the manuscript, nephrectomy was considered mandatory due to the patient's infectious condition, it serves as a cautionary example that highlights the need to be vigilant and cautious when considering nephrectomy before kidney transplantation in ADPKD patients. The appropriate timing for native nephrectomy in ADPKD remains debated, with several critical factors to consider. Liver involvement, often neglected in the current decision-making process, deserves greater attention. Recognizing and assessing the potential impact of liver cysts and associated complications is essential when evaluating nephrectomy suitability in ADPKD patients. Incorporating liver assessment into the criteria can enhance patient care and offer a more comprehensive approach to managing ADPKD before kidney transplantation.

Statement of Ethics

This retrospective review of patient data did not require ethical approval in accordance with local guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

All authors declare that they have no conflicts of interest.

Funding Sources

The authors did not receive support from any organization for the submitted work.

Author Contributions

Liliana Italia De Rosa, Martina Catania, Francesca Tunesi, Marta Vespa, Romina Bucci, Kristiana Kola, Giuseppe Vezzoli, and Maria Teresa Sciarrone Alibrandi contribute equally to the conception of the work, the acquisition, analysis, and interpretation of data for the case report. They reviewed it critically and approved the present version to be published. They agreed to be accountable for all aspects of the work.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material. Further inquiries can be directed to the corresponding author.

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