Massive Renal and Retroperitoneal Hemorrhage in a Patient with Acquired Cystic Kidney Disease

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CASE PRESENTATION

Initial Presentation and History

A 50-year-old African American man with a history of end-stage renal disease (ESRD) due to long-standing hypertensive nephropathy was transferred to the emergency department (ED) after becoming severely hypotensive during a regularly scheduled hemodialysis session. In the ED, he complained of constant dull pain in the left flank and left lower quadrant with no radiation; he stated that the pain had been present for the past 2 to 3 days. Urine output was minimal, and he denied hematuria. He denied fever or chills, nausea, vomiting or diarrhea, rectal bleeding, or dark stools but did report feeling weak and sleepy. He also denied having previous episodes of abdominal or flank pain or hematuria.

The patient's medical history was significant for ESRD treated with hemodialysis for the past 7 years, hypertension with hypertensive nephropathy, chronic pancreatitis, hepatitis C virus infection, and severe Barrett's esophagitis. The only surgical intervention he had was the creation of a left arm arteriovenous fistula for hemodialysis. The patient reported smoking 1 pack of cigarettes per day for approximately 28 years, drinking alcohol daily for the past 15 years, and using recreational drugs, including injecting heroin, snuffing cocaine, and smoking marijuana. His most recent use of illicit drugs was smoking marijuana 8 days prior to this presentation. Family history according to the patient was negative for members with heart disease, high blood pressure, kidney disease, or cancer. His parents died in their eighties from natural causes, and his 2 brothers were alive and healthy. Current medications included Nephrocaps and Renagel for renal failure, pantoprazole for esophagitis, and clonidine for hypertension. He denied using over-the-counter drugs or herbal remedies.

Physical Examination and Laboratory Studies

On physical examination, blood pressure was 72/35 mm Hg, heart rate was 100 bpm, temperature was 98.3°F, and respiratory rate was 20 breaths/min. The remainder of the physical examination was normal except for mild left flank tenderness and left costovertebral angle tenderness. Initial laboratory studies showed severe anemia (**Table 1**). The basic metabolic panel showed normal serum electrolytes and elevated creatinine and blood urea nitrogen, but these results were similar to the patient's baseline levels. Stool testing for occult blood was negative, and urinalysis was normal. Intravenous fluid resuscitation was initiated along with transfusion of 2 U of packed red blood cells. The patient's hemoglobin and hematocrit remained stable for more than 36 hours after blood transfusion.

Imaging Studies and Diagnosis

Computed tomography (CT) scan of the abdomen and pelvis showed massive hematoma inferior and anterior to the left kidney (**Figure 1**) with streaks of blood descending down to the left inguinal area. A possible mass in the left kidney was noted. In addition, the kidneys were significantly small in size, with very thin cortex; multiple small cysts (< 2 cm) were observed in both kidneys (**Figure 2**). After urology and nephrology consultations, the cause of the patient's symptoms and findings was believed to be acquired cystic kidney disease (ACKD) with rupture of one of the cysts.

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Table 1. Results of Complete Blood Cell Count in Case Patient

Laboratory Test	Result	Normal Range
White blood cell count ($\times 10^3/\mu L$)	6.38	4.4–10.5
Red blood cell count ($\times 10^6/\mu L$)	2.68	4.0–5.6
Hemoglobin (g/dL)	8.4	13.1–16.7
Hematocrit (%)	25.0	36–50
Mean corpuscular volume (fL)	93.3	82–98
Mean corpuscular hemoglobin (pg/cell)	31.3	28–33
Mean corpuscular hemoglobin concentration (g/dL)	33.6	32–36
Red blood cell distribution width (%)	20.3	12.1–14.9
Platelet count ($\times 10^3/\mu L$)	75	148–380

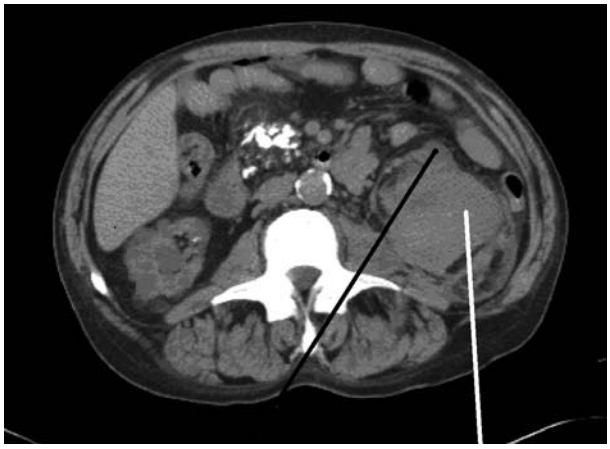

Figure 1. Computed tomography scan of the abdomen showing multiple small (0.5–2.2 cm) renal cysts (*black rule*). High-attenuation fluid is seen collected around the left kidney representing acute perirenal hemorrhage (*white rule*).

Nevertheless, the possibility of a bleeding renal mass could not be excluded. The patient was subsequently discharged home with a plan to repeat CT of the abdomen and pelvis in 2 months to differentiate between retroperitoneal bleeding due to cyst rupture and a bleeding renal mass. The repeat CT scans showed partial resolution of the hematoma with no evidence of any renal mass. Two months after the CT, ultrasonographic evaluation of the kidneys was performed to reassess the hematoma and the renal cysts; this evaluation showed a hypoechoic spherical area measuring 5.5 × 4.1 × 4.5 cm below the left kidney. Color flow studies revealed no blood flow associated with this structure, which was believed to represent a residual hematoma.

Review of the patient's hospital records showed that he had hypertension and hypertensive nephropathy for at least 15 years. A renal sonographic evaluation performed 8 years ago, or approximately 1 year prior to initiating hemodialysis, showed increased echogenicity of the renal cortex related to medical renal disease, with no apparent cystic masses in the kidneys. Review of the results of the patient's renal ultrasonographic and CT studies obtained over the 7 years he was on hemodialysis showed a gradual progression of cyst formation in both kidneys with no evidence of renal cysts prior to initiating hemodialysis. These studies were performed mainly in the ED for vague abdominal complaints. The CT scan performed during this admission showed a significant increase in the number and size of cysts as compared to the most recent previous scan done 2 years ago. The patient's extensive history of polysubstance abuse and noncompliance significantly delayed the diagnosis of ACKD.

DISCUSSION

ACKD is a complication of long-standing ESRD. Initially reported in 1847, ACKD was extensively described in 1977 as a potential cause of renal neoplasia or massive hemorrhage.[1] ACKD is characterized by multiple bilateral cysts that are less than 0.5 cm in diameter but can be as large as 2 to 3 cm. The cysts start to appear in the end-stage of renal failure and increase in number once patients are started on dialysis, whether the modality is hemodialysis or peritoneal dialysis.

Epidemiology

ACKD can begin prior to dialysis, but its incidence rises progressively with increasing time on dialysis, with most cases seen in patients with a 10-year history of dialysis.[1] The prevalence of ACKD ranges from 30% to over 95%.[1] This broad range can be partly explained by the differences in populations studied, as the disease will be infrequent in a group of patients recently started on dialysis compared with groups treated with dialysis for a longer period of time. Multiple studies have shown that the prevalence of ACKD is a function of time on dialysis.[2] In a study of 54 children undergoing continuous ambulatory peritoneal dialysis, the prevalence of ACKD was 9%, 50%, and 80% among those who had undergone dialysis for 0 to 4 years, 5 to 9 years, and longer than 10 years, respectively.[3] An increased prevalence of ACKD has been observed over the past several decades, which may be due to the development of ACKD in patients' retained kidneys after transplantation, growth in the dialysis population, and longer survival of dialysis patients. Both sexes are equally affected by ACKD, and patients of any age-group can

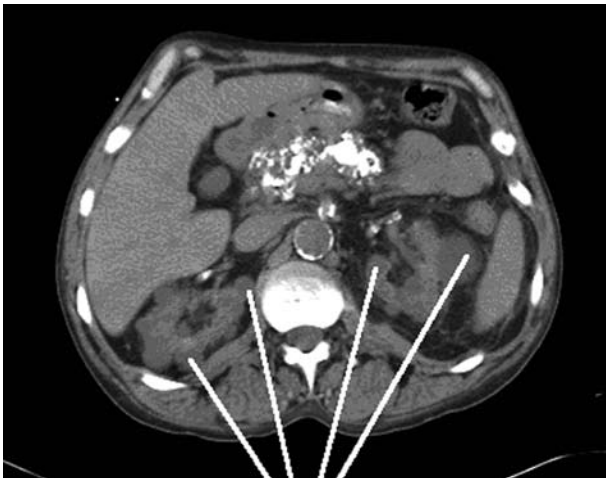

Figure 2. Computed tomography scan showing sharply demarcated cysts with smooth thin walls in both kidneys; these cysts occupy more than 25% of the renal cortex. The fluid within the cysts is homogenous and has low density (typically a density of < 20 Hounsfield units is a feature of benign cysts).

develop the disease. There appears to be a higher prevalence of ACKD in black patients with ESRD as compared with white patients.[1,2,4,5]

Pathogenesis

The pathogenesis of ACKD is not completely understood. The cysts are limited to the kidney, in contrast to polycystic kidney disease, which involves other organs, suggesting that local intrarenal events are of primary importance. It is well known that nephron loss from any cause leads to compensatory hypertrophy in normal nephrons. This response is driven by activation of proto-oncogenes and release of growth factors, which, over a prolonged period of time, can lead to tubular hyperplasia and cyst formation. Cystic fluid analysis reveals a composition similar to that of plasma; this finding plus the presence of a brush border on the luminal membrane of the cysts suggests that these cysts arise primarily from proliferation of proximal tubular epithelial cells.[6]

The cysts of ACKD tend to stabilize or even regress in most patients after renal transplantation. This is believed to be caused by the decrease in levels of growth factors after the transplanted kidney starts functioning. Interestingly, kidney transplant patients who receive cyclosporine continue to develop renal cysts at a rate similar to dialysis patients; the continued development of cysts may result from a direct effect of cyclosporine on the kidneys.[7] In addition, ACKD can develop in the transplanted kidney that has failed due to chronic rejection.[8]

Table 2. Distinctive Features of Acquired Cystic Kidney Disease

Parameter	Features
Kidney size	Usually small but may be normal
Cyst size	Usually 0.5–2 cm; may get bigger with time Size correlates with duration on dialysis
Location in the kidney	Any
Extrarenal cysts	None
Renal function	End-stage renal disease
Relation to renal parenchyma	Involves > 25% of the parenchymal tissue
Number of cysts	At least 1–5; number increases with duration on dialysis
Age of onset	Any age, usually 2–3 years after starting dialysis
Sonographic features	Anechoic, sharply defined, wall enhancement Nearly imperceptible cyst-wall thickness Round or ovoid shape
Family history	Negative
Histopathology	Covered by a single line of flat or cuboidal epithelium Brush border present on luminal membrane Cystic fluid is clear and noninflammatory

Diagnosis

Diseases of the kidney that cause cyst formation include autosomal dominant polycystic kidney disease, autosomal recessive polycystic kidney disease, renal cell carcinoma, simple renal cysts, and ACKD, among others. The clinical presentation of ACKD and the radiologic features of the cysts are important tools to establish the diagnosis of this disease.[5,9,10] Most patients with ACKD are asymptomatic. Hematuria is the most common symptom. Rupture of an unsupported blood vessel into the cyst results in lower back or flank pain. The diagnosis of ACKD is established by ultrasonography or CT scanning. Biopsy is not recommended for diagnosis.[2,4] Features of ACKD that can help establish the diagnosis are presented in **Table 2**.

Complications

Although most patients with ACKD are asymptomatic, this disorder may be complicated by bleeding, lithiasis, infection, and malignant transformation. Rare cases of severe hypertension have been reported in cases of cyst hemorrhage leading to the release of high amounts of renin from the cystic fluid with subsequent absorption into the blood stream.[11] Other patients have been reported to develop polycythemia

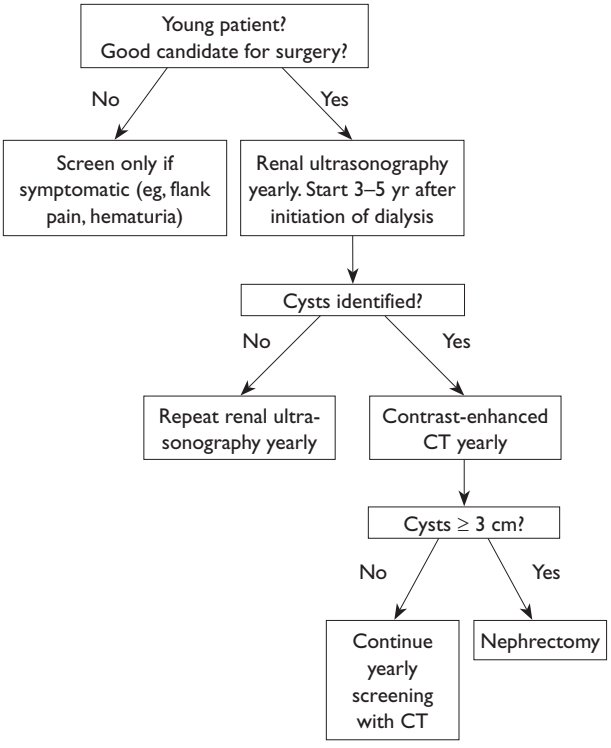

Figure 3. Suggested screening algorithm for acquired cystic kidney disease in patients receiving dialysis. CT = computed tomography. (Data from references 20, 22–25.)

due to high levels of erythropoietin secreted by the renal cysts.[12]

Flank pain is the most common symptom of cyst hemorrhage. This pain is accompanied by hematuria if the cyst bleeds into the renal calyx, but hematuria will not be present if there is intracystic bleeding or retroperitoneal hemorrhage. Nontraumatic rupture of a large renal cyst in patients with ACKD may lead to massive retroperitoneal bleeding, but patients may still present initially with mild vague symptoms. This scenario can cause significant delay in the diagnosis and may lead to a fatal outcome. Therefore, dialysis patients with acute anemia and abdominal pain should be evaluated for a possible renal origin of the blood loss.[1,13,14]

Cyst infection is a rare complication of ACKD and usually develops as a progression of urinary tract infection. This development should be suspected in patients with ACKD who do not respond to a 7-day regimen of antimicrobial therapy for urinary tract infection. The diagnosis of infected renal cyst is best established by CT, which shows thick walls and a slightly dense cyst.[15,16]

Between 1% and 2% of patients with ACKD will develop malignant transformation of their renal cysts.[17,18] The mechanism of this transformation is unclear.[14] When compared with the general population, patients with ACKD have a nearly 100-fold increase in the prevalence of renal cell carcinoma,[5] with papillary renal cell type being the most common.[10] ACKD-associated renal cell carcinoma is frequently asymptomatic (86%) but may be associated with bleeding, abrupt changes in hematocrit, fever, and flank pain or rarely with hypoglycemia, hypercalcemia, or metastases at presentation.[19]

Screening

Because of the significant association between ACKD and kidney cancer, it has been suggested that patients who have been on dialysis for 3 to 5 years undergo yearly screening for ACKD to facilitate early detection of premalignant or malignant lesions. However, studies have shown a low mortality rate from metastatic renal cell carcinoma in dialysis patients. This is attributed to the significant comorbid cardiovascular diseases that occur in this patient population, with the highest percentage of patients dying from cardiovascular events. In addition, it is estimated that screening could result in a 1.6-year gain in life expectancy over a 25-year period.[20] Hence, it is recommended that only young patients and those with long life expectancy undergo yearly screening for ACKD (**Figure 3**).[12]

It is recommended that initial screening be done with ultrasonography.[21] Once the ultrasonogram is positive for cysts, the more sensitive contrast-enhanced CT scan should be performed at yearly intervals.[22] Contrast-enhanced CT scanning is more sensitive than ultrasonography in detecting and characterizing cysts, but ultrasonography is more helpful in visualizing early cystic changes.[23] Prospective evaluations of helical CT and ultrasonography showed that CT was 96% sensitive and 95% specific for the detection of renal malignancy,[24] while ultrasonography was 87% sensitive and 83% specific.[22,25]

Treatment

Cysts larger than 3 cm are associated with a significant increase in the risk for malignancy,[14,19] and total nephrectomy should be performed in these cases. Management for cysts smaller than 3 cm with persistent symptoms, such as back pain or hematuria, remains controversial, but nephrectomy may be recommended as many of these tumors turn out to be unequivocal renal cell carcinoma.[14,19] Asymptomatic tumors smaller than 3 cm should be serially screened yearly, and tumor enlargement may be an indication for nephrectomy.

Bleeding episodes, either intrarenal or perirenal, often may be treated conservatively with bed rest and analgesics, followed by serial CT scanning to rule out

occult renal carcinoma. If the presence of renal cancer cannot be completely ruled out, then nephrectomy is indicated. In addition, persistent hemorrhage may require nephrectomy or renal artery embolization.[26]

Infected cysts should be treated with intravenous trimethoprim-sulfamethoxazole. Ciprofloxacin and chloramphenicol are considered second-line agents. Patients who do not respond to antibiotics alone require ultrasonography- or CT-guided drainage of the infected cyst.[15,16]

SUMMARY

Patients with ESRD are at risk for developing ACKD with its potential complications. The incidence of ACKD increases with time on dialysis, with most cases seen in patients with a 10-year history of dialysis. Most patients with ACKD are asymptomatic, but potential complications can develop, some of which present major health risks. The diagnosis of ACKD is established by ultrasonography or CT scanning. Young patients and those with long life expectancy should undergo yearly screening for ACKD. **HP**

REFERENCES

1. Piccoli GB, Bermond F, Mezza E, et al. Kidney rupture: an unusual and oligosymptomatic complication in a dialysis patient with acquired cystic disease. J Nephrol 2002; 15:394–7.
2. Matson MA, Cohen EP. Acquired cystic kidney disease: occurrence, prevalence, and renal cancers. Medicine (Baltimore) 1990;69:217–26.
3. Acquired cystic kidney disease in children undergoing continuous ambulatory peritoneal dialysis. Kyushu Pediatric Nephrology Study Group. Am J Kidney Dis 1999; 34:242–6.
4. Grantham JJ. Acquired cystic kidney disease. Kidney Int 1991;40:143–52.
5. Choyke PL. Acquired cystic kidney disease. Eur Radiol 2000;10:1716–21.
6. Dinda AK, Mathur M, Guleria S, et al. Heat shock protein (HSP) expression and proliferation of tubular cells in end stage renal disease with and without haemodialysis. Nephrol Dial Transplant 1998;13:99–105.
7. Lien YH, Hunt KR, Siskind MS, Zukoski C. Association of cyclosporin A with acquired cystic kidney disease of the native kidneys in renal transplant recipients. Kidney Int 1993;44:613–6.
8. Chung WY, Nast CC, Ettenger RB, et al. Acquired cystic disease in chronically rejected renal transplants. J Am Soc Nephrol 1992;2:1298–301.
9. Neureiter D, Frank H, Kunzendorf U, et al. Dialysis-associated acquired cystic kidney disease imitating autosomal dominant polycystic kidney disease in a patient receiving long-term peritoneal dialysis. Nephrol Dial Transplant 2002;17:500–3.
10. Denton MD, Magee CC, Ovuworie C, et al. Prevalence of renal cell carcinoma in patients with ESRD pretransplantation: a pathologic analysis. Kidney Int 2002;61: 2201–9.
11. Bongu S, Faubert PF, Porush JG, Gulmi F. Uncontrolled hypertension and hyperreninemia after hemorrhage in a patient with end-stage renal disease and acquired renal cysts. J Am Soc Nephrol 1994;5:22–6.
12. Edmunds ME, Devoy M, Tomson CR, et al. Plasma erythropoietin levels and acquired cystic disease of the kidney in patients receiving regular haemodialysis treatment. Br J Haematol 1991;78:275–7.
13. Levine E. Acquired cystic kidney disease. Radiol Clin North Am 1996;34:947–64.
14. Chandhoke PS, Torrence RJ, Clayman RV, Rothstein M. Acquired cystic disease of the kidney: a management dilemma. J Urol 1992;147:969–74.
15. Bonal J, Caralps A, Lauzurica R, et al. Cyst infection in acquired renal cystic disease. Br Med J (Clin Res Ed) 1987;295:25.
16. Rizk D, Chapman AB. Cystic and inherited kidney diseases. Am J Kidney Dis 2003;42:1305–17.
17. Levine E, Slusher SL, Grantham JJ, Wetzel LH. Natural history of acquired renal cystic disease in dialysis patients: a prospective longitudinal CT study. AJR Am J Roentgenol 1991;156:501–6.
18. Allan PL. Ultrasonography of the native kidney in dialysis and transplant patients. J Clin Ultrasound 1992;20: 557–67.
19. Truong LD, Krishnan B, Cao JT, et al. Renal neoplasm in acquired cystic kidney disease. Am J Kidney Dis 1995; 26:1–12.
20. Sarasin FP, Wong JB, Levey AS, Meyer KB. Screening for acquired cystic kidney disease: a decision analytic perspective. Kidney Int 1995;48:207–19.
21. Marple JT, MacDougall M, Chonko AM. Renal cancer complicating acquired cystic kidney disease. J Am Soc Nephrol 1994;4:1951–6.
22. Yip SK, Chee C. Clinics in diagnostic imaging (46). Renal cell carcinoma in acquired cystic kidney disease. Singapore Med J 2000;41:89–91.
23. Taylor AJ, Cohen EP, Erickson SJ, et al. Renal imaging in long-term dialysis patients: a comparison of CT and sonography. AJR Am J Roentgenol 1989;153:765–7.
24. Takebayashi S, Hidai H, Chiba T, et al. Using helical CT to evaluate renal cell carcinoma in patients undergoing hemodialysis: value of early enhanced images. AJR Am J Roentgenol 1999;172:429–33.
25. Schmidt T, Hohl C, Haage P, et al. Diagnostic accuracy of phase-inversion tissue harmonic imaging versus fundamental B-mode sonography in the evaluation of focal lesions of the kidney. AJR Am J Roentgenol 2003;180:1639–47.
26. Levine E, Grantham JJ, MacDougall ML. Spontaneous subcapsular and perinephric hemorrhage in end-stage kidney disease: clinical and CT findings. AJR Am J Roentgenol 1987;148:755–8.