THORACIC AORTIC DISSECTION IN A PATIENT WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE

Tolulola Adeola, MD, Olufemi Adeleye, MD, James L. Potts, MD, Marquetta Faulkner, MD, and Ayodeji Oso, MD

Nashville, Tennessee

Autosomal dominant polycystic kidney disease is one of the most common hereditary diseases, and frequently has well defined extrarenal manifestations. Very few cases of aortic aneurysms associated with this disorder are described in literature. We report a 42-year-old male with autosomal dominant polycystic kidney disease presenting with dissecting aneurysm of the thoracic aorta. (*J Natl Med Assoc.* 2001;93:282–287.)

Key words: aortic aneurysm, thoracic ♦ complications, etiology, diagnosis ♦ kidney, polycystic, autosomal dominant ♦ physiopathology, genetics, epidemiology, complications

Autosomal dominant polycystic kidney disease (PKD) is a systemic disorder primarily affecting the kidneys that develops multiple bilateral cysts that are characteristic of this condition. Extrarenal manifestations of PKD include hepatic cysts,[1] colonic diverticula,[2] intracranial berry aneurysms,[3] cardiac valvular anomalies, particularly mitral valve prolapse,[4] pancreatic,[5] and splenic cysts.[6] Association with aortic aneurysm is uncommon, and the majority of reported cases involve abdominal aortic aneurysms.[7,8] Descriptions of thoracic aortic dissection complicating PKD are rare.[9,12] We present one such case.

 From the Department of Internal Medicine, Meharry Medical College, Nashville, Tennessee. Request for reprints should be addressed to Dr. Olufemi Adeleye, Department of Internal Medicine, Meharry Medical College, 1005 D. B. Todd Boulevard, Nashville, TN 37208.

CASE REPORT

A 42-year-old African-American male presented to the emergency room with complaints of constant, nonradiating substernal chest tightness occurring at rest, of about 24 hours' duration. There were no associated symptoms. Past medical history is significant for hypertension since age 22.

On physical examination, the patient was not in apparent distress and had normal habitus. He was afebrile, blood pressure was 214/148, pulse rate of 104/min, and respiratory rate of 16/min. He had a heaving apical impulse, S4 gallop rhythm, grade 2/6 holosystolic murmur at the left lower sternal border, and equal carotid and peripheral arterial pulsations bilaterally.

Relevant laboratory test results were: creatinine kinase 95 U/L, troponin I 0.12 ng/mL, blood urea nitrogen 28 mg/dL, serum creatinine 3.1 mg/dL, serum potassium 4.2 mEq/L, hemoglobin 9.9 g/dL, hematocrit 30.1%, and MCV 84.8 fl. There were no baseline laboratory test results for comparison as this was the patient's first visit to our facility. Urinalysis showed 3 + protein, no red blood cells or casts, and urine drug screen was positive for benzodiazepines. Electrocardiogram showed normal sinus rhythm with T wave inversion in leads V4 through

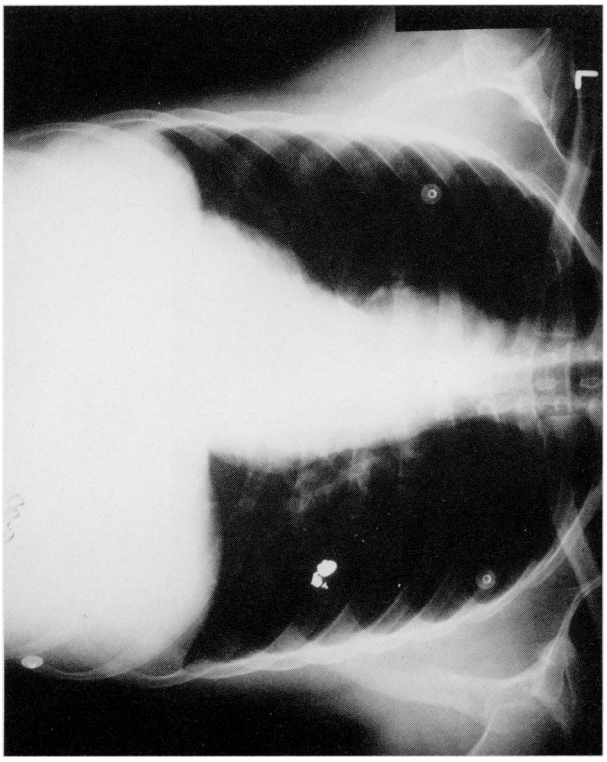

Figure 1. Posterior-anterior chest radiograph showing prominent aortic knob.

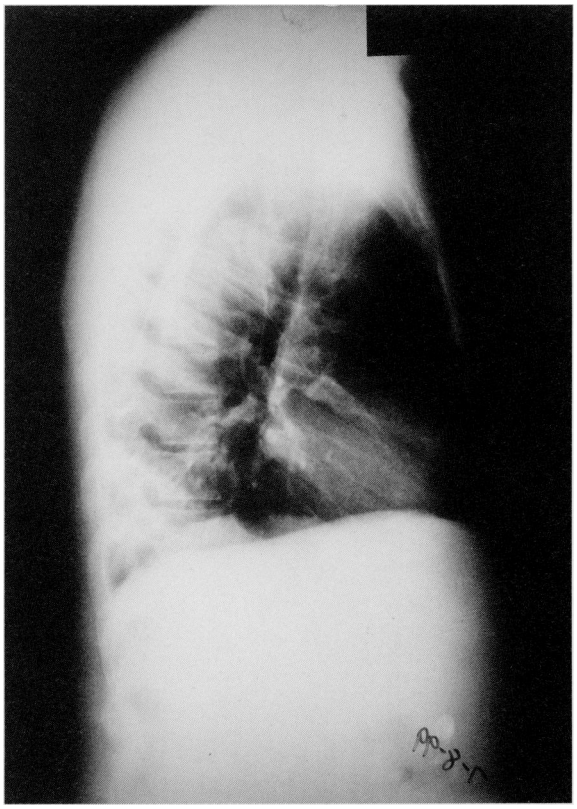

Figure 2. Lateral chest radiograph showing posterior blunting of the left costophrenic angle.

V6. Chest x-ray revealed prominence of the aortic knob, and blunting of the left costophrenic angle posteriorly (see Figs. 1 and 2).

The patient was admitted to the coronary care unit and intravenous nitroprusside and labetalol administered for blood pressure control. Magnetic resonance imaging of the thorax was done, because patient's renal function precluded contrast-enhanced computed tomography, and it revealed a 4-cm aneurysm of the thoracic aortic arch with Stanford Type B dissection (Figs. 3 and 4) and fluid in the left pleural space presumed to be blood. Subsequent transesophageal echocardiography confirmed the above finding and did not show evidence of mitral valve prolapse. Myocardial infarction was ruled out and blood pressure controlled. Renal ultrasound was done as part of work-up for renal failure and it showed multiple cysts bilaterally consistent with PKD (Fig. 5). Left and right kidney sizes were 19.1 cm and 20.7 cm, respectively. Three small hepatic cysts were also noted on ultrasonography.

Surgical opinion was sought, and surgical intervention was recommended based on an increase in size of pleural fluid on subsequent imaging. However, surgery was not done as patient declined perioperative blood transfusion based on religious beliefs. He was thus managed medically. Serial hemoglobin and hematocrit monitoring showed no appreciable change. The remainder of his hospital stay was uneventful, and hemoglobin and hematocrit were 9.6 and 29.9, respectively, on discharge.

Incidentally, a left popliteal Baker's cyst was detected on duplex sonography performed to rule out deep venous thrombosis. At last follow-up, he was asymptomatic, blood pressure was controlled, and there had been no deterioration in his renal function.

DISCUSSION

Autosomal dominant polycystic kidney disease has a prevalence of 1:400 to 1:1000 in live births.[13] Approximately 90% of cases are inherited in an

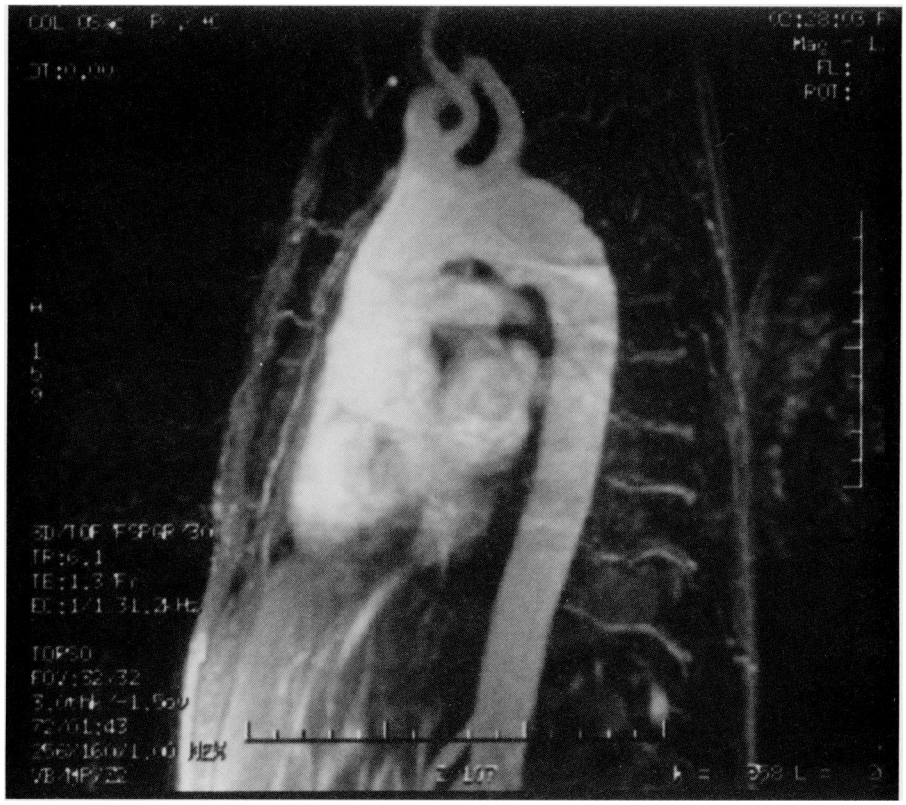

Figure 3. Magnetic resonance image showing aortic aneurysm.

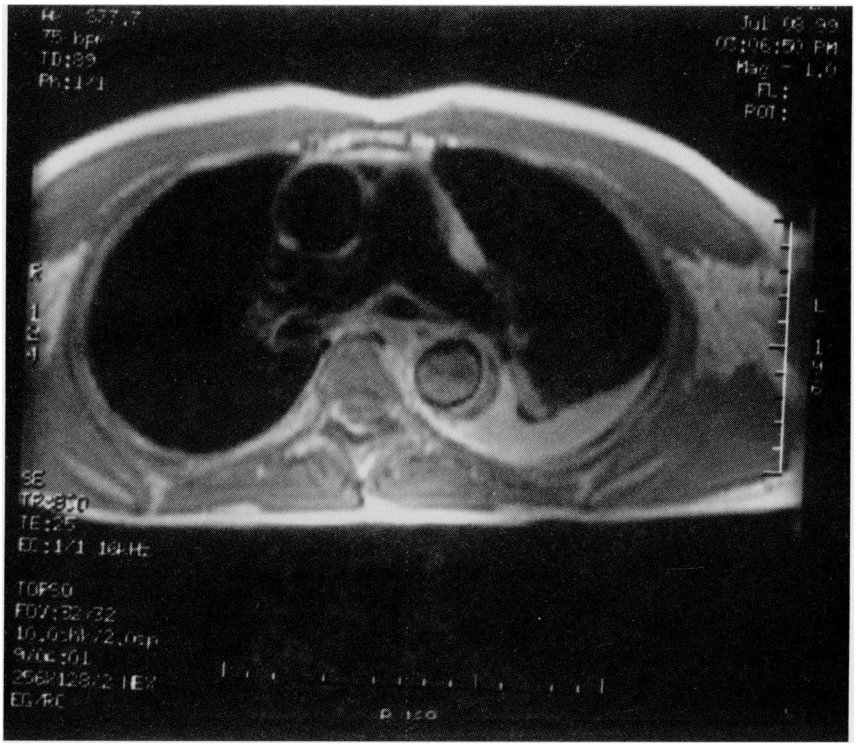

Figure 4. Magnetic resonance image showing aortic dissection and left-sided pleural effusion.

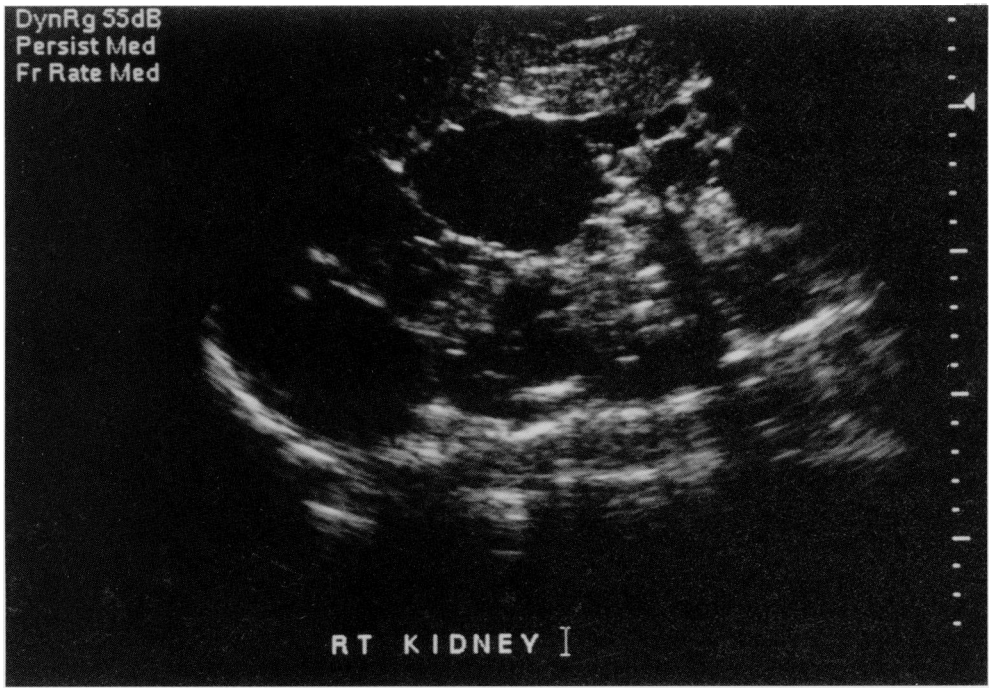

Figure 5. Ultrasound of right kidney showing multiple cysts.

autosomal dominant fashion whereas the remainder result from genetic mutations. The genes involved have been identified. Eighty-five to ninety percent of patients have the PKD1 gene on the short arm of chromosome 16,[14] whereas 10% to 15% have the PKD2 on the long arm of chromosome 4.[15] The mechanisms involved in cyst formation are still poorly understood. The PKD1 gene codes for a membrane glycoprotein called polycystin, which appears to function as a receptor for cell-cell or cell-matrix interactions, whereas the PKD2 gene product has significant homology to a family of voltage-activated calcium channels. It is thought that polycystin has an essential role in epithelial cell differentiation. When defective, there is impaired cell maturation, abnormal cell proliferation, and expression of altered amounts of otherwise normal electrolyte transport proteins, culminating in cyst formation.[16,17] Abnormalities in extracellular matrix components have been demonstrated,[18] which may be related to defective polycystin and are likely contributory to cyst formation.

Ultrasonography is the diagnostic procedure of choice because of its high sensitivity and safety. Sensitivity increases with patient's age and almost all individual over the age of 30 have cysts. Detection of at least three cysts in each kidney in an individual with a family history of PKD is generally considered as diagnostic.[13] A positive family history was not elicited in our patient. One explanation for this is that the disease could have resulted from genetic mutation. The other is the inability to rule out autosomal dominant inheritance based on family history alone. Only 60% of patients will report a family history of the disease, whereas renal imaging of patient's parents reveals the disease and autosomal dominant inheritance in another 30%.[13]

Currently, association of thoracic aortic dissection with PKD is not well recognized. To our knowledge, there are only four previously reported cases of this association in the absence of Marfan's syndrome.[7,10] Incidence of thoracic aortic dissection has been reported to be seven times more common in patients with PKD than in the general population at autopsy.[19] There are two reported cases of patients with both Marfan's syndrome and PKD who developed thoracic aortic dissection.[20,21] Marfan's syndrome is a well-recognized predisposing factor to aortic dissection and accounts for 6% to 9% of all thoracic dissections.[22,23] Other predisposing factors

include Ehlers-Danlos syndrome, hypertension, age, bicuspid, aortic valve, iatrogenic trauma, and pregnancy.[24,25]

Apart from hypertension, none of the abovementioned factors was present in our patient. Hypertension is frequently present in patients with aortic dissection and one study reports a history of hypertension in almost 80% of 236 cases of aortic dissection.[22] The opinion that polycystin and extracellular matrix abnormalities may primarily predispose individuals with PKD to thoracic aortic dissection is supported by a recent study. In that study, immunohistochemistry was used to demonstrate expression of polycystin in normal arterial smooth muscle cells, and an altered pattern of expression in specimens of intracranial aneurysms, thoracic aortic dissection, and dolichoectatic arteries of ten patients with PKD.[26] In our patient, it is more likely that the marked hypertension was the major predisposing factor, with vascular anomalies secondary to PKD being contributory.

Management of thoracic aortic dissection depends on the site. Proximal dissections involve the ascending aorta (Stanford type A or DeBakey types I and II), and are managed surgically. In-hospital mortality rate after surgery is 15% to 20%. Distal dissections involve the descending aorta (Stanford type B or DeBakey type III) and are managed medically with certain exceptions. The in-hospital mortality rate of medically managed treated patient with distal dissection is 15% to 20%. Indications for surgery in distal dissection include clinical evidence of propagation, compromise of major branches of the aorta, rupture or impending rupture, and continued pain.[27]

This case further emphasizes the systemic nature of PKD, and clinicians should bear this in mind when evaluating these patients. A high index of suspicion for thoracic aortic dissection should be entertained when these patients present with chest pain and appropriate work-up initiated. In the event of misdiagnosis when chest pain is the presenting symptom, use of anticoagulation to treat presumed myocardial ischemia could be catastrophic.

REFERENCES

1. Gabow PA, Johnson AM, Kaehny WD, et al. Risk factors for the development of hepatic cysts in autosomal dominant polycystic kidney disease. *Hepatology.* 1990;11:1033–1037.
2. Scheff RT, Zuckerman G, Harter H, et al. Diverticular disease in patients with chronic renal failure due to polycystic kidney disease. *Ann Inter Med.* 1980;92:202–204.
3. Chapman AB, Rubenstein D, Hughes R, et al. Intracranial aneurysms in autosomal dominant polycystic kidney disease. *N Engl J Med.* 1992;327:916–920.
4. Hossack KF, Leddy CL, Johnson AM, et al. Echocardiographic findings in autosomal dominant polycystic kidney disease. *N Engl J Med.* 1988;319:907–912.
5. Torra R, Nicolau C, Navarro S, et al. Ultrasonographic study of pancreatic cysts in autosomal dominant polycystic kidney disease. *Clin Nephrol.* 1997;47:19–22.
6. Liu Y, Zhang h, Zhong H. Systemic manifestations of adult polycystic kidney disease: an analysis of 205 cases. *Chung Hua Nei Ko Tsa Chih.* 1995;34:612–615.
7. Chapman JR, Hilson AJW. Polycystic kidneys and abdominal aortic aneurysms. *Lancet.* 1980;1:647–648.
8. Vanmaele R, Witbreuk M, De Broe M, et al. Abdominal aortic aneurysm and polycystic kidneys. *Nephron.* 1995;69:107–108.
9. Paynter HE, Parnham A, Feest T.G, et al. Thoracic aortic dissection complicating autosomal dominant polycystic kidney disease. *Nephrol Dial Transplant.* 1997;12:1711–1713.
10. Hartman D. Autosomal dominant polycystic kidney disease complicated by thoracic aortic dissection. *Am Roentgenol.* 1994;162:1454.
11. Biagini A, Maffei S, Baroni M, et al. Familial clustering of aortic dissection in polycystic kidney disease. *Am J Cardiol.* 1993;72:741–742.
12. Robertson A.J, Morris P.J. Dissection of the thoracic aorta in renal transplant patients with polycystic kidney disease. *Aust N.Z J Surg.* 1999;69:326–328.
13. Gabow PA. Autosomal Dominant Polycystic Kidney Disease. *N Engl J Med.* 1993;329:332–342.
14. Reeders ST, Breuning MH, Davies KE, et al. A highly polymorphic DNA marker linked to adult polycystic kidney disease on chromosome 16. *Nature (Lond).* 1985;317:524–544.
15. Kimberling WJ, Kumar S, Gabow P, et al. Autosomal dominant polycystic kidney disease: Localization of the second gene to chromosome 4q13–q23. *Genomics.* 1993;18:467–472.
16. Watnick T, Germino GG. Molecular basis of autosomal dominant polycystic kidney disease. *Semin Nephrol.* 1999;19:327–343.
17. Grantham JJ. The etiology, pathogenesis, and treatment of autosomal dominant polycystic kidney disease: recent advances. *Am J Kidney Dis.* 1996;28:788–803.
18. Wilson P, Schrier RW, Breckon RD, et al. A new method of studying human kidney disease epithelia in culture. *Kidney Int.* 1986;30:371–378.
19. Torres VE. Systemic manifestations of renal cystic disease. In: Gardner KD, Bernestein J, eds. *The Cystic Kidney.* Dordrecht, The Netherlands: Kluwer; 1990:295–326.
20. Somlo S. Rutecki G, Giuffra LA, et al. A kindred exhibiting cosegregation of an overlap connective tissue disorder and the chromosome 16-linked form of an autosomal dominant polycystic kidney disease. *J Am Soc Nephrol.* 1993;4:1371–1378.
21. Biermann CW, Rutishauser G. Polycystic kidneys associated with Marfan's syndrome in an adult. *Scand J Urol Nephrol.* 1994;28:295–296.

22. Spitell PC, Spitell JA Jr, Joyce JW, et al. Clinical features and differential diagnoses of aortic dissection: experience with 236 cases (1980 through 1990). *Mayo Clin Proc.* 1993; 68:642.

23. Larson EW, Edwards WD. Risk factors for aortic dissection. A necropsy study of 161 patients. *Am J Cardiol.* 1984;53:849.

24. Jacobs LE, Fraifeld M, Kotler MN, et al. Aortic dissection following intraaortic balloon insertion: Recognition by transesophageal echocardiography. *Am Heart J.* 1992;124:536.

25. Williams GM, Gott VL, Brawley RK, et al. Aortic disease associated with pregnancy. *J Vasc Surg.* 1988;8:470.

26. Griffin MD, Torres VE, Grande JP, et al. Vascular expression of polycystin. *J Am Soc Nephrol.* 1997 8:616–626.

27. Dzau VJ, Creager MA. Diseases of the Aorta. In: Fauci et al, eds. *Harrison's Principles of Medicine,* 14th ed. New York: McGraw-Hill; 1998:1395–1397.