CLINICAL VIGNETTE

Diagnosis of Autosomal Dominant Polycystic Kidney Disease in a Patient Presenting with Acute Stroke

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Case Report

A 54-year-old El Salvadorian woman with a long history of hypertension presented to the emergency department with acute onset dysarthria, right-sided facial droop, and right-sided hemiparesis. Her blood pressure on arrival to the emergency room was 230/100 mm Hg. She was afebrile, her white blood cell count was normal at 4,500/uL, sedimentation rate was 26, and serum creatinine was 0.7 mg/dl. Her brain MRI showed a parenchymal hematoma measuring 23 x 32 mm in the left basal ganglia, and therefore she was admitted to the hospital for management of acute hemorrhagic stroke.

Our patient reported severe hypertension since age 30 that had been well controlled on four antihypertensive medications: amlodipine 10 mg daily, benazepril 40 mg daily, hydrochlorothiazide 12.5 mg daily, and atenolol 50 mg daily. She had run out of one of these medications a few days prior to presentation. She has no other chronic medical problems and has no history of previous strokes. Interestingly, her mother also had extreme hypertension starting in her 30s, and she died of an acute stroke at age 54. Upon further questioning, we learned that the patient's younger brother was concurrently being evaluated at a different hospital for renal cysts and renal failure. She has two adult children who are healthy with no known renal disease or hypertension.

She denied previous workup for secondary causes of hypertension. Further work-up for her long-standing hypertension included normal patent renal arteries on renal ultrasound, but numerous bilateral renal cysts with mild renal enlargement. Right upper quadrant ultrasound also revealed several hepatic cysts without pancreatic cysts. She denied any current or previous symptoms of flank pain, hematuria, or nephrolithiasis. Given her positive family history, large numbers of bilateral renal and hepatic cysts, and malignant hypertension starting at a relatively young age, we diagnosed her with autosomal dominant polycystic kidney disease (ADPKD).

Discussion

ADPKD is an autosomal dominant inherited disease with offspring of affected patients having a 50% chance of inheriting the mutated PKD gene, which in most cases, is completely penetrant. Spontaneous mutations occur in approximately 5% of cases and in one fourth of newly diagnosed patients there is no family history of the disease. Mutation in the PKD1 and PKD2 genes encode polycystins, which regulate tubular and vascular development in the kidneys and other organs including liver, brain, heart, and pancreas. Hepatic cysts are present in more than 80% of patients with ADPKD and cysts are usually larger in women than in men[1].

Hypertension is present in nearly all patients with renal insufficiency and affects approximately 50% of patients aged 20-34 years with normal renal function. ADPKD is a more progressive disease in men compared to women. Hematuria is common affecting 60% of patients. Complications of ADPKD include intracranial aneurysms as well as pyelonephritis and renal-cyst infections, which require aggressive antimicrobial therapy. Renal colic due to clots from intraparenchymal or extrarenal hemorrhage can occur and can be severe, and

nephrolithiasis is also more common[1,2]. Kidney failure requiring renal-replacement therapy occurs in approximately 50% of patients and typically develops in the fourth to sixth decade of life[1]. Criteria for the diagnosis of ADPKD in individuals with likely or known family history of ADPKD include at least two unilateral or bilateral cysts in persons younger than 30 years of age, at least two cysts in each kidney in persons 30 to 59 years of age, and at least four cysts in each kidney in persons 60 years of age or older[1,2,3]. In 25% of ADPKD cases, there will not be a known family history and will be likely secondary to mild familial disease or undiagnosed disease[1]. In these cases, presence of numerous and bilateral renal cysts, enlarged kidney size, and/or hepatic cysts should raise suspicion for ADPKD and may warrant further imaging and possible genetic testing[1,3].

Renal ultrasound is the recommended imaging modality and can reliably detect cysts that are 1 cm or larger in diameter and is highly sensitive for the diagnosis of ADPKD[1]. The identification of associated liver cysts, pancreatic cysts, or both confirms the diagnosis of ADPKD[1]. The differential diagnosis for renal cystic disease includes benign simple cyst, acquired cystic disease, tuberous sclerosis, autosomal recessive polycystic kidney disease, and hereditary cystic diseases with interstitial nephritis[1,4]. Current genotype testing for PKD mutations (I and 2) only identifies 60-70% of known pathogenic mutations[1].

In patients with ADPKD, arterial hypertension should be treated aggressively with target levels of less than 130/80 in adults. Patients should be monitored with serial creatinine measurements and when levels start to rise above baseline, more than 50% of functioning parenchyma has typically been destroyed. Magnetic resonance angiography is recommended for patients with a family history of aneurysm or stroke and for any known ADPKD patient with new-onset or severe headache or other CNS signs and symptoms, as intracranial aneurysms are present in 5-10% of patients with ADPKD[1]. Unfortunately, no current therapies have been shown to slow the formation of cysts or disease progression in randomized clinical trials. Current treatment guidelines target blood pressure control with salt restriction and antihypertensive medications. In particular, angiotensin-converting-enzyme (ACE) inhibitors and angiotensin II-receptor blockers (ARBs) have been associated with preservation of renal function in patients with ADPKD[1,2]. Patients should be counseled to avoid sports in which abdominal trauma may occur. Significant hepatic cystic enlargement has been linked to exogenous estrogens and multiple pregnancies. Pregnancy in women with ADPKD also increases the risk for severe hypertension and preeclampsia. Screening of asymptomatic children using genetic or imaging studies is not currently recommended as there are no current interventions shown to be effective in preventing progression of disease[1].

Conclusion

Our case demonstrates the importance of evaluation for secondary causes of hypertension in young patients, especially if multiple medications are needed for optimal blood pressure control. It also highlights the importance of the family history and how it can increase suspicion for genetic conditions, prompting additional testing, and eventual diagnosis. Finally, our case presents an example in which ADPKD should be included in the differential for hypertensive emergencies and refractory hypertension, especially in young patients. Although there are no specific therapies for ADPKD, patients can benefit from early identification and measures to detect potential complications. Our patient did undergo screening for intracranial aneurysms prior to hospital discharge and will be following-up regularly with her neurologist for routine interval screening. Additionally, she was educated on her multiple diagnoses and counseled on the importance of medication adherence and lifestyle modifications to aid in controlling her blood pressure.

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