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Case Report

Noncompaction of the Ventricular Myocardium and Polycystic Kidney Disease: A Case Report

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Autosomal dominant polycystic kidney disease (ADPKD) is one of the most common hereditary disorders, characterized by the formation of multiple cysts in the kidneys and other organs, as well as noncystic manifestations such as cerebral aneurysm. The most common cardiovascular disorders associated with ADPKD include valvular abnormalities and aortic aneurysm. An association between ADPKD and impaired left ventricular function has occasionally been reported. We describe a 74-year-old woman with ADPKD and exertional dyspnea. Impaired left ventricular function resulting from noncompaction of the ventricular myocardium (NVM) and secondary left ventricular aneurysm were diagnosed. Cardiac sarcoidosis and ischemic heart disease were ruled out. Myocardial ischemia resulting from NVM was the presumptive cause of the ventricular aneurysm. To our knowledge, this is the first report of concurrent isolated NVM and left ventricular aneurysm in a patient with ADPKD. ADPKD and various cardiomyopathies, including NVM, are all reported to involve mutations of sarcomere genes, suggesting a possible link between the conditions.
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INDEX WORDS: Autosomal dominant polycystic kidney disease (ADPKD); non-compaction of the left ventricular myocardium (NVM); left ventricular aneurysm; microcirculation; sarcomere genes; cardiomyopathy; PKD2.

Autosomal dominant polycystic kidney disease (ADPKD) is the most frequently inherited nephropathy, characterized by its progressive nature and multiple organ involvement.[1-3] Commonly reported cardiac abnormalities associated with ADPKD include valvular disease (eg, mitral valve prolapse), aortic regurgitation (often caused by enlargement of the aortic root and annulus), tricuspid regurgitation, aortic and coronary aneurysm, and coronary dissection.[4-9] Noncompaction of the ventricular myocardium (NVM) is a rare cardiomyopathy with a prevalence of 0.014% to 0.7% and is characterized by increased ventricular trabeculation and intertrabecular recesses communicating with the ventricular cavity.[10,11] NVM often occurs concomitantly with other cardiac abnormalities. Isolated NVM and the possibility of postnatal development of noncompaction have been described,[12] although the pathogenesis remains unclear. Cases of ADPKD with concomitant cardiomyopathy have been reported,[13] including several cases of isolated NVM.[14-17] However, the association between these 2 conditions remains unclear. We report a case of ADPKD, isolated NVM, and left ventricular aneurysm with markedly reduced left ventricular function. To our knowledge, this is the first report of isolated NVM with left ventricular aneurysm in a patient with ADPKD.

CASE REPORT

A 74-year-old woman presented to our outpatient clinic with worsening exertional dyspnea, occasional palpitations, and bilateral pitting edema of the lower limbs. She reported that the exertional dyspnea had started several years earlier and had become obvious in the previous 2 years. Because her symptoms had always alleviated with rest, she had not sought prior medical evaluation until 2 weeks prior to presentation, when she first experienced orthopnea. She had blood pressure of 147/88 mm Hg at admission and reported having had mild hypertension for many years. Ten years earlier, she underwent surgical resection of a liver abscess; at that time, multiple liver and kidney cysts were diagnosed. Abdominal ultrasonography and computed tomography on admission (Fig 1) revealed more than 10 cysts in each kidney, resulting in organ enlargement, but she did not report abdominal pain. We diagnosed ADPKD based on the criteria of the Japanese clinical practice guideline for PKD.[18]

The patient's mother had valvular heart disease and multiple kidney cysts; her daughter had had systemic lupus erythematosus and multiple kidney cysts diagnosed. Genetic testing of the patient revealed 2 sequence variants in *PKD2* (a guanine to thymine substitution at nucleotide 784 of the coding DNA sequence [c.784G>T] and a thymine deletion at nucleotide 2830 [c.2830delT]) that to our knowledge have not been reported previously. No mutations were detected in *PKD1*. The patient showed mildly decreased kidney function with estimated glomerular filtration rate of 40 to 50 mL/min/1.73 m^2, as calculated using the revised serum creatinine–based Japanese equation.[19] Her mother and daughter did not have severely decreased kidney function or

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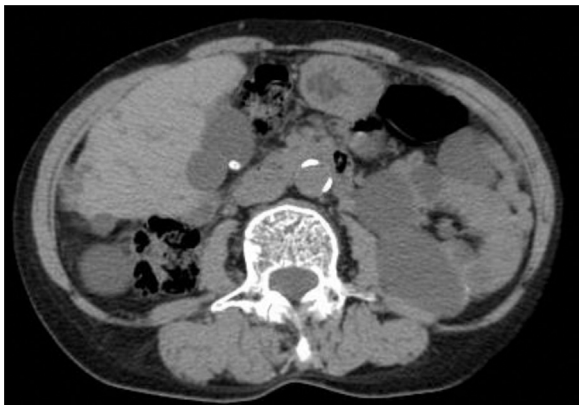

Figure 1. Computed tomographic scan on admission shows multiple bilateral kidney and liver cysts, resulting in enlargement of the organs.

require maintenance hemodialysis therapy. Further details of her family's genetic information and history of kidney disease were not available.

On chest auscultation, coarse crackles were recognized in both lower lung fields. Chest radiographs showed severe cardiac enlargement with a cardiothoracic ratio > 60% and congested lungs. An echocardiogram showed severely impaired left ventricular function (ejection fraction, 27%) and left ventricular enlargement (73 mm at end-diastole). Marked trabeculation was observed, most prominently affecting the left ventricular apex. Mild to moderate mitral regurgitation resulting from tethering with slight prolapse of the anterior leaflet was reported. The patient was given a diagnosis of congestive heart failure resulting from noncompaction or dilated cardiomyopathy. She was immediately admitted to our institution. She responded well to treatment with intravenous infusion of furosemide and carperitide. Within the first several days, her symptoms alleviated. She began oral treatment with furosemide, spironolactone, enalapril, and bisoprolol.

Transthoracic echocardiography on admission and after discharge showed that the ratio of maximal thickness of the noncompacted to compacted layers was >2.0. Cardiac catheterization revealed intact coronary arteries and left ventricular aneurysm (Fig 2A). Myocardial biopsy revealed fibrosis, which was consistent with cardiomyopathy. ^{99m}Tc-tetrofosmin myocardial perfusion single-photon emission computed tomography at rest showed a perfusion defect in the anterior wall of the left ventricle (Fig 2B). There was no abnormal ^{67}Ga uptake on scintigraphy, including the perfusion defect area. No hilar lymphadenopathy was observed on chest computed tomography. Serum angiotensin-converting enzyme and lysozyme levels were within reference ranges. The patient was discharged with oral treatment, and as of 6 months postdischarge, has remained ambulatory.

DISCUSSION

ADPKD is a hereditary disease characterized by kidney enlargement resulting from progressive expansion of multiple cysts and by extrarenal involvement, including noncystic manifestations (eg, vascular, cardiac, and connective tissue abnormalities).[2] Mutations in 2 genes, *PKD1* and *PKD2*, are responsible for the development of ADPKD; up to 85% of cases are attributed to *PKD1* abnormalities.[20-22] *PKD1* and *PKD2* encode polycystin 1 and polycystin 2, respectively. Polycystin 1 is a transmembrane protein, and polycystin 2 is located predominantly on the endoplasmic/sarcoplasmic reticulum, where the 2 proteins act together as a nonselective cation-regulated calcium channel.[23,24]

NVM is a rare cardiomyopathy associated with arrest of the normal compaction process of the embryonic myocardium. Trabeculation of the human embryo usually starts at the end of week 4 of embryonic life, when looping of the primitive heart tube is complete and the myocardium has a spongy appearance. Trabecular solidification starts at week 8, when compaction or trabecular remodeling begins. Concomitant invasion of coronary arteries from the epicardium to the endocardium occurs, transforming large intertrabecular spaces into capillaries, thereby creating the foundation of coronary circulation. The severity of NVM depends on the timing of the arrest of the normal ventricular myocardium compaction process. A genetic study revealed a possible association between the disease and certain mutations, including sarcomere protein gene defects.[25] NVM is often associated with other congenital cardiac abnormalities;[26] however, an isolated form is occasionally seen in adults. Whether NVM can be acquired remains controversial because a later-life presentation of NVM may simply be on account of not having been recognized in an earlier echocardiogram. However, the fact that patients with dilated cardiomyopathy, hypertrophic cardiomyopathy, and NVM share common mutations in sarcomere protein genes supports the hypothesis of postnatal NVM development. A recent study[13] using a zebrafish model of isolated *PKD2* mutation reported aberrant intracellular calcium signaling and impaired cardiac function, suggesting a possible association between polycystin 2 abnormalities and cardiac function. In the same study, the authors also analyzed ADPKD database records from 1984 to 2010 and reported an increased prevalence of idiopathic dilated cardiomyopathy among patients with ADPKD, particularly those with *PKD2* mutations. Because isolated NVM was described as a distinct condition in 1984, some of the patients with a diagnosis of concomitant dilated cardiomyopathy and ADPKD early in that study might have had NVM. Although the association between ADPKD and NVM remains unclear and the coexistence of these 2 diseases may be coincidental, abnormalities in sarcoplasmic proteins in both disorders suggest a possible link between polycystin abnormalities, impaired cardiac function, and NVM development. The finding that homozygous deletions of *PKD1* and *PKD2* can lead to a disorganized myocardium[24] also supports this hypothesis.

In our case, not only NVM but also left ventricular aneurysm was detected. The location of the latter was not associated with the territory of major coronary arteries, suggesting a different cause than coronary