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Multiple Cardiovascular Manifestations in a Patient with Autosomal Dominant Polycystic Kidney Disease

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Autosomal dominant polycystic kidney disease (ADPKD) is a systemic disorder associated with various extrarenal complications. The major cardiovascular complications of ADPKD include valvulopathies and vascular ectasia. A 64-year-old man who was diagnosed with ADPKD seven years previously was admitted to our hospital for heart failure. Pelvic computed tomography revealed multiple variable-sized cysts in both kidneys. Transthoracic echocardiography showed enlargement of the left ventricle and left atrium. Severe mitral regurgitation and moderate aortic regurgitation with annuloaortic ectasia were observed. The left main coronary artery was dilated. The patient had various cardiovascular features associated with ADPKD.

KEY WORDS: Cardiac manifestations · Autosomal dominant polycystic kidney disease · Heart failure.

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) has various extrarenal manifestations. The major extrarenal complications of ADPKD include cerebral aneurysms, hepatic and pancreatic cysts, cardiovascular diseases, colonic diverticula, and malignancies.[1)2)] In cardiovascular diseases, the most common abnormalities include mitral valve prolapse and aortic regurgitation, which occur less frequently in ADPKD.[3)4)] In addition, aortic[4)] and coronary aneurysms[5)] and coronary artery dissection[6)] have been described in patients with ADPKD. Here, we report a case of a patient with ADPKD who presented with complex cardiovascular manifestations, as well as a literature review on the cardiovascular complications of ADPKD.

Case

A 64-year-old man was referred to our hospital because of worsening dyspnea and peripheral edema. He had a 2-week history of shortness of breath on exertion. Seven years previously, he visited an outpatient clinic for dyspnea on exertion. At that time, atrial fibrillation on electrocardiography and mild mitral regurgitation and moderate aortic regurgitation on echocardiography were detected. His medical record listed the following values: left ventricular (LV) end-diastolic dimension/body surface area (BSA), 33 mm/m^2; LV end-systolic dimension/BSA, 28 mm/m^2; left atrial (LA) antero-posterior diameter, 40 mm; and ejection fraction, 57% by M-mode. Abdominal computed tomography performed for abdominal distension revealed multiple cysts compatible with ADPKD. He was diagnosed with heart failure caused by atrial fibrillation with aortic regurgitation. His mother and maternal uncle, who both had ADPKD, died suddenly at the age of 40 years. The patient did not smoke or drink alcohol. On admission, his blood pressure was 134/80 mmHg and his heart rate was 85 bpm. Cardiac auscultation revealed a holosystolic murmur at the apex and diastolic murmur in the right upper parasternal area. A coarse crackle was audible in both lower lung fields. An engorged jugular vein and mild pretibial pitting edema were noted. The patient's abdomen was distended and soft. Shifting dullness was not observed. Laboratory test results revealed elevated levels of brain natriuretic peptide to 272 pg/mL and creatinine to 1.78 mg/dL (estimated glomerular filtration rate, 23.1 mL·min^{-1}·1.73 m^{-2}). Electrocardiography showed atrial

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fibrillation and intraventricular conduction delay. Chest radiography revealed massive cardiomegaly with a cardiothoracic ratio of 90% and bilateral pulmonary congestion (Fig. 1). Two-dimensional echocardiography showed an extremely dilated LA with LV end-diastolic dimension/BSA of 44 mm/m^2, LV end-systolic dimension/BSA of 30 mm/m^2, LA antero-posterior diameter of 93 mm, and LA volume index of 614 mL/m^2 (Fig. 2). The LV ejection fraction calculated by the modified Simpson method was 55%. There was no regional wall motion abnormality. Color Doppler imaging revealed severe eccentric mitral regurgitation jet toward the lateral side (Fig. 3A). Mitral leaflets showed tethering and incomplete coaptation (Fig. 2). Moderate regurgitation of the aortic valve was evaluated as a central flow with vena contracta of 6 mm. Incomplete coaptation of the aorta with dilatation of the aortic root and annulus resulted in aortic regurgitation (Fig. 3B and C). Severe dilatation of the left main coronary artery (15 mm) was noted at the aortic valve level of the parasternal short-axis (Fig. 3D). This echocardiographic finding suggested combined coronary aneurysm, although angiographic evaluation for coronary aneurysm was not performed owing to poor renal function. A small amount of pericardial effusion and patent foramen ovale also was observed. Multiple variable-sized cystic lesions in the liver and both kidneys observed on abdominal-pelvic computed tomography were compatible with ADPKD (Fig. 4). In the abdominal aorta and its branches, there were no specific findings. The patient was diagnosed with decompensated heart failure caused by complex cardiovascular abnormalities of ADPKD. He was treated with oxygen supplementation and intravenous diuretics. The patient was discharged with heart failure medications, and his follow-up course has been uneventful.

Discussion

ADPKD is characterized by the progressive expansion of numerous cysts, resulting in substantial enlargement of the kidneys.[1] In addition, patients exhibit a variety of extrarenal complications and concomitant systemic disorders with extrarenal cyst formation in the liver, pancreas, seminal vesicles, and meninges.[2] Noncystic manifestations of ADPKD-related extrarenal complications affect mostly the vascular, cardiac, and connective tissues. The cardiovascular complications are the major cause of morbidity and mortality in patients with ADPKD.[7] The most common cardiovascular complication is hypertension.[7] In structural cardiovascular abnormalities, mitral and aortic valvular prolapse with regurgitation and dilatation of the aortic root and annulus are considered as important

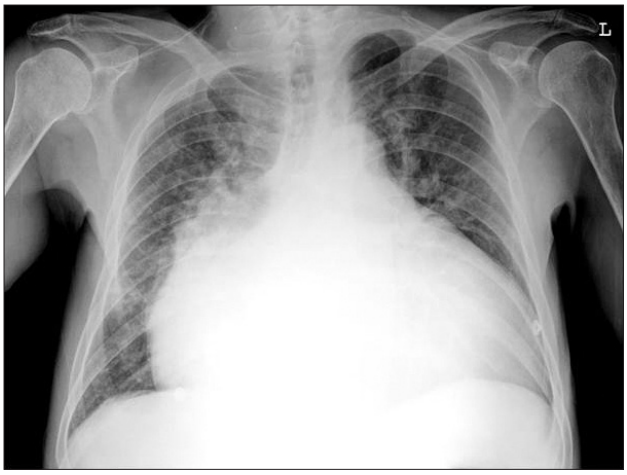

Fig. 1. Initial chest radiography. Chest radiography shows severe cardiomegaly and pulmonary congestion in both lung fields.

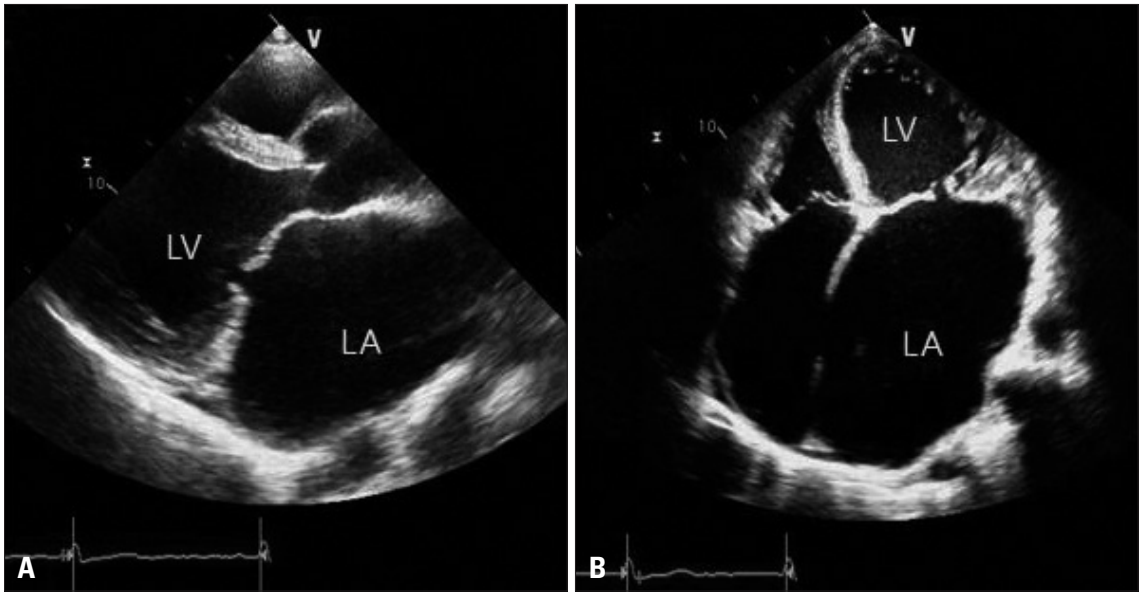

Fig. 2. Two-dimensional echocardiography. The left ventricular end-diastolic dimension/body surface area was approximately 44 mm/m^2 and the left atrial volume index was calculated to be approximately 614 mL/m^2 by the area-length method. Tethering and malcoaptation of the mitral valve are observed at end diastole. A: Parasternal long-axis view. B: Apical four-chamber view. LA: left atrium, LV: left ventricle.

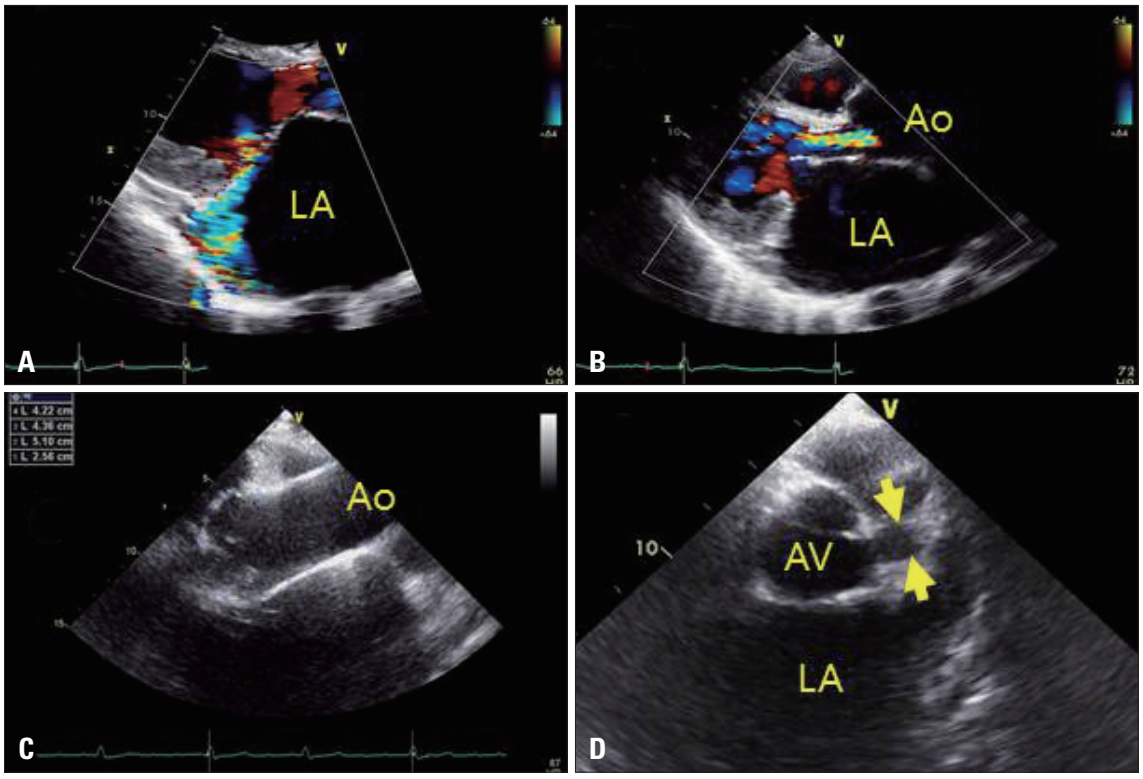

Fig. 3. Transthoracic echocardiography. A: Eccentric and severe mitral regurgitation is observed on the parasternal long-axis view. B: Moderate aortic regurgitation is shown on the parasternal long-axis view. The size of the vena contracta is approximately 6 mm. C: The modified parasternal long-axis view shows annuloaortic ectasia. D: At the aortic valve level of the parasternal short-axis view, 15-mm dilatation of the left main coronary artery (arrows) is seen. LA: left atrium, Ao: aorta, AV: aortic valve.

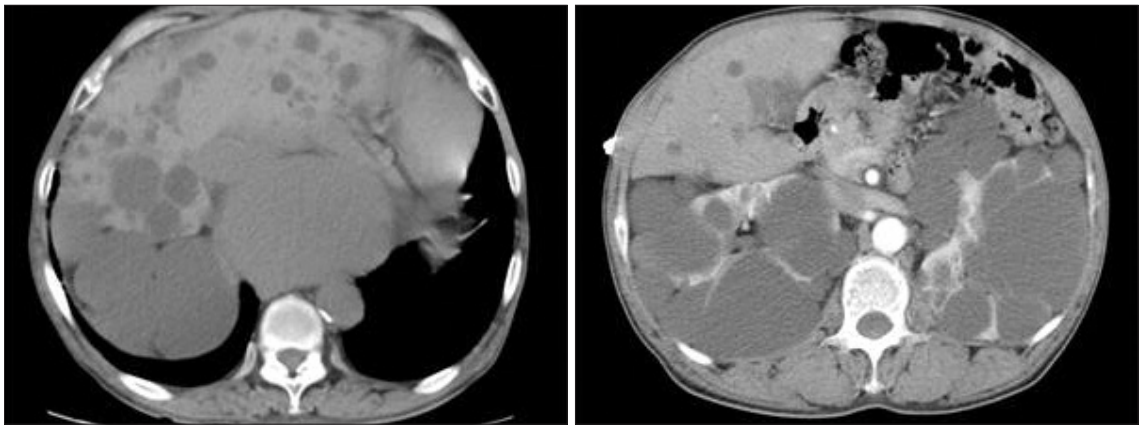

Fig. 4. Abdominal computed tomography. Abdominal enhanced computed tomography shows multiple variable-sized cysts in both the kidney and liver. The abdominal aorta and branches are normal.

extrarenal manifestations of ADPKD.[2-4] Lumiaho et al.[8] reported an increased prevalence of valvular abnormalities in patients with ADPKD, such as mitral valve prolapse, mitral regurgitation, aortic regurgitation, and tricuspid regurgitation. ADPKD also may be associated with an increased incidence of coronary aneurysm and coronary artery dissection.[5] The mechanism underlying the development of valvulopathies and annuloaortic ectasia in ADPKD is uncertain. ADPKD is related to mutations in the *PKD1* and *PKD2* genes, which encode polycystin-1 and polycystin-2.[9] These proteins are expressed in vascular smooth muscle cells and are associated with increased rates of proliferation and apoptosis. These changes may increase susceptibility to vascular injury, and result in direct aneurysmal changes and rupture of the vasculature.[9] A few studies have discovered that abnormalities in collagen and extracellular matrix may be responsible for valvular disease in ADPKD.[4][10] On the other hand, polycystin-2 is a nonselective cation channel capable of transporting calcium ions,[11] which plays an important role in the regulation of intracellular calcium stores and calcium homeostasis. Reduced calcium stores in the sarco-

plasmic reticulum resulting from a lack of polycystin-2 may be related to cardiac systolic dysfunction.[11] This mechanism supports the notion of intrinsic myocardial dysfunction in patients with ADPKD. Previously, Choe et al.[12] reported a case of dilated cardiomyopathy associated with ADPKD.

In this case, moderate aortic regurgitation, annuloaortic ectasia, severe mitral regurgitation, and coronary aneurysm were observed concurrently. Seven years previously, echocardiography showed mild mitral regurgitation and moderate aortic regurgitation. Therefore, the main cause of mitral regurgitation progression was believed to be a tethering effect and that of LV dilatation to be aortic regurgitation. Because the dilatation of the LV and LA was extensive, even considering valvular regurgitation, we could not rule out that this intrinsic myocardial dysfunction may be combined with valvular and vascular diseases.

Herein, we described a case of ADPKD with multiple cardiovascular manifestations. Although routine screening of all ADPKD patients using echocardiography is not recommended, we suggest careful evaluation and serial follow-up of these patients presenting with symptoms or signs of cardiac disease to enable early decision-making regarding treatment.

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