Atrioventricular Block and Diastolic Dysfunction in a Patient with Sanfilippo C

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Abstract

A 39-year-old woman with Sanfilippo C syndrome was referred to our department for the treatment of bradycardia. An electrocardiogram revealed a second degree atrioventricular block, and pacemaker implantation was performed with the patient under general anesthesia. A transthoracic echocardiogram showed normal left ventricular systolic function, moderate mitral regurgitation due to mitral valve prolapse, and a high E/e’ ratio, indicating left ventricular diastolic dysfunction. The present patient exhibited a rare case of Sanfilippo syndrome complicated with conduction disturbances, mitral regurgitation, and diastolic dysfunction.

Key words: atrioventricular block, diastolic dysfunction, sanfilippo C

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Introduction

Mucopolysaccharides are produced by all cells of the body and are particularly abundant in connective tissues. Mucopolysaccharides are degraded by lysosomal enzymes, and the deficiency of these enzymes causes mucopolysaccharidosis. Mucopolysaccharidosis III (Sanfilippo syndrome) is caused by the intralysosomal storage of heparan sulfate-like mucopolysaccharide fragments in all organs (1).

We encountered a case of atrioventricular block and diastolic dysfunction in association with mucopolysaccharidosis III C (Sanfilippo syndrome, type C).

Case Report

A 39-year-old woman was referred to our department for the treatment of bradycardia. She was asymptomatic at birth and showed normal development until 2 years of age. In elementary and junior high school, she attended special classes for handicapped children because she exhibited slow mental development. At age 14 years, she experienced trouble while walking. At age 19 years, she became bedridden and was diagnosed with mucopolysaccharidosis.

The patient had severe dementia with loss of hearing, eyesight, and speech. She flailed her head and arms restlessly. Laboratory examination revealed a normal creatinine level (0.6 mg/dL), a high B-type natriuretic peptide (BNP) level (246.8 pg/mL), increased urinary excretion of heparan sulfate. Sanfilippo syndrome type C was diagnosed by the basis of an assay of enzyme levels in the peripheral blood leukocytes. An electrocardiogram (ECG) showed a 2 : 1 atrioventricular block with negative T waves in leads I, II, aVL, and V3-V6 (Fig. 1, left). A Holter ECG showed a second degree atrioventricular block with a minimal heart rate of 27 beats/min. A chest roentgenogram showed a high cardiothoracic ratio (53%) and pulmonary congestion (Fig. 1, right). A transthoracic echocardiogram showed normal left ventricular systolic function (ejection fraction, 79%) and mild pericardial effusion. Doppler echocardiography revealed moderate mitral regurgitation.

Pacemaker implantation was performed with the patient under general anesthesia and after successful endotracheal intubation with a 6.5F tube. Ten days after the operation,
Figure 1. Left: Electrocardiogram showing 2:1 atrioventricular block and negative T wave in leads I, II, aVL, V3 to V6. Right: Chest roentgenogram showing high cardiothoracic ratio (53%) and pulmonary congestion.

Figure 2. Two-dimensional apical long axis view in diastole (left) and in systole (right). Patchy edematous, high- and low- intensity areas at left ventricle were observed. Left ventricular wall motion was normal.

Anesthetic drugs and artificial respiration were discontinued without any complication.

Two months later, a follow-up transthoracic echocardiography was performed. Two-dimensional echocardiography showed patchy edematous, high- and low- intensity areas (Fig. 2). Mild left ventricular hypertrophy was observed at the septum. The left atrial size (29 mm) and left ventricular mass (83 g) were normal (2, 3). Moderate mitral regurgi-
Figure 3. Two-dimensional echocardiography showed mitral valve prolapse at the anterior leaflet (left) and color Doppler echocardiography showed moderate mitral regurgitation (right).

Figure 4. Pulse Doppler echo at the mitral valve and tissue Doppler at the septum showed a high E/e’ ratio (E/e’ ratio 19) indicating left ventricular diastolic dysfunction.

Pulse Doppler and tissue Doppler echocardiography revealed a high ratio of early mitral inflow to early diastolic tissue velocity (E/e’ ratio = 19) (Fig. 4) indicating left ventricular diastolic dysfunction due to mitral valve prolapse was observed (Fig. 3).
Discussion

Sanfilippo syndrome is a distinctive mucopolysaccharidosis and involves the combination of severe mental retardation with mild somatic features (5). Sanfilippo syndrome manifests in childhood, with progressive symptoms that evolve into severe neurological deterioration causing hyperactivity, sleep disorders, loss of speech, mental retardation, and hearing loss. Death usually occurs in the late teens (6). In the present case, Sanfilippo syndrome followed its typical course, except for the unusually long life-span of patient.

Sanfilippo syndrome is classified into 4 types on the basis of the specific enzyme deficiency. The present patient was diagnosed with Sanfilippo syndrome, type C because the deficient enzyme was acetyl-CoA: alpha-glucosaminide N-acetyltransferase. The prevalence of Sanfilippo syndrome, type C is reported to be 1 in 1,407,000 (7).

Mucopolysaccharidoses are frequently associated with severe cardiac diseases such as cardiomyopathy and valvular heart diseases due to thickening of the mitral and aortic valves (8). Although cardiac abnormalities are very rare in Sanfilippo syndrome (1), there have been reports of deposition of mucopolysaccharides in the heart. A 6-year-old girl with Sanfilippo syndrome, type B was diagnosed with severe mitral regurgitation and consequently underwent mitral valve repair (9). Further, the autopsy of 39 year-old woman with Sanfilippo syndrome, type C, who died of acute cardiac failure, revealed focal myocardial necrosis replaced by vacuolated cells and fibrosis (10). The present patient may be the first patient with Sanfilippo syndrome, type C to have developed an atrioventricular block. The echocardiographic findings in our patient suggested myocardial involvement by mucopolysaccharides. Two-dimensional echocardiography revealed patchy edematous and high-and low-intensity areas in the left ventricle. Doppler echocardiography revealed moderate mitral regurgitation due to mitral valve prolapse and left ventricular diastolic dysfunction, as indicated by a high E/e' ratio.

Pacemaker implantation was performed under general anesthesia. Although mucopolysaccharidosis may cause throat problems and lead to intubation failure (11), we could successfully intubate the patient with a 6.5F endotracheal tube which was removed 10 days after the operation.

The present patient exhibited a rare case of Sanfilippo syndrome complicated with conduction disturbance, mitral regurgitation, and diastolic dysfunction.

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References