Successful Outcome in a Pregnant Woman with Isolated Noncompaction of the Left Ventricular Myocardium

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Abstract

A 24-year-old pregnant woman was referred to our hospital for the evaluation of her cardiac function. An electrocardiogram showed Wolff-Parkinson-White syndrome. Echocardiography revealed prominent trabeculation and deep intertrabecular recesses at the left ventricular apex and mid-portion of the inferior and lateral wall, with an impaired ejection fraction. She was diagnosed as having an isolated noncompaction of the ventricular myocardium (INVM). As the pregnancy progressed, severe restrictive hemodynamics became apparent. In consideration of the fetal growth, we decided to deliver the fetus by cesarean section at 32 weeks gestation; the patient successfully delivered a female infant. Interestingly, echocardiography demonstrated INVM in both the child and mother. This report is the first description of a successful pregnancy in a patient with familial INVM.

Key words: cesarean section, noncompaction, pregnancy, Wolff-Parkinson-White syndrome

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Introduction

Isolated noncompaction of the ventricular myocardium (INVM) is a rare disease resulting from the arrest of endomyocardial morphogenesis (1). The diagnosis can be made based on echocardiography findings showing numerous areas of prominent trabeculation and deep intertrabecular recesses, with no other cardiac malformation (2, 3). To date, noncompacted myocardium has tended to be recognized as a disease during childhood. However, some cases have recently been reported in adults (4).

The present findings are of special interest from two points of view. First, we believe this report describes the first attempt to deliver a child by cesarean section in a pregnant woman with INVM. Second, echocardiographic screening of the first-degree relatives of this patient demonstrated familial INVM occurring in three generations.

Case Report

A 24-year-old asymptomatic woman with previously diagnosed dilated cardiomyopathy (DCM) was referred to the Department of Cardiology at 5 weeks of gestation for an ante partum evaluation of cardiac function. She had a history of heart failure at the age of 4 months, but her first degree relatives had not been diagnosed with any cardiac disease. On physical examination, the patient appeared well, without obvious abnormal findings. The hematological and biochemical parameters were within physiological ranges, except for an elevated plasma brain natriuretic peptide (BNP) concentration (33.1 pg/ml). An electrocardiogram (ECG) showed Wolff-Parkinson-White (WPW) syndrome with sinus rhythm (Fig. 1). She had never felt any rapid palpitation, and no supraventricular or ventricular arrhythmia was observed on Holter ECG. Echocardiographic imaging showed a mildly enlarged left ventricle with an impaired ejection fraction (EF) of 0.45. A thickened myocardium with prominent trabeculation and deep intertrabecular recesses

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were observed in the left ventricular apex and mid portion of the inferior and posterolateral wall (Fig. 2a, b). Color Doppler imaging at the apical myocardium revealed blood flow throughout the trabeculations (Fig. 2c). The thickened left ventricular wall consisted of two layers, compacted epicardial and noncompacted endocardial layers. The end systolic ratio of the noncompacted/compacted layer thickness was 2.3. No other cardiac malformations were detected.

Based on these findings, we diagnosed the patient as having INVM. A Doppler investigation of the transmitral flow indicated restrictive hemodynamics, in which the ratio of early to late diastolic flow (E/A ratio) was 2.4 and the deceleration time of the E wave was 78 ms (Fig. 2d).

The patient had a miscarriage in August 2003 and had become pregnant again in January 2004. Throughout the pregnancy, we continued to monitor her hemodynamics, including the echocardiographic parameters of left ventricular end-diastolic (LVDd) and end-systolic (LVDs) dimensions, end-systolic left atrium diameter (LAD), EF, and the tricuspid regurgitant (TR) jet peak velocity, as well as the plasma BNP concentration (Fig. 3). At 8 weeks of gestation, LVDd was 54 mm, LAD was 44 mm, pulmonary artery systolic pressure (PASP) calculated from the TR velocity was 32

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Figure 1. ECG showing sinus rhythm and Wolff-Parkinson-White syndrome.

Figure 2. Echocardiographic image showing a thickened myocardium with prominent trabeculation and deep intertrabecular recesses in the left ventricular apex and mid portion of the inferior and lateral wall, in a parasternal long axis view (a) and short axis view (b). (c) Color Doppler image demonstrating blood flow throughout the trabeculations. (d) Doppler image of transmitral flow. The E/A ratio is 2.4, and the deceleration time is 78 ms.
Figure 3. (a) Left ventricular end-diastolic (LVDd) and end-systolic (LVDs) dimensions, predicted pulmonary artery systolic pressure (PASP), and plasma brain natriuretic peptide (BNP) concentration. LVDd did not change, whereas LAD, PASP, and plasma BNP concentration gradually increased. After cesarean section, these parameters returned to normal values. (i) Miscarriage, (ii) 5 weeks of gestation, and (iii) delivery by cesarean section. (b) Echocardiography in the parasternal long axis view showing left atrium dilatation at 31 weeks of gestation.

As the pregnancy progressed, neither the E/A ratio nor the deceleration time of the E wave changed markedly; however, LAD, predicted PASP, and plasma BNP concentration increased. At 31 weeks of gestation, LVDd remained stationary and EF was preserved, whereas LAD, predicted PASP, and plasma BNP concentration had increased to 52 mm, 52 mmHg, and 222 pg/ml, respectively. These findings indicated that the maternal cardiac status was under severe restrictive condition (Fig. 3). We therefore decided to discontinue the pregnancy, and we performed a cesarean section under general anesthesia. She safely delivered a female infant. After childbirth, the patient was given warfarin, enalapril, and carvedilol to improve myocardial contractility and sympathetic dysfunction by reducing the abnormal release of noradrenalin in INVM (4).

When examined by echocardiography, the infant showed well-preserved systolic function; however, a trabecular meshwork was observed predominantly in the mid-posterior and apex of the left ventricle (Fig. 4a). Color Doppler imaging revealed blood flow communication between the intertrabecular spaces and the left ventricular cavity. In addition, we screened the mother of the patient and identified INVM in her heart; a trabecular meshwork was present in the mid-posterior and apex of the left ventricle (Fig. 4b), and an ECG showed WPW (Fig. 4c). In contrast to the patient, the mother had often felt rapid palpitations due to paroxysmal supraventricular tachycardia. We performed a genetic analysis of the G4.5, DRP3, and Cypher/ZASP genes, but no mutations were found in this family.

Discussion

Recently, some cases of INVM have been reported in adults (5, 6). To our knowledge, only one report has described a pregnancy complicated with INVM. Kitao et al reported a pregnant woman with INVM who showed acute heart failure, which resulted in neonatal death (7). The present case is believed to be the first report of a successful pregnancy outcome in a patient with INVM.

In 599 pregnancies of women with heart disease, Siu et al reported that the fetal/neonatal mortality rate was 2% and that the rate of preterm labor was 10%, despite the medical advances that have improved the overall prognosis for pregnancy complicated with heart disease (8). In a recent survey of the prognosis of completed pregnancies in women with cardiac disease, five predictive factors were indicated: 1) prior cardiac event, 2) prior arrhythmia, 3) NYHA functional class >II or cyanosis, 4) valvular and outflow tract obstruction, and 5) myocardial dysfunction with LVEF < 40%, restrictive cardiomyopathy, or hypertrophic cardiomyopathy (9). The present case was categorized as NYHA class I, but we regarded the subject to be a moderate to high risk patient because of myocardial dysfunction with restrictive hemodynamics. Although a large number of studies have evaluated maternal hemodynamics, little has been reported about a reliable index for describing maternal cardiac function in restrictive cardiomyopathy. By monitoring the
maternal echocardiographic parameters and BNP concentration throughout the pregnancy, we found that LAD and predicted PASP were sensitive indices for restrictive hemodynamics; however, the E/A ratio and deceleration time of the E wave remained unchanged. One possible explanation for the invariability of these latter two parameters is that the patient had already reached a restrictive hemodynamic state at the beginning of her pregnancy. The plasma BNP concentration has been reported to be ~30 pg/ml in the third trimester (weeks 28-36) in a normal pregnancy (10, 11). In the present case, the plasma BNP concentration had increased to 222 pg/ml at 31 weeks of gestation, implying that plasma BNP is a sensitive biomarker for maternal hemodynamics. At 31 weeks of gestation, maternal hemodynamics showed a severely restrictive pattern, suggesting that the maternal condition may deteriorate during labor and delivery. As fetal growth had reached a stage at which we expected a good chance for postnatal survival, we decided to perform a cesarean section at 32 weeks of gestation, rather than risk a vaginal delivery at full gestation. An early diagnosis and careful continuous observations enabled the patient to safely deliver her child.

According to the echocardiographic criteria advocated by Jenni et al (12), we diagnosed this patient as having third generation familial INVM. INVM is thought to be a genetically heterogeneous disorder. A point mutation in the G4.5 gene encoding taffazin has been reported to cause INVM and Barth syndrome, among other conditions (13-17). A mutation in the gene for α-dystrobrevin, a cytoskeletal protein in the dystrophin-associated glycoprotein complex, has also been reported as a cause of this disease (14). Recently, mutations in the Cypher/ZASP gene have also been identified in patients with DCM and INVM (18). Although no mutations could be identified in this family, the inheritance pattern suggests that some unknown genetic abnormality might have caused this familial INVM.

Interestingly, despite the common presence of familial INVM, each cardiac malformation was slightly different among the family members. The location of the noncompacted myocardium was identical, but the left ventricle in both the mother and infant resembled apical hypoplasia, in which the longitudinal length of the left ventricle was much shorter than that of the right ventricle, and the elongated right ventricle wrapped around the hypoplastic apex of the left ventricle. Restrictive hemodynamics were only observed in the heart of the patient. In addition, the patient and mother both had abnormal ECG findings showing WPW syndrome, in which a presumptive localization of the accessory pathway in the patient was in the right anterior area, and that in mother was in the posterior area. In contrast, the

Figure 4. (a) Echocardiography of the infant showing a trabecular meshwork, predominantly in the posterior wall of the mid portion and apex of the left ventricle. (b) Echocardiography of the mother, demonstrating INVM. The right ventricle is enlarged and wrapped around the apex of the left ventricle. (c) ECG of the mother revealing WPW syndrome.
ECG of the infant showed no WPW syndrome. It is conceivable that cardiac phenotypes may tend to vary in familial INVM.

In conclusion, this report is believed to be the first description of a successful pregnancy in a patient with familial INVM, which was identified to span three generations. During pregnancy, careful monitoring using echocardiography and BNP measurements made it possible for us to determine both the optimal timing and the most appropriate therapeutic maneuvers to safely deliver the child.

References