Fetal Case of Rare Association of Hypoplastic Left Heart Syndrome and Absent Atrial Septum Accompanied by Mixed Form of Supracardiac Total Anomalous Pulmonary Venous Connection

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Abstract

Abnormal pulmonary venous flow patterns on fetal echocardiography and a nutmeg lung pattern on fetal magnetic resonance imaging are seen in patients with pulmonary venous stenosis. The association between these findings and the degree of pulmonary venous stenosis remains unknown. We report an extremely rare case of a fetus diagnosed with hypoplastic left heart syndrome complicated by an absent atrial septum and supracardiac total anomalous pulmonary venous connection with left pulmonary venous congestion. This case suggests that compared to non-pulsatile continuous pulmonary venous flow, the nutmeg lung pattern can only be observed with severe pulmonary congestion and advanced pulmonary lymphangiectasia.

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Running head: Rare case of hypoplastic left heart syndrome

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Abstract

Abnormal pulmonary venous flow patterns on fetal echocardiography and a nutmeg lung pattern on fetal magnetic resonance imaging are seen in patients with pulmonary venous stenosis. The association between these findings and the degree of pulmonary venous stenosis remains unknown. We report an extremely rare case of a fetus diagnosed with hypoplastic left heart syndrome complicated by an absent atrial septum and supracardiac total anomalous pulmonary venous connection with left pulmonary venous congestion. This case suggests that compared to non-pulsatile continuous pulmonary venous flow, the nutmeg lung pattern can only be observed with severe pulmonary congestion and advanced pulmonary lymphangiectasia.

Keywords: case report, hypoplastic left heart syndrome, absent atrial septum, supracardiac total anomalous pulmonary venous connection

Introduction

Hypoplastic left heart syndrome is rarely complicated by the absence of an atrial septum.[1] In addition, the incidence of complications of total anomalous pulmonary venous connection (TAPVC) in patients with hypoplastic left heart syndrome is low (2.3%), and the prognosis is poor. The prognosis may even be poorer if the condition is further complicated by pulmonary venous stenosis.[2,3]

The nutmeg lung pattern refers to the heterogeneous appearance of the lung parenchyma, identified as the presence of subtle T2-hyperintense branching tubular structures that emanate from the hila on fetal magnetic resonance imaging (MRI). Previous studies have shown that this pattern suggests the presence of pulmonary lymphangiectasia and, in relation to congenital heart disease, may be considered indicative of secondary lymphangiectasia caused by pulmonary venous congestion.[4,5] However, few studies have investigated this condition. The association of the nutmeg lung pattern with the degree of pulmonary congestion and prognosis remains unclear. This study reports an extremely rare case of hypoplastic left heart syndrome complicated by an absent atrial septum and a mixed form of supracardiac TAPVC accompanied by pulmonary venous stenosis. This article discusses fetal echocardiographic and MRI findings as well as the postnatal course of the neonate.

Case Presentation

The mother was a 43-year-old G2P2 woman. She was referred to our hospital when the fetus was suspected to have heart disease at 26 weeks of gestational age. Fetal echocardiography at gestational week 33 showed that the main pulmonary artery arose from the right single ventricle; on the right side of the main pulmonary artery, a hypoplastic ascending aorta with reverse blood flow from the ductus arteriosus was observed. The fetus was diagnosed as having hypoplastic left heart syndrome (Fig. 1a). The interatrial septum was completely absent, presenting anatomically as a single atrium; however, the inferior vena cava and right superior vena cava returned to the right side of the atrium. A residual left superior vena cava (SVC), which returned to the left side of the single atrium, was observed. The pulmonary veins did not return to the atrium. The right pulmonary veins returned to the right SVC and the left pulmonary veins to the left SVC. Therefore, the fetus was diagnosed with a mixed form of supracardiac TAPVC. The left pulmonary veins returning to the left SVC were severely constricted to a diameter of 1.3 mm, with an increased velocity of 1.2 m/s. Part of the left pulmonary veins ran to the right, through the narrow tortuous abnormal vessels behind the atrium, to join the right pulmonary veins. The diameters of these anomalous vessels were small (1.0 mm). They were tortuous and did not have a structure that could be described as a common chamber (Fig. 1b). Doppler waveforms from the pulmonary veins were normal and biphasic on the right side; however, they showed non-pulsatile continuous flow on the left side, suggesting left pulmonary congestion (Fig. 1c).

Fetal MRI performed at 35 weeks of gestation revealed no difference in appearance between the left and right lungs, indicating no laterality of the lungs. No nutmeg lung pattern was observed (Fig. 1d). However, because fetal echocardiographic findings were suggestive of advanced left pulmonary venous stenosis, interventions

such as stent placement at the site of stenosis could be required directly following birth. Therefore, a cesarean section was performed.

The baby was born with a birthweight of 2618 g at 38 weeks and 2 days of gestation. Immediately after birth, the following conditions were observed: an oxygen saturation (SpO_2) of 90% on room air, tachypnea, and retractive breathing. High-flow nasal cannula therapy with a low oxygen concentration was administered. Based on the findings of chest computed tomography (CT) and echocardiography performed on the day of birth, it was determined that the diagnosis had not changed since gestation (Fig. 2a–d). Marked congestion was observed in the left lung (Fig. 2a). On echocardiography, blood flow velocity was approximately 1.5 m/s at sites where the left pulmonary veins returned to the left SVC, and blood flow to the left pulmonary artery was maintained. As the patient was inhaling low-oxygen air (17% of oxygen) under hypoxia inhalation therapy with a nitrogen gas mixture and the patient's SpO_2 was 80–89%, it was determined that the patient's course could be observed without performing additional interventions. Therefore, no interventions were performed for pulmonary venous stenosis during the early neonatal period. Bilateral pulmonary artery banding was performed at 6 days of age. The patient has been scheduled to undergo another operation after weight gain has occurred.

Discussion

The peripheral pulmonary venous plexus and systemic archenteron plexus are initially connected; however, their connection regresses after the pulmonary veins and left atrium connect to each other. The common pulmonary vein develops from the posterior wall of the left atrium embryologically. TAPVC occurs if the fusion of the pulmonary veins and left atrium via the common pulmonary vein is interrupted before the network between the pulmonary venous plexus and archenteron plexus regresses.

In the present case, narrow tortuous networks of anomalous vessels between the left and right pulmonary veins were observed on the posterior side of the atrium; however, the common pulmonary venous chamber could not be clearly observed. Therefore, it may be deduced that the fusion of the pulmonary veins and left atrium was not the result of the agenesis of the common pulmonary vein, leading to TAPVC. Rather, it is thought that the anomalous vessels on the posterior side of the left atrium were part of the remaining archenteron venous plexus.

Meanwhile, there was only a single atrium, in which complete absence of the septum was observed. The left atrial appendage was present, and there were no issues with the returning systemic veins. Hence, it was thought that laterality was maintained while the atria were developing, although a single atrium was formed due to the malformation of the interatrial septum.

During normal development, the atria are formed by the following four components: (1) smooth-walled lower atrial rim derived from the atrioventricular canal myocardium; (2) atrial appendages derived from the primitive cardiac tube; (3) caval vein myocardium (systemic inlet); and (4) mediastinal myocardium (pulmonary inlet), including the atrial septa derived from the dorsal mesocardium.[6] In this case, the absence of the common pulmonary vein, which would have formed an inflow portion to receive blood from the pulmonary veins and interatrial septum, was observed. Hence, it was believed that the sequence of cardiac malformations in the present case occurred due to the incomplete development of the dorsal mesocardium.

The nutmeg lung pattern can be observed in pulmonary lymphangiectasia on fetal MRI. Secondary pulmonary lymphangiectasia due to congenital heart disease is caused by the following conditions: pulmonary venous stenosis/atresia, mitral stenosis/atresia, cor triatriatum, and hypoplastic left heart syndrome.[4] Furthermore, the pulmonary venous flow has been reported to be continuous or monophasic on fetal echocardiography in TAPVC patients with pulmonary venous stenosis.[7] However, no studies have reported the relationship between the nutmeg lung pattern and pulmonary venous flow patterns. In this case, fetal echocardiography showed non-pulsatile continuous flow in the left pulmonary veins as well as increased flow velocity at the entry point of the pulmonary vein to the left SVC, suggesting severe pulmonary congestion. On the other hand, no marked nutmeg lung pattern was observed on fetal MRI. Additionally, while left pulmonary congestion was suggested on postnatal CT, blood flow in the left pulmonary artery was main-

tained. Therefore, it was not necessary to perform interventions for pulmonary venous stenosis directly following birth. The above findings suggest that the nutmeg lung pattern can only be observed if more severe pulmonary congestion and more advanced pulmonary lymphangiectasia are present, compared with non-pulsatile continuous pulmonary venous flow patterns. Going forward, it is necessary to report more cases such as this in order to more accurately predict the postnatal course of fetuses with TAPVC accompanied by pulmonary venous stenosis based on fetal echocardiography and pulmonary MRI. This may help develop effective treatment plans.

A cknowledgement

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Statement of Ethics

This study was approved by the Institutional Review Board of Osaka City General Hospital (approval number: 2012135). Informed consent was obtained in the form of opt-out on the website of Osaka City General Hospital.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Author Contributions

All authors discussed and planned the treatment. WM, TS, EE, and KK carried out the treatment. WM and YK drafted the manuscript. All authors critically reviewed and approved the final manuscript.

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Figure Legends

Fig. 1. Fetal echocardiography at 31 weeks of gestational age. (**a**) i. Single atrium and single right ventricle. ii. Narrow ascending aorta (AAo) is observed on the right side of the main pulmonary artery. iii. Color Doppler image of (a)-ii. (**b**) i. An abnormal pulmonary vein (PV) is behind the single atrium (dotted arrow). ii/iii. Left PV blood flow runs off to the right side at increased flow velocity. (**c**) i. Doppler wave

form in the right PV is rich and biphasic. ii. Doppler wave form in the left PV is non-pulsatile continuous flow. (**d**) Axial single-shot spin echo magnetic resonance image at 35 weeks of gestational age. Bilateral lungs are heterogeneous without nutmeg lung pattern. DAo, descending aorta; LSVC, left superior vena cava; mPA, main pulmonary artery.

Fig. 2. Computed tomography angiography with three-dimensional reconstruction. (**a**) Pulmonary window setting. Severe pulmonary congestion in the left lung. (**b**) The right pulmonary vein (PV) entered the left superior vena cava (LSVC). (**c**) Anterior-posterior image of three-dimensional reconstruction. An extremely narrow ascending aorta (AAo) is observed. (**d**) Posterior-anterior image. The right PV enters the right superior vena cava (SVC) without stenosis. The left PV enters the LSVC with stenosis. Bilateral PVs have communication by a tortuous vessel.