A case of prenatally diagnosed extrapulmonary arteriovenous malformation associated with a complex heart defect

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Pulmonary arteriovenous malformations are rare vascular anomalies of the lung, only a few cases of which have been diagnosed prenatally. The diagnostic clue for prenatal diagnosis was cardiomegaly with a particularly enlarged left atrium. All previous cases of pulmonary arteriovenous malformations diagnosed prenatally have been reported as an isolated anomaly or in association with simple heart defects. We here describe the first case of a pulmonary arteriovenous malformation with a complex heart defect that was diagnosed prenatally at 21.0 weeks of gestation and confirmed by postmortem autopsy.

Keywords: Congenital heart defects; Prenatal diagnosis; Pulmonary arteriovenous fistulas

Introduction

Pulmonary arteriovenous malformations (PAVMs) are abnormal communications between the pulmonary arterial and venous system. They are quite rare and only a few reports of prenatal diagnosis have been described [1-9]. The cases diagnosed prenatally were reported as an isolated anomaly or in association with simple cardiac defects. Here, we present the first case of prenatally diagnosed PAVM associated with double outlet right ventricle (DORV) with ventricular septal defect (VSD) that was confirmed by autopsy.

Case report

A 32-year-old primigravida woman was referred to our center at 21.0 weeks of gestation with suspicion of fetal DORV with VSD. The non-invasive prenatal test was normal. The ultrasound examination showed cardiomegaly (cardiothoracic area ratio, 0.47; normal range, 0.25 to 35) with a particularly enlarged left atrium (Fig. 1A). Both great arteries arose from the right ventricle with a dextro-transposition relationship, and a huge VSD (6.5 mm) was present (Fig. 1B). The aortic and ductal arches were observed on the left side of trachea. However, the main pulmonary artery was widened (Z-score 2.19) and coursed abnormally to the right side of the trachea, turned to the left behind the lower level of the trachea, and joined to the left atrium. Pulsed wave color Doppler was applied to the area of the junction of the pulmonary artery and left atrium and showed an arterial flow pattern, which confirmed it as a right-to-left shunt with suspicion of a PAVM (Fig. 1C). The pulmonary valve appeared normal without thickening and laminar antegrade flow with normal velocity was demonstrated at color and pulsed Doppler. The blood flow through the ductus arteriosus was reversed. The baby was delivered due...
to impending fetal death but expired. The autopsy confirmed the extrapulmonary PAVM between the main pulmonary artery and the left atrium, which was associated with DORV and VSD (Fig. 1D-F). The histological investigation could not differentiate between the pulmonary artery and vein due to the small size of the heart. There was no evidence of telangiectasia or further malformations.

**Discussion**

PAVMs result from persistent capillary anastomoses or defects in the terminal capillary loops allowing dilatation and formation of vascular sacs [10,11]. The incidence of this disease is 2 to 3 per 100,000 people, and more than 80% of PAVMs are congenital [5,12]. They may be an isolated anomaly or associated with hereditary hemorrhagic telangiectasia in about 70% of cases [2]. The clinical symptoms of patients are variable from asymptomatic to dyspnea depending on the degree of right-to-left shunt through PAVMs [13]. Patients with small lesions remain asymptomatic and may not present until the fourth decade of life [2]. The frequent complications are cerebrovascular attacks or brain abscesses by emboli entering the systemic circulation in the absence of the pulmonary capillary filter [14].

Technological advancements of ultrasound such as color and pulsed wave Doppler help an earlier prenatal diagnosis of congenital abnormalities. Similar with previous reported cases, PAVMs could be diagnosed prenatally by ultrasonographic findings of cardiomegaly particularly left atrium, abnormal course of pulmonary artery and pulsed Doppler of arterial drainage into left atrium. In addition to these findings, it is the first case of a PAVM associated with a complex heart defect diagnosed prenatally. In previous cases of PAVM diagnosed prenatally, three were associated with a congenital heart defect, but a simple disease such as valvular pulmonary stenosis,
In our case, a complex heart defect of DORV with VSD might add the hemodynamic effect to the already exiting shunting through a PAVM. Several studies have reported that PAVMs occurred after a palliative operation with cavopulmonary anastomoses in patients with a congenital heart defect [15]. However, they were not congenital, but acquired conditions.

In eight previous cases of prenatally diagnosed PAVMs, four infants survived after successful treatment (Table 1) [1,3-9]. Among four survived infants, one was diagnosed as late as 37 weeks. Although the other three fetuses were diagnosed early at 21 to 22 weeks, none of them had signs of heart failure during pregnancy, and all were born at or near term. This may mean that the degree of shunting was insufficient to cause heart failure prenatally.

In contrast to the small PAVMs, large PAVMs might cause a hyperdynamic circulatory status leading to heart failure, even in the antenatal period. As a result, preterm delivery was needed and infants could not survive even after an immediate treatment postnatally [3,6]. The earliest diagnosed case showed a PAVM between the main pulmonary artery and the right pulmonary vein. Similarly, this case was confirmed as an extrapulmonary PAVM with direct connection between main pulmonary artery and the left atrium. It might make the larger amount of shunting than the other seven cases with localized communication between either the right or left pulmonary artery and pulmonary vein inside the lung. As a result, the larger hemodynamic change would occur.

It is difficult to evaluate the prognostic factors of PAVMs diagnosed prenatally because of its rarity. However, this case was suggested as the worst condition showing the hemodynamic change prenatally, the extrapulmonary connection of main pulmonary artery and the additional complex heart defect. In cases of large PAVMs like this, antenatal intervention such as coiling of shunt before fetal heart failure or irreversible pulmonary hypoplasia may be helpful for improvement of

| Reference | Center | GA at diagnosis (wk) | Site of PAVM | Associated anomaly | GA at delivery (wk) | Fetal hydrops | Perinatal outcomes |
|-----------|--------|----------------------|--------------|--------------------|---------------------|--------------|-------------------|
| Kalugdan et al. (1989) [8] | Fukuoka, Japan | 28 | In RUL RPA to RPV | | 31 | + | Expired after 4 hours before treatment |
| Heling et al. (2002) [3] | Berlin, Germany | 27 | In RUL, RLL RPA to RPV | | 30 | + | Expired during transcatheter occlusion |
| Russell et al. (2002) [6] | Michigan, USA | 23 | In RLL RPA to RPV | Valvular PS | NA | - | EXIT, ECMO, surgical ligation → expired due to pulmonary hypoplasia |
| Kenny et al. (2007) [4] | Bristol, UK | 37 | In RML, RLL RPA to RPV | | Term | NA | Transcatheter occlusion at HD 1 → survived |
| Sinkovskaya et al. (2009) [7] | Virginia, USA | 22 | RPA to RPV | | 39 | - | Transcatheter occlusion at HD 1 → survived |
| Akler et al. (2012) [1] | Tel Aviv, Israel | 16 | MPA to RPV | Muscular VSD | - | NA | Termination of pregnancy |
| Hellmund et al. (2014) [9] | Bonn, Germany | 22 | In RLL RPA to RPV | ASD, muscular VSD | 36 | - | Surgical closure at HD 1 → survived |
| Ostras et al. (2015) [5] | Kyiv, Ukraine | 21 | LPA to LPV | | 38 | - | Surgical repair at HD 2 → survived |
| Current study | Seoul, Korea | 21 | MPA to LPV | DORV with VSD | - | - | Preterm delivery due to impending fetal death but expired |

PAVM, pulmonary arteriovenous malformation; GA, gestational age; RUL, right upper lobe; RPA, right pulmonary artery; RPV, right pulmonary vein; RLL, right lower lobe; PS, pulmonary stenosis; NA, not available; EXIT, ex utero intrapartum treatment; ECMO, extracorporeal membrane oxygenation; RML, right middle lobe; HD, hospital day; MPA, main pulmonary artery; VSD, ventricular septal defect; ASD, atrial septal defect; LPA, left pulmonary artery; LPV, left pulmonary vein; DORV, double outlet right ventricle.
the perinatal outcome in future.

PAVMs are rare, but can be diagnosed prenatally with typical ultrasonographic findings in cases with large hemodynamic change. It may be an isolated form or associated with congenital heart defect ranging variously from simple to complex.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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