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Case Reports

Large Fetal Pulmonary Arteriovenous Fistula: Impact on Pulmonary Development

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Abstract. A case report of a patient with a large pulmonary arteriovenous fistula and valvar pulmonary stenosis is presented. The fistula was diagnosed prenatally and its effect on in utero cardiovascular growth and development documented. Due to concerns about massive intrapulmonary shunting potentially causing profound cyanosis after delivery, an EXIT (EX-utero Intrapartum Treatment) procedure was used to transfer the infant from placental to extracorporeal membrane oxygenation (ECMO) support. Severe pulmonary microvascular disease resulted in prohibitive pulmonary hypertension despite surgical ligation of the fistula. Prenatal and postnatal hemodynamic assessments of the fistula are presented and are compared to the pathologic findings.

Key words: Pulmonary arteriovenous fistula — In utero diagnosis — pulmonary development — Valvar pulmonary stenosis

Pulmonary arteriovenous fistulas are congenital communications between the pulmonary arterial and pulmonary venous systems that usually present with exertional dyspnea and cyanosis in the third or fourth decades of life [9]. The timing of the onset of symptoms is primarily dependent on the percentage of cardiac output that passes through the fistula. Extremely rarely, the fistula is of sufficient hemodynamic significance to cause profound cyanosis, acidosis and death in the neonatal period [4, 6]. In the present case, the development of a fetus with an unusually large pulmonary arteriovenous fistula (PAF) is tracked from 23 weeks gestation through delivery. The implications of this connection on pulmonary vascular development and on pre- and post-natal care are discussed.

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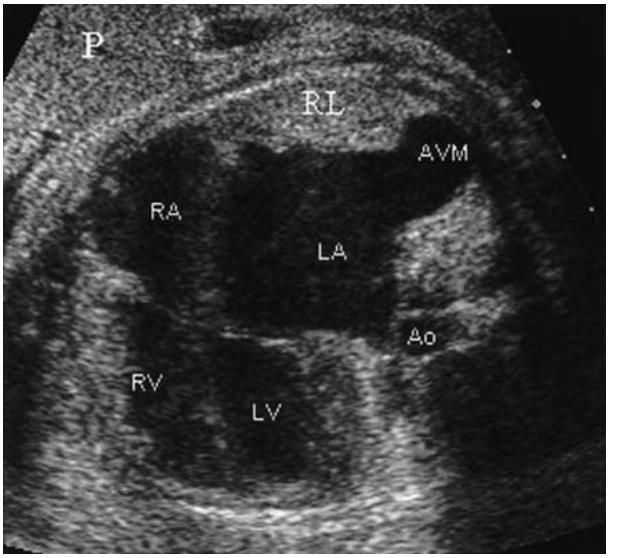

Fig. 1. Fetal echocardiographic image obtained during diastole at 23 weeks gestational age. Note the four chamber cardiac enlargement (*RA*, *LA*, *RV*, and *LV* denote the right and left atria and ventricles). Also indicated are the arteriovenous malformation (*AVM*), the descending aorta (*Ao*), right lung (*RL*) and placenta (*P*).

Case History

A patient presented to our institution with a 23 week gestational age fetus that had been determined to have marked four-chamber cardiomegaly on a screening obstetrical ultrasound. At the initial presentation there was severe, cardiomegaly with a cardiothoracic ratio of 0.73 (normal < 0.35), good biventricular function, markedly dilated right and main pulmonary artery, valvar pulmonary stenosis, a reverse-oriented patent ductus arteriosus, and an abnormal vascular connection in the right posterior lung field. A gradient of 42 mm Hg was obtained across the vascular connection that appeared to be multiple, small arteriovenous channels adjacent to the pleural surface. During the course of the pregnancy, there was progressive four chamber cardiac enlargement (Fig. l), continued dilatation of the main and right pulmonary artery, and gradual formation of a pulmonary venous lake. However, there were never indications of impending heart failure; there was normal umbilical vessel and inferior vena cava flow patterns and no significant effusions.

Due to concerns about pulmonary arterial and venous hypoplasia, airway compromise, pulmonary parenchymal hypoplasia

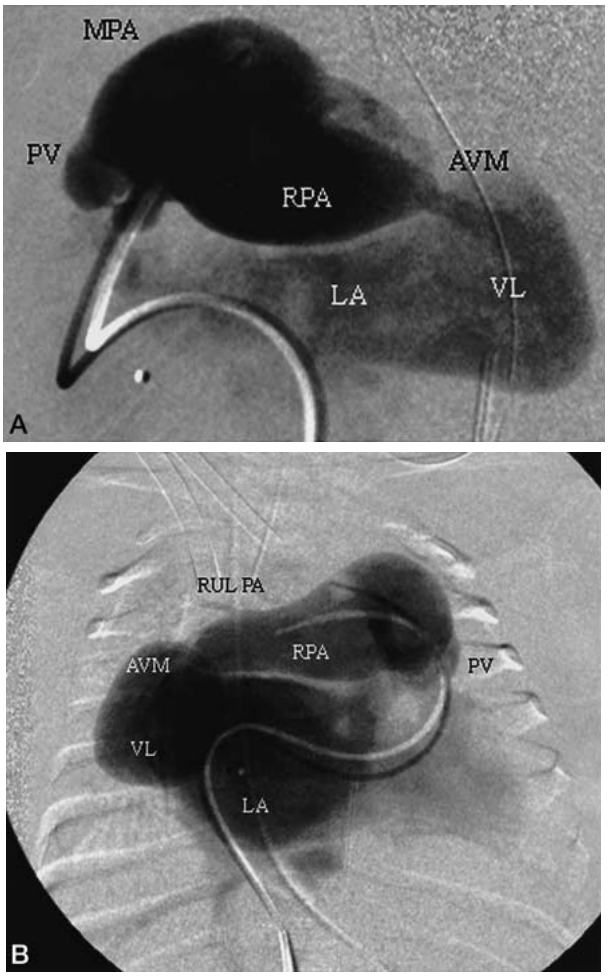

Fig. 2. Digital image of contrast injection in the main pulmonary artery at the time of catheterization. **A** Lateral projection. Note the dysplastic pulmonary valve (PV), the dilated main and right pulmonary arteries (MPA and RPA), connection between the RPA and the right pulmonary vein (AVM) and the dilated venous lake (VL) that drains into the left atrium (LA). **B** Anterior-posterior projection. Note the marked cardiac dilation, and the diminutive right upper lobe pulmonary artery (RUL PA).

and massive intrapulmonary right to left shunt, the team of physicians caring for the patient elected to perform an EXIT (EX-utero Intrapartum Treatment) procedure [9] in which the patient was transferred directly from placental support to veno-arterial extracorporeal membrane oxygenation (ECMO). With the mother under general anesthesia, the head and thorax of the fetus was delivered by cesarean section. A peripheral intravenous line was placed and the infant was sedated, paralyzed, and intubated. The right internal jugular vein and the carotid artery were cannulated and ECMO support was initiated. The remainder of the infant was delivered and the umbilical cord was clamped and divided.

The transition to ECMO was uncomplicated and, after stabilization, an echocardiogram confirmed the prenatal diagnoses. The patient underwent cardiac catheterization to further define the anatomy of the fistula and its blood supply. At catheterization, a single connection between the right lower lobe pulmonary artery and the right lower pulmonary vein was identified (Fig. 2). There was marked hypoplasia of the right middle, right upper and left pulmonary artery, and no significant contrast could be visualized in the pulmonary venous system of the left lung or the uninvolved segments of the right lung. Due to the large size and short length of the communication, non-surgical intervention via coil occlusion was determined to be higher risk than surgery.

The patient was taken for surgical ligation of the right lower lobe pulmonary artery proximal to the fistula. The friable nature of the ductus arteriosus necessitated institution of cardiopulmonary bypass and complete repair of the cardiac anomalies. The fistula, which arose from the very dilated main right pulmonary artery and drained directly into the left atrium via a large sinus cavity, was ligated and divided. The right pulmonary artery was reduced in size to relieve the tracheobronchial compression caused by its severe dilatation. Examination of the right upper, middle and lower lobe and left main pulmonary arteries showed them to be quite hypoplastic, accepting only 3–4 mm dilators. A valvotomy was performed to separate the fused raphe of the thickened pulmonary valve (Fig. 3). After rewarming, the patient was weaned from cardiopulmonary bypass and noted to have a pulmonary arterial pressure approximately 20 mmHg suprasystemic. The lungs accepted tidal volumes of 6–8 cc/kg with minimal end-tidal CO_2 return suggesting pulmonary parenchymal hypoplasia. Therefore, the patient was placed back on ECMO support and returned to the intensive care unit.

Two additional days of ECMO support failed to yield any progress in decreasing the amount of cardiopulmonary support required. The lung fields were extremely congested on chest X-ray and any weaning of the ECMO flow was accompanied by hypotension, hypoxia and decreasing mixed venous oxygen saturation. After discussion of the short and long-term prognosis with the family, the decision was made to discontinue ECMO support. Shortly after discontinuing support, the patient expired and an autopsy was performed.

On pathologic examination, the left pulmonary artery and left lung were noted to be markedly hypoplastic. There was diffuse bilateral congestion with hyaline membrane formation. The small arteries were noted to have marked medial hypertrophy and rare thrombi (Fig. 4).

Discussion

PAFs are thought to occur either secondary to incomplete degeneration of the vascular septae between the arterial and venous plexuses at the level of the pulmonary bud [1] or to a defect in the terminal capillary loops allowing dilatation and formation of thin-walled vascular sacs fed by a single artery and drained by a single vein [3]. Only rarely are they sufficient size to cause symptoms in the perinatal period. If a PAF is hemodynamically significant in the perinatal period, it is commonly fatal [7]. With prompt diagnosis and treatment, several cases of neonatal PAF have been successfully treated by resection of the involved lung segment [2, 5]. However, it is evident that the present case had a greater compromise of pulmonary parenchymal and vascular development.

What is striking about this case are the secondary effects of the fistula on the growth of the heart and on the development of the pulmonary vascular system.

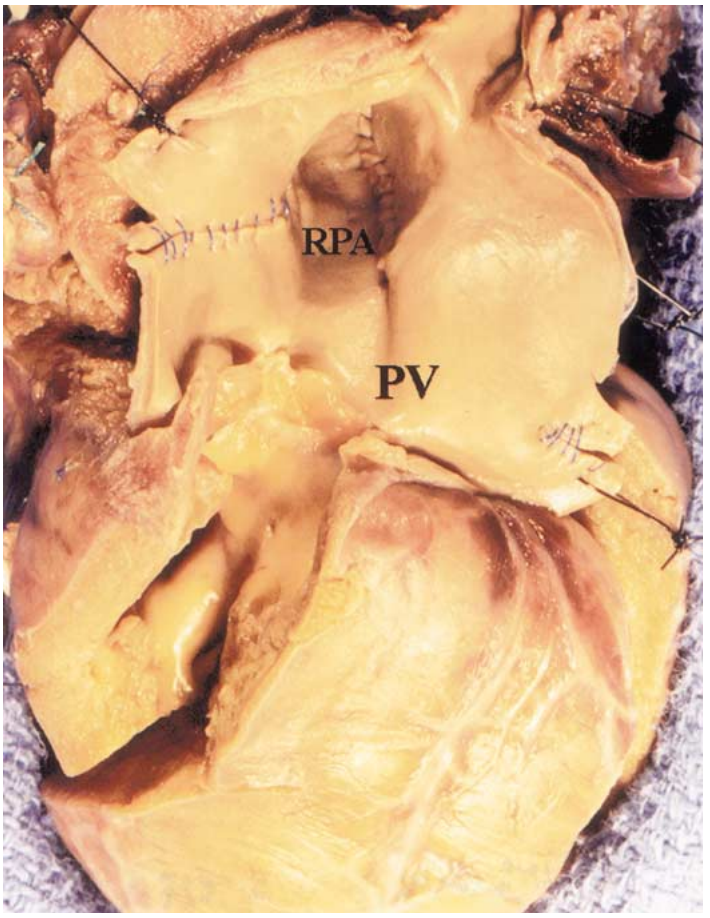

Fig. 3. Pathologic specimen demonstrating the thickened, dysplastic pulmonary valve leaflets (PV), and the dilated main and right pulmonary artery (RPA) (after surgical reduction).

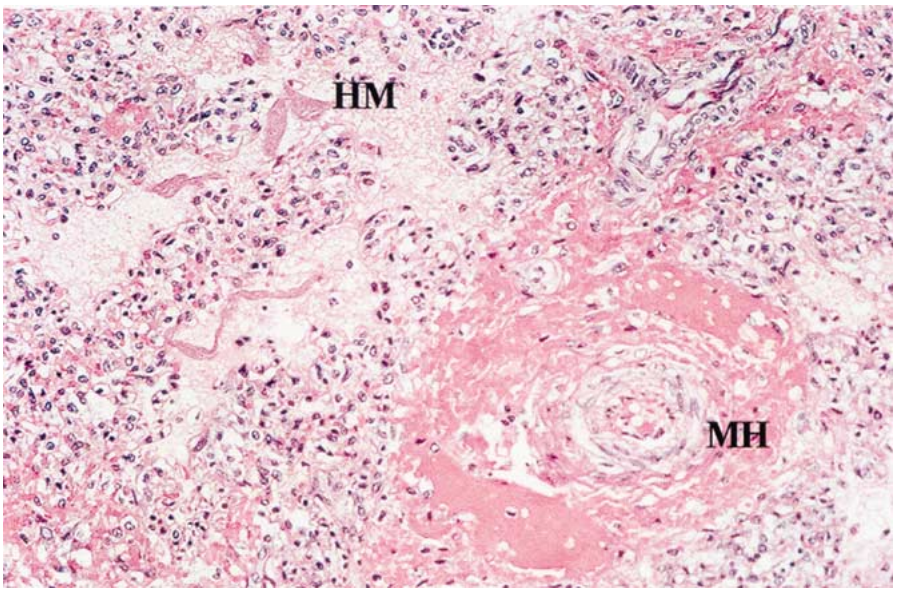

Fig. 4. Pathologic specimen examining the microvasculature of the right lung demonstrates medial hypertrophy (MH) of the small arterioles and hyaline membrane (HM) formation.

Due to the low resistance provided by the PAF in utero, there was retrograde flow into the pulmonary artery across the ductus arteriosus. This increased pulmonary arterial flow and increased return to the left atrium. Elevated left atrial filling caused left to right shunting at the atrial level. The increased right-sided filling led to right atrial and ventricular dilatation and marked dilatation of the main pul-

monary artery. The increased bilateral ventricular filling resulted in four chamber cardiac enlargement (Fig. l). Evidently, the rate of flow across the fistula allowed the heart to compensate with cardiac growth and dilatation as opposed to heart failure. The cardiomegaly resulting from increased cardiac output was sufficient to markedly inhibit normal lung growth as evident from the reduced lung volume.

It is also interesting to note that in this patient, the pulmonary valve was mildly thickened and stenotic, requiring separation of the raphe at the time of surgery. Since pulmonary stenosis and PAF have not been previously reported, it is possible that the pulmonary valve abnormality, which appeared to be progressive based on the fetal echocardiographic evaluations, may have been secondary to a jet lesion produced by the reverse-oriented patent ductus arteriosus. The high volume of flow into the pulmonary artery from the ductus arteriosus inhibited opening of the pulmonary valve and may have caused mild valvar dysplasia and fusion of the raphe.

Perhaps the most dramatic effect of this fistula was the effect it had on the peripheral pulmonary vasculature. The resistance vessels in the lung were small and hyperplastic. The lungs were diffusely congested and the chest X-ray reminiscent of pulmonary venous obstruction. In addition to the large vessel, pulmonary arterial hypoplasia, there appears to have been substantial compromise of the pulmonary arterial and venous microvasculature. It is possible that the "stealing" of flow by the fistula away from the developing pulmonary capillary beds inhibited their normal arborization and development. This is consistent with the finding that, once the fistula was ligated, there was suprasystemic right ventricular pressure and the lungs were markedly congested despite full ECMO support. Some of the arteriovenous connections may not have fully developed, leading to thrombi in some of the blind vascular pouches.

In retrospect, the best chance for successful outcome for this patient would have been blockage or removal of the fistula early in the pregnancy in a manner that would have allowed the pregnancy to continue. In discussing the case with institutions adept at *in utero* intervention, no intervention could be envisaged that had a reasonable likelihood of allowing for continued *in utero* development. It was decided that, to deliver the fetus prematurely, would further compromise the infant's respiratory status and would preclude the use of ECMO support during evaluation and treatment. The transfer from placental support to ECMO at the time of Cesearean delivery, prevented significant hypoxia, and allowed full assessment of the patient's condition. This approach to the management of severe pulmonary or airway abnormalities may be beneficial in some cases with more treatable abnormalities.

This case highlights the vital role of normal in utero pulmonary blood flow on the maturation of the pulmonary vascular bed. This patient demonstrated marked impairment of the pulmonary microvascular development likely secondary to arterial steal through the fistula. Reversing this process early in development may be required in patients with large PAFs, even without evidence of hydrops, to prevent inoperable pulmonary vasculopathy. As in utero cardiovascular interventions advance, it may become possible to intervene, at low risk, early enough to improve the outcome of these patients.

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