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In Utero Premature Closure of the Ductus Arteriosus Presenting as Isolated Right Ventricular Hypertrophy

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ABSTRACT

Background: The etiology of isolated right ventricular hypertrophy (RVH) is distinct from other forms of hypertrophic cardiomyopathy. RVH is typically seen in the setting of pulmonary valve stenosis or Tetralogy of Fallot. A rare cause of isolated RVH is premature closure of the patent ductus arteriosus (PDA) in utero that results in pulmonary hypertension. This can have a range of outcomes, from spontaneous resolution to fetal demise.

Methods: This case report describes a term infant who presented with respiratory distress and striking isolated RVH, pulmonary hypertension, and no PDA. She was treated conservatively with supplemental oxygen.

Results: The patient was gradually weaned off oxygen over the course of two weeks and follow-up echocardiography showed resolution of her RVH and pulmonary hypertension by 14 weeks of age.

Conclusions: The presentation and course of this patient with severe isolated RVH is consistent with spontaneous premature closure of the ductus arteriosus in utero.

CASE

A full-term girl was born via Cesarean section for face presentation and fetal distress after an uncomplicated pregnancy. She required continuous positive airway pressure and blow-by oxygen in the delivery room for approximately 10 minutes. Apgar scores were 6 at 1 minute and 9 at 5 minutes. She was transported to the neonatal intensive care unit (NICU) for presumed transient tachypnea of the newborn, with tachypnea, nasal flaring, and decreased oxygen saturation. A plain film chest radiograph demonstrated cardiomegaly. She failed a hyperoxia test, with an arterial partial pressure of oxygen of 41 mm Hg on 38% fraction of inspired oxygen (FiO_2) via head hood oxygen increasing to only 58 mm Hg on 94% FiO_2.

An echocardiogram (echo) was performed at approximately 8 hours of life to evaluate for congenital heart disease. She had a structurally normal heart with the exception of striking right ventricular hypertrophy (RVH) (Figure 1, Views A and C). No patent ductus arteriosus was identified. In addition, there was no evidence for outflow tract obstruction. Right ventricular function was mildly diminished, and left ventricular function was hyperdynamic (shortening fraction of 47%) with no evidence of left ventricular hypertrophy or chamber dilation. Pulmonary hypertension was suspected based on bidirectional flow across the patent foramen ovale, flattened ventricular septal wall motion, and an elevated right ventricular systolic pressure.

The patient was conservatively managed with supplemental oxygen. She showed gradual clinical improvement and was slowly weaned off her supplemental oxygen over the course of 2 weeks. Repeat echocardiography demonstrated resolution of RVH, normalization of pulmonary artery pressures, and improvement in right ventricular function. She was clinically stable and discharged to her home on day 18. An echo performed at 14 weeks of life showed nearly complete resolution of RVH and normalization of pulmonary artery pressures (Figure 1, views B and D).

DISCUSSION

This patient presented with respiratory distress and isolated RVH that resolved spontaneously within the first several months of life. The etiology of isolated RVH is distinct from other forms of hypertrophic cardiomyo-

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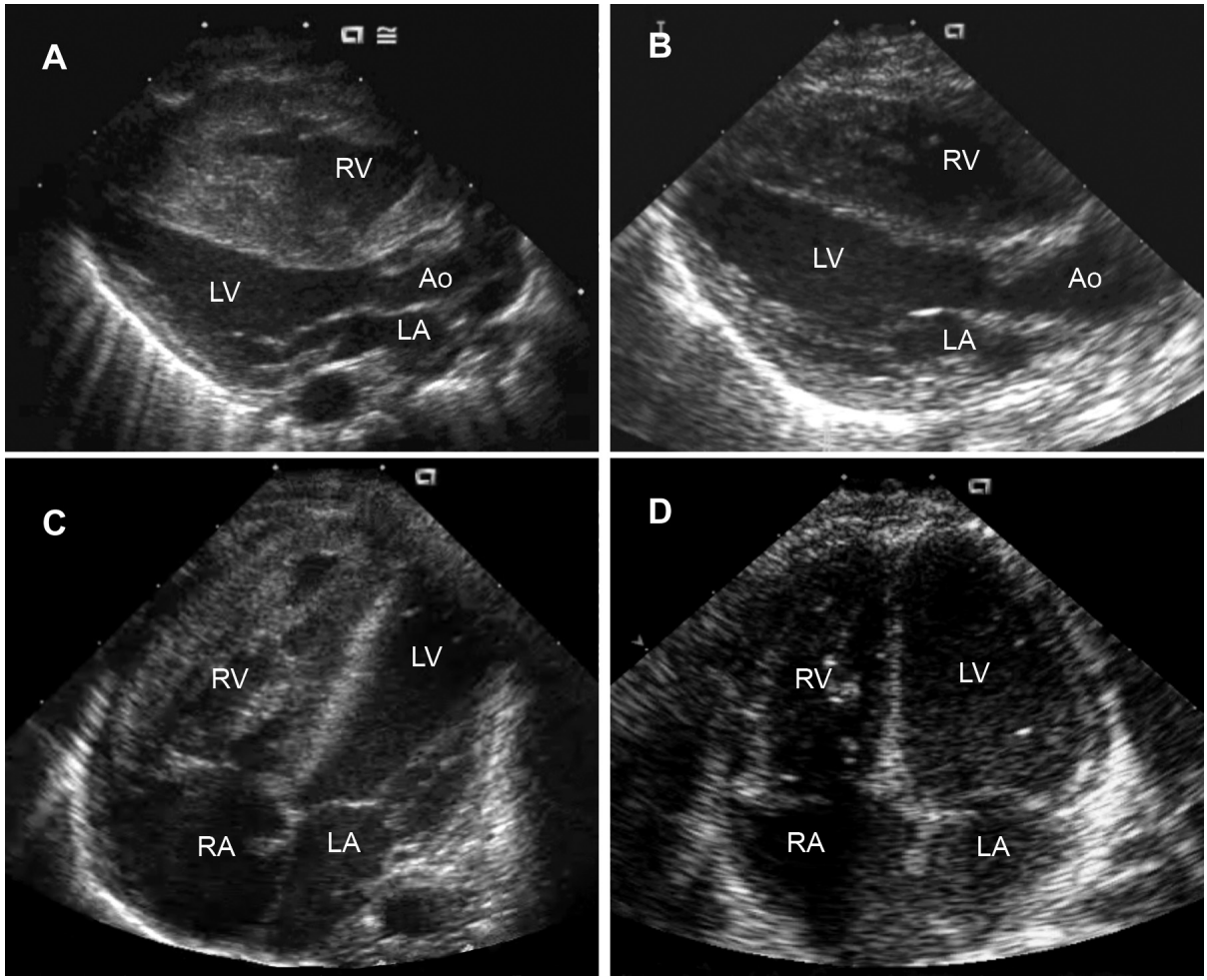

Figure 1. Transthoracic echocardiogram. Parasternal long axis view (A) and apical 4-chamber view (C), demonstrating striking right ventricular hypertrophy (RVH). Parasternal long axis view (B) and apical 4-chamber view (D) 14 weeks later, demonstrating resolution of RVH.

pathy that affect both ventricles. RVH in the fetal and newborn period typically occurs from congenital heart disease lesions that cause obstruction to the right ventricle such as valvar pulmonary stenosis or Tetralogy of Fallot. Isolated RVH is also noted in the setting of elevated afterload on the fetal right ventricle, as in the case of premature constriction of the ductus arteriosus or the recipient twin-to-twin transfusion syndrome. Rarely, isolated RVH may present in fetal life, in the setting of Noonan's syndrome.[1] Premature closure of the ductus arteriosus is a rare cause of isolated RVH. This was the presumed etiology of our patient, based on her presentation and course.

In utero premature closure of the ductus arteriosus has been shown to result in pulmonary arterial hypertension. It is postulated that the increased workload demanded by directing flow through the high-resistance fetal pulmonary vascular circuit results in compensatory right ventricular hypertrophy.[2-3] The variation in severity (from postnatal resolution to right heart failure, fetal hydrops, or death) is presumably correlated to the degree of ductus constriction, as well as the size of the foramen ovale and the gestational age at the time of ductus closure.[4]

The vasodilatory effects of the prostaglandins PGE1 and PGE2 play a vital role in maintaining the patency of the ductus arteriosus. Prostaglandin synthetase inhibitors have been shown to cause constriction of the ductus arteriosus in the human fetus.[5] Indomethacin for tocolysis is a well-documented cause,[6] and maternal nonsteroidal anti-inflammatory drug (NSAID) use during the third trimester is the most commonly reported etiology of premature closure of the ductus arteriosus.[7-8] However, this patient's mother had no history of NSAID use during the pregnancy, nor of any other prostaglandin synthetase inhibitors.

A recent report, describing 20 cases of intrauterine PDA constriction, demonstrated maternal NSAID use in only 7 cases and found no underlying etiology in the remaining 13 cases, suggesting that idiopathic constriction has been underappreciated.[9] The idiopathic group had similar outcomes to those cases secondary to maternal NSAID use, with a range of results, from fetal demise to persistent pulmonary hypertension of the newborn to complete postnatal resolution. Fetal hypoxemia is a potential etiology for these cases, based on the observation that asphyxia causes constriction of the ductus arteriosus in fetal lambs, with sympathetic amines thought to be the responsible agent.[10] Our patient had signs of perinatal distress, which could indicate a causative hypoxic event.

Regardless of the inciting event, it is important to recognize the potentially fatal consequences of premature constriction of the ductus arteriosus and to search carefully for reversible causes, such as maternal NSAID use. If no such cause can be found, prompt delivery of the fetus can allow for postnatal resolution.

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