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Brief Report

Pulmonary arterial and intracranial calcification in the recipient of a twin–twin transfusion

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Abstract Pulmonary arterial and intracranial calcifications are rarely found in children. A female infant, the recipient of a twin–twin transfusion syndrome was found, by ultrasound and computed tomography, to have both pulmonary arterial and intracerebral calcification. A rare condition, termed idiopathic arterial calcification of infancy, is the likely cause. This condition carries a poor prognosis and is usually fatal.

Keywords: Arterial calcification; pulmonary artery; twin–twin transfusion

PULMONARY ARTERIAL AND INTRACRANIAL calcifications are unusual in children.[1,2] Pulmonary calcifications are known only to occur in cases of severe underlying valvar disease,[1] while intracranial calcifications are usually associated with transplacental viral infection.[2] We report a unique case in which both pulmonary arterial and intracranial calcifications were identified in the recipient of a twin–twin transfusion. To our knowledge, this is the fourth report of pulmonary arterial calcification in this setting.[1,3,4] This association should be more widely recognized.

Case report

Twin A

Our index case, a female infant, twin A of monochorionic, diamniotic twins, was born at 29 weeks gestation to a 30-year-old multiparous white female. She had previously undergone 10 pregnancies, losing 5 prior to delivery. The pregnancy was complicated by twin–twin transfusion syndrome, in which the index case was the "recipient". A fetal echocardiogram revealed twin A to have mild to moderate hydrops, with moderate pericardial effusion, polyhydramnios, mild myocardial hypertrophy, and biventricular enlargement, with the right ventricle being larger than the left. Cardiac function appeared normal, with no hemodynamic disturbance or outflow obstruction.

Delivery was by repeat Cesarean after spontaneous onset of labor. Twin A was born at 1395 grs, with Apgar scores of 6 and 8, at 1 and 5 min, respectively. At 4 min of life, the baby had poor respiratory effort and was intubated. Chest X-ray showed diffuse cardiomegaly and normal pulmonary blood flow. Examination revealed good perfusion, and normal oxygen saturation. Heart sounds were normal with no murmurs. An echocardiogram confirmed normal cardiac connections and relations. The arterial duct was open, with left-to-right shunting at low velocity. All valves were normal. Prominent echogenecity of the wall of the pulmonary trunk was detected (Fig. 1), along with milder evidence of increased echogenecity of the aorta. Diffuse non-obstructive myocardial hypertrophy was also noted. Cranial ultrasound revealed a small cyst, measuring 0.3 by 0.35 cm, within the choroid plexus of the anterior horn of the left lateral ventricle. Prominent linear echogenic lines were observed at the peripheral edge of the thalamus on both sides, thought to be related to calcification within the thalamostriate vessels. Subsequent chest computed tomography confirmed the presence of calcification of the pulmonary trunk (Fig. 2). The cranial computed tomography showed two intra-cerebral

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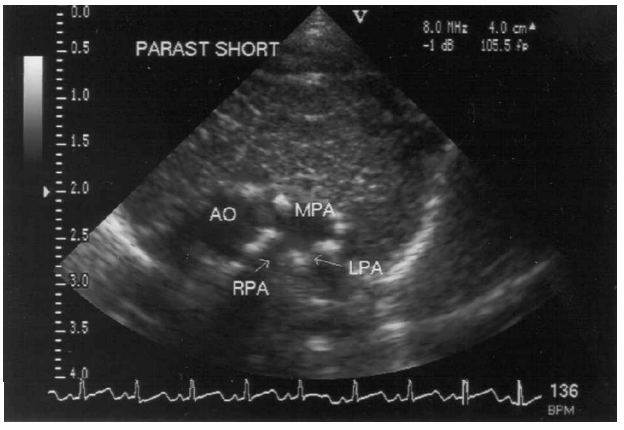

Figure 1.
Parasternal short-axis echocardiographic view of great vessels shows echodense material within wall of pulmonary trunk in the recipient of a twin transfusion syndrome. AO: aorta; MPA: pulmonary trunk; RPA: right pulmonary artery; LPA: left pulmonary artery.

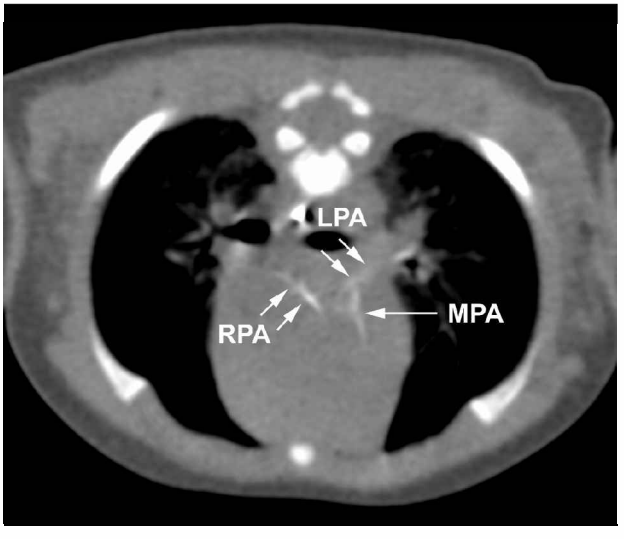

Figure 2.
Chest computed tomography shows linear calcification adjacent to the distal aspect of the pulmonary trunk extending into the right and left pulmonary arteries. Abbreviations as for Figure 1.

focuses of calcification, with the remainder of the cerebral parenchymal densities being normal. There was no evidence of hypervitaminosis D, hyperparathyroidism, renal disease, congenital syphilis, abnormal lipid metabolism, or inborn metabolic defects. Levels of calcium, phosphate and magnesium in the serum were found to be normal. Furthermore, calcification of placenta was not found.

Twin B

On fetal echosonography, twin B had oligohydramnios, a small pericardial effusion, good cardiac function and unusual echogenicity of the brain. This female infant, the donor in the twin–twin transfusion, was born at 1075 g, with Apgar scores of 2, 3, and 5, at 1, 5, and 10 min, respectively, and was severely depressed with poor response to intubation and ventilation. She required prolonged resuscitation, but eventually made good progress. Post-natal cranial ultrasonography and echocardiography were normal.

At examination four months later, the child was gaining weight and asymptomatic, on no medications. The cardiac findings were consistent with stenosis of the pulmonary arterial branches, with bilateral prominent systolic murmurs. The echo-Doppler examination confirmed a modest increase in flow velocities into both pulmonary arteries consistent with increased obstruction. This abnormality will be followed at 3 monthly intervals.

Discussion

Calcification of vessels in neonates can result from either a dystrophic or a metastatic process. Fetal insult or injury can lead to necrosis, hemorrhage, or fibrosis that precedes dystrophic calcification.[1] Metastatic arterial calcification can result from renal insufficiency, hypervitaminosis D, or hyperparathyroidism.[5] The rare entity, termed idiopathic arterial calcification of infancy, of unknown etiology, is the likely cause in this case.[5–8]

The incidence of such idiopathic arterial calcification of infancy is undetermined, but approximately 100 cases have been reported. Arterial changes are usually widespread throughout the body. There is usually coronary arterial involvement, and relative sparring of the cerebral vessels. It is characterized by deposition of calcium in the internal elastic lamina, and simultaneous proliferation of intimal fibrous tissue involving large and medium-sized arteries, resulting in luminal narrowing.[5–8] Polyhydramnios and cardiac failure at birth is commonly seen.[8] Marked cardiomegaly is often seen, most commonly described as biventricular or left ventricular enlargement. Clinically, patients often present with non-specific symptoms, secondary to congestive heart failure with abnormal vascular compliance.[5] Death usually ensues from right heart failure induced by the high pulmonary vascular resistance, congestive heart failure, or myocardial ischemia. Seven-eighths of affected patients die within 6 months of age.[5,7]

Our index case had many features consistent with idiopathic arterial calcification of infancy, including absence of abnormal laboratory findings, myocardial hypertrophy, biventricular enlargement, and polyhydramnios. There was an absence of calcification of other vessels, however, particularly the coronary arteries and renal vasculature, findings usually present in cases of idiopathic arterial calcification of

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infancy.[3] Furthermore, there was cerebral vascular involvement, which is seldom reported in this condition. There was no evidence of idiopathic arterial calcification in the other twin. Based on normal laboratory findings, other conditions leading to arterial calcification were excluded.

The status of our index case, being the recipient of a twin–twin transfusion, further enhances the uniqueness of our case, and casts doubt on the theory that idiopathic arterial calcification of infancy is inherited by an autosomal recessive manner.[6] Twin–twin transfusion syndrome complicates up to one-quarter of diamniotic monochorionic twin gestations, in which the donor twin supplies all or partial blood to the recipient co-twin via placental vascular anastomoses.[4] Popek et al.[1] reported one case of pulmonary arterial calcification in a recipient of the syndrome, and proposed a relationship between the presence of pulmonary arterial calcification and increased cardiac output during fetal life of the volume overloaded recipient. According to one study, calcifications are frequently found in the iliac arteries of neonates. The authors of this study suggested that this phenomenon represented a structural accommodation to the increased hemodynamic load on the common and internal iliac arteries that receive the full impact of blood flowing from the placenta.[9] Although the increased hemodynamic load from the donor twin may play some part, recent work suggests another possible explanation.

Lougheed et al.[4] reviewed 73 cases with twin–twin transfusion syndrome, identifying obstruction of the right ventricular outflow tract in 7 cases. The obstruction developed during fetal life and was frequently progressive, leading to complete atresia in 2 of the 7 cases. Pulmonary arterial calcification was described in one case, with subsequent death at 4–5 months of age, related to chronic lung disease. Abnormal circulatory growth factors and vasoactive peptides may also play a part in this process, as the recipient twin has greater exposure to these substances. Endothelin levels are known to be increased in the recipient as compared to the donor and controls.[4,10] Endothelin is a potent vasoconstrictor, as well as a smooth muscle mitogen.[4] These processes may explain the right ventricular hypertrophy that is seen in recipients of twin–twin transfusion.

The limited distribution of arterial calcification, and presence of intracranial calcifications, in our index case may be a variable presentation of idiopathic arterial calcification of infancy, as part of the twin–twin transfusion syndrome. Though rare in occurrence, the diagnosis of this condition is of great importance, since the prognosis is usually poor. The echogenecity of the cardiac or valvar structures should alert the clinician to the possibility of calcification, for which computed tomography will be diagnostic and permit better definition of the process in the distal pulmonary arterial vessels. The clinical presentation can be quite nonspecific. It is often sudden in onset, with a rapid progression to death. The majority of patients die within hours or days of onset of illness.[7] We could not find another reported survivor of pulmonary arterial calcification associated with the twin–twin transfusion syndrome.

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