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Brief Report

Pulmonary diffuse arterial calcifications: a very rare complication in the recipient of a twin-to-twin transfusion syndrome

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Abstract The syndrome of twin-to-twin transfusion is known potentially to be associated with the development of right ventricular obstruction, albeit rarely at supravalvar levels, in the recipient twin. We report the case of a recipient twin with diffuse hypoplasia and calcification of the pulmonary arterial tree, confirmed by postnatal thoracic angioscan. When aged 2 years, the child was moderately symptomatic with mild cyanosis, in spite of suprasystemic right ventricular systolic pressure as revealed by follow-up echocardiography.

Keywords: Monochorionic twins; right ventricular outflow tract obstruction; endothelin-1

The chronic twin-to-twin transfusion syndrome develops in up to one-tenth of all monochorionic twin pregnancies, and may be diagnosed following detection of the sequence of oligo- and polyhydramnios on ultrasonic examination.[1] The cardiovascular consequences of the syndrome vary for the twins. A significant number of recipient twins have systemic arterial hypertension, systolic and diastolic ventricular dysfunction, myocardial hypertrophy, and staged right ventricular obstructions.[2–5] We report the prenatal diagnosis and postnatal treatment of diffuse hypoplasia and calcification of the pulmonary arterial tree in a recipient twin.

Case report

A 39-year-old woman in her third pregnancy was referred for prenatal care because of discovery of a monochorionic diamniotic twin gestation, complicated by severe twin-to-twin transfusion syndrome. Ultrasonic examination at 20 weeks gestation revealed hydramnios, with ascitis, circumferential pericardial effusion, ventricular dilation, and tricuspid insufficiency in the recipient twin (Fig. 1). The examination of the donor twin proved normal. Two amnioreductions were undertaken, resulting in disappearance of the pericardial effusion and a decrease in tricuspid regurgitation. Subsequent scans at 25 weeks of gestation indicated development of biventricular hypertrophic cardiomyopathy and pulmonary arterial hypoplasia. The diameter of the right pulmonary artery was measured at 1 millimetre, with parietal thickening and hyperechogenicity. No fetal hydrops or right ventricular failure was observed at this stage. A caesarean section was performed at 33 weeks of gestation. No signs of dyspnea or cyanosis were observed, and arterial saturation of oxygen in room air was 96%. Blood tests, including analyses for calcaemia and phosphoraemia, were normal. Serial cardiac ultrasonic assessments showed regression of the cardiomyopathy, but confirmed hypoplasia of the pulmonary trunk, showing parietal mural thickening and hyperechogenecity. The estimated systolic right ventricular pressure was suprasystemic. The child had a left-to-right shunt through the arterial duct, giving

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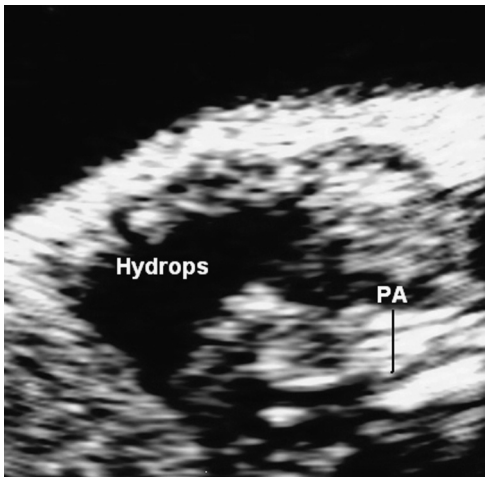

Figure 1.
Fetal cross-sectional echocardiography showing fetal hydrops with pulmonary hypoplasia and pulmonary mural hyperechogenecity. PA: pulmonary trunk.

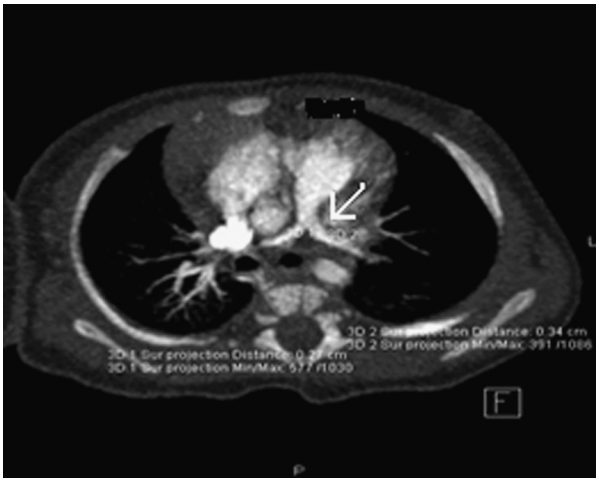

Figure 2.
Cardiothoracic spiral scan showing diffuse pulmonary arterial hypoplasia, extending from the trunk to the segmental arterial branches, as well as hyperdense images within the arterial walls. The arrow shows the left pulmonary artery.

evidence of a significant obstruction between the right ventricle and the distal pulmonary arteries, and a bidirectional shunt at the atrial level through the oval fossa. A cardiothoracic spiral scan showed diffuse pulmonary arterial hypoplasia, with circumferential mural calcifications. Given the extent of these lesions, therapeutic options, especially surgical ones, were limited. Treatment with bosentan (Tracleer®) at 2 mg/kg twice daily, combined with furosemide, was started on the 14th day after birth. The child developed well, and was discharged when aged one month. Subsequent monthly follow-up visits showed that he had gained weight regularly, developing no signs of cardiac failure. Levels of saturation of oxygen measured peripherally, however, decreased progressively to 80%, with an exclusive right-to-left atrial shunt. A second cardiothoracic scan was performed when the patient was aged six months, in the absence of parental consent for an angiographic examination. This scan showed no change in pulmonary hypoplasia, which extended from the trunk to the lobar and segmental arterial branches. The left and right pulmonary arteries measured 2.7 and 2.6 mm in diameter, respectively, while the trunk measured 8 mm in diameter (Fig. 2). At the age of 24 months, a cardiac ultrasound revealed highly elevated right ventricular systolic pressure, measured at 230 mmHg, with tricuspid regurgitation. The pulmonary arteries remained hypoplastic and hyperechogenic. The right ventricle was slightly dilated, albeit in the absence of any systolic dysfunction. Surgical decalcification of the pulmonary arteries was not indicated because of the global extension of the calcification.

Discussion

The occurrence of infundibular or valvar pulmonary obstruction is well documented in recipient twins suffering twin-to-twin transfusion syndrome.[4–6] The underlying aetiology, however, remains unclear. Hypertrophy of the right ventricle occurs to varying degrees in the majority of recipient twins suffering the syndrome. Significant hypertrophy of the infundibular musculature may cause a direct obstruction to the flow of blood to the lungs. Such a decrease in forward flow across the right ventricular outflow tract may then result in diminished growth, causing progression to more severe pulmonary stenosis, or even pulmonary atresia and right ventricular hypoplasia during fetal life. Almost one-tenth of instances of pulmonary stenosis (9.6%) were diagnosed in a series of 73 cases of the syndrome, with the obstruction found at infundibular level in 2, valvar level in 4, and the other showing pulmonary and aortic calcifications.[5] Monitoring in one fetus revealed critical pulmonary stenosis, with retrograde flow through the arterial duct, a finding confirmed on postnatal ultrasound. In this case, the child died when aged less than 2 weeks. Autopsy showed moderate thickening of the pulmonary valvar leaflets, but with significant right ventricular hypertrophy, and severe subvalvar stenosis. To our knowledge, at least 5 other reports of right ventricle hypertrophy, pulmonary valvar stenosis, and tricuspid insufficiency acquired during fetal life have been published, albeit in the absence of subsequent systemic hypertension.[3] Indeed, supravalvar pulmonary arterial stenosis and calcifications in the recipient twin has rarely been described. Saxena and colleagues[6] reported 3 cases of pulmonary arterial calcifications in

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recipient twins. In the first case, the diagnosis of pulmonary and aortic calcifications was made postnatally, and the child underwent successful surgery when aged 4 months. The obstructions were less severe in the other 2 cases. Popek and colleagues[7] reported 3 neonates with calcified pulmonary arterial rings, one being the recipient of twin-to-twin transfusion, this neonate dying 24 hours after delivery. Microscopy of the autopsied pulmonary trunk revealed intimal and medial hyperplasia, with disruption and calcification of the elastic fibres. Nicosia and colleagues[8] reported intimal thickening of the aorta, albeit without calcification, in another recipient of twin-to-twin transfusion. The intimal remodeling may have arisen in response to endothelial injury caused by excessive volume load, and early or premature arterial ageing. Pulmonary arterial thickening and calcification may also result from vascular injury caused by volume overload.

Endothelin-1 is an important growth factor and a potent vasoconstrictor. Its concentrations are known to be increased during fetal life and at birth in recipient twins suffering severe twin-to-twin transfusion.[9] Endothelin-1 exerts its effects on pulmonary and systemic vascular myocytes, and has also been shown experimentally to induce proliferation of fetal ventricular myocytes. The mitogenic and vasoconstrictor effects of endothelin-1 on vascular myocytes may also contribute indirectly to ventricular hypertrophy and hypertension in the recipient twin during the neonatal period. In a large series of cases of the syndrome in which mean levels of endothelin-1 were measured at birth, nonetheless, values were noted to be similar in the donors and recipients.[10] Bosentan, a potent dual antagonist of endothelin receptors, is primarily used for the treatment of pulmonary arterial hypertension. The compassionate use of bosentan in our patient may have enabled clinical stabilization by delaying right ventricular remodeling and insufficiency. Further prospective haemodynamic studies are warranted to elucidate the role of endothelin and other growth factors in the genesis of right ventricular obstructions.

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