Rapid regression of primary pulmonary hypertension

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Abstract
A 14 month old child presented for investigation of tachypnoea. No parenchymal lung disease was shown on chest x-ray. On echocardiography there was normal intracardiac anatomy with significant pulmonary hypertension. At cardiac catheterisation the presence of primary pulmonary hypertension was confirmed, with a partial response to inhaled nitric oxide (80 ppm) and 100% oxygen. The child was referred for assessment for heart–lung transplantation while maintained on oxygen, inhaled nitric oxide, and nifedipine. Repeat cardiac catheterisation two months after presentation showed complete normalisation of the pulmonary artery pressures.

Keywords: pulmonary hypertension; infancy; resolution

CASE REPORT

A 14 month old Latin American girl was admitted with a one week history of tachypnoea. There was no history of previous febrile illnesses, drug ingestion, upper airway obstructive symptoms, obstructive sleep apnoea, or residence at high altitude. There was also no family history of pulmonary hypertension or parenchymal lung disease.

Physical examination showed her to be acyanotic, with a respiratory rate of 40/min, heart rate 110 beats/min, blood pressure 90/45 mm Hg (right arm), and a systemic oxygen saturation of 96% in room air by pulse oximetry. The apex beat was in the fourth intercostal space in the left mid-clavicular line. There was a prominent right ventricular impulse. On auscultation there was a normal first heart sound, a split second heart sound, and an accentuated pulmonary component. There was a II/VI pansystolic murmur, loudest over the epigastrium. The liver was enlarged 2 cm below the right costal margin. The pulses were normal. The chest was clear to auscultation.

An ECG showed normal sinus rhythm with right ventricular hypertrophy. A chest x-ray was normal with no evidence of infiltration or atelectasis. On echocardiography there was normal intracardiac anatomy with a tricuspid regurgitation jet of 4.3 m/s, confirming systemic right heart pressures in the absence of right ventricular outflow tract obstruction. There was right to left bowing of the atrial septum. The white cell count was normal, blood cultures were negative, and antimitochondrial antibodies were negative. Nasopharyngeal aspirates were negative for viral studies.

At cardiac catheterisation the pulmonary artery pressure was at systemic level, at 91/50 mm Hg, and the cardiac index was 1.8 l/min/m². The pulmonary arteriolar resistance measured 26 Wood units in 100% fractional inspired oxygen (FiO₂). This decreased to 13 Wood units in additional nitric oxide, 20 and 40 ppm, and the cardiac index increased to 3.2 l/min/m². There was a slight further drop in pulmonary arteriolar resistance to 11 Wood units on 100% FiO₂, and 80 ppm nitric oxide (table 1).

Wedge angiography in the right lower lobe showed a decrease in supernumerary vessels during the early arterial phase, consistent with a vasoconstrictive pattern (fig 1A). There was a normal capillary blush around each vessel during the late arterial–capillary phase (fig 1B). A blade atrial septostomy was performed using a 9.4 mm Park blade in two planes through the atrial septum and this communication was inflated twice with an 8 mm balloon. There was an acute drop in systemic saturation to 84% post-septostomy on room air. The systemic saturation later fell to 40%, so the patient was maintained on 100% FiO₂ and 5 ppm nitric oxide. The administration of nifedipine
study showed a median survival of 2.8 years from time of diagnosis (95% confidence interval 1.9 to 3.7 years), with survival rates of 68% at one year, 48% at three years, and 34% at five years. Rapidly progressive pulmonary hypertension may, however, occur in paediatric patients, death being reported as early as six months after the onset of symptoms.7

The underlying aetiology remains poorly understood and necropsy examination invariably reveals a normal lung parenchyma, the disease being limited to the small muscular pulmonary arteries. These changes are not pathognomonic, occurring in Eisenmenger’s syndrome and scleroderma.4 To date, vasoconstriction has been the primary underlying mechanism proposed, with medial hypertrophy the predominant reported pathological finding in younger patients.6 This has been supported by an often dramatic response to calcium channel blockers and by an association with Raynaud’s phenomenon in up to 10% of female patients with primary pulmonary hypertension.7

Our patient was asymptomatic for her first 14 months of life and her pulmonary hypertension resolved within two months of its onset. To our knowledge this is only the third case in which “spontaneous” resolution of primary pulmonary hypertension has been described, previous cases having been reported by Bourdillon and Oakley,5 and by Fujii and colleagues.7 The authors of those reports speculated that the resolution of the disease may have been mediated by changes in growth factor or hormone concentrations, as in both cases resolution occurred in conjunction with puberty. Our case, however, appears to be the first in which resolution has occurred before puberty.

In conclusion, we present a very rare case of rapid regression of primary pulmonary hypertension in childhood, occurring significantly earlier than in the two previously reported cases. Whether resolution occurred spontaneously or secondary to treatment with nitric oxide and calcium channel blockers remains an unanswered question, but the rapidity of resolution was nevertheless striking.

Discussion

Primary pulmonary hypertension is associated with significant morbidity and mortality, with the highest mortality in infants and African American women.1,2 One large multicentre

Figure 1  (A) Wedge angiography in the right lower lobe with early arterial phase showing a decrease in supernumerary vessels. (B) Late arterial–capillary phase showing normal capillary blush around each artery.

(2.5 mg sublingually) during the catheterisation failed to reduce the pulmonary arteriolar resistance any further than 80 ppm nitric oxide.

The patient was anticoagulated with warfarin (coumadin) and referred for evaluation for heart–lung transplantation seven weeks after diagnosis on nifedipine (1 mg/kg six hourly orally), nasal continuous airways positive pressure (CPAP), and nitric oxide 5 ppm. Two months after the initial presentation she was weaned from CPAP and nitric oxide but continued on nifedipine (1 mg/kg six hourly orally). Repeat cardiac catheterisation showed complete normalisation of pulmonary arterial pressures, with a main pulmonary artery pressure of 25/10 mm Hg (mean 16 mm Hg) and a persistent mild elevation of pulmonary arteriolar resistance (4 Wood units).

Six months after initial presentation she was asymptomatic with a normal physical examination. A repeat echocardiogram showed spontaneous closure of the atrial septal defect and complete resolution of the pulmonary hypertension.