Premature infants with bronchopulmonary dysplasia (BPD) are at increased risk of developing pulmonary hypertension (PH). The incidence of PH ranges from 18 to 37% with an associated mortality of 50 to 80% within 3 years of diagnosis. Presence of an atrial septal defect (ASD) or a patent ductus arteriosus (PDA) in these infants poses a therapeutic dilemma. If untreated, these communications expose the pulmonary arterial bed to increased flow and may accelerate the adverse pulmonary vascular remodeling and thus worsen PH. Conversely, closing these communications in the presence of PH may result in acute right ventricular (RV) failure with subsequent PH crisis. Here, we describe two premature infants with pulmonary hypertension who developed acute pulmonary hypertensive crisis after closure of these shunts and hence advise caution.

Case Report 1

Baby boy P was born at 27 weeks’ gestation, weighing 675 g. Pregnancy was complicated by severe preeclampsia, fetal intrauterine growth restriction and lobar holoprosencephaly. Hospital course included development of severe BPD (need for ≥30% supplemental oxygen at 36 weeks’ postmenstrual age), large PDA, cholestasis, and hypothyroidism. At 4 months of life, he developed respiratory failure from a viral pneumonia; at that time his echocardiogram showed a large PDA with PH (bidirectional shunting at PDA, flattening of interventricular septum, and an estimated RV systolic pressure [eRVSP] of 45 mm Hg). He was initially treated with mechanical ventilation with 100% O2, inhaled nitric oxide (iNO) and subsequently transitioned to Sildenafil. His respiratory status improved and was weaned to a nasal cannula (NC). One month later, on 25% NC, his echocardiogram showed a PDA with bidirectional shunting, estimated pulmonary artery (PA) pressure of 76 mm Hg (based on PDA gradient) with a hypertrophied RV and normal systolic function (fractional area change [FAC] of 39%). The decision was made to obtain a cardiac catheterization at 6 months, which on 21% O2 showed a large PDA with a left-to-right shunt (Qp:Qs of 4.2:1), systemic PA pressures, and PVR of 3 Wood units. PDA was closed with an Amplatzer (St. Jude Medical, Plymouth, Minnesota, United States) vascular plug and post closure had half systemic PA pressures. After the procedure, he remained stable on 25% O2 via NC, but 7 days later, he developed acute respiratory deterioration and PH crisis. Echocardiogram showed a small PFO with right-to-left shunt, systemic RV systolic pressures, and poor RV...
systolic function (FAC of 14%). Despite increasing PH treatment and RV support with iNO, Sildenafil, inotropes, and milrinone, he expired.

Case Report 2

Baby boy T was born at 26 weeks’ gestation, weighing 780 g. Hospital course was complicated by congenital cutaneous herpes simplex viral infection, prenatally diagnosed supraventricular tachycardia, large secundum ASD, and development of severe BPD. Serial echocardiograms after birth showed a large secundum ASD (range, 8–9 mm) and subsequent evidence of PH (eRVSP > two-thirds systemic at 41 weeks’ corrected age). Sildenafil therapy was initiated with improvement in the follow-up echocardiograms. He underwent ASD patch closure at 7 months of age. His respiratory status improved after ASD closure with weaning off the ventilator to NC, but the echocardiograms continued to show PH, dilated and hypertrophied RV with adequate systolic function (FAC > 35%). One month after ASD closure, he developed acute respiratory failure with worsening PH, RV failure (severe RV dilation with severe systolic dysfunction FAC of 4%), and cardiac arrest. Work up for bacterial and viral infectious etiology was negative. He was resuscitated and treated with inotropes and pulmonary vasodilators (iNO, Sildenafil, intravenous prostacyclin, and milrinone). His PH and RV function improved gradually over the next 3 weeks. He was discharged home at 11 months of age with O2, sildenafil, and diuretic therapy. He continues to be well at 18 months of age without further exacerbations.

Discussion

Closure of left-to-right shunts in premature infants with BPD and PH poses a dilemma. PH in these infants is because of both hypoxia-induced structural changes and increased vasoreactivity.6–9 Echocardiogram is commonly used to screen for PH, but it correlates poorly with cardiac catheterization especially in estimating the severity.10 Although the structural component could be evaluated during studies at baseline, vasoreactivity to acidemia and hypoxemia could be underestimated. In our first patient, measurements obtained during cardiac catheterization with sedation, mechanical ventilation, and arterial pH of 7.5 and PO2 of 40 torr could have underestimated the vasoreactivity component. Infants with BPD are prone to acute exacerbations of their pulmonary disease.11,12 These exacerbations may worsen the PH and if severe can result in acute RV failure as happened in our patients. The presence of a left-to-right conduit may act as a pop off for the RV during such episodes and prevent acute RV failure. But when the pulmonary pressures are sub systemic, patients with left-to-right shunts may benefit from closure of such shunts by preventing pulmonary edema and adverse pulmonary vascular changes from increased pulmonary blood flow.13 Experience with closing such shunts in the presence of PH in infants with BPD is limited. A staged approach by optimizing pulmonary vasodilator therapy before PDA closure and a balloon test occlusion at cardiac catheterization has been suggested.14 del Cerro et al reported their experience with closure of PDAs and ASVs in infants with BPD and PH. In their cohort of five PDA closures, three required prolonged treatments for PH after closure and in five cases with ASD, two spontaneously closed and one not closed because of severe PH. They reported two sudden deaths, one who had undergone aortopulmonary collaterals closure and another with spontaneous ASD closure.15 Andrews et al reported a case of ASD closure in an infant with PH who required a patch fenestration to be able to come off bypass.5 Atrial septal fenestration was considered in both of our patients, but it was not performed.

With current data, we cannot estimate which BPD patients will benefit from closure of left-to-right shunts. However, if PH is well established, there is a potential association between closure of these shunts and RV failure. Because death is possible in the event of a severe PH crisis, caution is advised.

References

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