Persistent pulmonary hypertension of the newborn (PPHN) due to aseptic thrombotic endocarditis: a rare but potentially treatable disorder
This male term infant was delivered by elective Caesarean section after an uneventful pregnancy. The Apgar scores were 8, 9, 9 at 1, 5 and 10 minutes, respectively. Arterial cord pH was 7.13. Birth weight was 3150 g. He rapidly developed profound respiratory distress leading to intubation and mechanical ventilation. Echocardiography ruled out structural heart disease but revealed pulmonary hypertension (tricuspid valve regurgitation with a pressure gradient of 60 mmHg) with right-to-left-shunting across the patent ductus arteriosus and the foramen ovale. In addition, there was marked mitral valve insufficiency despite proper performance of the left ventricle. The mitral valve itself appeared fragile and not malformed. There was no parenchymal lung disease on chest X-ray and sepsis was ruled out. PPHN was initially treated successfully with inhaled nitric oxide (iNO) and cardiovascular support. On day 2 of life, pulmonary hypertension again worsened with suprasystolic pulmonary pressure on echocardiography. The mitral valve was now heavily thickened and its function was severely impaired (Fig. 1). Marked thrombocytopenia and coagulopathy developed and thrombotic heart disease was suspected. Despite intensive care therapy including maximum circulatory support, high frequency oscillatory ventilation, administration of iNO and additional pulmonary vasodilator therapy with sildenafil and prostacyclin, the infant deteriorated further and died on the 3rd day of life before systemic lysis with recombinant tissue plasminogen activator (rt-PA) was initiated.
Post mortem examination revealed aseptic thrombotic endocarditis of the mitral valve (Fig. 2) and multiple thromboemboli in the small pulmonary arteries (Fig. 3). There was no evidence systemic microembolism.

_Echocardiography on day 2 of life: marked thickening of the mitral valve (arrow heads; A) mitral valve closed, B) mitral valve open)._
Verrucous transformation of the mitral valve (arrows).
Thrombotic material (asterisk) on the mitral valve (H&E stain).
Thrombotic endocarditis is rarely diagnosed in the neonatal period. If present, the right side of the heart is predominantly affected, either due to ventricular dyskinesia after perinatal asphyxia, true septic endocarditis, intracardiac location of central lines or rare congenital endocardial lesions (1-4). Already more than 25 years ago, Morrow and colleagues have described thrombotic endocarditis and widespread microembolism (including the small pulmonary arterial vascular bed) at autopsy of newborn infants who succumbed to persistent fetal circulation (5).

In our patient, PPHN was refractory to multimodal pulmonary vasodilator therapy most likely because of widespread microembolism into the pulmonary arterial vascular bed combined with profound functional impairment of the thrombotic mitral valve. We speculate that the combination of mitral regurgitation and bidirectional atrial shunting was responsible for selective pulmonary microembolism.

In our patient, none of the known predisposing factors for aseptic thrombotic endocarditis could be elucidated: pregnancy was reported to have been uneventful, particularly without any substance abuse or inappropriate medication. Intrauterine development seemed undisturbed without any evidence for episodes of intrauterine asphyxia. The ductus arteriosus did not close prematurely but was found patent at birth. Congenital endocardial malformations as well as septic
endocarditis were both ruled out at autopsy. Finally, maternal evaluation for hereditary or acquired thrombophilias revealed heterozygosity for APC resistance (Factor V Leiden), however, this mutation was not found on postmortem examination in our patient.

In conclusion, in the presence of PPHN refractory to standard vasodilator therapy, the possibility of thrombotic endocarditis with pulmonary microembolism should be considered. If confirmed on echocardiography, systemic lysis with rt-PA is a promising therapy and should be initiated without delay (6, 7).


