Systemic Sirolimus: a new era for pulmonary veins stenosis treatment?

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Introduction: Pulmonary veins stenosis, though rare, represents a challenging condition. Even when prompt surgical or percutaneous intervention is performed, early and symptomatic recurrence is often observed, with progressive and potentially fatal decline of clinical status. However, researchers are testing new pharmacological therapies, systemically or through drug-eluting stents administrated, in order to improve overall survival. We describe a case of an infant in which percutaneous intervention followed by systemic sirolimus medication ameliorated short-term prognosis.

Case description: A male baby was born at 30+5 weeks of gestational age of twin pregnancy by urgent caesarean section, due to IUGR condition. Jaundice and preterm anaemia characterized neonatal period and X-ray showed progressive bronchodysplasia. The baby needed non-invasive ventilatory support with low levels of oxygen supplementation, for his first 3 months of life. At 2 months old, he reported cardiorespiratory depression requiring cardiopulmonary resuscitation. After this episode, he remained hemodynamically stable for the following period. Screening echocardiography documented spontaneous arteriosus ductus closure, ostium secundum atrial defect with left-to-right shunting and, by the 4th month of life, gradual onset of indirect signs of pulmonary artery hypertension with right chambers' dilatation (Figure 1) and progressive development of three pulmonary veins stenosis. Sildenafil treatment was set up, then the infant was transferred to our centre at 6 months of age with high flow ventilatory support. Our first assessment confirmed the diagnosis of severe pulmonary veins stenosis with pulmonary artery hypertension (mean pressure of 50 mmHg detected through pulmonary regurgitation). The baby underwent cardiac catheterization under general anaesthesia and intubation. Post-capillary pulmonary artery hypertension, severe stenosis of left superior, right superior and right inferior pulmonary veins were documented and treated through multiple angioplasties, with both conventional and sirolimus drug-coated balloons (Figure 2). Severe bradycardia and desaturation temporally complicated the procedure, but subsequent respiratory and hemodynamic stability was obtain. Post-procedural echocardiography showed successful reduction in pulmonary veins gradient and a mean pulmonary artery pressure of 23 mmHg. Sildenafil treatment was withdrawn, whereas systemic sirolimus administration at the doses of 0,05 mg/kg was started and, as blood chemical tests were in range, it was titrated to 0,07 mg/kg. The following course was uncomplicated and subsequent echocardiography confirmed the persistence of optimal post-procedural result. No more episodes of cyanosis or hemodynamic failure occurred. The patient was discharged with loop diuretic and sirolimus medications. CT scan angiography was scheduled at follow-up.

Conclusions: Despite the natural predisposition to severe recurrence of pulmonary veins stenosis, aggressive combination of interventional treatment and target therapies against neo-intimal and myo-fibroblast proliferation may slow the progression of the disease and improve short-term prognosis. However, major evidence regarding the real efficacy on long-term outcomes is still lacking, and larger studies are further required.

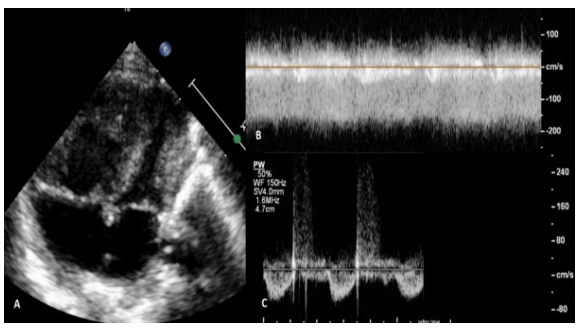

Figure 1. A. Right chambers' dilatation with signs of pressure overload.[X1] B. Pulmonary veins' CW Doppler. C. Pulmonary artery PW Doppler.

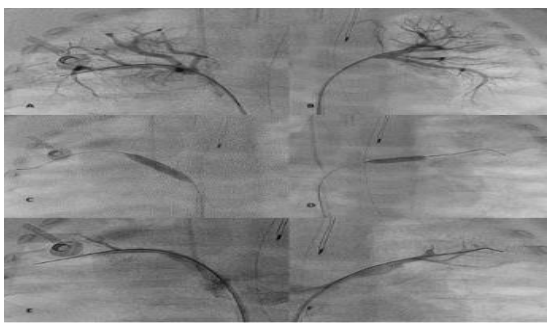

Figure 2. Pulmonary veins angiography and subsequent angioplasty through conventional and drug-coated balloons.