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Intrauterine Pompe disease

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Introduction. Pompe disease is a rare autosomal recessive disease, caused by the lack of acid maltase, which is responsible for an increase in the lysosomal storage of glycogen. In children it causes heart failure, cardiac hypertrophy, and arrhythmias. Prenatal onset is very rare. We report the case of a child affected by Pompe disease presenting in uterus with hypertrophic cardiomyopathy in a decompensated dilated phase.

Case description. The case is that of a second-child male born prematurely at 34 weeks+4 days of pregnancy through an emergency C-section performed for hydrops fetalis, polyhydramnios and abnormal cardiotocographic monitoring. At birth the weight was normal (3500g), the patient presented with cardiorespiratory depression (Apgar 3 at 1 minute and 7 at 5 minutes), which required intubation. Cardiac evaluation showed biventricular hypertrophy and prominent trabeculations at the apex and the free wall of left ventricle, which was dilated and showed an EF of 35%. Moreover, the patient had moderate to severe mitral and tricuspid insufficiency with pulmonary hypertension (PASP 90 mmHg). Furosemide was administered (1mg/kg/day), with the addition of captopril (0.1mg/kg TID) in the following days. The patient was able to eat adequately and regularly; a modest generalized hypotonia was observed. No dysmorphic stigmata were noticed. The patient had IgGs anti-SARS-CoV-2 (but no IgMs), secondarily to the previous infection of the mother during the fifth month of pregnancy. Due to an increase in cytolytic enzymes (CPK 698 U/L - nr 46-171; LDH 503 U/L - nr 158-234; myoglobin 261ng/ml - nr <110), the suspicion of metabolic disease was raised. Two pathogenic mutations were found in the GAA gene: c.2238G>A; c.1465G>A; p.(Trp746Term); p.(Asp489Asn). The patient was CRIM positive. At 18 days of life, enzyme replacement therapy (ERT) was administered in a protected environment because of the unstable hemodynamic status of the patient, after immunomodulation with methotrexate and premedication with paracetamol and chlorphenamine. In the first three cycles of therapy, during the administration of ERT the hemodynamics worsened, and the dose of furosemide was increased. Blood tests showed an improvement in cardiac function (NT-proBNP 7628 after ERT vs. 11137 pg/ml before ERT). At three months of life, during the fourth cycle of ERT, the patient had acute cardiorespiratory failure and irreversible cardiac arrest.

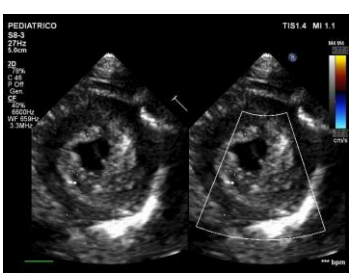
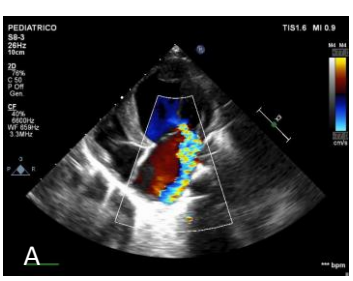


Fig. 1 Severe symmetric concentric LV hypetrophy



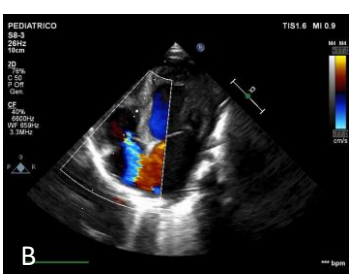


Fig 2. A Severe mitral regurgitation. LV and LA dilation.
B. Moderate tricuspid regurgitation (PASP 90 mmHg)

Conclusion. The patient we report was affected by Pompe disease with intrauterine onset. He had positive anti-SARS-CoV-2 antibodies. The clinical status of the patient was severe, there were adverse events in the course of ERT administration and exitus occurred three months after birth. Seven other cases of intrauterine onset have been reported. The disease onset before birth is rare, and negatively affects the severity and the prognosis, which are worst in comparison to the later onset forms. Today, ERT is the gold standard for treatment of Pompe disease, and if promptly administered it can improve cardiac function. However, in the case we report, it was poorly tolerated perhaps because the disease started prenatally and the baby was preterm. Further studies are needed to assess the prenatal occurrence of Pompe disease, the predisposing causes and to improve its management.