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Mitral Valve Thrombosis in a Neonate: Thrombolysis with rTPA and Unfractionated Heparin

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Abstract

We report on a term neonate with idiopathic left heart Intracardiac Thrombus formation (ICT), mitral valve insufficiency and as a result heart failure. Thrombolysis with recombinant tissue plasminogen activator (Alteplase) and Heparine was performed successfully. ICT dissolved completely without occurrence of severe complications, such as embolism or hemorrhagic complications. Therefore, we suggest consideration of Alteplase for ICT treatment in neonates.

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Introduction

Left intracardiac thrombus formation is a rare complication in neonates. Thrombolysis using Alteplase has been described as a possible therapeutic approach.

Case presentation

We report on the case of a term male born (gestational age 38/0 weeks, birth weight 3380 g, height 51 cm, Apgar scores 9/10/10, umbilical artery pH 7.3) with left Intracardiac Thrombosis (ICT). The pregnancy of his 35 years old mother without known previous disease or medication was uneventful. At 5 hours, the neonate presented with respiratory distress, lethargy, hypotension, episodes of bradycardia and increasing oxygen demand. He required respiratory support including non-invasive and invasive ventilation, as well as surfactant treatment. Due to suspected septicaemia (maximum C-reactive Protein 68 mg/l) the boy received antibiotics and supportive treatment. Correctly positioned venous and arterial umbilical catheters, as well as peripheral catheters were used. Unfractionated heparin

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(UFH, 100 IE/ kg BW and day) was administered from day 1.

An echocardiography on day 2 did not show any abnormalities. ICT was discovered coincidentally during routine follow up intensive care echocardiography on day 5. Echocardiography showed two vegetations on the mitral valve, each measuring 6 x 5 mm (Figure 1) and mitral valve insufficiency. Signs for endocarditis were not observed.

Further aggravation of the clinical situation, including tachycardia, tachypnoea and impairment of the peripheral circulation led to the decision to attempt thrombolysis. Therefore, recombinant tissue plasminogen activator (Alteplase, Actilyse®, Boehringer-Ingelheim, Ingelheim, Germany) was administered. We used a treatment protocol consisting of 0.04 mg/kg/h Alteplase for 24 hours combined with 100 IE/kg/d UFH. UFH was continued for 14 days at 400 IE/kg/d and then adjusted to LMWH (2 mg/kg/d).

4 hours, following initiation of Alteplase infusion D-Dimers increases to a maximum of 18 mgL (normal range 0.11-0.42 mg/l, Figure 2). Echocardiography showed a decreasing size of the thrombi 12 hours after initiation of Alteplase. At 24 hours, the vegetations and mitral insufficiency disappeared completely. Cerebral ultrasound scans were performed before initiation of Alteplase treatment and repeated every 12 hours without any signs of haemorrhage. The patient recovered and was discharged healthy 26 days after birth.

At an age of 2 month, the boy was examined by a pediatric specialist in coagulation disorders. Hemostatic panel as well as genetic tests did not show any abnormalities. Therefore, LMWH treatment was ceased. Follow up examinations; including echocardiography and ultrasound scans at 4,8 and 12 weeks after discharge showed a healthy and normally developed boy without any signs of thrombolysis related complications or reoccurrence of ICT.

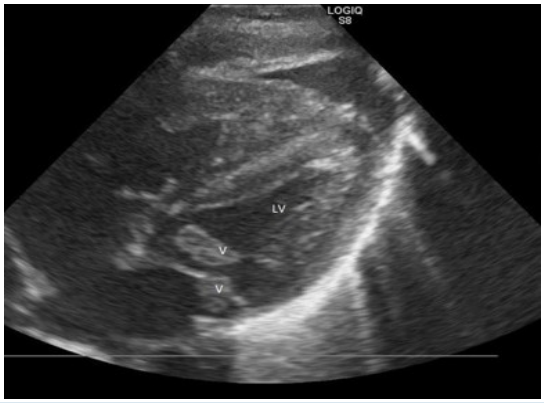

Figure 1: Frozen echocardiography frame of vegetation on mitral valve at start of lysis V- Vegetation on Mitral Valve; LV- left ventricle.

Discussion

ICT is a rare potentially life-threatening complication in neonates with uncertain aetiology. Left ICT may lead to systemic embolization and cause life threatening events, including cerebrovascular events, right heart ICT can cause pulmonary embolism. In most described patients ICT is located in the right atrium and associated with umbilical or central venous lines, ECMO, cardiac surgery and/or sepsis [1,2]. Additionally, neonates, especially preterm infants are at high risk of thrombus formation due to low levels of natural anticoagulants, as well as premature imbalances in their haemostatic systems [3,4].

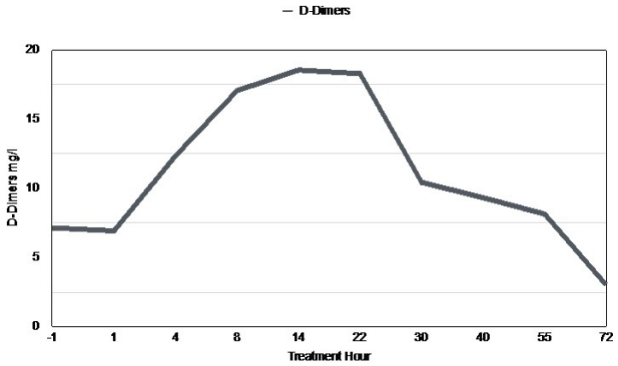

Figure 2: Line graph of D-dimer level against time of lysis in plasma.

Fibrinolysis of thrombus by administration of Alteplase is used as a matter of routine in adults [1]. Because of the enormous risk of severe bleeding, it is discussed controversial in the neonate [1,3,5-7]. Not surprisingly, only few authors report on therapeutic fibrinolysis of ICTs in neonatology [1,5,3,6,8-13]. However, some case reports and series suggest Alteplase as a promising approach to treat ICT in neonates [1,5,8,9,3,6,10,11]. Rimensberger et al. even suggest thrombolytic treatment as first choice treatment for ICT in paediatrics [3]. El-Segaier et al., performed lysis with Alteplase (0.5 mg kg^{-1} h^{-1}) and heparin infusions in six neonates with ICT or thrombi in great vessels and observed complete clot dissolution. In this study thrombus dissolution without complication happened within a median time of 60 h (range 6-72 h) [1].

Unlikely most reported studies our patient presented with a left heart ICT [14]. From our point of view, in our case there is no linking to the central venous line. In addition, further observations did not reveal any disturbance in the coagulation system. So, previous sepsis with cardiocirculatory failure and prematurity as known risk factors for ICT may have contributed to thrombogenesis.

In our patient therapeutic effect of fibrinolysis was mainly monitored by echocardiography and D-Dimers. As noted by other authors both methods are feasible tools to ensure the effectiveness of fibrinolysis. However, possible bleeding complications has to be monitored closely by ultrasound and constant laboratory checks.

Conclusion

The described report confirms the effectiveness and safety of intravenous Alteplase infusion in neonates with ICT. This case report requires further investigations, observations and tests to validate the safe use of tissue plasminogen activator in neonates.

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