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ADVANCED

CASE REPORT: CLINICAL CASE

Catheter-Guided Dissolution of a Giant Thrombus in the Left Ventricle in a Newborn

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ABSTRACT

A newborn with pulmonary hypertension due to the premature fetal arterial duct occlusion was diagnosed with a giant left ventricle thrombus. Cardiopulmonary compromise required multidrug therapy with vasopressors infusions, high-frequency oscillation, and nitric oxide. Alteplase infusion through a guiding catheter into the left atrium dissoluted the clot without sequelae. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2021;3:220–4) © 2021 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 1-day-old newborn was admitted to the Neonatal Intensive Care Unit from a district hospital with symptoms of progressive cardiopulmonary compromise requiring respiratory support.

Physical examination showed symptomatic dyspnea, tachycardia at 170/min, systolic heart murmur of 3/6 in Levine scale, and hepatomegaly. Blood pressure was 50/25 mm Hg with mean arterial pressure of 34 mm Hg.

LEARNING OBJECTIVES

- To make a differential diagnosis of thrombus formation in newborns.
- To consider early r-TPA infusion in LV thrombus threatening arterial stroke.

MEDICAL HISTORY

The medical history revealed diet-controlled maternal gestational diabetes mellitus. The newborn was delivered at 37 week's gestation via Caesarian section due to fetal transverse lie, weighing 3,470 g, scoring 8-8-9-9 points in Apgar scale at 1-3-5-10 min of life, respectively. Prenatal ultrasonography did not reveal any abnormalities.

Within the first hours of life the condition decreased rapidly requiring urgent mechanical ventilation for cardiopulmonary failure.

DIFFERENTIAL DIAGNOSIS

An initial diagnosis of a cyanotic congenital heart defect was established and prostaglandin E_1 infusion commenced. In differential diagnoses, pulmonary hypertension with severe respiratory distress was

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considered as well as sepsis, metabolic disorders, and intracranial hemorrhage.

INVESTIGATIONS

Pulsoximetry showed significant desaturation of 80% despite oxygen delivery. Arterial blood gasses with low pO_2 (38 mm Hg) and high pCO_2 (57 mm Hg) signaled progressive pulmonary failure, however, chest X-ray revealed normal lung fields and cardiomegaly. Cardiac monitoring showed tachycardia with P waves preceding narrow QRS complexes. Bilateral thalamic vasculopathy without hemorrhagic features was found on cranial ultrasound. Transthoracic echocardiogram (TTE) excluded congenital heart defect and displayed a dilated right atrium (RA), severely hypertrophied right ventricle (RV), right-to-left shunt via patent foramen ovale (FO), and tricuspid regurgitation with a pressure gradient of 90 mm Hg, indicating pulmonary hypertension with suprasystemic RV pressure. The heart chambers were free from clots. Alprostadil was stopped upon noticing an occluded arterial duct despite continuous infusion.

MANAGEMENT

Complex treatment began with respiratory support (High Frequency Oscillation Ventilation), oxygen delivery, nitric oxide (20 ppm), surfactant, empirical antibiotics (ampicillin and gentamycin), vasopressors, and inotropic infusions (dopamine, norepinephrine, dobutamine, and milrinone) due to hypotension. The neonate's condition gradually improved.

Subsequent TTE at 72 h revealed a massive intracardiac 18 mm x 4 mm thrombus in the left ventricle (LV) apex (**Figure 1**, Videos 1 to 3). A second large thrombus lay within the ductus venosus and left hepatic vein along the central catheter introduced through the umbilical vein (**Figure 2**).

Hemodynamic calculations showed moderate tricuspid valve regurgitation recording a pressure gradient of 32 mm Hg (the systemic pressure was 62/40 mm Hg). The interventricular septum deviated toward the LV with diminished end-diastolic volume and preserved contractility (ejection fraction 65%).

To differentially diagnose thrombus cause, laboratory tests were analyzed with coagulation assay and all results lay within the reference range (RR): Protein C 51.2% (RR: 28% to 54%), antithrombin III 77% (RR: 41 to 95), fibrinogen 3.16 g/l (RR: 1.5 to 4.5 g/l), activated partial thromboplastin time 27 to 33 s (RR: 33 to 50 s), and international normalized ratio 1.09 (RR: 0.98 to 1.32). However, significantly elevated D-dimers 13,537 μg/l (RR: 200 to 1,200 μg/l) and procalcitonin 4.39 ng/ml (<0.05) suggested thrombolysis or infection, yet C-reactive protein remained low at 1.6 mg/dl (RR: 0.0 to 1.0 mg/dl).

The child was qualified for catheter-guided alteplase infusion at 0.1 mg/kg/h without concomitant heparin. To commence, a 3-F central catheter was inserted into the right jugular vein for multidrug therapy and the umbilical catheter removed.

A 5-F sheath was introduced into the right femoral vein. Hemodynamic evaluation recorded low superior vena cava SaO_2 (60%), elevated central venous pressure (mean = 5 mm Hg), and high RV pressure (47/13 mm Hg). A multipurpose 4-F guiding catheter was traversed through the FO into the left atrium (LA) (**Figure 3**).

During the procedure atrial flutter appeared with heart rate of 230 beats/min requiring amiodaron infusion (5 mg/kg) and finally effective synchronized cardioversion (0.5 J/kg).

Using TTE we confirmed the position of the catheter tip in the LA and the clot in the LV before alteplase infusion (**Figure 4**). The thrombus diminished gradually and within 15 h completely dissolved (**Figure 5**, Videos 4 and 5).

Thromboembolism was sonographically excluded in major systemic arteries (anterior cerebral, basal, carotid, subclavian, celiac, mesenteric, kidney, and femoral) with normal color and pulse wave doppler flows. Alteplase was stopped and heparin infusion continued at 10 U/kg/h. Three days later prophylactic fraxiparin commenced for 14 days.

ABBREVIATIONS AND ACRONYMS

FO = foramen ovale

LA = left atrium

LV = left ventricle

RA = right atrium

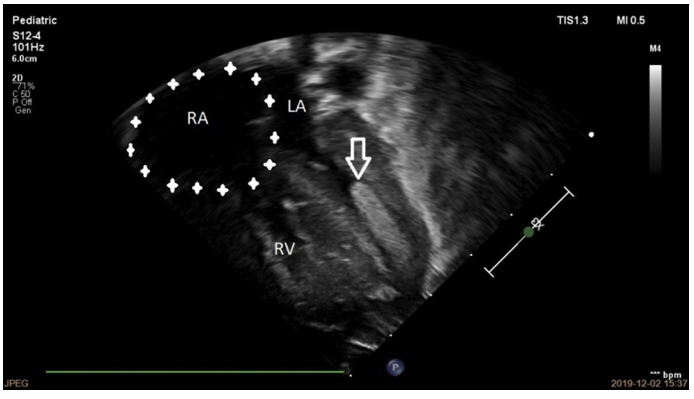
RR = reference range

rTPA = recombinant tissue plasminogen activator

RV = right ventricle

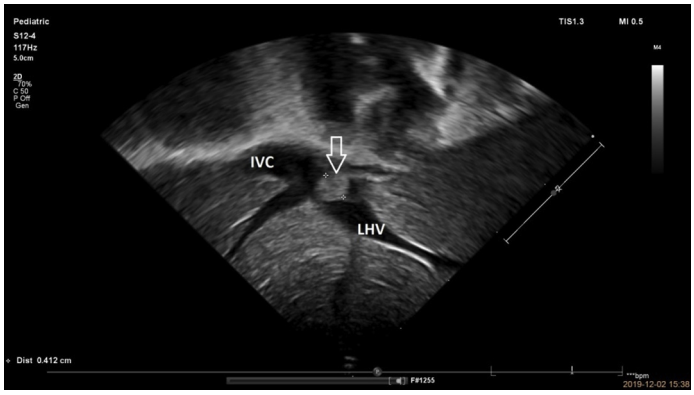
TTE = transthoracic echocardiogram

FIGURE 1 Transthoracic Echocardiogram: 4-Chamber View



A giant (18 mm × 4 mm) thrombus **(arrow)** in the left ventricle. Dilated right atrium **(stars)**, severe right ventricle hypertrophy. LA = left atrium; RA = right atrium; RV = right ventricle.

FIGURE 2 Transthoracic Echocardiogram: Subcostal View, Dilated Inferior Vena Cava and Hepatic Veins

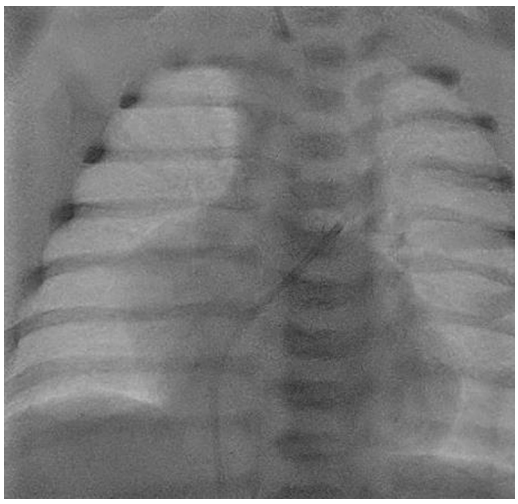


A large 4-mm thrombus **(white arrow)**. IVC = inferior vena cava; LHV = left hepatic vein.

The vasopressor dosages, nitric oxide, and diuretics were tapered then stopped whereas sildenafil was continued at 1 mg/kg every 8 h. In subsequent TTE, the RV and RA remained enlarged although LV end-diastolic volume improved.

The FO now showed left-to-right shunt with first degree tricuspid regurgitation. The flow through the pulmonary valve was normal with ratio of acceleration time to ejection time 0.49 The patient improved and at 24 days was discharged home in good condition.

FIGURE 3 Chest X-Ray



Antero posterior view. Multipurpose 4-F catheter in the left atrium.

DISCUSSION

Over recent decades our expanding knowledge has further recognized the incidence and causes of thrombosis in neonates. Thromboembolic events are rare complications in the newborn period. Clots are usually found incidentally during TTE screen, which is the gold standard for the diagnosis. Computed tomography or magnetic resonance imaging are also useful, but require general anesthesia. The majority of children with clots fulfill Virchow's triad (hypercoagulable conditions, endothelial damage, and abnormal venous or arterial flow); upon thrombus formation, they easily embolize when mobile or pedunculated (1–4).

Thromboembolic events in venous circulation are mostly due to central catheters or cardiopulmonary compromise with congestion and may lead to pulmonary embolism. In rare cases paradoxical embolism is possible when the FO or ventricular septal defect provides right-to-left shunt.

The clots may also appear in the LA appendage (secondary to tachyarrhythmias; e.g., atrial flutter or fibrillation) or the LV (in ischemic endothelial damage with poor myocardial contractility).

In the presented case the most probable cause of the clot formation included cardiopulmonary compromise due to pulmonary hypertension with LV compression and venous congestion as well as central venous catheter obturating the venous flow. The final

diagnosis was established in TTE with consistent features of premature intrauterine arterial duct closure: absence of ductal color doppler flow, RV hypertrophy with fibroelastotic papillary muscles, RA enlargement, patent FO with right-to-left shunt, and tricuspid valve regurgitation with increased pressure gradient.

The natural course described in the literature, whether asymptomatic or with cardiopulmonary compromise, depends on time and degree of arterial duct stenosis or complete obliteration (5,6). Persistent volume and pressure overload in the pulmonic arteries causes endothelial and media thickening with compromising vessel compliance. This may lead to long-standing pulmonary hypertension requiring complex therapy as in the presented case with respiratory support, oxygen delivery, pulmonary vasodilators (nitric oxide, sildenafil), inotropes, diuretics, and, in extreme cases, extracorporeal membrane oxygenation as a bridge to recovery.

Furthermore, adverse hemodynamics diminish LV end-diastolic volume and cardiac output, which inclines coagulation disturbances and thrombus formation.

Classic systemic treatment of the thrombus is with heparin infusion then warfarin for high-risk thromboembolism; larger obturating clots demand surgery or interventional therapy.

Our clinicians agreed on an interventional approach with the access through the FO for relatively low-dose recombinant tissue plasminogen activator (r-TPA) infusion (0.1 mg/kg/min) to minimize the risk of hemorrhage. This was based on our clinical experience without a preceding loading-dose bolus, although the guidelines recommend 0.01 to 0.03 μg/kg/h for targeted thrombolysis with concomitant heparin infusion (7). The dilemma between rapid, direct clot disintegration and the well-documented intracranial or pulmonary hemorrhage concerned us, thus balancing the safe and correct r-TPA dose to achieve resolution and abate hemorrhagic risk was vital.

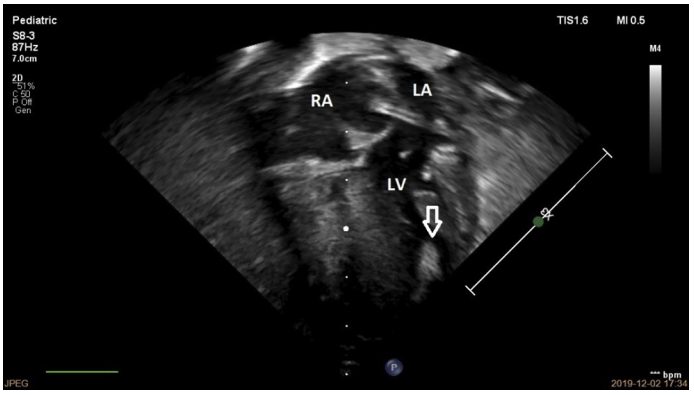
FOLLOW-UP

At 6-month follow-up the baby girl was asymptomatic with New York Heart Association functional class I. TTE showed normal anatomy and heart function without the need for pharmacotherapy.

CONCLUSIONS

Alteplase therapy is widely accepted although with high risk of hemorrhage especially in newborns. This risk may be significantly decreased by lowering the dose and precise delivery via a guiding catheter at the exact thrombosed site. The presented case is an alternative approach for effective treatment of life-threatening thrombi in newborns.

FIGURE 4 Transthoracic Echocardiogram: Subcostal View



Multipurpose 4-F guiding catheter introduced via foramen ovale into the left atrial (LA) appendage. Left ventricle (LV) thrombus **(white arrow)**.

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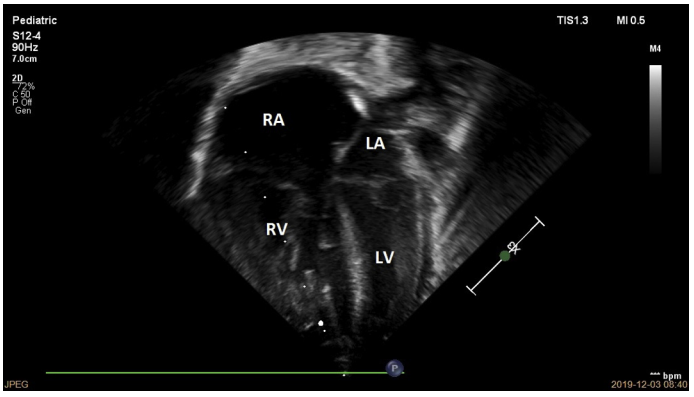
FIGURE 5 Transthoracic Echocardiogram: 4-Chamber View, Total Thrombus Dissolution



Four-chamber view. Total thrombus dissolution. Abbreviations as in Figures 1 and 4.

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KEY WORDS anticoagulation, atrial flutter, left-sided catheterization, pulmonary hypertension, thrombus

APPENDIX For supplemental videos, please see the online version of this paper.