3 A Newborn with a Mass on the Right Ventricle

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PRESENTATION

A male neonate is born at 36 2/7 weeks via vaginal delivery at a level 2 nursery. The mother is a 34-year-old, gravida 8, para 4, aborta 3 woman.

The maternal history is remarkable for chronic hypertension that was treated with labetalol and amlodipine; hypothyroidism that was treated with levothyroxine; and obesity and gestational diabetes that were controlled with diet. Maternal laboratory findings are as follows: human immunodeficiency virus, negative; rapid plasma reagin, nonreactive; hepatitis B, negative; group B *Streptococcus*, negative; blood type, O positive; and antibodies, negative. The mother has not received any medication at the time of delivery. The neonate is born via cesarean section for nonreassuring fetal heart tracing and clear amniotic fluids.

Anthropometric measurements at birth are as follows: weight, 2,740 g (45th percentile); head circumference, 34 cm (77th percentile); length, 45.5 cm (20th percentile); growth status: appropriate for gestational age; Apgar scores, 7 and 8 at 1 and 5 minutes, respectively. The neonate requires positive pressure ventilation for 1 minute after delivery.

On admission to the nursery, the neonate exhibits signs of mild respiratory distress and tachypnea, and is placed on continuous positive airway pressure (CPAP) of 6 cm H_2O with a fraction of inspired oxygen (FIO_2) of 50%; chest radiograph (Fig 1) shows mild ground glass appearance. Because of his worsening respiratory status, the neonate undergoes intubation and is administered surfactant. A few minutes after surfactant administration, the infant's condition suddenly deteriorates, requiring an increase in FIO_2 to 100%. Although the neonate receives maximal ventilator and oxygen support, his oxygen saturation remains under 80%. The presence of a pneumothorax prompts the placement of a left chest tube. He is transferred to a level IV NICU for further management of his condition. At admission, a diagnosis of severe respiratory distress, right pneumothorax, and persistent pulmonary hypertension of the newborn is rendered.

DISCUSSION

On admission, the infant was placed on high-frequency jet ventilation with peak inspiratory pressure (PIP) 40 mm Hg, positive end-expiratory pressure (PEEP) 10 mm Hg, rate of 360 BPM, an FIO_2 of 100%, and inhaled nitric oxide at 20 ppm. A cardiothoracic surgeon was consulted for potential extracorporeal membrane oxygenation.

Maternal and infant platelets were normal on admission. A complete blood cell count 12 hours later showed severe thrombocytopenia (15,000/μL [150$\times$ 10^9/L]); coagulation profile and liver function tests were normal for age; and

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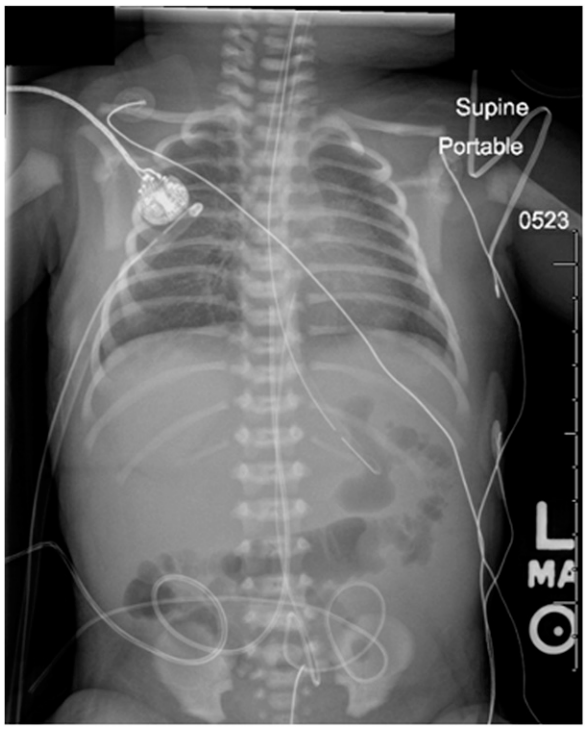

Figure 1. Chest radiography showing mild ground glass appearance.

brain ultrasonography findings were normal. Because of severe respiratory failure and absence of response to maximal respiratory support, echocardiography was requested, which showed 2 masses on the anterior and septal leaflets of the tricuspid valve and pulmonary hypertension with supra-systemic right ventricular pressure and septal bowing (Fig 2). A magnetic resonance imaging of the brain (Fig 3) showed a large area involving encephalomalacia in the posterior right cerebral hemisphere, possibly related to a prior infarction.

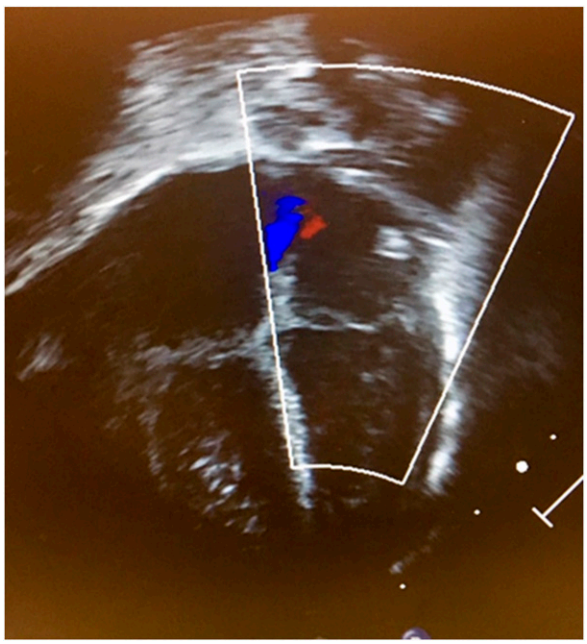

Figure 2. Echocardiogram showing 2 masses on the anterior and septal leaflets of the tricuspid valve and pulmonary hypertension with supra-systemic right ventricular pressure and septal bowing.

Echogenic material from the umbilical line/portal veins (Fig 4) was seen along the course of the umbilical venous line, probably reflecting thrombus. No flow could be elicited within the left portal vein. In addition, arterial flow was prominent in the proximity of the left portal vein, which was likely compensatory. The right and main portal veins were widely patent.

Hospital Course

The neonate was given anticoagulation treatment, and the thrombi started to decrease in size at 72 hours and pulmonary pressures dropped as well. We suspected pulmonary vein thrombosis caused by a decrease of the flow, though echocardiography was not able to show thrombosis. We were not able to perform cardiac catheterization at the time because of the cardiorespiratory compromise first and then the risk of bleeding with anticoagulation treatment. Inhaled nitric oxide was weaned after 48 hours, F_{IO_2} was weaned to 21% on day 5, and the infant underwent extubation on day 8 to receiving nasal CPAP. Feeding started on day 7. The infant was discharged after 2 weeks with subcutaneous low-molecular-weight enoxaparin; he received full feedings by mouth and was stable in room air.

Maternal laboratory findings, placental pathology, and infant sepsis screening were all negative. Testing of the mother for protein C and S deficiency showed normal results.

The Condition

Hyperhomocysteinemia, methylenetetrahydrofolate reductase (*MTHFR*) heterozygote mutation, associated with low protein C and S, severe respiratory distress syndrome, severe pulmonary hypertension, pneumothorax, hypotension, clinical sepsis, metabolic and respiratory acidosis, and placement of central catheters potentially contributed to this overwhelming presentation of multiple venous and arterial thrombosis (cardiac, portal vein, right nonocclusive venous thrombosis in the bilateral sigmoid sinuses of the brain, and encephalomalacia).

Carriers of *MTHFR* C677T/ A1298C are not at increased risk for thrombosis in the absence of hyperhomocysteinemia. (1)(2)(3)(4)(5) However, in the presence of other risk factors (perinatal asphyxia, septicemia, dehydration, and maternal diabetes), venous and arterial thrombosis can occur. (6) The infant described here had mild elevated homocysteine and the *MTHFR* heterozygote

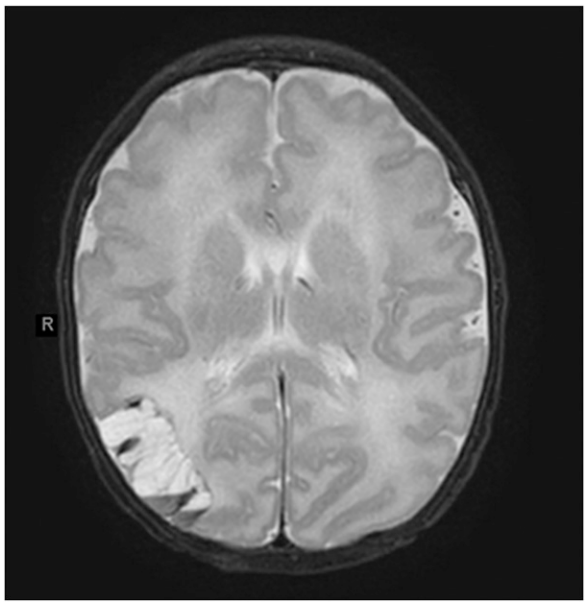

Figure 3. Magnetic resonance imaging of the brain showing a large area of encephalomalacia in the posterior right cerebral hemisphere, possibly related to a prior infarction.

mutation associated with other risk factors for thrombophilia. The single most important risk factor for the development of arterial or venous thrombosis events is an indwelling central catheter, with thrombi commonly involving large vessels. These events are unusual, but their occurrence increases in the presence of coagulation and other risk factors.

At birth, the hematologic system is not fully developed compared with adults. (6) The neonate described here presented with a relatively normal complete blood cell count, and in less than 12 hours, developed severe thrombocytopenia. Coagulation studies were within normal range at that time, with the prothrombin time being 15 seconds, partial thromboplastin time 40 seconds, and

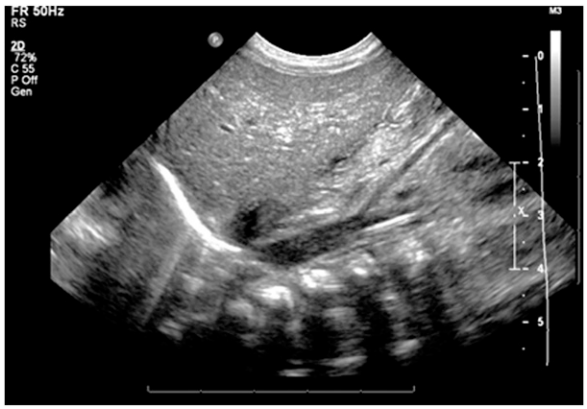

Figure 4. Echogenic material from the umbilical line/portal veins was seen along the course of the umbilical venous line, probably reflecting thrombus.

fibrinogen 150 mg/dL (4.4 μmol/L). Protein C and S activity was low (6% [normal 15%–50%] and 30% [normal ≥ 50%], respectively). The *MTHFR* C677T/ A1298C heterozygous gene mutation on a single allele was detected (heterozygous mutant), and homocysteine level was in the lower limit (6 μmol/L or 0.6 mg/L) (normal <5 μmol/L or 0.5 mg/L). Other tests included β_2-glycoprotein 1 immunoglobulin (Ig) G/IgM (negative), cardiolipin IgG/IgM (negative), factor VIII activity assay (WNL), lupus anticoagulant, protein C antigen 12% (mildly low), protein S antigen 43% (acceptable), and antithrombin III elevated (50 mg/dL [500 mg/L] normal value > 30 mg/dL or > 300 mg/L).

Compared with adults, procoagulant proteins, particularly the vitamin K–dependent and contact factors, are reduced in the term neonate. (7) Although α_2-macroglobulin is significantly increased at birth, inhibitors of coagulation, antithrombin, heparin cofactor II, protein C, and protein S are reduced. (7) The fibrinolytic system also appears different, with plasminogen concentrations around 50% of adult values. (8) Preterm infants have more pronounced variation in these factors. (9)

Management

The infant was given anticoagulation treatment at 48 hours after birth, and his venous and arterial thrombi started to decrease in size with improvement in his clinical condition. Enoxaparin failed to reach the target level of anticoagulation, thus requiring heparin infusion. We theorized that low-molecular-weight heparin absorption was decreased because of severe fluid retention and anasarca. Heparin treatment was associated with mild asymptomatic thrombocytopenia.

Echocardiography and abdominal ultrasonography showed a decrease in the size of the thrombi and improvement and resolution of pulmonary hypertension. On discharge, the patient was switched to enoxaparin, with adequate anti–factor X.

Lessons for the Clinician

- In the context of a critically ill neonate, central catheter placement can be associated with deep venous and arterial thrombosis.
- The presence of a thrombus in a sick neonate should trigger further hematologic evaluation and consultation.
- Management should include heparin infusion with anti–factor X levels within target goals.
- Multidisciplinary management with the inclusion of a hematologist and geneticist should be considered in cases with an abnormal coagulation profile and multiple thrombi.

American Board of Pediatrics Neonatal-Perinatal Content Specifications

- Know the inheritance patterns of the common coagulation factor deficiencies.
- Know the causes and pathophysiology of congenital and acquired thrombotic disorders.
- Know the causes and pathophysiology of congenital defects in hemostasis.
- Know the clinical manifestations, laboratory findings, and management of congenital defects in hemostasis.
- Know the pathogenesis and complications of catheter related thrombi including umbilical arterial and central venous catheters.

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