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Pulmonary Embolism Presenting with Sudden Respiratory Failure
in Two Previously Stable Neonates

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Abstract

Pulmonary artery embolism (PE) is a rare and life-threatening complication in the neonate. We describe two previously stable infants who incurred respiratory failure from PE. The first case is a late preterm infant with gastroschisis with autopsy confirmation of PE presumably as a result of a central venous line (CVL) with thromboembolism. The second case is an extreme low birth weight infant with sudden onset of respiratory failure, abnormal chest x-ray, disseminated intravascular coagulation (DIC), and echocardiographic confirmation of a thrombus at the junction of the superior vena cava and right atrium (SVC/RA) at the site of a previous CVL. This infant was successfully managed with thrombolytic therapy and anticoagulation. We suggest that PE be considered in an infant with a history of a CVL who presents with otherwise unexplained respiratory failure.

Introduction

Neonatal thrombosis occurs in 5.1 per 100,000 births^[1] and 2.4 per 1000 admissions to the neonatal intensive care unit.^[2] Excluding renal vein thrombosis, 45% of cases are arterial.^[2] PE occurs in 0.86 per 10,000 hospitalized children age one month to 18 years.^[3]

This report describes the clinical aspects of two previously stable premature infants with acute onset of respiratory failure from confirmed or suspected PE. One case has autopsy confirmed massive PE with a suspected source of a femoral venous line with venous thrombosis, and the other has presumed PE with echocardiographic evidence of a thrombus located at the junction of the SVC/RA, the site of a previous CVL.

We present these two cases to add to the body of literature on the clinical presentation of PE in the neonate and describe the successful medical treatment in one case.

Case One

A 2070 gram female with gastroschisis and colonic atresia was delivered at our hospital at 34 weeks by dates. After fluid resuscitation, a surgical repair was undertaken. A peripherally inserted central catheter (PICC) was placed for parenteral alimentation on the first day of life. On day of life 14 the PICC was replaced with a right femoral venous catheter. On day of life 39 the infant developed staphylococcus epidermidis sepsis treated with vancomycin through the central line. Doppler ultrasound of the inferior vena cava (IVC), SVC, jugular and subclavian veins showed no thrombus; however, the IVC and SVC were poorly visualized. On day of life 44 a left femoral venous catheter was placed. On day of life 45 swelling and bluish discoloration of the left leg were noted. Superficial veins on the abdominal wall were also more prominent. The femoral line was functioning well with good blood return. X-rays of the left hip and thigh were negative for fracture or osteomyelitis. Repeat doppler ultrasound of the iliofemoral veins and IVC showed no venous thrombus. The edema improved over the next twelve hours. Platelet counts ranged from 115,000-190,000. On day of life 50 the infant suddenly developed hypotension, hypoxemia, and bradycardia. The infant failed to respond to resuscitation and was pronounced dead. At autopsy the contents of the pulmonary artery showed an organized thrombus (Figure 1) characterized by red cells, layering fibrin, and inflammatory cells.



Figure 1. Cross-section through the pulmonary artery containing an organized, fibrous clot.

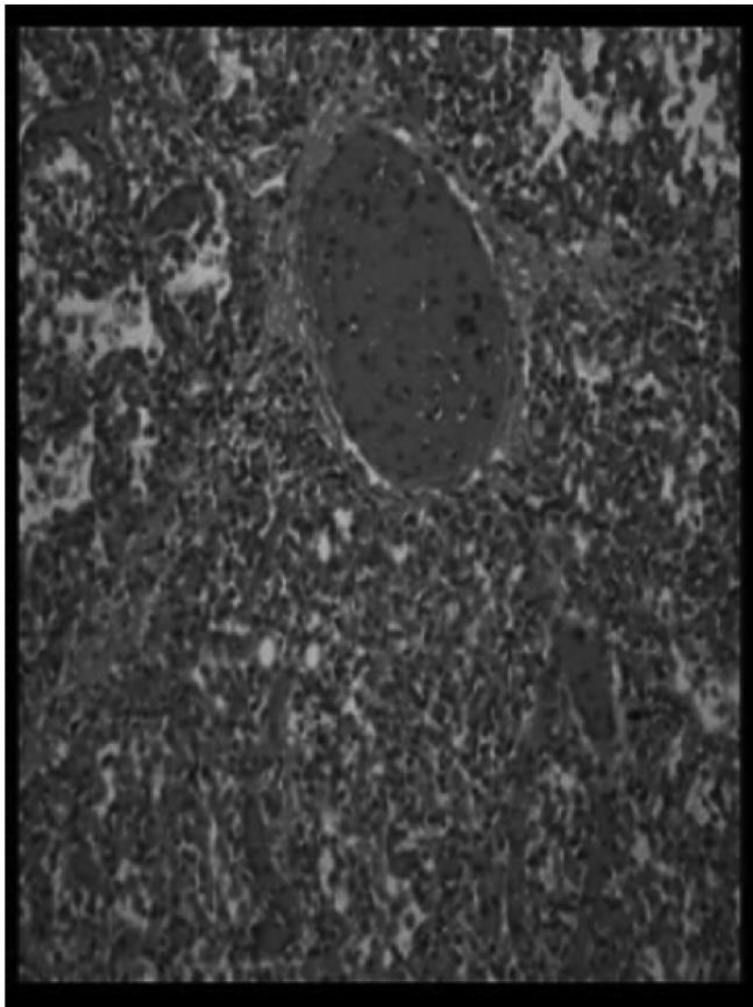


Figure 2. A peripheral lung vessel with an organized thrombus including fibrin and inflammatory cells.

Examination of the lungs revealed multiple microscopic emboli (Figure 2). No thrombophilia work-up was performed.

Case Two

A 740 gram female was delivered at our hospital at 26 weeks gestation by emergency cesarean section for abruptio placentae. The infant was initially managed with nasal intermittent positive pressure ventilation and was weaned to room air on day of life 4. No umbilical line was used. A

PICC was placed on the second day of life and was discontinued on day of life 14 when full enteral feedings were achieved. On day of life 16 the infant developed episodes of apnea and bradycardia requiring intubation and mechanical ventilation. No blood or milk was noted from the endotracheal tube. Chest x-ray showed diffuse bilateral pulmonary infiltrates. Because of worsening hypoxia, inhaled nitric oxide (iNO) was begun. CBC showed a white blood cell count of 4800 and evidence of DIC (platelet count 25,000, PT and PTT prolonged, D-dimer elevated). Platelets, fresh frozen plasma, and intravenous immune globulin were given. There was no fall in hematocrit, an echocardiogram showed a 7x3mm thrombus at the junction of the SVC/RA (Figure 3) corresponding to the position of the tip of the previous PICC.

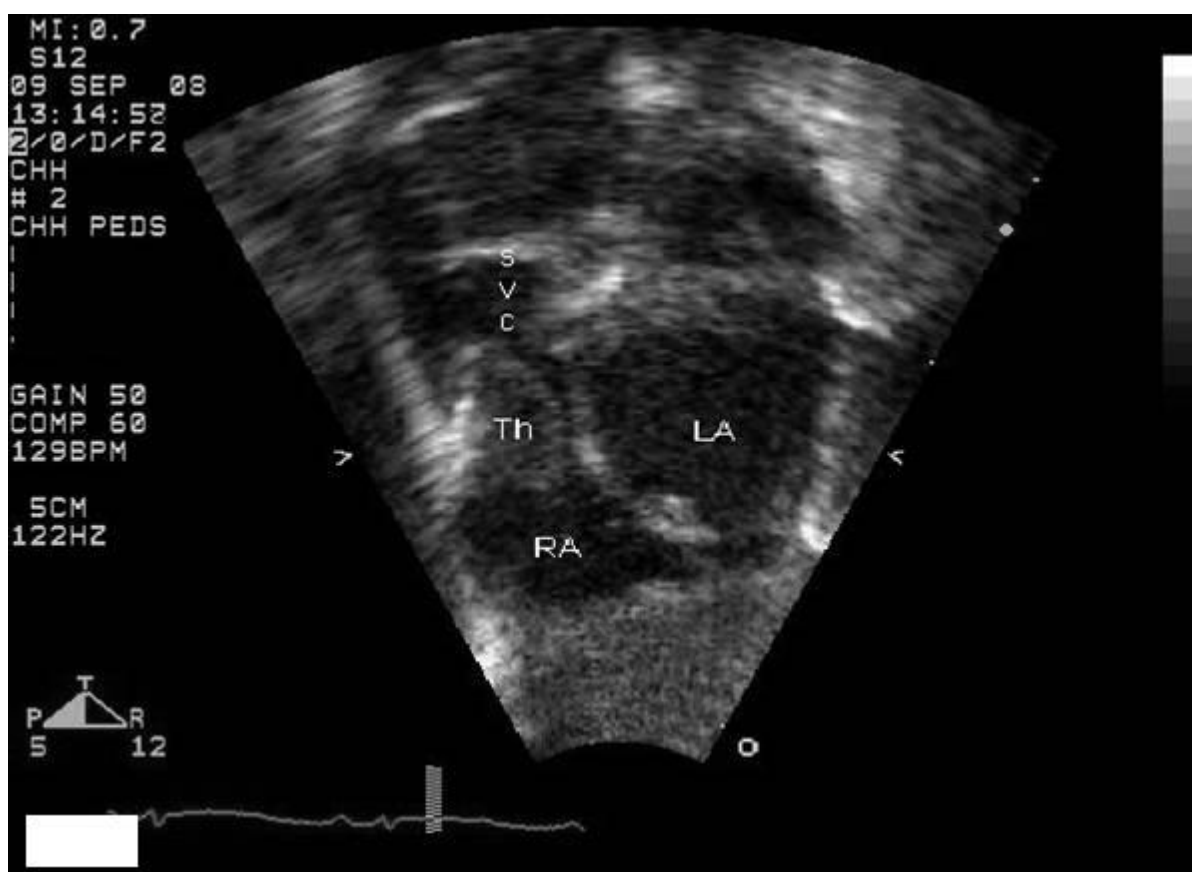


Figure 3. Subcostal sagittal view demonstrating a 7 x 4 mm thrombus (Th) at the junction of the superior vena cava (SVC)-right atrium (RA).

A PICC was inserted 1 cm proximal to the thrombus and tissue type plasminogen activator (t-PA) was administered at 0.2 mg/kg/hour. After 36 hours of t-PA administration, the thrombus measured 3x2mm. The t-PA was discontinued and low-molecular-weight heparin (LMWH) was begun at 2mg/kg SQ q12hours and adjusted to achieve target anti-factor X_a levels of 0.5-1.0 units/ml. No excess bleeding was noted except at venipuncture sites and this was controlled with pressure. Coagulation studies returned to normal. Head ultrasounds showed no intraventricular bleeding prior to or after t-PA administration. On day of life 25 the thrombus measured 1x1mm and the chest x-ray was clear of infiltrates. The LMWH was discontinued. All bacterial, fungal and viral cultures were negative and antibiotics were stopped after 72 hours. The infant was discharged home on day of life 86 weighing 1800 grams with resolution of the thrombus by echocardiogram. Laboratory evaluation at 4 months of age for prothrombotic disorders including Factor V Leiden, protein S, protein C, antithrombin, and prothrombin G20210A were negative.

Discussion

The frequency of PE in the first 30 days of life is unknown, but likely underestimated because clinical features are often masked by a primary respiratory illness. In a review of autopsy cases of PE in childhood, the antemortem diagnosis was considered in only one third of patients.^[4] PE in the neonate can be asymptomatic, mimic congenital heart disease, or present with respiratory failure, right heart failure, or persistent pulmonary hypertension of the newborn.^[5-7] In addition, PE in children has been reported in association with DIC.^[8] We have presented two cases with divergent histories who both presented with sudden onset of respiratory failure from confirmed or suspected PE. In Case One, despite clinical symptoms of venous obstruction, the diagnosis of PE was not considered until autopsy. In Case Two, either pneumonia or pulmonary

hemorrhage was thought to be the most probable diagnosis until an echocardiogram revealed a large thrombus at the SVC/RA junction. While the radiographic appearance of PE in the neonate is unknown, we speculate that the radiographic infiltrates in this case resulted from microthrombi similar to those seen at autopsy in Case One. Both the thrombus and infiltrates resolved with thrombolytic therapy.

89% of neonatal cases symptomatic venous thromboembolism (VTE) in the neonate are secondary to a CVL.^[2] Other reported risk factors include surgery and sepsis as seen in Case One, as well as other risks not seen in our cases including maternal diabetes, prolonged immobilization (with or without the use of paralytic drugs), polycythemia, asphyxia, hypotension, dehydration, closure of the ductus arteriosus, and hypercoagulable disorders.^[1, 2, 9-12, 23]

The standard for diagnosis of VTE is angiography. Doppler ultrasound is less invasive and can be performed at the bedside. In one reported series, however, the accuracy of ultrasound was poor when compared to contrast venography in detecting asymptomatic thrombi.^[13] We presume Case One had a thrombus of the iliofemoral veins or IVC with the observed clinical symptoms of leg discoloration and swelling, as well as prominence of the superficial abdominal wall veins despite two negative ultrasound studies. Because the thrombus found at autopsy in the pulmonary artery was well organized, we speculate that it likely formed over a prolonged period of time before terminally moving to obstruct the main pulmonary artery.

PE has been diagnosed in neonates by echocardiography,^[5-7, 9] cardiac catheterization,^[14] V/Q scan,^[6, 12] and CT angiography.^[6] Cardiac catheterization with angiography is the gold standard for diagnosis of PE and also provides a means for treatment via thrombectomy.^[15]

Optimal therapy for vascular thrombosis in the neonate has not been defined.^[16] Reported options include anticoagulation with heparin or LMWH, thrombolytic therapy with t-PA, surgery, and catheter-based embolectomy.^[6, 7, 9, 12, 14, 15, 17-19] We chose t-PA and LMWH because it is the most studied option. t-PA has a short half-life, nonantigenic qualities, and local specific action on plasminogen bound fibrin.^[20] Catheter directed therapy has been shown to be superior to systemic t-PA therapy in the rabbit model of SVC thrombosis.^[21]

In a literature review of 94 cases of neonatal thrombus treated with t-PA, infusion rate ranged from 0.02-1mg/kg/hour, a duration of administration from ½-264 hours, and an initial bolus of 0-0.75mg/kg.^[22] Thrombolysis with concomitant heparin may be synergistic; however, whether LMWH or unfractionated heparin (UFH) is better is still unclear. The potential advantages of LMWH when compared with UFH include a more predictable pharmacokinetic profile, minimal monitoring, subcutaneous administration and potentially less bleeding and osteopenia.^[6, 18]

In summary, we recommend PE be considered in any previously stable neonate with sudden onset of respiratory failure and history of CVL. We, like others, feel there is a need for a multicenter trial to evaluate the most effective therapeutic intervention for vascular thrombosis in the newborn.

References

- [1] U. Nowak-Göttl, R. vonKries, U. Göbel. Neonatal symptomatic thromboembolism in Germany: two year survey, *Arch Dis Fetal Neonatal Ed*, 76 (1997), F163-F167.
- [2] B. Schmidt, M. Andrew. Neonatal thrombosis: report of a prospective Canadian and international registry, *Pediatrics*, 96 (1995), 939-43.
- [3] M. Andrew, M. David, M. Adams, et al. Venous thromboembolic complications (VTE) in children: first analysis of the Canadian registry of VTE, *Blood*, 83 (1994), 1251-57.
- [4] J. R. Buck, R. H. Connors, W. W. Coon, W. H. Weintraub, J. R. Wesley, A. G. Coran. Pulmonary embolism in children, *J Pediatr Surg*, 16 (1981), 385-91.
- [5] K. J. Pugh, S. B. Jureidini, R. Ream, P. Syamasuendur Rao, J. Dossier. Successful Thrombolytic therapy of pulmonary embolism associated with urosepsis in an infant, *Pediatr Cardo*, 23 (2002), 77-79.
- [6] T. Sawyer, A. Antle, M. Studer, M. Thompson, S. Perry, C. Mahnke. Neonatal pulmonary artery thrombosis presenting as persistent pulmonary hypertension of the newborn, *Pediatr Cardiol*, [Epub ahead of print] 2008.
<http://www.ncbi.nlm.nih.gov/pubmed/19052800?dopt=abstractplus>
- [7] M. M. Goble, C. A. Gomez. Neonatal pulmonary artery thrombosis: echocardiographic characteristics and possible contributing factors, *J Am Soc Echocardiog*, 18 (2005), e1-e4.
- [8] L. A. Pyles, M.E. Pierpont, M.E. Steiner, P. S. Hesslein, C.M.Smith. Fibrinolysis by tissue plasminogen activator in a child with pulmonary embolism, *J Pediatr*, 116 (1990), 801-04.

- [9] S. Clapp, M. Bedard, Z. Q. Farooki, E. Arciniegas. Pulmonary artery thrombus associated with the ductus arteriosus, *Am Heart J*, 111 (1986), 796-7.
- [10] E. H. Oppenheimer, J. R. Esterly. Thrombosis in the newborn: comparison between infants of diabetic and nondiabetic mothers, *J Pediatr*, 67 (1965), 549-56.
- [11] D. S. Beardsley. Venous thromboembolism in the neonatal period, *Semper*, 31 (2007), 250-53.
- [12] J. Arnold, H. O’Brodivich, R. Whyte, G. Coates. Pulmonary thromboemboli after neonatal asphyxia. *J Pediatr*, 106 (1985), 806-9.
- [13] M. Roy, S. Turner-Gomes, G. Gill, C. Way, J. Mernagh, B, Schmidt. Accuracy of Doppler echocardiography for the diagnosis of thrombosis associated with umbilical venous catheters, *J. Pediatr*, 140 (2002), 131-34.
- [14] A. Greenway, M. Massicotte, P. Monagle. Neonatal thrombosis and its treatment, *Blood Rev*, 18 (2004), 75-84.
- [15] J. Feldman, J. Feinstein, J. Lamberiti, S. Perry. AngioJet catheter – based thrombectomy in a neonate with postoperative pulmonary embolism, *Catheter Cardiovasc Interven*, 66 (2005), 442-45.
- [16] C. M. John, C. Harkensee. Thrombolytic agents for arterial and venous thromboses in neonates (review), *Cochrane Database Syst Rev*, Issue 1(2005) CDOO4342. DOI:10.1002/14651858.CD004342.pub2.
- [17] E. Chalmers. Neonatal thrombosis, *J. Clin Pathol*, 53 (2000), 419-23.
- [18] D. Kenny, B. Tsai-Goodman. Neonatal arterial thrombus mimicking congenital heart disease, *Arch Dis Child Fetal Neonatal Ed*, 92 (2007), F59-F61.

- [19] A. Gamillscheg, J. Nürnberg, V. Alexi-Meskishvili, et al. Surgical emergency embolectomy for the treatment of fulminant pulmonary embolism in a preterm infant, *J. Pediatr Surg*, 32 (1997), 1516-18.
- [20] R. W. Holden. Plasminogen activators: pharmacology and therapy, *Radiology*, 174 (1990), 993-1001.
- [21] D. Collen, J. M. Stassen, M. Verstraete. Thrombolysis with human extrinsic (tissue-type) plasminogen activator in rabbits with experimental jugular vein thrombosis, *J Clin Invest*, 71 (1983), 368-76.
- [22] J. Hartman, A. Hussein, B. Trowitzsch. Treatment of neonatal thrombus formation with recombinant tissue plasminogen activator: six years experience and review of the literature, *Arch Dis Child Fetal Neonatal Ed*, 85 (2001), F18-22.
- [23] M. J. Manco-Johnson. Disorders of hemostasis in childhood: risk factors for venous thromboembolism, *Thromb Haemost*, 78 (1997), 710-14.