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PATIENT SAFETY NETWORK

Central Line Clot

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Case Objectives

- List the complications of central line manipulation
- Appreciate the limitations of diagnostic studies for PE in children
- Describe modalities for prevention of catheter-related venous thrombosis

Case & Commentary: Part 1

An 8-month-old girl had been in the intensive care unit for 6 days for treatment of septic shock secondary to meningococcemia, and was ready to be transferred to a general pediatrics ward. In preparation for transfer, the nurse flushed the patient's central venous catheter with heparin and "hep-locked" the line. Within minutes, the infant became cyanotic and apneic. A full code ensued and after a brief time, the patient was stabilized with a blood pressure of 95/55, heart rate of 120, a RR of 35, and an O2 sat of 90% on 100% non-rebreather.

Manipulation of central venous catheters can lead to arrhythmias, venous air embolism, and thromboembolism.(1) If the tip of the catheter is in the heart, irritation of the cardiac conducting system by the catheter can cause premature atrial and ventricular contractions and arrhythmias. Although rhythm disturbances can lead to cardiac arrest requiring resuscitation, this usually occurs in children with depressed cardiac function and/or abnormal electrolytes.

For the infant in this case, the acute onset of a high O2 requirement raises the suspicion of sudden embolism of air or clot. Immediate aspiration of the central venous catheter, ideally with the patient positioned with the right side up, can help diagnose and treat venous air embolism. This maneuver would be less effective if performed after CPR, such as in this patient, because it is likely that any air would be dislodged by the chest compressions. In this patient, venous thromboembolism must be strongly suspected because she is recovering from a hypercoagulable state; meningococcemia is associated with acquired deficiency of Protein C.(2)

Pulmonary thromboembolism is reported much less frequently in infants and children than in adult patients, with scattered case reports and autopsy studies in the literature.(3) It is not clear if this is due to a true lower incidence or underdiagnosis. Radiographic studies for pulmonary embolism are not always readily available in children's hospitals. Thus, therapeutic anticoagulation is not recommended without very high suspicion of or confirmation of a clot or pulmonary embolism. In this patient, the suspicion of pulmonary embolism is high, and starting anticoagulation with unfractionated heparin while further studies are pending would be acceptable but not mandatory. If this infant did not regain hemodynamic stability, it would be prudent to obtain an emergent echocardiogram to evaluate the function of the right ventricle, looking for evidence of septal deviation and pulmonary hypertension. This would be evidence of submassive pulmonary embolism that may require thrombolytic therapy after confirmation.(4)

The gold standard test for diagnosing pulmonary embolism is a pulmonary angiogram.(Figure 1) Alternative tests are spiral computed tomography (CT) (Figure 2) and ventilation-perfusion (VQ) scan.(5) (Figure 3) In adults, spiral CT has been shown to have good sensitivity for diagnosing large, centrally located pulmonary emboli and good specificity when read by experienced radiologists.(6) Because pulmonary embolism is rarely reported in infants and children, many pediatric radiologists do not have experience interpreting spiral CT scans. No studies have been done to evaluate the performance of spiral CT in infants and children for diagnosing pulmonary embolism. Ventilation-perfusion scans can be useful if the patient has relatively normal lungs. Areas of atelectasis or infiltrate can hinder accurate interpretation as blood flow to those areas may be constricted due to decreased ventilation. Because pediatric angiograms are rarely performed, they are not always readily available. Therefore, despite the limitations of spiral CT and VQ scan, these are often the first-line diagnostic studies. A readily available study that may rule out the diagnosis of pulmonary embolism in low-risk patients is a negative D-dimer test.(7) However, this test has not been validated in children, and due to poor specificity, the test cannot be used to confirm pulmonary embolism. In this case, the patient may have a positive D-dimer because of her meningococcemia, and therefore the D-dimer result may not help diagnostically.

Case & Commentary: Part 2

A spiral CT revealed multiple pulmonary emboli. Anticoagulation therapy was started. The patient improved and was discharged home several days later without sequelae from this event.

The coagulation system of prepubertal children is different from that of adults, making spontaneous clots less likely.(8) The incidence of DVT and pulmonary embolism is not well studied in children. One prospective study of 59 hospitalized children with two or more risk factors identified only one patient with a DVT.(9) A retrospective study of pediatric trauma patients identified three cases of DVT in 2,746 admissions.(3) The incidence in the critically ill pediatric population is not known. Almost all deep venous clots in neonates, and one-third in infants and young children, are related to central venous access devices.(10) Catheter-related DVTs are reported in 8% to 25% of infants and children in the ICU, as detected by ultrasound.(11,12) Even more may be seen by venography, a more sensitive test for detecting DVT. However, other factors also put children at risk including congenital or acquired abnormalities of anticoagulant factors including Protein C, Protein S, antithrombin III deficiency, Factor V Leiden mutation, and other medical comorbidities.(Table 1) This patient had at least two risk factors, including acquired

hypercoagulability from meningococcemia and a central venous catheter.

It is unclear how many catheter-related thrombi result in pulmonary emboli in children. This is partly because no prospective studies have been done performing spiral CT, VQ, or angiogram in pediatric populations with documented DVT. A more commonly detected problem is thrombus propagation from the tip of the catheter, ultimately resulting in inferior vena cava or subclavian vein occlusion.(13) Clinically, this can lead to swelling and discoloration of the extremity for femoral catheters or swelling of the head or arm for subclavian or internal jugular catheters. For most otherwise healthy children, catheter removal and anticoagulation results in recannulation of the vessel and/or good collateral blood flow over time. However, clotting of the major vessels is a serious problem for chronically ill children who require repeated central venous access, and postphlebitic syndrome can develop.(13) Registries of serious thrombotic complications in infants and children have been developed in Canada and the Netherlands.(10,13,14) These registries show that DVT in infants and children can have very serious morbidity. Although registry data has serious limitations in assessing actual incidence of these severe complications, pediatric intensivists are now becoming more concerned about catheter-related thrombosis and are looking at ways to prevent it.

To date, the best evidence for preventing catheter-related thrombosis in children supports use of heparin-bonded central venous lines.(11,12) A single-center randomized controlled clinical trial and a before-after trial have shown that heparin-bonded catheters not only markedly decrease the incidence of thrombus formation but also decrease the incidence of catheter-related infection.(11,12) Low-dose heparin flushes (10 u/ml) through the catheter are not beneficial for adults and probably would not be for children.(15,16) Higher doses may be effective but could result in systemic anticoagulation in children. Dosing of low molecular weight heparin (LMWH) in children is similar to the adult population.(17,18) However, there have been no clinical trials evaluating LMWH for DVT prophylaxis in this population. Since other measures to prevent DVT such as pneumatic compression boots and compression stockings are available only in adult size, these measures are unsuitable for neonates and children.

In conclusion, lack of strong evidence (Table 2) makes it difficult to write practice recommendations for prevention of DVT in prepubertal children. There is not enough data, even in adult patients, to determine whether thrombus associated with central venous catheters is preventable with heparin. A multicenter randomized clinical trial is needed to confirm whether heparin-bonded catheters or heparin in the infusate should become standard of care to prevent DVT. Until adequate data is available, it would be risky to write practice recommendations, as heparin is not without side effects. For adolescents, evidence-based recommendations for prophylaxis, diagnosis, and management that are available for adult patients can be applied. Once DVT or pulmonary embolism is recognized in a young child, anticoagulation and close follow-up are required.

Take-Home Points

- Complications of central line manipulation include arrhythmias, thrombosis, and embolism.
- The incidence of DVT/pulmonary embolism in infants and children is thought to be much lower than in adults; however, sub-optimal diagnostic modalities in this population may result in underestimation of these events.

- The majority of thrombotic episodes in the pediatric population occur as a complication of central venous catheters.
- Central line thromboses can result in serious morbidity, including emboli, SVC syndrome, and iliofemoral and IVC clots.
- Heparin-bonded catheters may be an effective modality for prevention of central venous catheter-related thrombosis.

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References

1. Polderman KH, Girbes AJ. Central venous catheter use. Part 1: mechanical complications. Intensive Care Med. 2002;28:1-17.[go to PubMed]

2. Faust SN, Levin M, Harrison OB, et al. Dysfunction of endothelial protein C activation in severe meningococcal sepsis. N Engl J Med. 2001;345:408-16.[go to PubMed]

3. Grandas OH, Klar M, Goldman MH, Filston HC. Deep venous thrombosis in the pediatric trauma population: an unusual event: report of three cases. Am Surg. 2000:66:273-276.[go to PubMed]

4. Konstantinides S, Geibel A, Heusel G, Heinrich F, Kasper W. Management strategies and prognosis of pulmonary embolism-3 trial investigators. Heparin plus alteplase compared with heparin alone in patients with submassive pulmonary embolism. N Engl J Med. 2002;347:1143-50.[go to PubMed]

5. Velmahos GC, Vassiliu P, Wilcox A, et al. Spiral computed tomography for the diagnosis of pulmonary embolism in critically ill surgical patients: a comparison with pulmonary angiography. Arch Surg. 2001;136:505-11.[go to PubMed]

6. Baile EM, King GG, Muller NL, et al. Spiral computed tomography is comparable to angiography for the diagnosis of pulmonary embolism. Am J Respir Crit Care Med. 2000;161:1010-5.[go to PubMed]

7. Kelly J, Rudd A, Lewis RR, Hunt BJ. Plasma D-dimers in the diagnosis of venous thromboembolism. Arch Intern Med. 2002;162:747-756.[go to PubMed]

8. Chan AK, Berry LR, Monagle PT, Andrew M. Decreased concentrations of heparinoids are required to inhibit thrombin generation in plasma from newborns and children compared to plasma from adults due to

reduced thrombin potential. Thromb Haemost. 2002;87:606-13.[go to PubMed]

9. Rohrer MJ, Cutler BS, MacDougall E, Herrmann JB, Anderson FA Jr, Wheeler HB. A prospective study of the incidence of deep venous thrombosis in hospitalized children. J Vasc Surg. 1996;24:46-9.[go to PubMed]

10. van Ommen CH, Heijboer H, Buller HR, Hirasing RA, Heijmans HS, Peters M. Venous thromboembolism in childhood: a prospective two-year registry in the Netherlands. J Pediatr. 2001:139:676-81.[go to PubMed]

11. Pierce CM, Wade A, Mok Q. Heparin-bonded central venous lines reduce thrombotic and infective complications in critically ill children. Intensive Care Med. 2000;26:967-72.[go to PubMed]

12. Krafte-Jacobs B, Sivit CJ, Mejia R, Pollack MM. Catheter-related thrombosis in critically ill children: comparison of catheters with and without heparin bonding. J Pediatr. 1995;126:50-4.[go to PubMed]

13. Monagle P, Adams M, Mahoney M, et al. Outcome of pediatric thromboembolic disease: a report from the Canadian Childhood Thrombophilia Registry. Pediatr Res. 2000;47:763-6.[go to PubMed]

14. Andrew M, David M, Adams M, et al. Venous thromboembolic complications (VTE) in children: first analyses of the Canadian Registry of VTE. Blood. 1994;83:1251-7.[go to PubMed]

15. Randolph AG, Cook DJ, Gonzales CA, Andrew M. Benefit of heparin use in central venous and pulmonary artery catheters: a meta-analysis of randomized controlled trials. Chest. 1998;113:165-71.[go to PubMed]

16. Smith S, Dawson S, Hennessey R, Andrew M. Maintenance of the patency of indwelling central venous catheters: is heparin necessary? Am J Pediatr Hematol Oncol. 1991;13:141-3.[go to PubMed]

17. Albisetti M, Andrew M. Low molecular weight heparin in children. Eur J Pediatr. 2002:161;71-7.[go to PubMed]

18. Massicotte P, Adams M, Marzinotto V, Brooker LA, Andrew M. Low-molecular-weight heparin in pediatric patients with thrombotic disease: a dose finding study. J Pediatr. 1996;128:313-8.[go to PubMed]

Tables

Table 1. Risk Factors for DVT in Infants and Children

Central venous catheter
Sepsis and other acute states with disseminated intravascular coagulation
Hereditary or acquired abnormalities of anticoagulant factors

Immobility
Cancer
Nephrotic syndrome
Moderate to severe dehydration
Greater than 150% ideal body weight
Use of oral contraceptives
History of DVT or pulmonary embolism in the past

Table 2. Possible Interventions to Prevent Catheter-Related Thrombosis in Children

Intervention	Supportive Evidence in Children
Heparin infusate	Ineffective at low doses (15,16) May be dangerous in small children at high doses due to amount of heparin exposure
LMWH prophylaxis	No data on efficacy in children
Heparin-bonded catheters	One RCT in 228 patients showed markedly decreased thrombosis (ARR 8%, 95% CI 2.6% to 13%) and infection (ARR 88%, 95% CI 67% to 95%).(11) A smaller before-and-after prospective study also showed decreased thrombosis and infection.(12)

Figures

Figure 1. Pulmonary angiogram in a patient with PE. The clot appears as a filling defect (arrow).

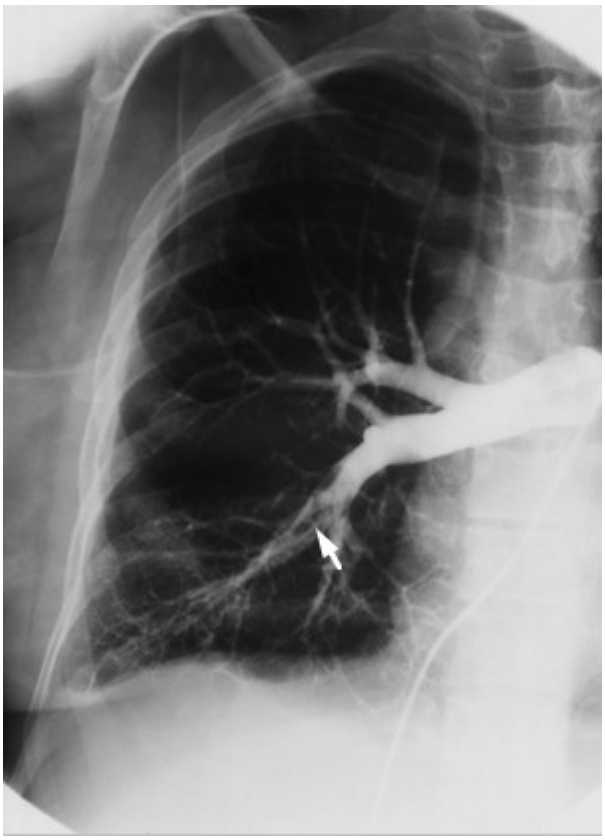


Figure 2. Spiral CT in a patient with PE. The clot appears as a filling defect (arrow).

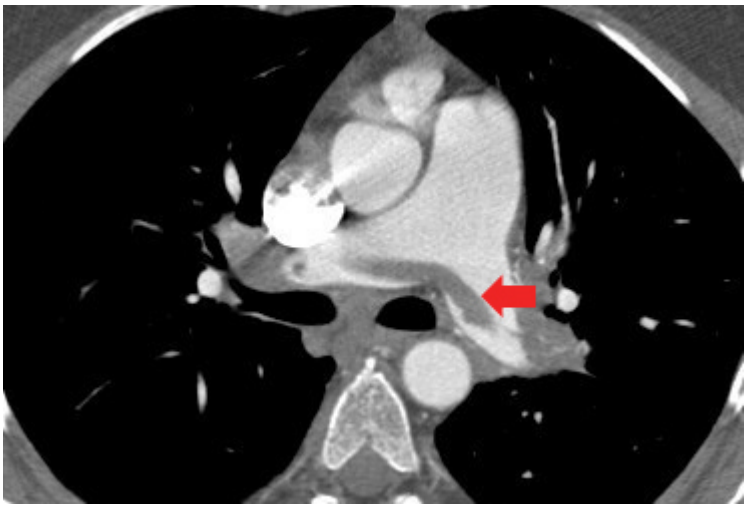
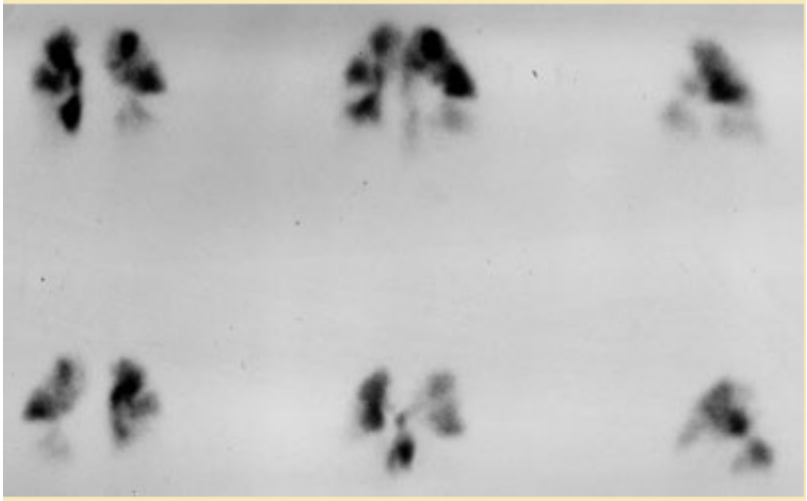


Figure 3. Ventilation-Perfusion (VQ) Scan. Clots appear as perfusion defects, without corresponding defects on the ventilation scan ('mismatched defects').

Ventilation



Perfusion

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