

Bilateral chylothoraces and  
intraventricular hemorrhages  
secondary to catheter-related  
vena cava syndrome in a  
preterm infant

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This 1150 g male infant was delivered at 29 4/7 weeks of gestation by Cesarean section following premature contractions and prolonged rupture of membranes. The mother had received antenatal corticosteroids at 25 weeks of gestation. Apgar scores were 5, 7 and 7 at 1, 5 and 10 minutes, respectively, and arterial cord pH was 7.32. Respiratory support with nasal CPAP was required for only 24 hours because of wet lung (Fig. 1). The differential blood count revealed borderline polycythemia with a hematocrit of 65%.

A peripherally inserted central venous catheter (PICC) was placed in the superior vena cava for parenteral nutrition. At the age of 7 days, the infant developed respiratory distress with tachypnea and plethora of the upper body. Blood cultures were obtained and antibiotic therapy with amoxicillin and gentamicin was started. The chest X-ray showed diffuse bilateral opacifications of the lung fields with evidence of bilateral pleural effusions. A contrast agent injection through the catheter demonstrated thrombosis of the superior vena cava (Fig. 2). Pleurocentesis was performed and examination of the fluid was consistent with the diagnosis of bilateral chylothoraces.

Cerebral ultrasound revealed bilateral intraventricular hemorrhages (IVH) and unilateral thalamic hemorrhage. After detailed discussion with pediatric hematologists no anticoagulant or fibrinolytic therapy was

started at this point because of IVH, and the PICC was removed.

Between 9 and 16 days of age, the patient developed progressive edema of the head, neck and upper torso. At this point, anticoagulant therapy with low molecular weight heparin (LMWH) was begun. Repeated pleurocenteses were necessary. Serial cerebral ultrasound scans demonstrated progressive enlargement of the ventricles. The infant showed a gradually increasing oxygen requirement which would have necessitated mechanical ventilation. Because of extensive IVH, lack of valid therapeutic options, life support was withdrawn after detailed discussion with the parents, and the patient died.

Autopsy confirmed venous thrombosis starting from the superior vena cava with extension into the superior sagittal sinus, bilateral intraventricular hemorrhages, unilateral thalamic hemorrhage and ventricular enlargement. Family history was negative for thrombosis, but the mother was found to be heterozygous for Factor V Leiden mutation.

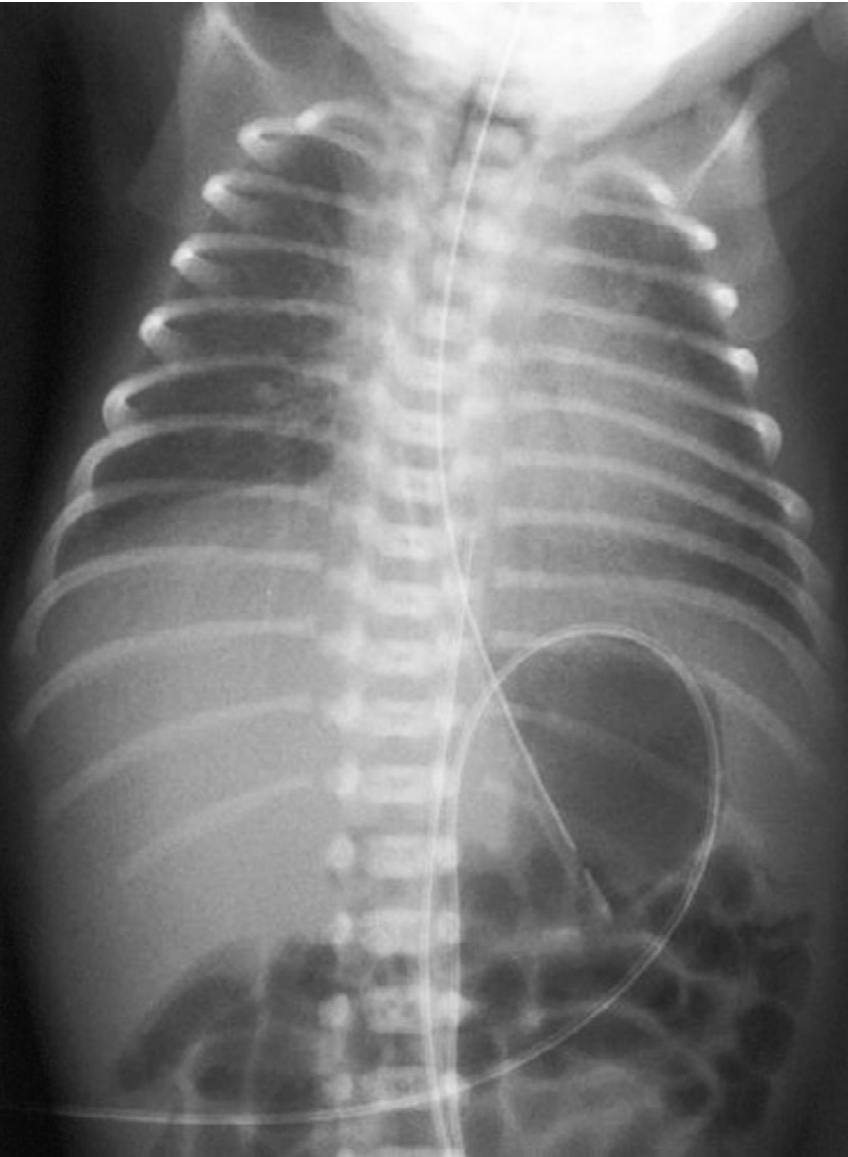


Fig. 1

*CXR on 1st day of life: wet lung.*



Fig. 2

*Contrast injection (8th day of life): thrombosis of vena cava superior, bilateral pleural effusions.*



Fig. 3

*US: bilateral IVH with dilated ventricles.*



**Fig. 4**

*Autopsy specimen: bilateral IVH and unilateral thalamic hemorrhage.*



Thrombosis of the superior vena cava in infancy is an unusual, but often fatal complication. It is often associated with the use of central venous catheters. In a prospective Canadian and international registry of neonatal thrombosis, mortality rate of central venous catheter-associated thrombosis affecting the right atrium or the superior vena cava was 33% (1).

Prothrombotic states may cause or contribute to venous thrombosis. Factor V Leiden mutation (heterozygous or homozygous) is the major genetic risk factor in catheter-related thrombosis in infancy (2,3). No evaluation for a hypercoagulable state was performed in the infant but his mother was found to be heterozygous for factor V Leiden mutation.

Bilateral chylothoraces secondary to superior vena cava obstruction is a known complication of central venous catheters. Based on analysis of a case series, Dhande concluded that the pleural effusions resulted from obstruction of thoracic lymph flow into the venous system (4). Elevation of cerebral venous pressure can contribute to the occurrence of cerebral and intraventricular hemorrhages (5). The progression of venous thrombosis of the superior vena cava into the sagittal sinus leads to an immense increase of cerebral venous pressure. Ventricular enlargement is a well known complication of IVH. McLaughlin described development of hydrocephalus due to elevation of cerebral venous pressure in infants with superior vena cava syndrome

(6). He explained this association with an inadequate pressure gradient at the level of the arachnoid granulations secondary to elevated venous pressures. All infants developed hydrocephalus within a time interval of several weeks. Acute ventricular enlargement over a period of only one week is more likely due to obstruction by particulate blood clots (5), but when thrombosis of the superior vena cava extends into the sagittal sinus, an inadequate pressure gradient at the level of the arachnoid granulations may also play an important role.

Effectiveness and safety of thrombolytic and anticoagulant therapies in very preterm infants with extended venous thrombosis is not well established, even less so in the presence of severe IVH. Therefore, anticoagulant therapy with LMWH was only reluctantly begun in our patient. The PICC was removed before the possibility of local thrombolysis was discussed. Intracranial bleeding is an important and serious complication of thrombolytic therapy and intraventricular hemorrhage within the last 10 days is considered an absolute contraindication for thrombolysis (7). Local thrombolysis or systemic low-dose tissue plasminogen activator therapy is perhaps an alternative strategy with less risks, but randomized clinical trials are lacking (8). LMWH is an effective and well tolerated drug for prophylaxis and therapy of thrombosis in infancy (9). In premature infants, higher doses are required as compared with the healthy term neonate and achieving thera-

peutic levels is often difficult (10). The administration, dosage and monitoring of LMWH therapy in children has recently been reviewed by Albisetti (11).

## REFERENCES

1. Schmidt B, Andrew M. Neonatal thrombosis: Report of a prospective Canadian and international registry. *Pediatrics* 1995;96:939-943 (*Abstract*)
2. Nowak-Gottl U, Dubbers A, Kececioglu D, et al. Factor V Leiden, protein C and lipoprotein(a) in catheter-related thrombosis in childhood: A prospective study. *J Pediatr* 1997;131:608-612 (*Abstract*)
3. Munchow N, Kosch A, Schobess R, Junker R, Auberger K, Nowak-Gottl U. Role of genetic prothrombotic risk factors in childhood caval vein thrombosis. *Eur J Pediatr* 1999;158: S109-112 (*Abstract*)
4. Dhande V, Kattwinkel J, Alford B. Recurrent bilateral pleural effusions secondary to superior vena cava obstruction as a complication of central venous catheterization. *Pediatrics* 1983;72:109-113 (*Abstract*)
5. Volpe J. Intracranial hemorrhage: Germinal matrix-IVH of the premature infant. In: *Neurology of the newborn*, 4th edition (2001)
6. McLaughlin J, Loeser J, Roberts T. Acquired hydrocephalus associated with superior vena cava syndrome in infants. *Childs Nerv Syst* 1997;13:59-63 (*Abstract*)
7. Gupta AA, Leaker M, Andrew M, et al. Safety and outcomes of thrombolysis with tissue plasminogen activator for treatment of intravascular thrombosis in children. *J Pediatr* 2001;139:682-688 (*Abstract*)
8. Wang M, Hays T, Balasa V, Bagatell R, Gruppo R, Grabowski EF, Valentino LA, Tsao-Wu G, Manco-Johnson MJ; Pediatric Coagulation Consortium. Low-dose plasminogen activator thrombolysis in children. *J Pediatr Hematol Oncol* 2003;25:379-386 (*Abstract*)

9. Nohe N, Flemmer A, Rumler R, Praun M, Auberger K. The low molecular weight heparin dalteparin for prophylaxis and therapy of thrombosis in childhood: a report of 48 cases. *Eur J Pediatr* 1999;158:S134-139 (*Abstract*)
10. Michaels LA, Gurian M, Hegyi T, Drachtman RA. Low molecular weight heparin in the treatment of venous and arterial thromboses in the premature infant. *Pediatrics* 2004;114(3):703-707 (*Abstract*)
11. Albisetti M, Andrew M. Low molecular weight heparin in children. *Eur J Pediatr* 2002;161:71-77 (*Abstract*)

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