Neonatal venous cerebral hemorrhage

Report of two cases

SANJAY N. MISRA, M.D., AND ASHISH K. MISRA, M.D.

Department of Neurosurgery, Denver Health Medical Center, University of Colorado Health Sciences Center, Denver, Colorado; and Department of Hematology Oncology, Children’s Hospital at Westmead, Sydney, New South Wales, Australia

Intracranial pathological changes can occur as a result of impaired craniocervical venous return. Thrombosis of central venous access catheters was demonstrated in two neonates born at 38 and 27 weeks’ gestation. Neither infant developed hemorrhage of prematurity as confirmed on cranial ultrasonography. Clinical evidence of vena cava thrombosis and associated spontaneous intraventricular hemorrhage developed on Day 24 and 36, respectively, and these findings were confirmed on imaging studies. In one infant the hemorrhage was accompanied by communicating hydrocephalus.

The cause of the intracranial disease was attributable to the retrograde cerebral venous congestion. This, together with the primitive venous bed developing in the periventricular region, was associated with the spontaneous hemorrhage in the region of the foramen of Monro.

To the authors’ knowledge, this is the first report in the English-language literature of spontaneous neonatal intracerebral hemorrhage, due to thrombosis of the superior or inferior vena cava.

The natural history of this condition is resolution without sequelae after appropriate therapeutic intervention for the vena cava thrombosis.

KEY WORDS • cerebral hemorrhage • neonate • venous congestion • thrombosis

Abbreviations used in this paper: CSF = cerebrospinal fluid; ICU = intensive care unit; IVH = intraventricular hemorrhage.
instituted. Repeated cranial ultrasonography at 2 weeks demonstrated clearance of the intracerebral blood and no change in the ventricular status. The circumference growth of the patient’s head remained appropriate for age and there were no neurosurgical sequelae.

Case 2

This female infant with an unexpected birth at 27 weeks’ gestation was admitted to the neonatal ICU, requiring ventilation and the placement of an internal jugular line for venous access.

Routine cranial ultrasonography was performed at the time of neonatal ICU admission, and findings were normal (Fig. 1 upper). Because of line-related sepsis, prolonged venous access was required to administer broad-spectrum antibiotic agents and provide venous access. Routine cranial ultrasonography on Day 23 revealed no change. On Day 36, facial swelling and suffusion were noted. Chest radiography demonstrated bilateral pleural effusions. Cervical ultrasonography revealed the presence of superior vena cava thrombosis extending from the level of the internal jugular vein to the distal superior vena cava (Fig. 1 center). Cranial ultrasonography demonstrated the presence of IVH and communicating hydrocephalus (Fig. 1 lower).

Venography confirmed the complete occlusion of the superior vena cava (Fig. 2 left). Low–molecular weight heparin therapy was instituted at a dose of 1.5 mg/kg subcutaneously twice daily. A central venous line was placed at an alternate site and the offending central line was removed. Cranial ultrasonography performed 1 week following treatment demonstrated increased subdural collections and expanded ventricles (Fig. 2 center). There were no further untoward clinical events. The patient’s head circumference remained appropriate for her age. She experienced no apneic or bradycardic episodes suggestive of clinically significant intracranial hypertension. Repeated cranial ultrasonography was conducted at 4 weeks after removal of the jugular line and treatment with heparin. This demonstrated clearance of the IVH and decreasing communicating hydrocephalus (Fig. 2 right).

DISCUSSION

Venous thrombosis resulting from the presence of neonatal central venous access catheters is a recognized complication. The incidence varies (4.5–28%) depending on the primary vessel involved and is significantly greater for femoral access lines.9,16,20 In addition to the presence of an intravascular foreign body, an important predisposing factor is the hematological profile of the developing fetus in the third trimester and in the neonatal period. In the third trimester, there is a progressive increase in hemoglobin. There is a progressive increase in the hemoglobin concentration during the gestational period. By 39 weeks of gestation it has increased to 16.5 ± 4 g/dl.18 This relatively high level of hemoglobin is accompanied by a commensurate change in hematological viscosity. In general, neonatal circulating blood has a greater viscosity than that in older patients at a comparable packed cell volume. In both of our cases, the infants were preterm. On examining the temporal profile of the intracerebral hemorrhage, one can attribute the hemorrhage to the obstruction of cranio-cerebral venous drainage. The usual form of germinal matrix hemorrhage of prematurity is by the 5th day of life in 95% of cases. In each case presented here, the hemorrhage occurred more than 4 weeks after birth and in association with the onset of clinical signs of vena cava thrombosis.

The presence of venous hypertension with retrograde pressure into the cerebral tissue predisposes it to intracranial changes.2,4,5,11,12,21,22 The predilection for this in infants is believed to be multifactorial, with important factors being the open cranial sutures and compliance of the neonatal brain and venous system.2,4 The development of macrocephaly or neurological instability in infants, accompanying upper- or lower-body congestion, may herald the occurrence on intracerebral hemorrhage with or without communicating hydrocephalus.
Neonatal cardiovascular investigations have demonstrated that 49% of the cardiac output in neonates is superior vena cava return. One can surmise therefore that in neonates with obstructed superior vena cava flow this blood volume would need to be accommodated in other parts of the venous system. The presence of increased volumes in these vessels would then result in decreased flow and relative return pressure via the collateral venous channels.

The distribution of neonatal cerebral and systemic venous return also explains the pathogenesis of the cerebral venous congestion as a result of inferior vena cava thrombosis. There is significant flow of cerebral return via the inferior vena cava with the potential for retrograde venous congestion. Conversely inferior vena cava thrombosis results in retrograde venous congestion and increases impedance to venous flow.

In studies of retrograde venous cerebral perfusion in canines, investigators have demonstrated intracerebral water content and intracranial pressure elevation as a result of retrograde cerebral perfusion. This observation is in keeping with current knowledge that CSF circulation disturbance occurs due to impaired cerebral venous return. Superior vena cava pressure elevation has been associated with an elevation in CSF pressure. This is important to note that hemorrhages in the region of the germinal matrix have been demonstrated at the capillary–venule junction and small venules. The explanation for this may be that these vessels have minimal mesenchymal supporting structures whose development begins to be prominent after 31 to 32 weeks’ gestation. These intrinsically weak developing vessels are less able to resist elevated venous pressure.

As demonstrated in these cases, the pathophysiological changes predisposing to intracerebral venous hemorrhage and CSF resorption are corrected by treating the thrombosis. Superior or inferior vena cava thrombosis in neonates results in cerebral venous congestion and responds to the appropriate therapeutic intervention.

**CONCLUSIONS**

Interference with central venous return from the head and neck is a predisposing factor for spontaneous neonatal intracerebral hemorrhage. The physiological interference with craniocervical venous return can result from both superior or inferior vena cava obstruction in neonates.

**References**


