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CASE OF THE MONTH

November 1996 - Premature Baby with Lethargy and Coma

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Clinical History

An 18-year-old primigravid mother with preeclampsia gave birth by Cesarean section to a premature male baby (28 weeks gestational age). During the first postnatal week, the neonate required artificial ventilation for respiratory distress syndrome. Two weeks postnatally, the baby was re-intubated for recurrent respiratory distress. Four weeks postnatally, he had an episode of transient renal failure with acidosis, hyperkalemia, and hypernatremia, followed by neurological deterioration with lethargy leading to coma, prompting ultrasound examinations. High signal intensity in the germinal matrix bilaterally (Figure 1, arrow) was interpreted by the radiologist as intraventricular hemorrhage, grade 2. The baby died 31 days after birth.

Gross

General autopsy findings included a venous thrombosis involving the right kidney. External examination of the brain revealed the presence of small subarachnoid hemorrhages. Coronal sections revealed massive bilateral internal lesions (Figure 2).

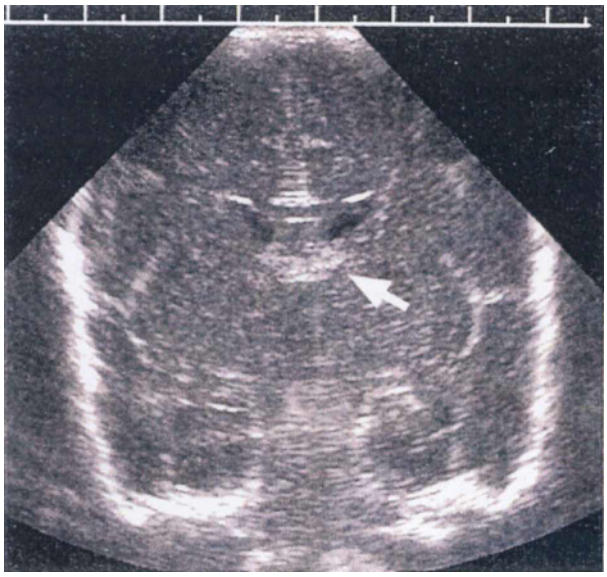

Figure 1.

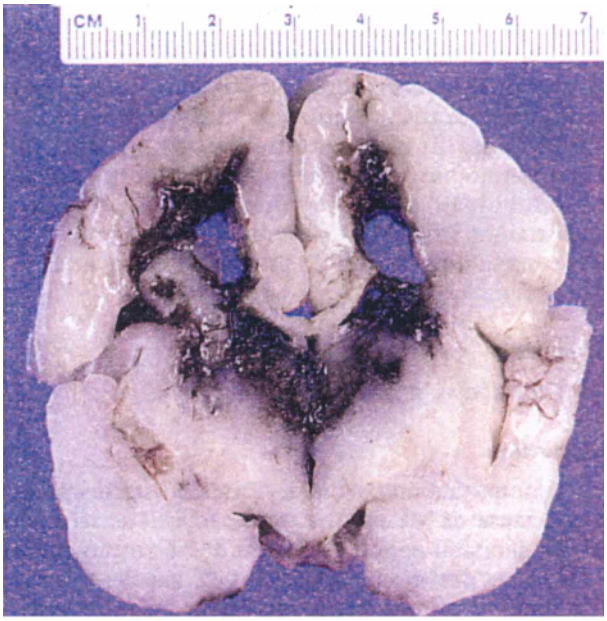

Figure 2.

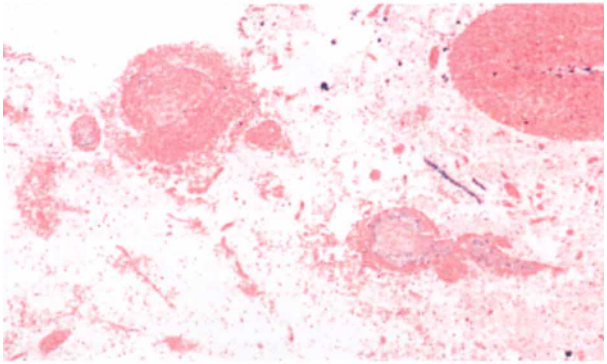

Figure 3.

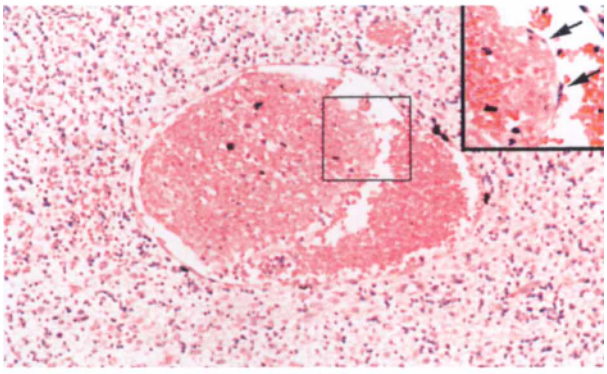

Figure 4.

The periventricular white matter was completely necrotic. Subcortical white matter and the corpus callosum remained intact.

Microscopic

In a Bielschowsky preparation, the necrotic deep white matter was clearly demarcated by its pale appearance and by a surrounding rim of brown/black argyrophilic debris. Veins in necrotic areas, such as the thalamus (Figure 3), were surrounded by petechial hemorrhages and contained organizing thrombi. Endothelialization of thrombi was clearly visible, e.g., in the germinal matrix (Figure 4). The choroid plexus was hemorrhagic, and the ventricles contained clotted blood. The vein of Galen and straight sinus were distended and engorged by large organizing thrombi, showing typical lines of Zahn (Figure 5).

Diagnosis

Thrombosis of internal cerebral veins

Discussion

Venous thrombosis is a clinically under-recognized cause of lethargy or coma, as well as seizures, in the neonatal period (1-3). The dural venous sinuses are most commonly affected (1,3), but the internal (Galenic) venous system may also be involved—either in conjunction with the dural sinuses or in isolation, as in the present case. In some cases, neonatal cerebral venous thrombosis may have a favorable outcome with normal subsequent neurodevelopment (2); however, a poor outcome is more likely when the internal venous system is involved (3).

The pathogenesis of perinatal cerebral venous thrombosis was discussed thoroughly by Ehlers and Courville in their classic article published in 1936 (3). They classified intracranial venous thrombosis into primary (marantic), secondary (infectious) and combined types and reported that whereas thrombosis of the dural sinuses is most often secondary to a suppurative process such as meningitis, thrombosis of the internal venous system is usually of the primary or combined type. In infants, important factors associated with primary thrombosis of the internal cerebral veins include diarrhea, vomiting, and dehydration (3); any factors causing increased coagulability of the blood may also contribute.

The presence of hemorrhagic venous infarcts bilaterally in the deep hemispheres is characteristic of thrombosis of the internal cerebral venous system (3). In normal anatomy, blood from the deep structures drains via bilaterally paired internal cerebral veins into the unpaired midline vein of Galen, which in turn drains into the straight sinus. Thus, thrombosis of the vein of Galen or straight sinus leads to bilateral congestion of internal cerebral veins and retrograde spread of thrombosis, followed by hemorrhagic infarction. Thrombosis of the internal cerebral venous system should be considered in the differential diagnosis of neonatal intraventricular hemorrhage and periventricular leukomalacia, particularly when the infant is near term and has bilateral hemorrhagic lesions.

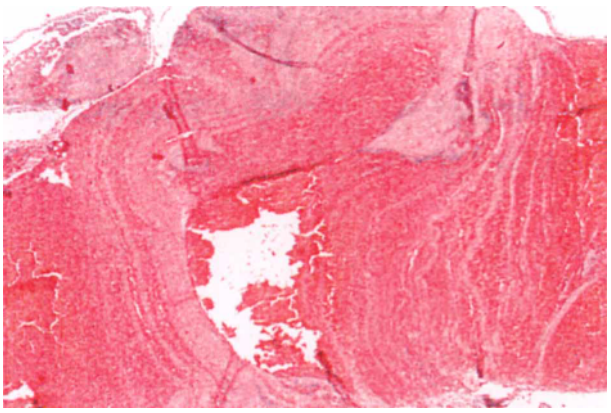

Figure 5.

The present case illustrates a close correlation between the postmortem brain specimen and the pattern of lesions as seen by ultrasound exam. MRI methods that reveal the absence of blood flow are also useful for diagnosing intracranial venous thrombosis (2).

References

1. Volpe JJ (1995) *Neurology of the Newborn*, Third Edition, W.B. Saunders: Philadelphia, pp. 300-301
2. Rivkin MJ, Anderson ML, Kaye EM (1992) Neonatal idiopathic cerebral venous thrombosis: an unrecognized cause of transient seizures or lethargy. *Ann Neurol* 32:51-56
3. Ehlers H, Courville CB (1936) Thrombosis of internal cerebral veins in infancy and childhood: review of literature and report of five cases. *J Ped* 8: 600-623

Case Abstract

A premature male baby (28 weeks gestational age) was delivered by Cesarean section and required ventilation for respiratory distress syndrome during the first postnatal week. Four weeks postnatally, he had an episode of transient renal failure followed by lethargy leading to coma. Ultrasound changes were interpreted as intraventricular hemorrhage, grade 2. The baby died 31 days after birth. Autopsy showed bilateral thrombosis of the deep cerebral veins.

For a more complete discussion of this case and additional micrographs, please access this case on the WWW at: http://path.upmc.edu/divisions/neuropath/bpath/cases/case8.html. We welcome comments about these or similar cases our readers may have encountered.
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