

Deep cerebral venous thrombosis in thalamo-ventricular hemorrhage of the term newborn

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Abstract. Unilateral thalamic bleeding with associated intraventricular hemorrhage is reported in three full-term neonates. The first presented within 48 hours from birth with early onset streptococcal meningitis, persistent pulmonary hypertension, tonic seizures and a tense fontanelle. The second presented 6 days after birth with irritability, opisthotonus, a tense fontanelle and tonic seizures. The third was admitted three days after birth with seizures and a tense fontanelle. In the latter two infants NMR and CT imaging documented thrombosed superficial and deep cerebral veins. The etiopathogenesis of intracranial venous thrombosis in the neonate is diverse: asphyxia, dehydration, polycythemia, sepsis-meningitis and difficult delivery are the main causes. In one of our patients jugular vein compression by the collar of a negative-pressure ventilation chamber probably initiated the intracranial events. More than half of the survivors sustain severe neurological impairment.

Bleeding into the basal ganglia of the newborn can be associated with a myriad of events: severe birth asphyxia [12, 18], generalized hemorrhagic diathesis [15], extension from a germinal layer hemorrhage or from a choroid plexus bleeding in the lateral or third ventricle [5], bleeding from a micro-angioma [1, 19], or into an intracranial tumor [15]. The event of a unilateral thalamic hemorrhage with or without intraventricular clot formation, has been recognized sporadically in the at or near term newborn since the advent of CT. From personal experience with 3 recent observations and a review on 22 instances from the literature, we propose deep cerebral venous thrombosis as the main etiopathogenetic mechanism of this old clinical syndrome [6].

Case reports

First case (BW, 89/2534, °04.12.89)

Following an uneventful pregnancy this girl was born at term by spontaneous vaginal delivery. The membranes had ruptured one week earlier, but oligohydramnios and clinical chorioamnionitis

were absent. Her birthweight was 3430 g for a length of 49 cm and a head circumference of 34 cm. The Apgar scores were 9 at 1 and at 5 minutes. Well into the second day of life the girl started grunting and became tachycardic. Because of increasing cyanosis, a tense fontanelle and generalized tonic seizures a septic screen was done, revealing purulent meningitis. After referral to our Neonatal Intensive Care Unit she was noted to have anisocoria (right pupil larger than left) and presented with obvious tonic seizures besides subtle convulsions. Her metabolic acidosis, hypotension and neutropenia were successfully treated but seizures persisted for 9 days despite phenobarbital, diphenylhydantoin, paraldehyde and diazepam. The lowest serum calcium was 5.8 mg/dL, but she was never hypoglycemic. Near the end of the first week a transient mild thrombocytopenia was documented. Blood and CSF cultures both grew Streptococcus agalactiae. After an initial period of persistent pulmonary hypertension with corresponding ventilatory treatment, she was slowly weaned from the ventilator 2 weeks after admission. It took 1 week to switch from nasogastric to oral feeding. On day 16 of life she had an EEG recording which showed epileptical activity covering the whole left hemisphere. Her eye grounds were unremarkable. Serial ultrasound examinations revealed a unilateral thalamic bleeding with minor intraventricular clot formation on the same side (Fig. 1). A CT scan was delayed for practical reasons until day 16 (Fig. 2). At the end of the first month she was hypotonic with bilateral ankle clonus. Her right pupil remained unresponsive to light and mydriatic for 2 months. In the absence of maintenance anticonvulsant therapy her EEG had a good structural basis on day 30, with intercurrent runs of irritative slow wave activity without persistent lateralisation. At the age of 6 months she was slightly hypotonic and had a high pitched cry, but was not suffering from cerebral palsy and found to be appropriate for age on a Denver Developmental Screening test. The thalamic density had disappeared on ultrasound in the beginning of the second month, not leaving a posthemorrhagic hydrocephalus.

Second case (VLL, 90/754, °08.12.90)

This boy presented in breech position at term, following an unremarkable pregnancy. Delivery of the aftercoming head created some difficulty: the chin was locked behind the symphysis and a rotational manoeuvre was necessary before proceeding to delivery according to Mauriceau. He weighed 3100 g for a length of 49 and a head circumference of 34 cm. The Apgar scores were 5 and 9 at 1 and 5 minutes. His postnatal course was uneventful until the sixth day of life. Irritability, opisthotonic posturing and a tense fontanelle preceded sudden generalised tonic seizures. He had a high pitched cry and started vomiting. Following an ultrasound examination he was referred to our Neonatal Intensive Care Unit. Upon admission his pupils were symmetrically responsive to light and isocoric. Tran-

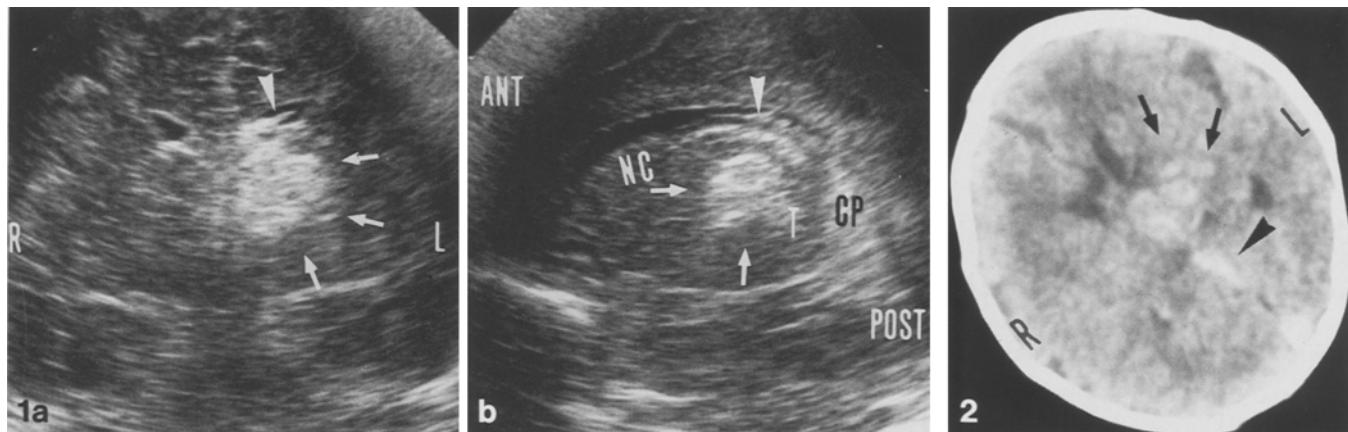


Fig. 1a,b. (first patient) US scan of the brain (7.5 MHZ) on day 3: a coronal section behind the foramina of Monro: hemorrhagic density within the left thalamo-caudate region (arrows); limited ventricular clot formation (arrowhead). **b** left parasagittal section: density restricted to upper left thalamus (T) in front of the choroid plexus (CP) and behind the nucleus caudatus (NC) (arrows); intraventricular clot (arrowhead)

Fig. 2. (first patient) uncontrasted CT scan of the brain on day 16: spontaneous opacification within the great cerebral vein (arrowhead); hemorrhagic opacities in the left basal ganglia (arrows)

sient right facial palsy was noticeable together with lateroflexion of the head due to bleeding within the right sternocleidomastoidus muscle. The seizures subsided with loading doses of phenobarbital and diphantoin. A thorough coagulation screen was normal except for a fibrinogen level of 99 mg/dL with a normal platelet count. US demonstrated a large bleed within the left thalamus, bilateral intraventricular bleeds and suspected white matter ischemia around the left lateral ventricle (Fig. 3). The hemorrhagic mass crossed the midline. High frequency sonographic scanning (10 MHZ) through the posterior fontanelle suggested limited densities within the tip of the superior sagittal sinus but on Colour Doppler flow imaging the vessel showed presence of venous flow. An uncontrasted CT scan the same day revealed additional spontaneous densities within the torcular Herophili and the great cerebral vein of Galen besides the bleeding suspected on ultrasound (Fig. 4). One week later an NMR scan documented extensive thromboses within the superior sagittal sinus, the straight sinus and several deep cerebral venous structures (Fig. 5). It confirmed unilateral white matter changes. At the age of 5 months he had mild spastic diplegia.

Third case (GO, 91/58, °02.04.91)

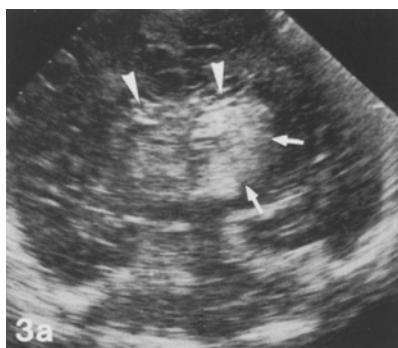
This boy was born after a pregnancy of 36 weeks complicated by pre-eclampsia. Oligohydramnios and fetal growth retardation had been recognized with prenatal echography. Following onset of labor, oxytocin augmentation was started. The delivery was spontaneous vaginal with a second stage of 20 minutes. The cord was tightly wrapped twice around the neck. His birthweight was 2000 g for a length of 43 and a head circumference of 33 cm respectively. Apgar scores were 4 and 6 at 1 and 5 minutes. The remaining liquor was meconium stained. Because of respiratory difficulties the newborn was nursed in a negative-pressure respirator [10] and received parenteral antibiotic treatment with ampicillin and netromycin. Despite an uneventful recovery on the first day of life sudden fever (39.5 °C), paleness and obvious generalized tonic seizures necessitated endotracheal ventilation and referral to our Neonatal Intensive Care Unit on day 2. On admission tonic and clonic seizures were noticed. The fontanelle was tense. There were no abnormal eye movements. In the neck a single deep and hemorrhagic pressure mark was pre-

sent on the right side: we felt this to be compatible with a local injury by the ventilator collar (Fig. 6). Hemoglobin in blood was 12.3 g/dL, platelets were 44.000/mm³ and fibrinogen 111 mg/dL. Lumbar CSF was uniformly hemorrhagic and did not clot. The clinical evolution excluded early onset septicemia. US scan on the third day of life disclosed bilateral intraventricular bleeding with extension of the coagulum into the right intercaudo-thalamic fissure; both the left and especially the right periventricular white matter contained cloudy echodensities suggestive of severe ischemia (Fig. 7). CT and NMR scan on day 4 revealed additional densities within the straight sinus, the occipital and transverse sinus and several cerebral bridging veins, corresponding to venous thrombi (Fig. 8). His clinical course went downhill with obvious bilateral leucomalacia on US scan and cerebral atonia preceding neonatal death on day 14.

Discussion

Including three described here, 25 instances of thalamoventricular bleeding in at or near term newborns were reviewed [11, 14, 15, 17, 20]. All had a birthweight above 2000 g (mean 3078). Seventeen were male (68%). Birth trauma was responsible for the event in 4 infants, birth asphyxia contributed in another 4. Delivery was spontaneous vaginal in 8, with low outlet forceps in 2, by caesarean section in 1 and by the breech in still another (no data in 13 neonates). Probable etiopathogenetic factors were dehydration in 3, hyponatremia in 1, polycythemia in 1, sepsis in 3, meningitis in 1 (case 1 in this report), hemorrhagic diathesis in 2 and jugular vein compression in 1 (case 3 in this report). The clinical features are gathered in Table 1.

In 1979 Palma et al. reported on 2 full-term neonates with CT-confirmed intraventricular hemorrhage and associated bleeding in the basal ganglia on one side [15]. Both presented several days from birth with an acute neurological deterioration not related to birth asphyxia or infection. The authors suggested the occurrence of delayed germinal matrix bleeding, in one infant probably facilitated by vitamin K deficiency. A few months later Mitchell and O'Tuama widened the age spectrum of intraventricular hemorrhage from the neonatal to the infantile period [14]. In a newborn girl they detailed a thalamoventricular bleed on day 12. A four-vessel angiogram at 20 days of age revealed a normal arterial and superficial cerebral venous phase, but failed to visualise the deep cerebral venous system. These authors chose the eponym "spontaneous" to describe the event, but obvious dehydration may have been an etiological factor. They specu-



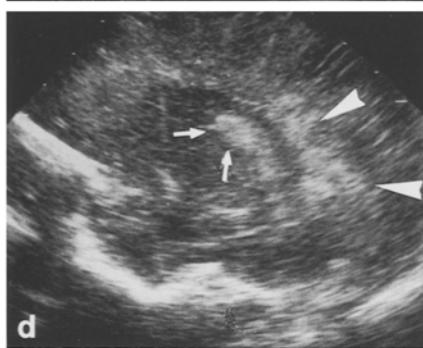
3a



c



b



d

Fig. 3a-d. (second patient) US scan of the brain (7.5 MHZ) on day 7:
a coronal section behind the foramina of Monro: hemorrhage within the left basal ganglia (arrows); bilateral ventricle clots (arrowheads)

b sagittal section: the density crosses the midline (arrow) (V4 = fourth ventricle, CC = corpus callosum)
c left parasagittal section: large intrathalamic density (arrows); intraventricular hemorrhage (arrowhead)
d left parasagittal section through centrum semiovale: hemorrhage in lateral basal ganglia (arrows); fluffy densities in the occipital periventricular white matter (arrowheads)

Fig. 4.a, b. (second patient) uncontrasted CT scan of the brain on day 7:
a section at the level of the basal ganglia: parasagittal hemorrhage mainly filling the left thalamic region and crossing the midline (arrows)

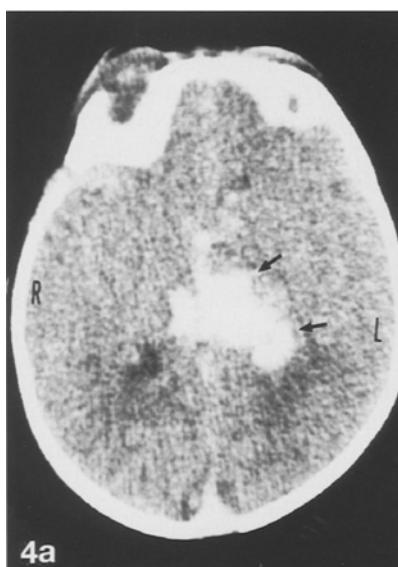
b section through the temporal horns of the lateral ventricles: hemorrhage within the left ventricle; spontaneous opacification of the great cerebral vein (GCV) and superior sagittal sinus (arrowheads)

Fig. 5a-c. (second patient) NMR images of the brain on day 14:

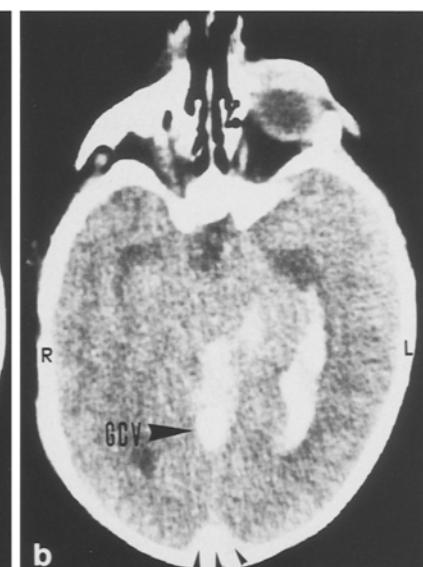
a left para-sagittal section (T1-weighted): increased signal intensity within the superior sagittal sinus (SSS), sinus rectus (SR), great cerebral vein (GCV), left thalamus (T) and left lateral ventricle (LLV); central less intense zones are characteristic of clot formation (arrows)

b axial section (T1-weighted): irregular signals of increased intensity in the superior sagittal sinus (arrowhead) and the left frontoparietal supraventricular white matter (arrows)

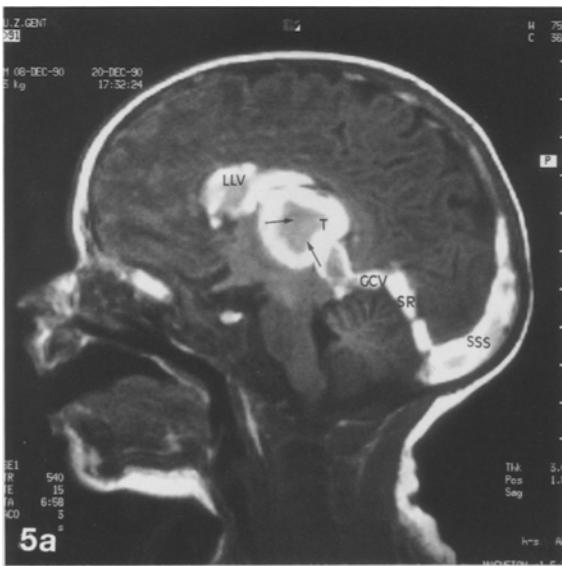
c axial section (T1-weighted) through the great cerebral vein (GCV): note the curvilinear high signal streaks sprouting from the thrombosed GCV (arrowheads) (possibly the internal cerebral veins and the basal vein of Rosenthal), the high signal intensity in a linear structure within the lateral ventricle (arrow) (choroid plexus vein), an ovoid hypersignal in the right parieto-temporal subarachnoid space (asterisk) (superficial cerebral vein or anastomosing vein of Labbé).



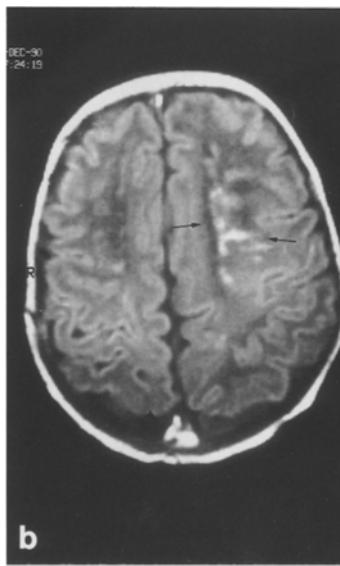
4a



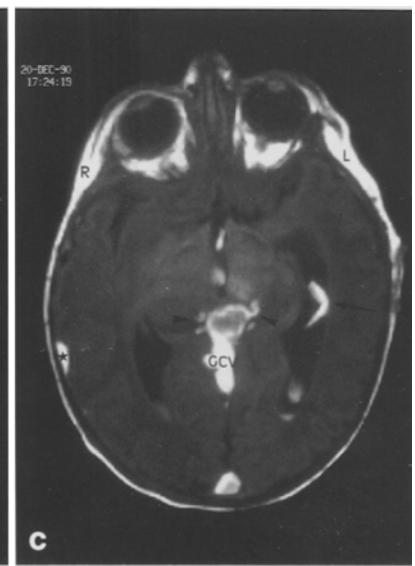
b



5a



b



c

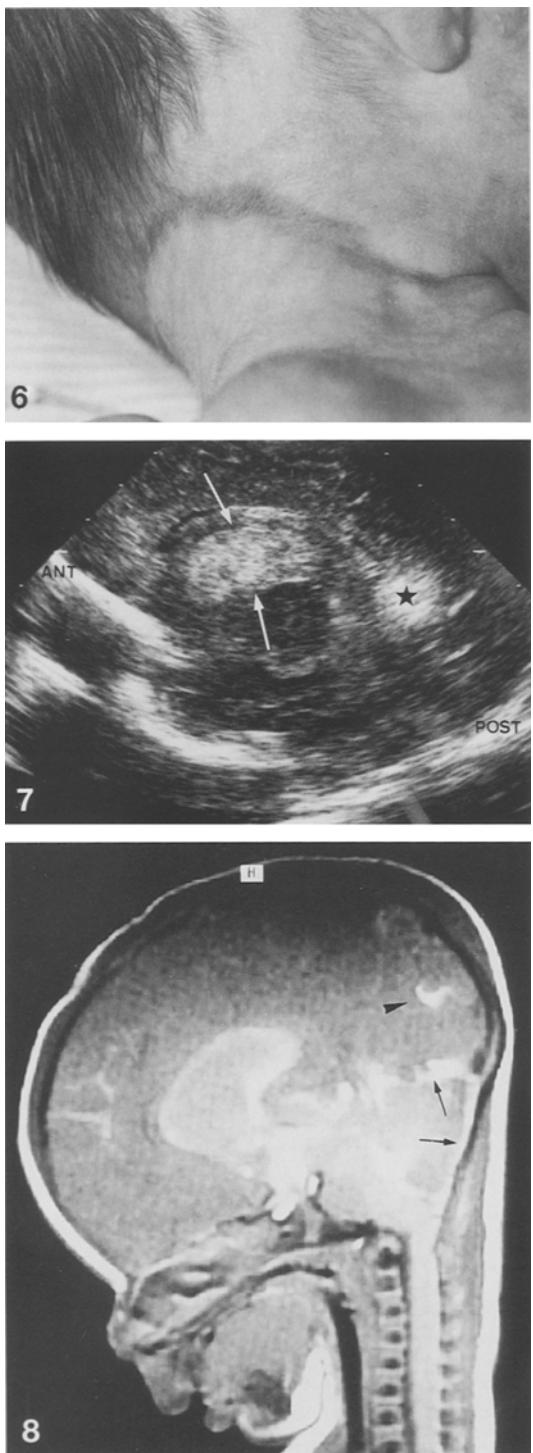


Fig. 6. (third patient): nuchal injury from an overtight seal by the collar of a negative-pressure ventilator

Fig. 7. (third patient) US scan of the brain on day 3: intraventricular clot extending between thalamus and caput nuclei caudati (arrows); periventricular white matter ischemia (asterisk)

Fig. 8. (third patient) T1-weighted NMR image of the brain on day 4: intravascular clots in the occipital and straight sinus (arrows) and in a cerebral bridging vein (arrowhead)

lated that, at least in some children, bleeding may originate in the choroid plexus as suggested in autopsy reports [5]. Trounce et al. accounted for 4 full-term newborns with

unilateral thalamic hemorrhage presenting unexpectedly in the second week of life [20]. Their main contribution was to specify the associated ophthalmological findings, possibly due to damage of the subthalamic frontomesencephalic optic pathway: vertical upward gaze palsy, deviation of the eyes towards the lesion, ipsilateral saccadic paresis and/or a flat visual evoked response. Three of the infants suffered from residual cerebral palsy and two needed ventriculoperitoneal shunting. In the discussion it was stipulated that one should differentiate this "new clinical entity" of unilateral thalamic bleeding from bilateral hemorrhagic infarction of the basal ganglia following severe birth asphyxia [12]. The first *NMR* images on this topic were reported in a dehydrated infant with extensive thrombosis of intracranial veins following misplacement of a central catheter up into the jugular vein [11]. The association with thalamic bleeding suggested deep cerebrovenous thromboses not shown in the figures of this report. A comprehensive review of *in vivo* diagnosed thalamo-ventricular hemorrhage in the full-term newborn is provided by Roland et al. [17]. At British Columbia Children's Hospital they recognized 19 instances of intraventricular hemorrhage diagnosed with CT and US scan in full-term neonates born between 1980 and 1987 and less than one month old. Twelve of these lesions were judged to follow a primary thalamic hemorrhage, 3 were thought to originate in residual germinal matrix and in 4 an indefinite source was suggested. The "thalamic" variety of intraventricular hemorrhage manifested mainly after the first 48 hours (10 of their 12 personal observations) whereas the "germinal matrix" variety invariably presented on the first or second day of life. In about half of their patients no etiological explanation was possible. Angiographic studies, normal in 2 neonates, disclosed impossible opacification of the deep venous system in one infant, despite absence of abnormal attenuation of the straight sinus on uncontrasted CT scan in this child. Only a minority of infants recovered completely.

Already in 1936 Ehlers and Courville summarized clinical and pathological findings on 26 children with deep cerebral venous thrombosis, including 5 of their own [6]. Three of those children were newborn. Both the existence of an association thalamic hemorrhage-ventricular bleeding and of an association deep venous thrombosis-thalamic hemorrhage was recognized. Throughout subsequent years a multitude of *etiopathogenetic mechanisms* were gradually associated with *deep cerebral venous thrombosis in newborn infants* (Table 2). An extensive amount of reports have documented the occurrence of deep venous thrombosis following *difficult delivery*. Nevertheless, the complete picture of bilateral thalamo-ventricular bleeding and a thrombosed, saccular and aneurysmal great cerebral vein of Galen has become a rare event in modern perinatology, probably due to the virtual disappearance of very prolonged labour [16]. On the other hand, this old concept of deep venous stasis in intracranial veins gained new interest in the study of germinal layer hemorrhage in preterm infants [23]. Several case reports mentioned the probable contribution of *dehydration* to thalamic hemorrhage [3]. Our first patient confirms the possibility of deep thrombophlebitis associated with men-

Table 1. Thalamo-ventricular bleeding in the full-term neonate. Clinical features (22 literature + 3 personal observations)

	<i>n</i> = 25
Free interval from birth (days)	
• mean	11
• range	1-27
• $\geq 8/\geq 15$	13/5
• $< 1/\leq 7$	3/12
Signs and symptoms	
• lethargy/irritability	4/10
• opisthotonus	6
• fontanelle: bulging/normal	7/2
• seizures: focal/general	8/9
• contralateral hemiparalysis ^a	3
• high pitched cry	3
• eye signs – sunsetting	5
– nystagmus	1
– saccadic paresis ^b	3
Neonatal death	2
Hydrocephalus requiring shunt	12
Normal survival	6
Cerebral palsy	14

^a except for one ipsilateral instance

^b ipsilateral [20]

Table 2. Etiology of deep cerebral venous thrombosis in the neonate

- Following difficult delivery
- Primary (marantic) thrombosis due to dehydration [3]
- Associated with leptomenitis and ventriculitis [2, 7]
- In association with cyanotic heart disease and polycythemia [4, 13]
- As a consequence of thrombosis in a major superficial cerebral vein or sinus, extending into deeper vessels via the straight sinus [3]
- Following severe birth asphyxia [22]
- In the vicinity of a germinal layer hemorrhage [8]

ingitis [2, 7]. *Polycythemia*, as in neonates with cyanotic heart disease, is a wellknown cause of venous occlusion and the case presented by Miller et al. is firmly suggestive of thalamic bleeding following polycythemia [13]. All etiological factors leading to *superficial cerebral venous thrombosis* in the neonate, are indirect causes of deep cerebrovenous thrombosis. One report suggests an important rôle for *asphyxia* in some instances of venous thrombosis within the cranium [22]. Finally, any severe (fatal) *intraventricular bleeding* may lead to hemorrhagic venous periventricular infarction [8].

Our second case is a unique example of *in vivo* diagnosed *deep cerebral venous thrombosis associated with late onset thalamo-ventricular bleeding in a full-term neonate*. Angiographic studies already suggested this phenomenon before [14, 17]. Evidently the postmortem observations referred to above firmly underscribe this cause and effect relation [6]. As the corpus striatum, dorsal thalamus, choroid plexus and subependymal matrix at the foramen of Monro are all drained by the internal cerebral veins, occlusion of these vessels or their tributaries can lead to deep hemorrhagic infarction and/or germinal layer bleeding and/or choroid plexus hemorrhage, explaining the frequent association of bleeding into the basal ganglia with intraventricular hemorrhage [6, 14, 15].

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