Eur. Radiol. (2001) 11: 1760–1765
DOI 10.1007/s003300100822

PEDIATRIC

Cerebral venous thrombosis in childhood

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Received: 1 September 2000
Revised: 19 December 2000
Accepted: 26 December 2000
Published online: 3 February 2001

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Abstract This was a retrospective study to determine different etiologies of cerebral venous thrombosis (CVT) in childhood and to correlate extent and location of thrombosis with the etiology and the age of the child as well as the final outcome. In addition, the radiologic approach is discussed. This was a retrospective analysis of 19 children with CVT. The children were examined by contrast-enhanced dynamic CT. Radiologic findings were correlated with the etiology of CVT. Cerebral venous thrombosis is not as infrequent in children as has been thought. Cerebral venous thrombosis in children can occur due to trauma ($n = 9$), infections ($n = 7$), or coagulation disorders ($n = 3$). Extent and location of thrombosis, as well as complications, final outcome, and therapy, depend on the etiology. Computed tomography remains a valuable primary imaging modality in the diagnosis of CVT in the acutely injured or diseased child.

Keywords Dural sinus · CT · Trauma · Infection

Introduction

Cerebral venous thrombosis (CVT) is a well-known clinical entity in adults. Morbidity and mortality vary and depend on the topography and extent of thrombosis. Clinical symptoms occur when a thrombus impairs the venous drainage of brain tissue with resultant venous (hemorrhagic) infarctions. Cerebral venous thrombosis in children is probably less frequent; however, exact statistics are unknown. Cerebral venous thrombosis may develop in neonates due to various etiologies including dehydration and hypoxia–ischemia [1, 2, 3, 4]. In infancy and childhood CVT is seen in association with infections such as mastoiditis [5, 6]. In addition, CVT may occur in other infections including common colds and trauma [7]. Intracranial (dural) arteriovenous shunts are known to induce or to be associated with CVT [8]. Cerebral venous thrombosis may also appear in malignant diseases such as lymphoma [9] and coagulation disorders such as protein-S deficiency or protein-C deficiency [10, 11]. Cerebral venous thrombosis is often misdiagnosed because of its non-specific clinical presentation [12]. Symptoms may vary from mild headache to coma with death. We retrospectively evaluated 19 children with CVT to correlate extent and location of thrombosis with the etiology, the age of the

Table 1 Etiology of CVT related to child's age

Group		Infants 0–12 months	Young childhood 1–6 years	Older childhood > 6 years
A	Head trauma ($n = 9$)	0	3	6
	Skull fracture crossing dural sinus	0	3	5
	Petrous bone fracture	0	1	4
	Epidural hematoma	0	2	0
	Brain contusion	0	1	1
B	Infectious ($n = 7$)	2	4	1
	Mastoiditis	1	4	1
	Meningitis	1	0	0
C	Coagulation disorders ($n = 3$)	3	0	0

child, and the final outcome. In addition, CT imaging findings which support the diagnosis of CVT were reviewed.

Patients and methods

Patients were retrospectively selected by a computer-assisted review, checking the CT diagnosis database for CVT in the time period between 1994 and 1998. Nineteen children (10 girls and 9 boys; age range 14 days to 14 years, mean age 5 years 2 months) were included. All children were suspected of CVT according to either clinical history and symptoms, or suspicious CT findings. In all children pre- and post-contrast CT was performed (slice thickness infratentorial: 3 mm; supratentorial: 5 mm). Non-ionic contrast was injected (2 ml/s) at the standard body-weight related dose. Scanning started after 60 % of the dose was administered. Scan duration varies depending on the size of the child's head/required number of slices. Different window-level settings were used including standard brain parenchyma and bone settings as well as a high window-level setting to differentiate contrast-enhanced dural sinus from adjacent hyperdense bone. Images were evaluated by at least two pediatric radiologists. Follow-up CT was acquired using the same acquisition technique and parameter. The CT was evaluated for the dense vein or cord sign which results from high-density blood clots within the course of either a dural sinus or cortical vein. The CT was also evaluated for the empty delta or sinus sign. Instead of a direct visualization of the hyperdense blood clot, contrast enhancement allows the indirect identification of blood clots because the vessel wall enhances strongly and the intraluminal blood clot enhances relatively poorly. Depending on the shape of the venous channel, either an empty delta (Δ) or an empty sinus (O) will be seen. The positive identification of the empty delta or empty sinus on multiple slices on initial CT and the resolution of this sign on follow-up imaging was considered to be diagnostic for CVT. In addition, secondary signs and complications of CVT; congested cortical veins, tentorial or gyral enhancement, venous infarctions, as well as hydrovenous disorders, defined as hydrocephalus due to impaired cerebrospinal fluid resorption at the venous channels, were evaluated. The extent and topography of CVT were correlated with clinical findings and the etiology.

Results

Three groups were defined as follows: group A, trauma ($n = 9$); group B, infectious ($n = 7$); and group C, coagulation disorders ($n = 3$; Table 1). Correlating the child's age and the etiology of thrombosis, CVT due to head trauma occurred in childhood, infectious CVT occurred in all age groups with a peak during young childhood, and CVT due to coagulation disorders occurred in infants.

In group A, 5 children showed a petrous bone/skull-base fracture. The remaining children had isolated fractures at different locations. In 2 children an epidural hematoma displaced the adjacent dural sinus (Fig. 1a). In 8 of 9 children the fracture crossed the dural sinus (Fig. 1b). One girl with fracture of the anterior skull base developed a frontal lobe abscess with subdural empyema. On follow-up, no patient developed venous infarction or hemorrhage. In one boy a discrete transient hydrocephalus was observed. All children showed a spontaneous recanalization on follow-up. No neurologic deficit correlated directly with the location and extent of thrombosis.

In group B, 6 children with mastoiditis developed thrombosis of the adjacent dural sinus. Presenting symptoms were malaise with fever (7 of 7), otalgia (5 of 7), headache (4 of 7), and febrile convulsions (3 of 7). Antegrade thrombus propagation from the sigmoid sinus into the jugular vein was seen in 5 children, and retrograde thrombus propagation into the transverse sinus was seen in 4 children. Compared with traumatic CVT, thrombosis was more extensive as well as its complications, e.g., internal carotid artery thrombosis (Fig. 2) or neck abscesses ($n = 2$; Fig. 3). All children underwent mastoidectomy with incision and drainage of the thrombosed sigmoid sinus. No ligation of the sinus was necessary. All children were treated with antibiotics. Five of 6 patients received anticoagulation with heparin for 2–5 weeks; however, therapeutic levels of anticoagulation were reached in only 2 patients. One child developed CVT due to extensive meningitis. On follow-up, venous infarctions occurred in 2 children.

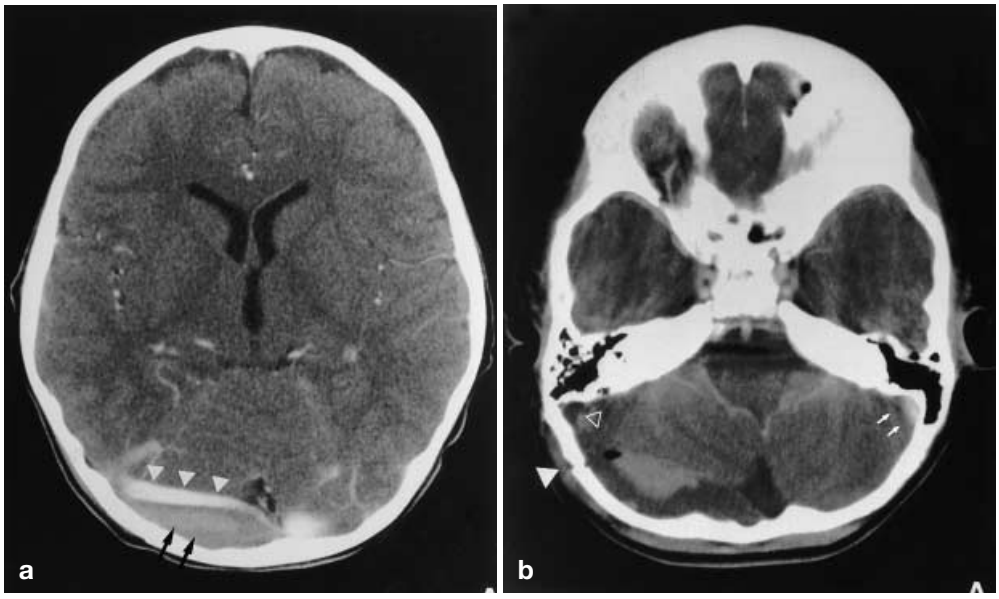

Fig. 1 a, b Computed tomography of two children with head trauma. **a** The first child shows an epidural hematoma *(arrows)* which displaced the transverse sinus *(arrowheads)* with thrombosis of the ipsilateral sigmoid sinus (not shown). **b** The second child suffered from a skull-base fracture *(arrowhead)* and developed sigmoid sinus thrombosis *(open arrowhead)*. Compared with the contralateral sigmoid sinus *(arrows)*, an empty sinus is seen

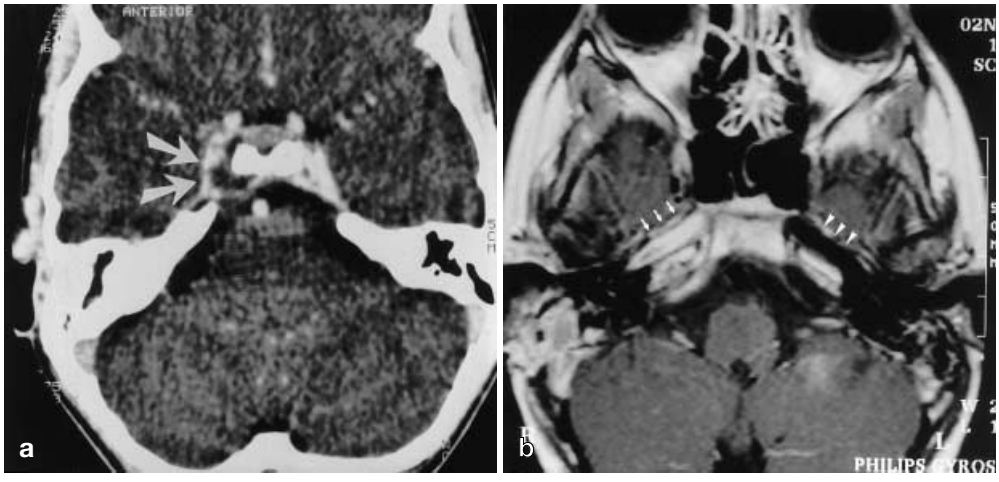

Fig. 2 **a** Computed tomography of a child with mastoiditis. Infection propagated along the superior petrous sinus with septic thrombosis of the right cavernous sinus, visualized as a hypodense filling defect within the right cavernous sinus *(arrows)*. **b** On follow-up, contrast-enhanced MRI showed thrombosis of the internal carotid artery *(arrows)*. The contralateral carotid artery shows a normal hypointense flow void *(arrowheads)*

With the exception of the child with meningitis, all children recovered without neurologic deficits.

In group C, 3 infants presented with extensive thrombosis of the deep and superficial venous system (Fig. 4a). In all 3 patients protein-C or protein-S deficiency was detected. On follow-up all children showed extensive venous infarctions with secondary hemorrhage (Fig. 4b). Follow-up CT showed the pattern previously described by Lasjaunias of a "melting brain" which is known as a devastating, progressive destruction/resorption of the telencephalon [8]. Only one child survived with severe neurologic deficits.

Evaluating the primary CT signs of CVT (Table 2), the empty delta or sinus sign was positive in all patients, the dense vein sign in 8 of 19, and the cord sign in 1 of 19 patients. From the secondary CT signs venous infarctions were seen in 5 of 19, congested cortical veins in 4 of 19, and hemorrhage and hydrovenous disorders in 3 of 19 patients. No increased tentorial or gyral enhancement was seen.

Discussion

Our series of 19 children in a time period of 43 months in a mid-sized children's hospital indicate that CVT is not as uncommon in childhood as thought. The condition is often missed because of the non-specific clinical presentation [2] and the variable natural history of CVT [4]. The presentation depends on the time course of thrombus formation (acute vs chronic), the thrombus location and extension, the individual anatomy of the

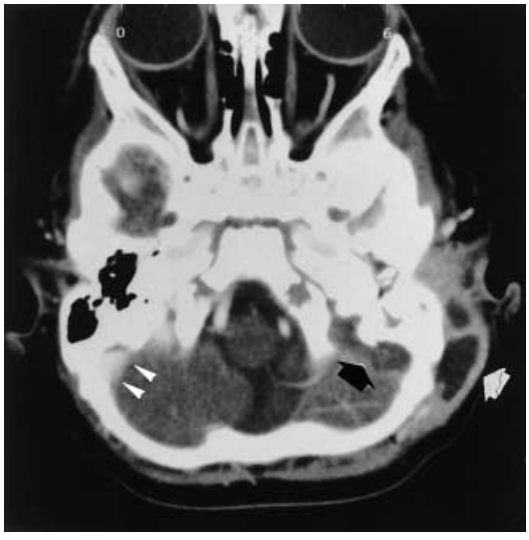

Fig. 3 Computed tomography showing a child with left-sided mastoiditis. A lateral neck abscess *(white arrow)* developed as well as thrombosis of the left sigmoid sinus *(black arrow)*. Regular enhancement of the contralateral sigmoid sinus *(arrowheads)*

child (presence of collaterals), and the age of the child [8]. In our population most children presented with nonspecific symptoms such as seizures (8 of 19), nausea (4 of 19), headache (4 of 19), and decreased level of consciousness (2 of 19). These symptoms are believed to be secondary to an increased intracranial venous pressure with resultant impairment of cerebrospinal fluid absorption at the venous channels. The radiologic manifestations include acute signs (venous ischemia), subacute signs (melting brain), and chronic signs (cerebral dysmaturation and hydrocephalus) [8]. These findings were also observed in our patient group with venous infarctions in 5 of 19 and mild hydrocephalus in 3 of 19.

Traumatic CVT occurred mainly in older childhood who are more at risk for trauma. The exact etiology of traumatic CVT is not known, but several theories have been suggested: obstruction of the dural sinuses from traumatic rifts of the venous channels, compression of the sinus by adjacent hematomas, intramural hemorrhage caused by rupture of small sinusoids, injury to the endothelial lining, or thrombus extension from injured emissary veins [13, 14]. In our series there were only minor clinical symptoms in traumatic CVT. In group A, despite the fact that no anticoagulation therapy was given, the sinus recanalized spontaneously in all children. Our findings indicate that in children with skull fractures crossing a dural sinus or with an epidural hematoma adjacent to a dural sinus, CVT should be excluded.

In group B no child was clinically suspected of CVT. Computed tomography was obtained because of the severity of infection. Cerebral venous thrombosis occurred in all age groups with a peak incidence in young childhood. Controversy exists about the appropriate treatment of septic CVT. The value of an antibiotic treatment is well established, but the role of anticoagulation is unclear [15, 16]. Our retrospective study does not allow us to study the value of systemic anticoagulation especially since therapeutic levels were reached in only 2 children. Contrast-enhanced CT showed recanalization of all sinuses on follow-up.

In group C, CVT due to coagulation disorders occurred exclusively in infancy. Sepsis, dehydration, shock, and hypoxia–ischemia are additional known etiological factors of neonatal CVT [17]. In our series, thrombosis was most extensive in group C with involvement of almost all deep and superficial venous outlets. Extensive venous/hemorrhagic infarctions occurred with the development of a "melting brain" on follow-up. To prevent this mostly lethal course, systemic

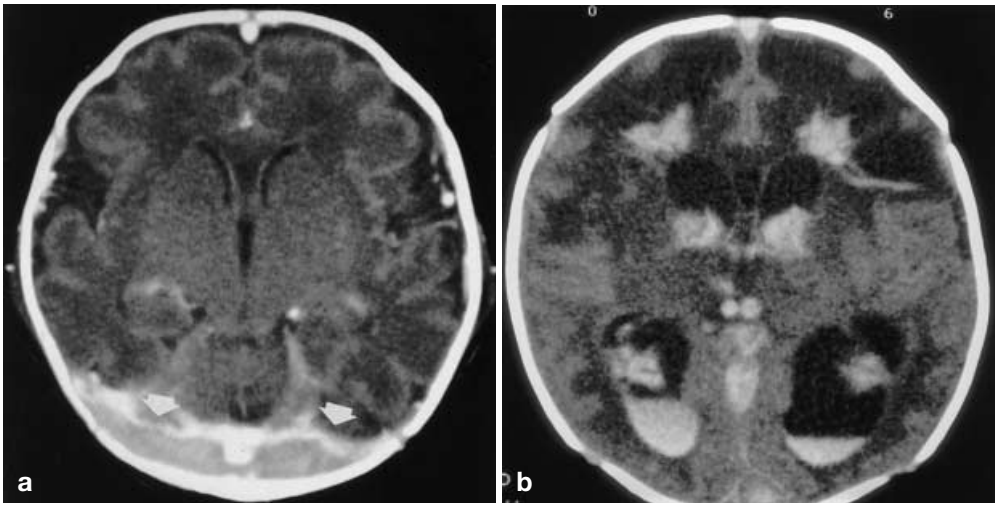

Fig. 4 **a** A CT image of a neonate with thrombosis of both transverse sinuses *(arrows)*. A residual wall enhancement is seen. **b** Follow-up CT shows extensive hemorrhagic venous infarctions in both hemispheres as well as intraventricular hemorrhage

Table 2 Primary and secondary CT signs of CVT

Group	A ($n = 9$)	B ($n = 7$)	C ($n = 3$)	Total ($n = 19$)
Primary CT signs				
Empty delta/sinus sign	9	7	3	19
Dense vein sign	2	3	3	8
Cord sign	0	1	0	1
Secondary CT signs				
Venous infarctions	0	2	3	5
Congested cortical veins	1	1	2	4
Hemorrhage	0	0	3	3
Hydrovenous disorders	1	1	1	3
Gyral/tentorial enhancement	0	0	0	0

anticoagulation should probably be started as early as possible before extensive venous infarction.

Computed tomography remains in most hospitals the first imaging modality in the work-up of acutely diseased/injured children. It has several key advantages in the acute setting: easy to perform; readily available; the child remains well accessible for emergency physicians during scanning; and short acquisition times reduce motion artifacts. The combination of pre- and post-contrast CT allows an exact evaluation of dural sinuses. Contrast-enhanced CT is especially helpful in differentiating the normal high attenuation of dural sinuses in neonates from thrombosis. The combined evaluation of different window-level settings and the use of thin slices reduces the likelihood that anatomic variations will be mistaken for filling defects from large arachnoid granulations, fibrous bands, or septa [18]. The use of high-speed CT scanners allows scanning during peak venous enhancement which will increase the sensitivity for filling defects. Consequently, all our patients showed an empty delta or empty sinus. Magnetic resonance imaging and MR angiography have often been reported as the most sensitive imaging methods for CVT; however, in the clinical setting of the acutely injured or diseased child, MRI has several practical drawbacks. Magnetic resonance imaging cannot be performed in the presence of most life-support systems used in emergency wards because these are frequently not MRI compatible. In addition, MR can be misleading, flow-related enhancement can mimic fresh thrombus on MRI, methemoglobin within a fresh thrombus can mimic flow on time-of-flight MRA, and in-plane flow can mimic thrombosis due to saturation effects [19]. In our series the empty delta or sinus sign was seen in all patients, whereas the dense vein sign was only seen in 42% of the children. The secondary CT signs that are of important clinical consequences should, however, not primarily be used for diagnosis of CVT.

A major limitation of our study is the retrospective character. A prospective study should show how often CVT is encountered in a non-selected series of children with head trauma or mastoiditis. The value of anticoagulation should also be investigated in a randomized study. The sensitivity and specificity of CT for CVT could not be established in our study. The diagnostic accuracy of dynamic contrast-enhanced CT compared with MRI/MRA should be established in a prospective double-blinded study where conventional cerebral venography can be used as gold standard.

In summary, CVT is more common in children than thought and usually presents with non-specific clinical symptoms. Cerebral venous thrombosis should be suspected if a fracture crosses a dural sinus or an epidural hematoma is located near a dural sinus. Traumatic thrombosis is usually focal, without major neurologic symptoms, and spontaneous recanalization usually occurs. Infectious CVT is more extensive and should be treated more aggressively. Neonatal CVT due to coagulation disorders occurs with high morbidity and mortality due to extensive thrombosis. Early anticoagulation could be life saving. Computed tomography with good contrast enhancement (during peak venous enhancement) and adequate window-level settings is easy to perform and readily available in the acutely injured or diseased child.

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