

Neonatal Idiopathic Cerebral Venous Thrombosis: An Unrecognized Cause of Transient Seizures or Lethargy

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Seven neonates who presented with either lethargy (four infants) or seizures (three infants) were found by magnetic resonance (MR) phase imaging to have idiopathic cerebral venous thrombosis (CVT). Examination showed only hypotonia or hyperreflexia. The presence of CVT was suggested by unenhanced cranial computed tomographic (CT) scans. Conventional MR T1- and T2-weighted images often indicated more extensive thromboses than were suggested by cranial CT. In all infants, MR phase imaging confirmed thromboses by establishing absence of blood flow in cerebral veins or sinuses. No infant received anticoagulation. Lethargy slowly resolved and seizures did not recur. Normal development has been observed thus far in brief follow-up. The occurrence of seven infants with idiopathic neonatal CVT within a 3-month period indicates that CVT may be a cause of neonatal seizures or lethargy of unclear cause. MR phase imaging provides a powerful, noninvasive means of confirming the diagnosis. Treatment with anticoagulants does not appear necessary.

Rivkin MJ, Anderson ML, Kaye EM. Neonatal idiopathic cerebral venous thrombosis: an unrecognized cause of transient seizures or lethargy. *Ann Neurol* 1992;32:51-56

Cerebral venous thrombosis (CVT) has been infrequently observed in neonates [1-6]. Although previous reports have provided radiological demonstration of dural sinus thrombosis, only scant documentation exists of thrombosis in the deep intracerebral venous system. Dehydration, polycythemia [5], sepsis [6], and protein C deficiency [7] have been implicated as causes of CVT. Despite extensive investigation, frequently no clear cause is found for dural sinus thrombosis occurring in neonates [1]. Little information exists about the clinical presentation and the necessity of treatment of CVT in this age group. Further, magnetic resonance (MR) phase images have not been used previously to document CVT in neonates. This MR technique, which can be obtained concomitant with conventional MR images, provides clear, noninvasive determination of blood flow within intracranial veins and greatly simplifies diagnosis of CVT in both dural and deep venous systems [8]. We report the clinical presentation and management of seven neonates encountered within a 3-month period who had idiopathic CVT diagnosed by MR spin echo T1- and T2-weighted images as well as phase-imaging technique.

Methods

All seven neonates (aged 1 day to 3 weeks) presented over a 3-month period. All infants were full-term except one born at 32 weeks' gestation. Each was evaluated as an inpatient in either the neonatal intensive care nursery or the step-down intensive care nursery at the Floating Hospital for Infants and Children. In each infant, neurological evaluation was obtained to explain either seizure or lethargy of unclear cause. All infants were examined initially and followed by a pediatric neurologist. Each patient was evaluated by complete blood count with differential; blood, urine, cerebrospinal fluid (CSF) cultures; serum electrolytes, blood urea nitrogen (BUN), creatinine, calcium, magnesium, phosphorus, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total protein, albumin, and total bilirubin; coagulation panel, including prothrombin time (PT), partial thromboplastin time (PTT), protein C, protein S, antithrombin III, and lupus anticoagulant; serum and urine amino acid and urine organic acid analyses. Unenhanced computed tomographic (CT) images were obtained on a Siemens DR3 scanner (Siemens Medical Systems, Iselin, NJ). The MR studies were performed on a Siemens 1 T Magnetom. Spin echo technique was used to obtain T1- and T2-weighted images. Two-dimensional phase images, to assess dural sinus and cerebral venous patency, were performed during the T1 data acquisition. The T1-

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Received Jul 31, 1991, and in revised form Nov 11 and Dec 24. Accepted for publication Dec 30, 1991.

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weighted and phase images were acquired in the sagittal, axial, and coronal planes. The T2-weighted images were performed in the axial plane. Follow-up neurological evaluation has been conducted (through 6 months of age) in the Pediatric Neurology Clinic of the Floating Hospital for Infants and Children.

Results

Seven neonates were identified (three girls, four boys). Four of the seven patients were delivered vaginally. Six of seven achieved an Apgar score of eight or greater at 5 minutes; all had Apgar scores of at least nine at 10 minutes. Meconium staining was found in only one infant (none below vocal cords) and none required intubation. Two representative infants are summarized below.

Patient 1

This infant was a 3.03-kg product of a full-term gestation, delivered by cesarean section for fetal distress detected after onset of labor. Apgar scores were 9 and 9 at 1 and 5 minutes. On the fifth day of life, a left flank mass was noted and subsequently a renal vein thrombosis was discovered. Anticoagulation therapy was stopped after a few days when improved renal blood flow was noted. On the twelfth day of life, the baby had synchronous jerking of the right arm and leg, which stopped spontaneously after 60 seconds. Neurological examination and electroencephalogram were normal. Laboratory studies were normal. An unenhanced head CT showed high attenuation in the superior sagittal sinus (SSS), straight sinus, torcular, and subependymal veins suggestive of venous thrombosis. Hemorrhage was present in the left anterior thalamus, and within choroid plexus in the left lateral ventricle (see Fig 1). The cranial MR study showed thromboses of SSS and straight sinus, left transverse sinus, vein of Galen, and both internal cerebral veins (see Fig 2). MR phase images demonstrated absence of flow in SSS, straight, and left transverse sinuses, the vein of Galen, and both internal cerebral and thalamostriate veins (see Fig 2). The patient never manifested signs of increased intracranial pressure and neurological examination remained normal. An MR imaging study, including phase images 3 weeks later, showed partial recanalization of deep and superficial venous systems (Fig 3). The infant has demonstrated normal neurodevelopment and is seizure-free on anticonvulsants.

Patient 2

This infant was the product of a full-term, uneventful gestation. Apgar scores were 5 and 8 at 1 and 5 minutes. Lethargy and a left Erb's palsy were noted after birth. The infant remained lethargic for the next several days. Neurological examination revealed lethargy and findings consistent with a left Erb's palsy. Labora-

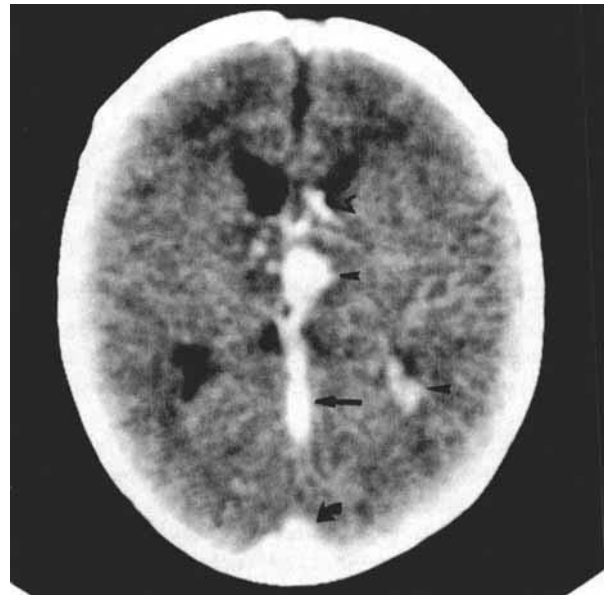
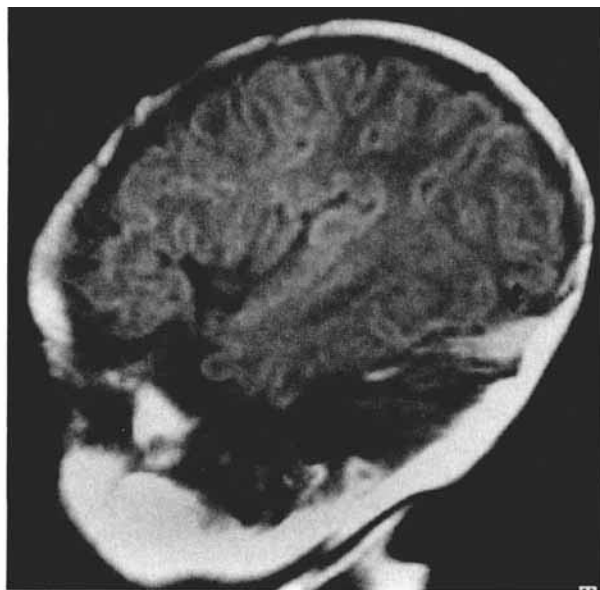


Fig 1. Patient 1. Unenhanced computed tomographic scan suggesting thrombosis of distal superior sagittal sinus (curved arrow), straight sinus (straight arrow), and subependymal veins (open arrow). Hemorrhage is seen in left thalamus and left choroid plexus (arrowheads).

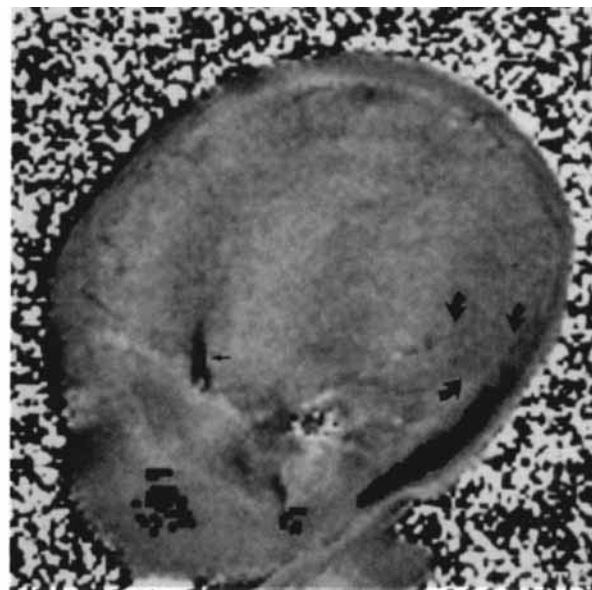
tory studies were normal. An unenhanced cranial CT done on the fifth day of life showed findings suggestive of a right transverse sinus thrombosis as well as deep white matter hemorrhagic infarcts greater in the right hemisphere than in the left hemisphere. A cranial MR spin echo study showed thrombosis of both transverse sinuses as well as biparietal hemorrhagic venous infarcts. MR phase images showed no flow in the transverse sinuses. At 3 months of age, neurodevelopment is normal.

Clinical signs at presentation as well as neuroradiological findings for all seven infants are summarized in the Table. Three infants were initially evaluated for seizures of unknown cause; in all three, seizures were of focal onset. Four neonates came to neurological attention as a result of unexplained lethargy.

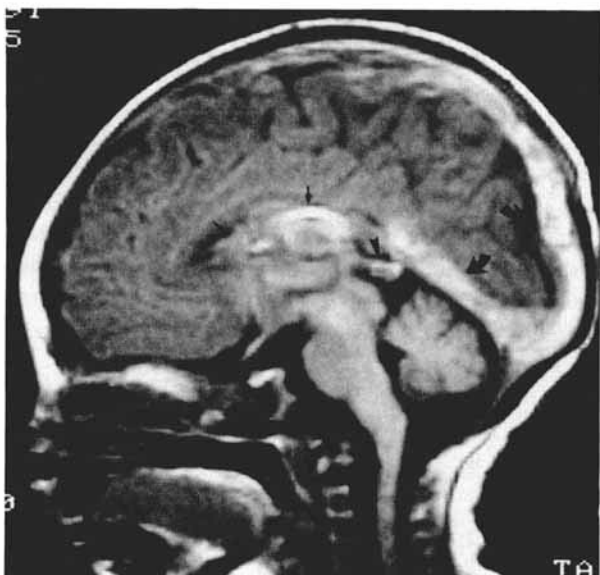
In six of seven infants, CT scanning revealed increased attenuation in a distribution suggesting either dural or venous thrombosis. In one infant, no such evidence was found. MR imaging consisted of simultaneously acquired T1, T2, and phase images on all patients. T1 and T2 MR images provided additional evidence of thrombosis in all six infants in which CVT had been suggested by CT. In the one infant with no CT evidence of CVT, MR images suggested thrombosis of the right basal vein of Rosenthal and the vein of Galen. Moreover, in four infants, MR T1 and T2 images provided evidence of more extensive thromboses of the dural and deep venous systems than that offered



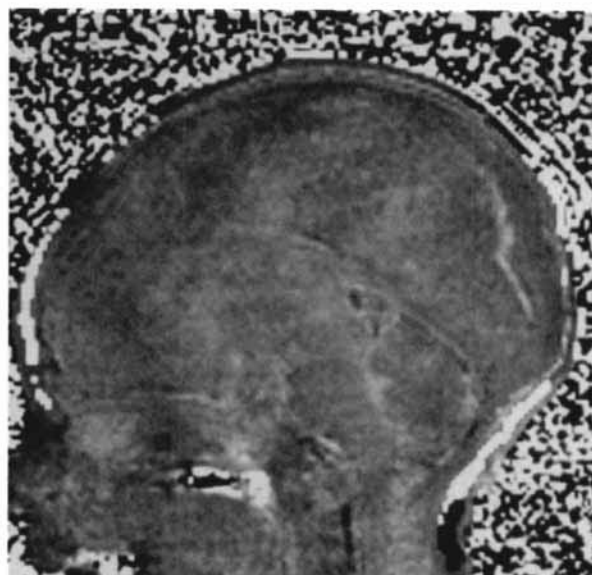
A



B



C

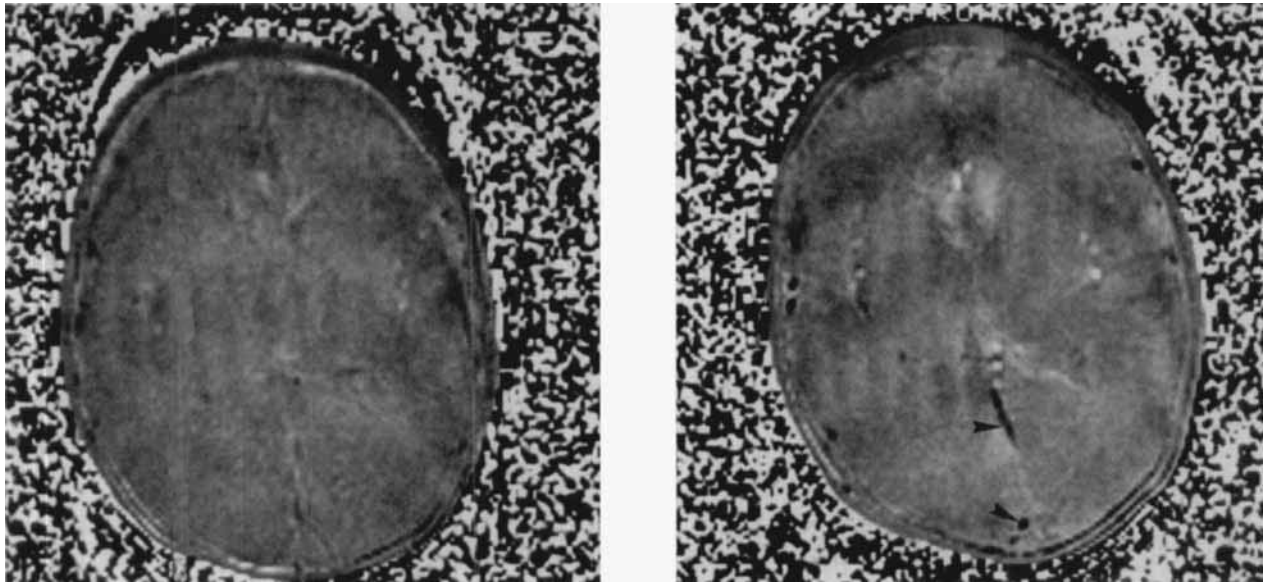


D

Fig 2. Patient 1. (A) Magnetic resonance (MR) T1-weighted image showing a high signal in left transverse sinus suggesting acute sinus thrombosis (curved arrow). (B) Corresponding MR phase image of demonstrating absence of flow signal in left transverse sinus (outlined by curved arrows) confirming sinus thrombosis. Flow signal is noted in the right superficial middle cerebral vein (small arrow). (C) MR T1-weighted sagittal image showing high signal in superior sagittal sinus and straight sinus (curved arrows), vein of Galen (arrowhead), internal cerebral veins, and subependymal veins (small arrows). (D) Corresponding MR phase image of C demonstrating absence of flow signals in venous structures, confirming thromboses.

by CT. In all seven infants, MR phase images demonstrated absent blood flow in the veins and sinuses, initially thought to be thrombosed on the basis of CT and MR T1 and T2 images (see Figs 2, 3).

Cultures (of urine, blood, and CSF) taken from each infant grew no organisms. Serum electrolytes, BUN, creatinine, calcium, magnesium, phosphorus, ALT, AST, total protein, albumin, and total bilirubin were normal in each infant. Serum and urine amino acid and urine organic acid profiles obtained in all seven infants were normal. Finally, coagulation studies (including PT, PTT, protein C, protein S, antithrombin III, and lupus anticoagulant) were normal in each infant.



A

B

Fig 3. (A) A magnetic resonance (MR) phase image demonstrating absent flow in distal superior sagittal sinus (SSS), straight veins, and subependymal veins. (B) An MR phase image taken 3 weeks later demonstrating partial return of flow signal in distal SSS and straight sinus (arrowheads).

Treatment of infants presenting with seizures has consisted of phenobarbital alone. These patients continue to receive phenobarbital but have suffered no recurrence of seizures. No patients received anticoagulant or thrombolytic therapy. Each infant has received follow-up neurological evaluation through the first 6 months of life. In two infants, repeat MR images have revealed recanalization of thrombosed areas. All infants, except one with frontal cerebral dysgenesis, have demonstrated normal neurodevelopment.

Discussion

Neonatal CVT is thought to occur rarely and is less well documented than in older children or adults. Indeed, this entity is not discussed in a comprehensive textbook of neonatal neurology [9]. Sinus thrombosis in neonates was first recognized by Parrot [10–12] in 1873. Bailey and Hass [6], Byers and Hass [13], and finally, Banker [14] described the neuropathology of CVT in infancy.

Contemporary pediatric and neurological literature contain only isolated case reports and one series of infants with neonatal CVT [1]. Marciniak and colleagues [7] reported a neonate with CVT who presented with purpura fulminans caused by a congenital absence of protein C. Konishi and associates [5] reported three term infants in whom sagittal sinus thromboses were discovered after each presented with seizures. In their report, polycythemia was found in two

of three infants. Two neonates with CVT were reported by Wong and coworkers [4]; in each case, the infants had suffered pronounced asphyxia. Both infants presented with seizures. Finally, Shevell and colleagues [1] in a retrospective series spanning 8 years identified 17 neonates with dural sinus thrombosis by using unenhanced cranial CT. Fifteen of these 17 infants presented with seizures. Dural sinus thrombosis was apparently idiopathic in the majority of neonates reported in this series [1].

Our series of seven neonates describes infants encountered over the relatively brief period of 3 months. In no infant were conditions felt to predispose to CVT, such as coagulopathy, metabolic defects, bacterial sepsis, perinatal birth trauma/asphyxia, dehydration, or polycythemia, found. Thus, five of the seven infants we report appear to have suffered idiopathic CVT (see Table). In the two remaining infants, associated clinical features somewhat obscure a clear idiopathic cause. In one infant (Patient 6), structural abnormalities of the brain may have included physical impediments to venous flow leading to stasis and resultant CVT. In the second infant (Patient 7), the CSF profile suggested viral meningitis. In both infants, no other evidence of conditions associated with CVT was found.

No infant developed signs of increased intracranial pressure. Either unexplained seizure (in three infants) or unexplained lethargy (in four infants) served as the clinical features leading to neurological evaluation and diagnosis of CVT. Although seizures have been reported in neonates with CVT [1, 4], lethargy has not been reported as a presenting sign of this disorder. No infants received anticoagulants. Follow-up neurological

Clinical Signs, Neuroradiological Findings, and Etiologies of Seven Neonates with CVT

Patient No.	Clinical Symptoms	CT Findings	MRI Findings	Cause
1	Seizure, beginning with right focal features	1. SSS thrombosis 2. Left parietal lobe infarct	1. SSS thrombosis; left parietal lobe infarct 2. Phase: absent blood flow at torcular and distal SSS	Idiopathic
2	Seizure, right arm rhythmic jerking	SSS and straight sinus thromboses	1. SSS, bilateral transverse sinus, bilateral internal cerebral vein thromboses 2. Phase: no flow in SSS, straight sinus, vein of Galen, bilateral internal cerebral veins	Idiopathic
3	Seizure, right arm and leg rhythmic jerking	1. SSS, straight sinus, and subependymal venous thromboses	1. SSS, left transverse sinus, bilateral internal cerebral vein, vein of Galen, straight sinus thromboses 2. Phase: no flow in distal SSS, left transverse, straight sinuses; vein of Galen, bilateral internal cerebral veins, thalamostriate veins	Idiopathic
4	Lethargy	SSS thrombosis	1. Distal SSS thrombosis; right cerebellar hemisphere hemorrhage 2. Phase: no flow in distal SSS	Idiopathic
5	Lethargy	1. Right transverse sinus thrombosis 2. White matter hemorrhages, R > L	1. Bilateral transverse sinus thromboses; biparietal hemorrhagic infarcts 2. Phase: no flow in both transverse sinuses	Idiopathic
6	Lethargy	1. Asymmetric extraaxial fluid 2. Bilateral frontal lobe hypoplasia	1. Right basal vein, vein of Galen thromboses; frontal lobe hypoplasia 2. Phase: no flow in right basal vein and vein of Galen	Structural flow impediment versus idiopathic
7	Lethargy	1. Inferior and superior sagittal sinus, straight sinus, vein of Galen, bilateral internal cerebral and thalamostriate vein thromboses	1. Inferior and superior sagittal, straight sinus, vein of Galen, bilateral internal cerebral and thalamostriate vein thromboses 2. Phase: no flow in superior, inferior sagittal, straight sinuses; bilateral internal cerebral and thalamostriate veins	Viremia versus idiopathic

CVT = cerebral venous thrombosis; CT = computed tomography; MRI = magnetic resonance imaging; SSS = superior sagittal sinus; R = right; L = left.

evaluation through 6 months of age in six of seven patients indicates normal development.

CT revealed evidence of cerebral venous system thrombosis clearly in five infants similar to previously described cases of CVT. In one infant, hemorrhagic infarction was seen, but its large size prevented distinction between arterial and venous infarction. In one neonate, however, no evidence of CVT was found on CT, but subsequent MR imaging showed thrombosis involving a cerebral vein. Radiological diagnosis of dural sinus thrombosis can be suggested by CT. Some have felt that CT alone is sufficient to diagnose CVT [15, 16], but the insensitivity of cranial CT for diagnosis of this disorder has been well documented [3, 17-19]. In our infants, MR spin echo images not only

confirmed the CT findings but demonstrated more extensive thromboses in four of seven infants.

While standard spin echo MR imaging is useful in the diagnosis of CVT [20, 21], variable signal intensities due to flow effects and breakdown of hemoglobin may cause confusion [8]. Phase images are flow-sensitive images that clearly and noninvasively demonstrate the absence or presence of venous flow in brain [8]. In all our patients, absent flow was evident in either dural sinuses or deep cerebral veins, or both, confirming the existence of CVT.

Our series constitutes the first cohort of neonates with CVT of either dural sinuses or the deep venous system documented using conventional MR as well as MR phase imaging. In particular, MR phase imaging

proved powerful in its ability to demonstrate absent flow in the cerebral venous system. CVT may well serve as an underlying cause of transient unexplained neonatal seizures or lethargy. The noninvasive, sensitive, and specific features of conventional MR and MR phase imaging make these the most desirable and definitive neuroradiological evaluations. Anticoagulation and thrombolytic therapy appear unnecessary.

Presented, in part, at the annual meeting of the Child Neurology Society, Portland, OR, October 3-5, 1991.

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