Cerebral Venous Thrombosis in a Child With Iron Deficiency Anemia and Thrombocytosis

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We describe a 22-month-old boy with iron deficiency anemia and reactive thrombocytosis who developed vomiting, headache, mental status changes, and seizures. Computed tomography showed infarction of the basal ganglia and thalami. Magnetic resonance imaging revealed cerebral venous thrombosis, delineated the extent of the vascular and associated parenchymal involvement, showed the infarcts to be hemorrhagic (a finding not imaged by computed tomography due to our patient's depressed hemoglobin level), and obviated the need for invasive angiography. (Stroke 1990;21:488-493)

Cerebral venous thrombosis is an infrequent cause of childhood stroke, occurring most often in the setting of systemic conditions causing significant morbidity. At times the diagnosis may be overlooked, particularly if there are no recognized antecedent risk factors or when presentation is atypical. To evaluate the intracranial and extracranial vasculature, cerebral angiography has been advocated as the most important diagnostic procedure in the workup of a child with stroke. Although accurate, angiography is invasive, and in young children anesthesia may be required. Therefore, computed tomography (CT) of the head has been used as a less invasive technique. However, CT is less sensitive than angiography and has a reported accuracy of only 60-75%. In addition, both angiography and CT require substantial amounts of iodinated contrast material as well as exposure to ionizing radiation. Magnetic resonance imaging (MRI), a noninvasive imaging modality, is increasingly being employed to evaluate intracranial pathology in children.

We describe a 22-month-old boy who presented with vomiting, headache, mental status changes, and seizures. The diagnosis of cerebral venous thrombosis was confirmed by MRI, and the extent of the vascular and associated parenchymal involvement was delineated. After an extensive evaluation, the only abnormality disclosed was iron deficiency anemia with reactive thrombocytosis, an unusual and, to our knowledge, a heretofore undescribed antecedent risk factor for cerebral venous thrombosis.

Case Report

A 22-month-old boy was transferred from a community hospital because of seizures. Three days before admission, his mother noted that he was unusually pale and irritable. The morning of admission he had two episodes of projectile vomiting. Examination by his family physician revealed a dull left tympanic membrane and a depressed hemoglobin level. He was hospitalized for the evaluation of anemia. A complete blood count was significant for a hemoglobin concentration of 4 g/dl, a hematocrit of 13.9%, and a platelet count of 1 x 10^5/mm^3; the reticulocyte count was 1.4%. There was no clinical or laboratory evidence of dehydration.

His mother said the child had been pale for approximately 6 months. He consumed 40 ounces of cow's milk daily and had become a "poor and picky eater." Melena and pica were denied. She described the child as "fussy, with a low frustration tolerance and not as even-tempered as his siblings." Treatment with supplemental oral iron, vitamins, and amoxicillin was instituted.

That night the child remained irritable, and he indicated that his head hurt. The following day he became increasingly irritable and agitated. He developed clonic movements of his right upper extremity followed by obtundation and intermittent tonic posturing. Cerebrospinal fluid analysis revealed 2,500 erythrocytes/mm^3, 0 leukocytes/mm^3, a protein concentration of 152 mg/dl, a hematocrit of 13.9%, and a platelet count of 1 x 10^5/mm^3; the reticulocyte count was 1.4%. There was no clinical or laboratory evidence of dehydration. Before transfer the child had received a transfusion of 80 ml packed
erythrocytes. Phenobarbital, ampicillin, and chloramphenicol were added to the therapeutic regimen.

On admission to the pediatric intensive care unit, the child was unresponsive. Noxious stimuli elicited hyperextension of the neck and trunk and extension of the lower extremities. Disk margins were blurred, his pupils reacted to light, and the left corneal reflex was depressed. There was bilateral asymmetric VI nerve paresis (left > right) and a mild right central facial paresis. His neck was rigid. Muscle tone in his lower extremities was asymmetrically increased (right > left). His deep tendon reflexes were active without knee or ankle clonus. His plantar reflexes were extensor. Dexamethasone was added to the medical regimen.

A complete blood count was notable for a hemoglobin concentration of 6 g/dl, a hematocrit of 19%, a platelet count of 540,000/mm³, a reticulocyte count of 1.75%, a mean corpuscular volume of 57 fL, a mean corpuscular hemoglobin of 18 mg, and a mean corpuscular hemoglobin concentration of 31.2 g/dl. The ferritin level was 5 ng/ml, with a total iron binding capacity of 427 µg/dl. Bone marrow aspirate revealed hypercellular bone marrow with erythroid dyspoiesis and absent iron stores. This confirmed the diagnosis of iron deficiency anemia (on a nutritional basis). A technetium-99 bone scan was normal. Head CT showed areas of decreased attenuation in the right basal ganglia and both thalami. There was a small area of increased attenuation in the right basal ganglia. Slight hyperdensity of the vein of Galen and straight sinus was noted. The lateral ventricles were dilated (Figure 1).

The next day, following the administration of iodinated contrast material, filling defects within the vein of Galen and straight sinus were visualized on repeat CT. The impression was acute infarction, possibly associated with venous thrombosis. Lumbar puncture revealed an opening pressure of 320 mm H₂O. Cerebrospinal fluid analysis showed 120 erythrocytes/mm³, 20 leukocytes/mm³, a protein concentration of 100 mg/dl, and a glucose concentration of 93 mg/dl. A ventriculostomy was performed for the management of increased intracranial pressure. MRI using a 1.5-T superconducting magnet showed hyperintense signals in the straight sinus, the vein of Galen, and the internal cerebral veins on both T1- and T2-weighted images (Figure 2, top and bottom right). Increased signal intensity was noted in the right thalamus as well. Proton density images also showed increased signal intensity in the straight sinus and right basal ganglia, suggestive of hematoma (Figure 2, bottom left). Another area of increased signal intensity was seen in the right basal ganglia (T2-weighted images), indicative of edema around the hemorrhage (Figure 2, bottom right).

The child gradually became more responsive, although for 1 week he remained irritable and had little spontaneous movements and vocalizations. Nuchal rigidity persisted. There was a left gaze preference, but he was able to follow an object. He kept his upper extremities close to his sides and had asymmetric pronation of the wrists (right > left). Tone was asymmetrically increased in the lower extremities, with rigidity and equinovarus posturing on the right. By the following week his mental status improved, and his gaze preference resolved. He now had profound nuchal and truncal hypotonia, a left hemiparesis, and a coarse action tremor of the right upper extremity without dysmetria. The reticulocyte count rose to 3% by the end of the first week, and by hospital day 14 it had peaked at 4.8%.

Extrapyramidal signs resolved completely within 1 month. Continued neurologic improvement was noted over the next 3 months. At age 25 months the child was alert and playful. He achieved a score of 85 on the Mental Developmental Index of the Bayley Scales of Infant Development. Neurologic examination was remarkable only for asymmetric deep tendon reflexes (left brisker than right). There was slight circumscription of his left lower extremity that was more pronounced when he fatigued. A complete blood count was normal. Follow-up MRI at age 27 months showed no evidence of high-intensity areas on T1-weighted sagittal views, suggestive of resolved thrombus and recanalization of the sinus (Figure 3).

The following laboratory studies were normal: urine analysis, SMA-22, rheumatoid factor, antinuclear antigen, hemoglobin electrophoresis (Aα and Aβ), antithrombin III, protein C and S antigen, Factor X antigen, osmotic fragility, bleeding time, prothrombin time, partial thromboplastin time, glucose-6-phosphate dehydrogenase, and pyruvate kinase.

Discussion

Strokes during childhood are uncommon. Their incidence in children <15 years of age is estimated to be 2.52/100,000/yr (excluding strokes during the perinatal period or related to intracranial infection or trauma).7 The incidence of cerebral venous thrombosis during childhood is unknown; it is reported most frequently in the setting of acute dehydration, cyanotic congenital heart disease, or the nephrotic syndrome.1-9 Before the effective use of antimicrobials, pyogenic infections of the face, mouth, sinuses, ear, mastoids, and leptomeninges were common antecedents of purulent cerebral venous thrombosis.1,9,13 Dural venous thrombosis has also been well described in the setting of malignancy, especially leukemia, and may result from leukemic infiltration of the dura and sinuses, from coagulation abnormalities, or as a complication of radiation or chemotherapy.14 Other less common hematologic conditions associated with thrombotic tendencies include disorders of coagulation and disorders of the formed elements of blood.15-21 The former includes deficiencies of the physiologic inhibitors of coagulation, proteins C and S, plasminogen, antithrombin III, and the lupus anticoagulant. Of these, antithrombin III deficiency (inherited or acquired) is increasingly recognized as a risk factor for stroke in children.19,15 Thrombotic tendencies may also occur in children with...
FIGURE 1. Computed tomograms. Top: Axial view without contrast showing area of increased density in vein of Galen and straight sinus. Bottom: Slightly lower slice showing areas of low attenuation in both thalami and in right basal ganglia. Note small area of increased density on right (arrow).
primary thrombocytosis (myeloproliferative disorders).\textsuperscript{12} A review of the literature, however, suggests that strokes are uncommon in children with these disorders; only five cases have been reported.\textsuperscript{22–25} Reactive (secondary) thrombocytosis may be associated with a myriad of pathologic conditions including

**FIGURE 2.** Magnetic resonance images. Top: \(T1\)-weighted (repetition/echo times [TR/TE] 600/20 msec) sagittal view near midline showing high-intensity signal in straight sinus (s), vein of Galen (arrowhead), and right thalamus and basal ganglia (arrow). Bottom left: Proton density (TR/TE) 2,040/25 msec) axial view shows increased signal intensity in straight sinus (s) and right basal ganglia (arrow). Bottom right: \(T2\)-weighted (TR/TE 2,040/80 msec) axial view again shows hyperintense signal in straight sinus (s) and right thalamus and basal ganglia, with increased intensity suggestive of edema surrounding hemorrhage (arrow).
iron deficiency anemia. Although a positive relation between chronic iron deficiency anemia and thrombocytosis is well documented in both children and adults, thrombotic tendencies have not been reported. In fact, current textbooks of hematology state that reactive thrombocytosis is usually asymptomatic, especially in children. An extensive evaluation in our patient ruled out the well-recognized causes of cerebral venous thrombosis. Iron deficiency anemia with reactive thrombocytosis was the only abnormality found, an unusual and, to our knowledge, a heretofore unreported risk factor for cerebral venous thrombosis during childhood in the absence of cyanotic congenital heart disease.

At times the diagnosis of cerebral venous thrombosis may be difficult, especially in children with no recognized antecedent risk factors or atypical symptoms. The clinical picture of cerebral venous thrombosis may be quite variable since it reflects the site and extent of involvement of thrombus within the venous system, the rapidity of occlusion, and the nature of the primary disease. Thus, the disorder is often not recognized, as documented by both Byers and Hass and more recently by Gates, who reported that cerebral venous thrombosis was not suspected in 15 of 29 fatal cases. Cerebral angiography has traditionally been considered the gold standard in the evaluation of cerebral venous thrombosis. Although accurate, long serial runs with subtraction techniques may be required to image subtle changes in the venous pattern. In our patient, MRI obviated the need for this invasive procedure with its exposure to ionizing radiation. In addition, MRI revealed the infarct to be hemorrhagic, a finding not well imaged by CT due to our patient's depressed hemoglobin level. Although we initially considered anticoagulation therapy (as advocated by some for the acute management of cavernous sinus and cerebral venous thrombosis), visualization of hemorrhages by MRI led us to more conservative management, thus avoiding the possibility of further intraparenchymal bleeding.

This case illustrates that MRI, because it is noninvasive and uniquely sensitive to blood flow, thrombus formation, and the evolution of hemorrhage, should be considered the neuroimaging procedure of choice in the initial evaluation and follow-up of childhood stroke syndromes. Moreover, the neurologic outcome of cerebral venous thrombosis may be favorable, as in our patient, with early recognition, control of increased intracranial pressure, supportive management, and treatment of the underlying condition.

References


**Key Words**: anemia, hypochromic • magnetic resonance imaging • thrombocytopathy • thrombosis
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