Ischemia

Sagittal Sinus Thrombosis following Minor Head Injury Treated with Continuous Urokinase Infusion

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BACKGROUND
Cerebral dural sinus thrombosis is a rare clinical entity. Symptoms may be vague, and left untreated thrombus progression may be fatal because of venous congestion and infarction.

METHODS
We report a case of post-traumatic dural sinus thrombosis treated with selective transfemoral, transvenous catheterization and infusion of urokinase.

RESULTS
Urokinase infusion into the dural venous sinuses using a microcatheter introduced from the femoral vein was successfully carried out, and patency of the venous sinuses was reestablished.

CONCLUSION
Venous sinus thrombosis can be an overlooked sequel to head injury. If the diagnosis is entertained, prompt performance of appropriate imaging studies should be instituted so that therapy can be initiated. The use of selective sinus catheterization using microcatheter techniques with instillation of urokinase is an excellent mode of therapy that should be considered in any patient with symptomatic occlusion. © 1998 by Elsevier Science Inc.

KEY WORDS
Sinus thrombosis, trauma, thrombolysis.

Intracranial dural venous sinus thrombosis remains a poorly understood condition. The disease process is unpredictable in terms of course and outcome. The potential for devastating consequences secondary to venous congestion and infarction makes recognition and treatment of paramount importance.

Case Report
A 22-year-old woman presented to the emergency room complaining of bi-frontal headache, progressive nausea over several days, emesis for 24 h, intermittent slurring of speech, and two brief episodes of unconsciousness on the day of admission. She had been in excellent health until 10 days earlier, when she was involved in a minor motor vehicle collision in which she struck her head against the steering wheel. She was evaluated at that time at another facility and discharged with no apparent injury. She returned to the hospital 36 h later complaining of a persistent headache. A head computed tomography (CT) demonstrated what was thought to be a small occipital subdural hematoma without mass effect (Figure 1). She was observed for 24 h and discharged. Upon presentation to our facility eight days later, a second CT was suggestive of sinus thrombosis (Figure 2). MRI and cerebral angiography confirmed the diagnosis of superior sagittal sinus (SSS) and transverse sinus (TS) thrombosis (Figures 3 and 4). Neurological examination was normal, except for papilledema.

While in the angiography suite, a 6F sheath was placed into the right femoral artery and a 6F sheath was placed into the left femoral vein. The artery and vein in a single leg were not catheterized for fear of creating an arteriovenous fistula when the sheaths were removed. A 5F angiographic catheter and guidewire were then advanced via the femoral vein through the right atrium and into the superior vena cava. The right internal jugular vein was selectively catheterized, and through it, a microcatheter was...
advanced over a guidewire into the right TS and then into the SSS. While the microcatheter was advanced through the thrombus, urokinase (UK) was instilled in 50,000-IU aliquots approximately every 15 minutes until a total dose of 250,000–500,000 IU was given. The catheter was positioned at the most anterior portion of the thrombus, and 3 million U of UK were infused over a 48-h period. Our technique and experience have been described extensively in a previous publication [1]. After 48 h of therapy, the SSS and TS were patent (Figure 5). The patient’s headaches and papilledema resolved, and she was discharged on the fifth hospital day on 6 months of warfarin with a target INR of 1.5. Follow-up MRI was obtained on the 10th postprocedure day, which showed a flow void in the area of previous thrombosis, consistent with patency (Fig. 6). She remained asymptomatic, and the warfarin was discontinued after 6 months. At 1-year follow-up, she remains symptom-free.

**DISCUSSION**

The first description of dural sinus thrombosis was made by Ribes, who in 1825 reported on a 45-year-old man with malignancy, headache, seizures, and delirium. Postmortem examination revealed SSS, TS, straight sinus, and cortical vein thromboses [2]. In 1915, Holmes and Sargent described posttraumatic thrombosis of the SSS [3]. Overall, since 1942, fewer than 250 cases of intracranial venous sinus thrombosis have been reported.

Predisposing factors and conditions associated with sinus thrombosis include puerperium, congenital and acquired cardiac diseases, blood dyscrasia, infection, medications (especially synthetic steroids), abnormalities in coagulation factors, autoimmune inflammatory diseases, connective tissue disorders, dehydration, and trauma [4–10]. The exact mechanism for the development of thrombosis after trauma is unclear. Bone fragments, sinus dissection, or sinus distortion can create obstructions to flow that in turn induce thrombus formation.

Signs and symptoms are numerous, and the time course during which they develop may be variable. These include headache, stroke, hydrocephalus, papilledema, visual loss, and pulmonary embolus [11].

CT, MR, and angiography are all used to assist in the diagnosis of dural sinus and cerebral vein thrombosis. Angiographic findings include partial or complete nonopacification of venous sinuses and veins, dilated cortical collateral veins with a cork-screw appearance, increased cerebral circulation time, and reversal of flow away from the obstructed sinus or vein [6,7]. CT images of the brain may be normal in 10%–20% of patients with venous thrombosis. Findings include hemorrhagic or nonhemorrhagic venous infarcts, cerebral edema, small ventricles, hydrocephalus, contrast enhancement of the tentorium and falx, thrombosed veins, a dense triangle sign representing fresh thrombus in the posterior SSS, and an empty delta sign on con-
trasted studies that represents enhancement of collateral veins in the SSS wall surrounding a nonenhancing thrombus. MRI and MR angiography represent noninvasive means of assessing the presence of thrombosed sinuses and veins [6].

The mortality rate of cerebral vein and sinus thrombosis ranges from 5.5%–30% [6]. Since 1980, 83% of reported patients survived [11]. If survival does occur, 15%–25% of patients demonstrate lasting abnormalities.

The management of dural venous and cerebral venous sinus thromboses is varied. Controlled, randomized studies are difficult to perform because of the rarity of symptomatic patients and the multiple causes, both of which make adequate randomization nearly impossible. Some physicians espouse a course of watchful waiting in view of the benign nature and uneventful recovery made by the majority of patients. In these instances, interventions are reserved for individuals whose condition worsens during observation [12–14]. Management of these patients includes cerebral dehydrating agents [15,
16], steroids [12,14,17], acetazolamide, cerebrospinal fluid, drainage, barbiturates, decompressive craniectomy [16], sinus thrombectomy [14,15], heparin/warfarin [15,17,25], urokinase [17,24–28], and tissue plasminogen activator [29].

Stansfield [18] was the first to use heparin in a puerperal woman with focal neurological deficits secondary to venous thrombosis. The patient recovered within 4 days after beginning therapy. Bousser and co-workers [20] managed 38 patients with cerebral sinus thrombosis. Some 23 were treated with heparin, none of whom died and 19 of whom made a complete recovery. While this report answers no questions about heparin therapy versus nonheparin therapy, it does point out the relative safety of using the former in a small group of patients. Einhaupl and associates [23] performed the only randomized, blinded study of adjusted-dose heparin in patients with venous sinus thrombosis. At 3 months after therapy, 80% of the heparin-treated patients were normal, and 20% had slight deficits. Only 10% of the nonheparinized patients were normal at 3 months, 60% had neurological deficits, and 30% were dead [23]. The authors went on to retrospectively study 102 patients with thrombosis, 43 of whom had intracranial hemorrhage. Some 27 of the 43 were treated with heparin. Some 4 (15%) of these patients died, and 14 had a normal recovery. The remaining 13 patients were treated without heparin. Some 9 (69%) died, and 3 had a normal recovery [23]. The authors concluded from this study that treatment with heparin was not only safe, but also beneficial, even in the setting of intracerebral hemorrhage.

Other practitioners have advocated the use of fibrinolytic agents with the goal of rapid clearance of thrombus from the venous system. In 1971, Vines and Davis [24] reported the use of urokinase and heparin in the treatment of four patients with sinus thrombosis, all of whom improved. As reported in
1988, Scott and co-workers [26] catheterized the sagittal sinus via a frontal burr hole and infused urokinase over an 8-hour period. The patient, who was initially decerebrate, had only a mild dysphasia 4 weeks after therapy.

In 1989, Higashida and coauthors [28] reported treatment of transverse sinus thrombotic occlusion in a newborn child with seizures by direct sagittal sinus puncture and installation of 12,000 units of urokinase over a 12-hour period. The thrombus cleared, and the child remained neurologically normal 3 years later. Nevertheless, the safety and efficacy of urokinase therapy have not been established in pediatric patients. There are case reports of urokinase infusions used to treat thrombosis in catheters or right atrial thrombi in infants. The dosage has ranged between 2000 and 8800 U/kg/hr [31–37]. Bolus doses of 5000–10,000 units have been used [35,36], as well as low-dose infusions of 70–500 U/kg/hr [35]. There are also published reports of urokinase treatment of arterial occlusions. Strife and colleagues [36] used urokinase to treat four neonates with central thrombosis, with the urokinase being administered via an umbilical artery catheter into the abdominal aorta. The urokinase dose used was a loading bolus of 4400 U/kg followed by a maintenance dose of 4000–20,000 U/kg/hr. The duration of therapy for these neonates ranged from 3–9 days.

In 1990, Persson and Lilja [14] performed an open thrombectomy and instilled urokinase into the sagittal sinus. Despite formation of a small cerebellar hematoma, the patient gradually improved, although never to baseline levels. In 1991, Barnwell and colleagues [24] reported three patients treated with transvenous catheterization and instillation of urokinase, and in 1992, Tsai and coauthors reported on five additional patients from the same institution [32]. Some 7 of the 8 patients had excellent neurological recoveries, and none had complications related to the therapy. Finally, in 1994, Smith and coauthors [28] described seven patients, two of whom had been previously reported by Barnwell (Dowd CF, personal communication, 1994).

Our previous series of 13 patients treated with transfemoral transvenous urokinase infusions directly into the cerebral dural sinuses demonstrated the efficacy that can be achieved using current catheter technology [1]. Some 12 of the 13 individuals reported had significant radiographic improvement (reestablished venous sinus drainage) or complete resolution of the thrombus along with rapid neurological improvement. One failure was in a patient who had at least a 2-month history of sinus thrombosis and protein C deficiency. We can only speculate that the clot was organized to the extent that it was resistant to urokinase’s thrombolytic properties. This concept is supported by a number of studies concerning thrombolysis for deep venous and pulmonary thrombosis and lower-extremity arterial occlusions. Genton and Wolf [17] noted that emboli estimated to be less than 72 hours old responded well to fibrinolysis, while lesions older than 2 weeks did not respond as well. Lesions at 6 weeks showed no appreciable change after therapy [36]. Amery and colleagues [3] confirmed these findings in patients with lower-extremity arterial occlusions. The frequency of thrombus clearing was significantly higher in patients who were treated within 72 hours than those who were treated later (68% versus 7%). The Urokinase-Pulmonary Embolism Trial also showed an advantage to acute treatment [33]. While venous and arterial thrombi are most susceptible to thrombolytic therapy early in their course, Duckert and co-workers [12] did achieve patency in 14% (2⁄13) of patients who were treated 22–56 days after the onset of deep venous thrombosis symptoms.

Conclusion

While neurologic changes following head trauma may result from concussion or more life-threatening injuries such as subdural and epidural hematomas, intracerebral hemorrhage, arterial dissection, and diffuse shearing of white matter tracts, we have shown in this report that venous sinus thrombosis should be considered when other etiologies are eliminated. Only through prompt identification can the patient receive appropriate treatment to avoid secondary complications that can at times be life-altering or fatal.

REFERENCES

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COMMENTARY

This is a very interesting article which draws the attention of the neurosurgical community to the fact that fibrinolysis of thrombosis of the SLS can be done easily with the microcatheter techniques now available. This potentially devastating complication can be treated with fibrinolysis of the clot, provided that it is not done too late. Therefore, recognition of the disease (by the use of CT and magnetic resonance, as in this case) is crucial to rapid initiation of fibrinolysis.

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This article is excellent. The report is very precise, without unnecessary details, and it is well documented with high quality neuroimages. The only concern is with the CT presented in Figure 1, which was considered to show a “small occipital subdural hematoma.” What is seen is more likely a section of the torcular and the right transverse sinus.

This case is an example of the efficacy of the continuous urokinase infusion at the level of the sinus thrombosis and its feasibility via the transvenous (femoral) route. Such a report argues for endovascular catheterization before considering direct catheterization of the sinus itself via a burr hole.

In the discussion, the authors provide a useful (if not exhaustive) review of the data from the literature. These data are in favor of active management if clinical symptoms worsen; namely emergency treatment with urokinase infusion not delayed beyond 72 h to make the chance of repermeation as high as possible.

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