Treatment of dural sinus thrombosis with local urokinase infusion

Case report

JOHN A. SCOTT, M.D., ROBERT M. PASCUZZI, M.D., PETER V. HALL, M.D., and
GARY J. BECKER, M.D.
Departments of Radiology, Neurology, and Neurological Surgery, Indiana University Medical Center Hospitals, Indianapolis, Indiana

Current therapy for dural sinus thrombosis consists of supportive measures, anticoagulation therapy, and in some cases intravenous infusion of a fibrinolytic agent. A patient with extensive dural sinus thrombosis was successfully treated with local urokinase infusion. The technique and rationale for this aggressive therapy are discussed.

KEY WORDS • dural sinus thrombosis • fibrinolysis • urokinase

THE treatment of dural sinus thrombosis with heparin anticoagulation and/or fibrinolysis is controversial. Favorable results have been reported; however, complications related to systemic fibrinolysis have also occurred.

A patient with widespread dural sinus thrombosis is described who was successfully treated with local infusion of the fibrinolytic agent urokinase (Abbokinase).

Case Report

This 33-year-old right-handed man was taken to the emergency room at a local hospital with a 24-hour history of progressive generalized headache culminating in a transient syncopal episode. He had previously been in excellent health. There was no medical history of thrombotic or ischemic disease. Upon arrival, he was found to be lethargic, oriented, and complaining of generalized headache. He rapidly became unresponsive and began vomiting. Vital signs were normal and the neurological examination was nonfocal. He was then transferred by helicopter to our institution. En route, he became completely unresponsive, with apnea and unreactive pupils. He was intubated, hyperventilated, and given intravenous mannitol.

Examination. Upon arrival, the patient was ventilating independently and had normal vital signs. On neurological examination, he was comatose and followed no commands. He exhibited nonpurposeful thrashing movements of all four extremities. The pupils were equal and normally reactive to light, and early papilledema was noted. The muscle stretch reflexes were brisk and symmetrical, and there were bilateral Babinski signs. The remainder of the neurological examination was nonfocal. No neck stiffness was found.

On laboratory evaluation, the following findings were normal: blood count with differential, platelet count, prothrombin time, partial thromboplastin time, electrolyte level, blood urea nitrogen level, creatinine content.
Dural sinus thrombosis

FIG. 2. Digital sinograms, lateral projection, with injection of contrast material. Left: Preoperative study outlining the thrombus (arrows). The diploic and meningeal venous collaterals also filled (arrowheads). Right: Postoperative study showing patency of the superior sagittal, left transverse, and left sigmoid sinuses. The catheter tip (arrow) can be seen in the superior sagittal sinus.

liver enzyme analysis, glucose level, and Westergren sedimentation rate. Urinalysis and a chest x-ray film were normal. Measurement of fibrin split products showed mildly elevated levels. An emergency computerized tomography (CT) scan demonstrated increased density in the region of the superior sagittal, straight, and both lateral sinuses with diffuse cerebral edema (Fig. 1). Cerebral arteriography confirmed thrombosis of the dural sinuses. The cerebral circulation time was markedly delayed.

Operation. Because of the widespread dural sinus thrombosis and severe acute neurological deficit, the patient was taken to the operating room. An intracranial pressure (ICP) monitor was placed in the right frontal epidural space through a burr hole. The initial ICP and mean arterial pressure were 60 and 90 torr, respectively. A midline frontal craniectomy was performed and a Tracker-18 angiographic infusion catheter* was placed into the superior sagittal sinus through a small incision. The tip of the catheter was advanced into the parietal segment of the sinus over a platinum-tipped 0.014-in. torque control guide wire.† The patient was then taken to the angiographic suite where a digital sinogram was performed by injection through the catheter (Fig. 2 left). A urokinase infusion through the Tracker catheter was begun at an initial rate of 4000 units/min. Sinograms were repeated at 1-hour intervals for 3 hours and showed no evidence of thrombolysis. The catheter was then advanced to the torcula and the rate of infusion was decreased to 1000 units/min. Local infusion was continued for the next 8 hours. A repeat sinogram showed patency of the superior sagittal and left lateral sinuses (Fig. 2 right). A CT scan at this time showed a left temporal hemorrhagic infarction. In view of this finding, it was decided to stop the urokinase infusion.

Postoperative Course. By 24 hours following the urokinase infusion, the ICP had fallen to between 25 and 30 torr; over the next 2 days the ICP gradually returned to normal. At 48 hours after infusion, a follow-up CT scan showed a nonhemorrhagic right temporal lobe infarction.

Decerebration was present at 24 to 48 hours with resolution at 72 hours, at which time the patient was moving semipurposefully. His subsequent course was one of gradual daily clinical improvement. On the 5th hospital day he was extubated and his eyes opened spontaneously. Over the next week as he became more alert, it was apparent that he was severely dysphasic, combative, and mildly paretic on the right side. Agitation required sedation. By 2 weeks, he was calm and sociable, with moderate dysphasia, severe short-term memory impairment, and limited insight. He was discharged and transferred to his local hospital for further rehabilitation.

During the subsequent 4 weeks, the patient's improvement continued. The dysphasia became mild with a moderate impairment in short-term memory. He was treated with anticonvulsant drugs from the time of his initial presentation, although there was no definite seizure activity. He was empirically treated with Coumadin (sodium warfarin) beginning 4 weeks after his first admission.

Pathological Examination. The etiology of the patient's dural sinus thrombosis was not determined. Laboratory examination revealed normal screens for hypercoagulable and hyperviscosity states, including normal serum viscosity and serum protein electrophoresis, and normal levels of immunoglobulins, fibrinogen, protein C, protein S, antithrombin III, fibrin split

* Infusion catheter manufactured by Target Therapeutics, Inc., Los Angeles, California.
† Torque control guide wire manufactured by Bard Interventional Products, Billerica, Massachusetts.
products, and serum complement. Studies of platelet aggregation, screens for hemolysis, and screens for paroxysmal nocturnal hemoglobinuria were normal. Tests for antinuclear antibodies and rheumatoid factor were normal. Multiple cultures were normal throughout the hospitalization.

Discussion

The first reported case of dural sinus thrombosis was that of Ribes who, in 1825, described a 45-year-old man found at autopsy to have thrombosis of the superior sagittal sinus in association with systemic malignancy. Since then, sinus thrombosis has been reported in virtually every setting in which thrombosis may occur elsewhere in the body, and has been associated with infection, the use of oral contraceptives, pregnancy, trauma, dehydration, disseminated intravascular coagulation, polycythemia, and thrombocytosis.

The natural course of the disease is highly variable. In most reports, mortality rates range from 10% to 20%. Factors associated with increased mortality include acute evolution of thrombosis, coma, and involvement of the deep venous system. General support, management of increased ICP and seizures, hydration, and treatment of underlying predisposing conditions constitute the mainstay of therapy.

There is disagreement over the use of anticoagulation therapy in the treatment of dural sinus thrombosis. Heparin has been used to limit the propagation of thrombus without definite complications. Its use has been advocated based on the notion that thrombus gradually spreads and may account for a gradually progressive poor clinical course. Reluctance to use heparin stems from the frequent occurrence of hemorrhagic venous infarction and fear of exacerbating such hemorrhage. Theoretically, anticoagulation therapy may be indicated when the thrombosis is early, partial, and actively propagating. Furthermore, if the patient has a demonstrable coagulopathy with significant risk of extracranial thrombosis, anticoagulation may be more strongly advocated. Presently, there are no clear guidelines for the use of anticoagulation therapy in the acute clinical setting.

Experience with fibrinolytic agents is limited to several small anecdotal series in which patients with dural venous thrombosis were treated by peripheral intravenous urokinase infusion. Three groups have reported successful treatment without significant hemorrhagic complications; however, others have cautioned against the use of fibrinolytic agents based on their unfavorable experience.

Success with local fibrinolytic therapy has been reported in the treatment of a variety of thrombotic and embolic conditions, including thrombosed coronary, visceral, renal, and carotid arteries. In addition, fibrinolysis has been used to treat thrombosed central veins' and occluded arterial grafts. The incidence of hemorrhagic complications is generally lower when fibrinolytic agents are administered locally rather than systemically.

To date, no experience with local fibrinolytic therapy has been described in cases of dural venous thrombosis. In view of our patient's grave clinical condition at the time of presentation and the finding of widespread dural sinus thrombosis, and based on experience with local fibrinolysis in other vascular systems, it was thought that local urokinase infusion would lyse the thrombus faster than any other therapy. It was therefore believed that this treatment would offer the patient the best prognosis. The decision to directly catheterize the superior sagittal sinus was based on similar reasoning. We were unsure of our ability to reach the dural sinuses via a femoral vein and considered that the fastest and most reliable method would be by direct cannulation of the superior sagittal sinus, a technique first described by Frenchner. With steerable guide wires and Tracker infusion catheters it should be possible to reach the superior sagittal, lateral, and possibly the straight sinus from the femoral vein, enabling local infusion to be performed without subjecting the patient to a craniotomy.

Conclusions

Direct infusion of urokinase into thrombosed dural sinuses can be accomplished with rapid dissolution of the thrombus in life-threatening situations. We do not advocate this mode of therapy in stable patients in whom more conventional anticoagulant therapy may be indicated. However, this case shows that, in patients with severe neurological dysfunction and with extensive dural sinus thrombosis, aggressive local fibrinolytic therapy may result in rapid clot lysis and improve an otherwise dismal prognosis. Newer catheters and steerable guide wires may enable this procedure to be performed from the femoral vein, thereby reducing the risk to the patient.

References

Dural sinus thrombosis


Manuscript received June 1, 1987.
Address reprint requests to: John A. Scott, M.D., Indiana University Hospital, Room X-64, 926 W. Michigan, Indianapolis, Indiana 46223.