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AJNR Am J Neuroradiol 1997, 18 (3) 502-506
http://www.ajnr.org/content/18/3/502

Endovascular Thrombolysis in Deep Cerebral Venous Thrombosis

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Summary: We present two cases of acute thrombosis of the internal cerebral veins, vein of Galen, and straight sinus without sagittal sinus involvement. Both patients had hydrocephalus and severe edema of the basal ganglia and thalami, one with hemorrhagic infarction of the thalamus. Because both patients rapidly deteriorated to a comatose state, endovascular thrombolysis was performed with urokinase infusion of the deep venous structures. Thrombolysis was continued until a patent channel with brisk flow in the venous structures was achieved. Both patients survived with minimal neurologic deficits.

Index terms: Thrombolysis; Thrombosis, venous

Acute deep cerebral venous thrombosis of the internal cerebral veins, vein of Galen, and straight sinus, without associated thrombosis of the superior sagittal sinus, is a rare disorder and can be associated with a poor outcome (1, 2). Clinical findings may be as vague as headaches, but patients can rapidly deteriorate into a comatose state. Radiologic imaging studies may show evidence of parenchymal edema in the corresponding territory of venous drainage with rapid progression to infarction and hemorrhage. The radiologic diagnosis of deep cerebral venous thrombosis, however, may be difficult. The characteristic delta sign of superior sagittal sinus thrombosis on contrast-enhanced computed tomographic (CT) scans may not be present. Flow-related signal in the straight sinus on magnetic resonance (MR) images normally can be variable, and is, therefore, difficult to evaluate. Diagnosis rests on the detection of hyperdense thrombus in the venous structures on CT scans or on the confirmation of the absence of flow on MR images.

One purpose of this article is to review the characteristic CT and MR imaging findings that can lead to a rapid diagnosis, thereby enabling early intervention. Both our patients deteriorated clinically and required endovascular thrombolysis of the deep venous system. Direct venous thrombolysis of the dural venous sinuses has been described previously (3, 4). In the past, however, the venous thrombolysis had a poorly defined end point (5). We propose that restoration of rapid flow fluoroscopically, despite some residual thrombus, is a sufficient goal of thrombolytic therapy, and we present two examples of the application of this theory.

Case Reports

Case 1

An 18-year-old right-handed man had a 24-hour history of progressive nausea, vomiting, and generalized headache. On examination he was found to be lethargic with slurred speech and had a right hemiparesis. CT of the head was performed, which revealed obstructive hydrocephalus with enlargement of the lateral ventricles and hypodensity in the left thalamus with associated mass effect. Hyperdense thrombus was present in the internal cerebral veins, vein of Galen, and straight sinus. The patient deteriorated to a comatose state during the ensuing 36 hours and was transferred to our medical center.

The patient's intracranial pressure was markedly elevated, and a right external ventricular drain was placed. A repeat unenhanced CT scan showed a small hemorrhage in the left thalamus and bilateral edema in the basal ganglia and thalami. The left lateral ventricle remained dilated owing to obstruction at the foramen of Monro from the edema, requiring placement of a left external ventricular drain. MR imaging showed severe parenchymal edema bilaterally at the level of the thalamus, lentiform nuclei, and caudate nucleus. MR venography confirmed the deep cerebral venous thrombosis of the internal cerebral veins, vein of Galen, and straight sinus with extension into the right transverse and sigmoid sinus. The superior sagittal sinus was normal. Endovascular thrombolysis was initiated and is described below.

Received November 17, 1995; accepted after revision April 11, 1996.

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AJNR 18:502–506, Mar 1997 0195-6108/97/1803–0502

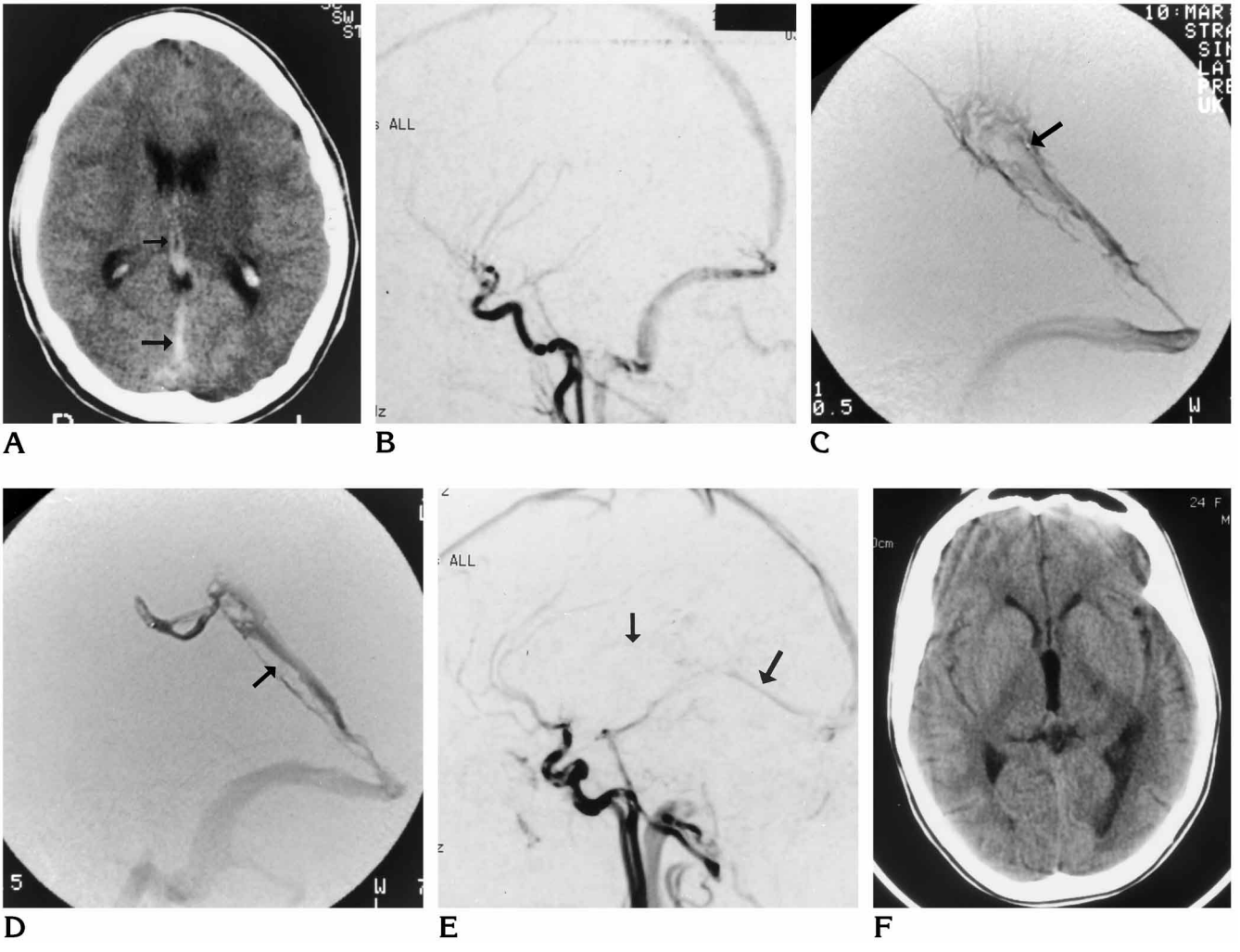

Fig 1. Case 2: 24-year-old woman with headache and confusion.

A, Initial unenhanced CT scan shows hyperdense thrombus in the internal cerebral veins (*small arrow*) and straight sinus (*large* arrow). Edema in the left thalamus and basal ganglia is present.

B, Sagittal phase-contrast MR venogram shows absence of flow in the internal cerebral veins, vein of Galen, and straight sinus. The sagittal sinus is patent.

C, Lateral view of the venogram shows the microcatheter (*arrow*) in the straight sinus with abundant thrombus. Virtual stasis of contrast material is noted; however, communication to the patent transverse sinus is present.

D, After thrombolysis of the internal cerebral veins, vein of Galen, and straight sinus, brisk flow to the transverse sinus is restored. Note some residual thrombus (*arrow*).

E, Repeat MR phase-contrast venogram 11 days after thrombolysis confirms flow in the straight sinus (*large arrow*) with only faint flow detected in the internal cerebral veins (*small arrow*).

F, Axial unenhanced CT scan after thrombolysis shows significant resolution of the parenchymal edema.

Case 2

A 24-year-old previously healthy right-handed woman had a headache of 3 days' duration. On the fourth day, she became confused and was brought to the emergency department. A CT scan of the head showed hypodensity in the left thalamus and basal ganglia. Hyperdense thrombus in the internal cerebral veins, vein of Galen, and straight sinus was present (Fig 1A). Her condition deteriorated, with development of a right hemiparesis and hemisensory deficit, and she was transferred to our medical center.

The patient was started on systemic heparin, and MR imaging was performed, which confirmed thrombosis of the internal cerebral veins with extension into the vein of Galen, straight sinus, and left transverse sinus. The superior sagittal sinus was normal (Fig 1B). The parenchymal edema had become severe, and edema developed in the contralateral thalamus, caudate nucleus, and lentiform nuclei during the 12 hours subsequent to the initial CT study. The patient's condition deteriorated to decerebrate rigidity during the following 24 hours.

Because both patients continued to deteriorate despite systemic anticoagulation, endovascular thrombolysis was requested. The procedure was similar in both patients and included cerebral venography from a femoral venous approach. The 5F base catheter was positioned in the jugular bulb draining the patent transverse sinus. A Tracker 18 microcatheter (Target Therapeutics, San Jose, Calif) was advanced coaxially over a 0.018-inch guidewire (Medi-Tech, Watertown, Mass) to the level of the torcular Herophili. The venogram confirmed the patency of the sagittal sinus and the catheterized transverse sinus. Repeated attempts at catheterization of the straight sinus from the patent transverse sinus were unsuccessful in both cases. The base catheter was then repositioned into the contralateral jugular bulb and the microcatheter was easily advanced coaxially over the guidewire through the thrombosed transverse sinus and into the straight sinus. The venogram confirmed the thrombosis of the straight sinus with virtual stasis of the contrast material and only minimal flow to the patent transverse sinus. The microcatheter was advanced to the junction of the vein of Galen with the straight sinus, where urokinase (5000 U/mL) was infused by hand at rates of 5000 to 10 000 U/min (Fig 1C).

As thrombolysis occurred and flow into the straight sinus became apparent, the microcatheter was advanced to the junction of the internal cerebral veins and vein of Galen, and the infusion was continued. Similarly, the internal cerebral veins were subsequently catheterized with the infusion proceeding. A total of 600 000 to 850 000 U of urokinase was infused over 3 hours. At the conclusion of the thrombolysis, brisk flow was observed in the internal cerebral veins, vein of Galen, and straight sinus despite some residual thrombus (Fig 1D). Prompt venous drainage into the contralateral transverse sinus was observed in both patients. No infusion was made directly into the thrombosed transverse or sigmoid sinuses. No immediate change in the clinical status was noted in either patient at the conclusion of the procedure. The patients were transferred to the intensive care unit and maintained on systemic anticoagulation with heparin.

In the first patient (case 1), a CT scan the next day showed a new, small area of hemorrhage along the left external ventricular drain tract. The repeat CT scan in the second patient (case 2) showed progression of the hydrocephalus owing to compression of the third ventricle from the severe thalamic edema, again requiring external ventricular drainage. This patient's condition improved rapidly over the next couple of days from decerebrate rigidity to the ability to follow commands. The hospital course consisted of management of the intracranial pressure with subsequent removal of the ventricular drains. In case 1 this required the patient to be placed in a pentobarbital coma for 3 days.

Repeat MR imaging with MR venography showed flow in the straight sinus in both patients. Eleven days after thrombolysis, phase-contrast venography with a velocity of 30 cm/s showed some flow in the internal cerebral veins, vein of Galen, and straight sinus (Fig 1E). Venography with a slower velocity was not performed at that time, which may have confirmed better flow in the internal cerebral veins. The spin-echo images, however, confirmed normal flow void in the internal cerebral veins and vein of Galen. Although the clinical status of the patients improved rapidly, the parenchymal edema was not significantly improved on the CT scan until 2 weeks after thrombolysis (Fig 1F).

Six months after the initial event, both patients had only minor neurologic deficits. The first patient had mild weakness in the right leg and went on to graduate from high school. The second patient had mild right arm drift at physical examination and returned to a high-level management position.

Discussion

Cerebral venous thrombosis may be associated with such widely disparate conditions as complications from infection, particularly mastoiditis (6), dehydration (7), hypercoagulable states (8), invasion of the venous sinus by neoplasm (9), the use of oral contraceptives (10), and pregnancy (11). The clinical severity of the disorder depends on the extent of the thrombosis in the involved vessels, the territory of the involved vessels, the establishment of venous collaterals, and the chronicity of the thrombus. In patients with acute occlusion of the superior sagittal sinus, particularly the posterior third or the dominant transverse sinus or sigmoid sinus, the occlusion is usually not tolerated, as adequate collateral venous drainage may not be available. Massive cerebral edema with venous infarction and/or hemorrhage may develop. Recently, staging of the degree of parenchymal signal change on MR images was found to correspond with the degree of venous congestion, which was, in turn, related to the venous sinus pressure (12).

Reports of deep cerebral venous thrombosis of the internal cerebral veins, vein of Galen, and straight sinus have been sporadic (13, 14). Many of the early cases were diagnosed only at postmortem examination. Because the clinical diagnosis can be quite confusing, accurate radiologic diagnosis is essential. In neither of our patients was the characteristic finding of thrombosis of the superior sagittal sinus present. The noncontrast CT images in both patients, however, showed hyperdense thrombus in the internal cerebral veins, vein of Galen, and straight sinus. This finding, suggesting venous thrombosis, is noteworthy and warrants further imaging. In both patients, this diagnosis was confirmed at MR imaging, in which the normal flow void in

the vein of Galen and straight sinus was lacking on the spin-echo sequences. MR venography confirmed the thrombosis of the involved vessels and showed the patency of the sagittal sinus.

Severe cerebral edema of the basal ganglia and thalami developed in both our patients, and hemorrhagic infarction of the thalamus developed in one patient. Although venous pressure measurements were not obtained, the parenchymal changes in the patients would be classified as stage IV by Tsai et al (12). These findings are characteristic for the territory of venous drainage collected by the deep cerebral venous system.

Hydrocephalus developed in both patients as a result of the deep cerebral venous thrombosis, which precipitated mass effect from the parenchymal edema with subsequent obstructive hydrocephalus. This obstruction occurred at the level of the foramen of Monro in case 1 and necessitated bilateral external ventricular drains in the lateral ventricles. In case 2, the third ventricle was compressed from the severe thalamic edema and a single external ventricular drain controlled the hydrocephalus. The natural course for thrombosis of the internal cerebral veins can be dismal, and it is diagnosed in many patients only at postmortem examination. Survivors often suffer severe neurologic compromise as a result of venous infarction with subsequent hemorrhage of the basal ganglia and thalamic structures (1). Management of venous thrombosis includes initiation of anticoagulation therapy with heparin to limit propagation of thrombus. Some authors have expressed a reluctance to use heparin because of its association with hemorrhagic venous infarction and the concern that it could directly exacerbate the process (15). Similar reservations hold for direct thrombolytic therapy with urokinase, but the total dose can be relatively low, and, presumably, the thrombus can be actively lysed and venous flow restored without the systemic side effects (16). Systemic heparin was tolerated in our cases, and theoretically does not initiate hemorrhage and should prevent rethrombosis.

It is possible for patients to recover from deep cerebral venous thrombosis if collateral venous drainage develops. Evidence that the thrombolysis contributed to the improved clinical outcome in our cases is that the patients made a relatively rapid recovery after treatment, with associated resolution of the parenchymal edema. One patient was able to follow commands within 24 hours after treatment; the other patient required management of his intracranial pressure before he improved. Subsequent imaging studies also confirmed the persistent recanalization of the deep venous structures.

Perhaps the most interesting aspect of our two cases was the end point for thrombolytic therapy. When fluoroscopic flow was established in a segment, the microcatheter was repositioned even if some thrombus remained. We relied on systemic heparinization to prevent rethrombosis. This end point has not always been used, and many days of infusion have been required in some cases (4). The good clinical outcome in both our patients appears to justify the process, although we recognize that the sample size is very small and the results could be misleading. Nevertheless, we have applied this therapy to subsequent patients with sagittal sinus thrombosis with hemorrhagic venous infarction and achieved similarly excellent clinical outcomes. In addition, no attempt was made to infuse urokinase at the level of the transverse or sigmoid sinuses, as the patients were not clinically deteriorating from thrombosis of those structures. The goal of the thrombolysis was to achieve flow and to relieve the severe parenchymal edema that had developed.

Interestingly, initial attempts at catheterization of the straight sinus from the patent transverse sinus were unsuccessful in both patients. This may have been due to the fact that the superior sagittal sinus often drains into the dominant transverse sinus. The contralateral transverse sinus may receive venous drainage primarily from the straight sinus. In both patients the microcatheter was easily advanced through the thrombosed segments of the sigmoid sinus and transverse sinus and into the thrombosed straight sinus.

In the first patient, a small area of hemorrhage developed along the tract of the external ventricular drain in the frontal lobe during the 24 hours after thrombolysis. This site was remote from the territory of edema associated with the venous congestion and was most likely related to the insertion of the external ventricular drain.

In conclusion, early diagnosis of deep cerebral venous thrombosis is critical for the initiation of proper clinical management. When pa-

renchymal edema in the thalamus and basal ganglia is present, one should suspect deep cerebral venous thrombosis as the underlying cause. Because severe clinical deficits can occur as a result of internal cerebral venous thrombosis, early application of direct endovascular thrombolytic therapy may dramatically improve the clinical outcome. Restoration of brisk flow, even if some thrombus remains, appears to be an adequate end point of intervention.

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