Intrasinus Thrombolysis by Mechanical and Urokinase for Severe Cerebral Venous Sinus Thrombosis : A Case Report

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Abstract-

Purpose: Cerebral venous and sinus thrombosis (CVST) is a rare stroke disorder, which requires prompt recognition and appropriate intervention to prevent a devastating outcome. Intrasinus thrombolysis is an alternative and effective method to anticoagulant therapy for the treatment of CVST, but is rarely used in Taiwan.

Case Report: A 46-year-old man presented with a one-week history of intractable headache and progressive weakness of his right lower limb. Magnetic resonance venography of the brain confirmed a diagnosis of extensive venous sinus thrombosis. The patient was successfully treated by direct intrasinus thrombolysis with urokinase.

Conclusion: This case highlights the benefit of early intrasinus thrombolysis for the treatment of CVST.

Key Words: Cerebral venous sinus thrombosis, intrasinus thrombolysis, urokinase

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INTRODUCTION

Cerebral venous and sinus thrombosis (CVST) is a rare disorder that accounts for 0.5% of all stroke cases and has a mortality rate of 10%[(1)]. Early diagnosis of CVST can be challenging because of nonspecific manifestations. This is concerning given that prompt treatment is essential to help reduce the likelihood of mortality. Anticoagulant therapy, either with intravenous unfractionated heparin or subcutaneous low molecular weight heparin, has traditionally been the first line of treatment for CVST, even in cases where there is hemorrhagic complication[(2)]. More recently, an increasing number of reports have described intrasinus thrombolysis (IST) to be an effective and advanced treatment for rapid recanalization of thrombosed sinuses, especially for patients who do not respond to anticoagulant therapy[(3-5)]. Herein, we report the case of a patient with CVST, confirmed by brain computed tomography (CT) and magnetic resonance (MR) imaging, who received immediate treatment with IST.

CASE REPORT

A 46-year-old man presented to our hospital with a one-week history of intractable headache. The headache was of sudden onset and originated from the occipital region with a band-like distribution. It was characterized

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as being persistent throughout the day, of moderate-to-severe intensity, and associated with nausea and vomiting. The patient had been prescribed ineffective pain killers. The patient denied having any medical conditions and did not take any illicit medications. He had no history of headache, trauma, or fever before the onset of the intractable headache.

On physical examination, the patient was alert and orientated. He had a body temperature of 37.1 ˚C, a regular pulse rate of 60 beats/min, blood pressure of 178/98 mm Hg, and normal heart sounds. He exhibited slight neck stiffness with a positive Brudzinski sign. Focal weakness of the patient's right lower limb was apparent (muscle power grade = 4 on the Medical Research Council Scale), as was an extensor plantar response. The deep tendon reflexes were relative brisk on the right lower limb without ankle clonus. Cranial nerve and other physical examination findings were unremarkable.

Laboratory testing revealed a high D-dimer titer of 1836 ng/mL. Other laboratory findings, including biochemical and serological, were within normal limits. Tests for hypercoagulable state, including autoimmune diseases, blood dyscrasias, inflammatory and infectious disease, were negative. There was no evidence of vasculitis or malignancy. Brain CT revealed a focal hypodense change at the left parietal lobe and high density (70 Hounsfield units) at the superior sagittal and right sigmoid sinuses. MR imaging and venography of the brain revealed extensive venous sinus thrombosis (Fig. 1 a & b & c) and infarction area at the left precentral gyrus and parietal lobe.

As the imaging finding and clinical deterioration, the patient underwent emergent IST via a femoral transvenous approach. Digital subtraction angiography by way of the right internal carotid artery (RICA) further confirmed the diagnosis of extensive dural sinus thrombosis. The cortical veins of the bilateral cerebral hemispheres were corkscrew in appearance, with increased venous stasis. Venous drainage was mainly from the cavernous sinus to the internal jugular vein through the clival and petrosal sinuses, with some drainage through the left transverse sinus to the internal jugular vein. The right superior ophthalmic vein appeared engorged and drained to the right angular and the facial veins. After introducing a guiding catheter in the right internal jugular vein, a microcatheter was advanced to the left transverse sinus and then the superior sagittal sinus (Fig. 2). Wire manipulation was performed step by step to the superior sagittal sinus with manual pulse injections of urokinase (1,250,000 units) for thrombus disruption. During the procedure, there was no regurgitation of contrast material into superficial cortical veins or extravasation. The blood pressure maintained in a normal range without significant signs of intracranial hemorrhage.

After thrombolytic therapy, cerebral angiography of the RICA revealed recanalization of most of the superior

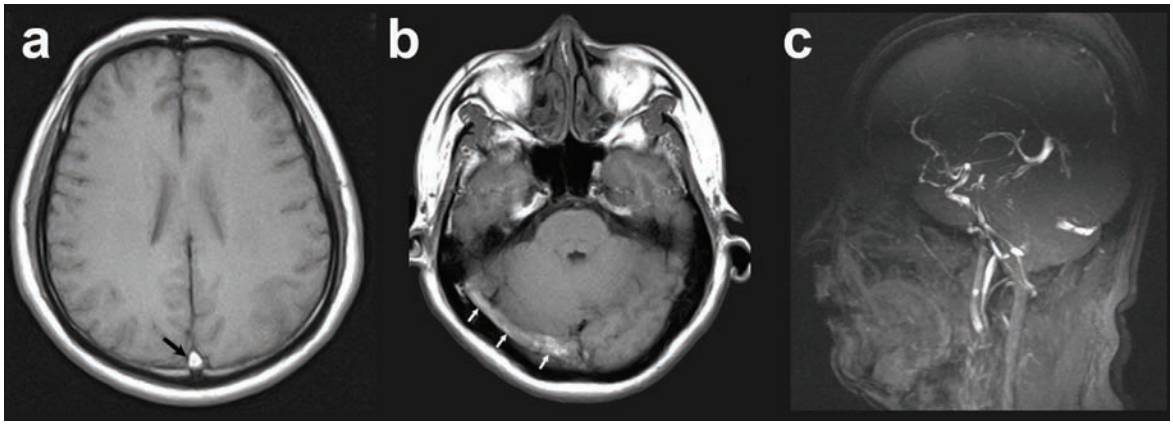

Figure 1. Axial T1 weighted image shows hyperintensities in the superior sagittal sinus (arrow in a) and the right transverse-sigmoid sinuses (arrows in b). Lateral MR venography confirms no flow signal of the superior sagittal, straight, bilateral transverse and sigmoid sinuses ©.

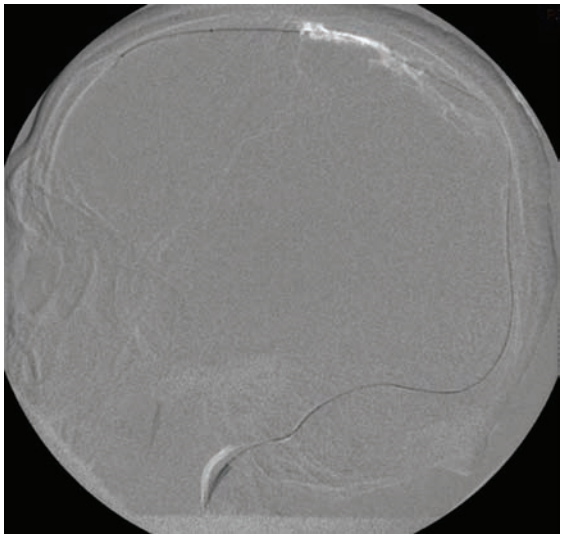

Figure 2. Angiography of the cerebral sinus venous system by way of the right internal jugular vein shows advancement of the microcatheter to the superior sagittal sinus with wire manipulation and injection of urokinase.

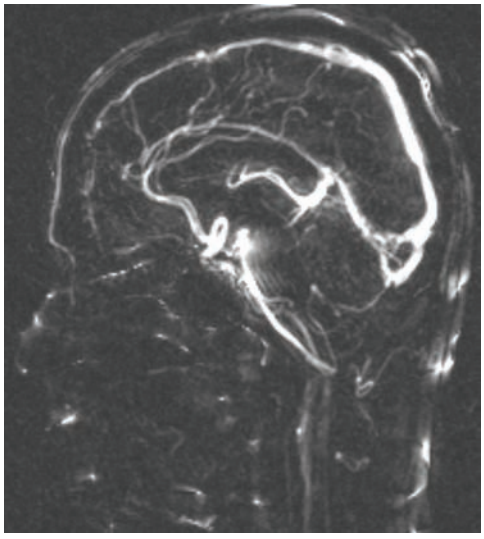

Figure 3. Lateral MR venography 1 week after IST shows restoration of the SSS while the bilateral sigmoid and right transverse sinuses remain occluded.

sagittal sinus. The venous systems were relatively patent at the time of the procedure. The patient experienced dramatic relief of the headache and the neurologic deficits resolved gradually. There was no hemorrhagic stroke after the procedure and the patient received anticoagulant therapy for the next 6 months. Follow-up MR venography one-week later revealed restoration of the superior sagittal and straight sinuses; the transverse-sigmoid sinuses remained occluded (Fig. 3).

DISCUSSION

IST is an effective and safe procedure for patients with severe CVST or for patients who fail to respond to conventional medical treatment. This procedure provides rapid recanalization and circulatory restoration, without significantly increasing the incidence of intracranial hemorrhage[3,4]. There are no established indications for IST; however, IST has been employed a rescue therapy for patients who are unresponsive to anticoagulant therapy or who have poor outcomes such as coma, intracranial hemorrhage, rapidly progressive clinical deficits, posterior fossa lesions, and involvement of the deep venous system[5,6]. This approach requires expertise in interventional radiology and is typically performed using a transfemoral or fontanelle puncture approach, with direct penetration of the catheter into the thrombic sinus. Urokinase is typically used as the thrombolytic agent; however recombinant tissue plasminogen activator and streptokinase have also been used[5].

To date, there are no established guidelines on thrombolytic agent dosage in IST. Described regimens vary from a bolus at the time of the intervention followed by a continuous infusion, to a bolus or a continuous infusion[5]. In the case described herein, we disrupted the thrombus with wire manipulation and followed this with urokinase injection. Angiography was performed to monitor the patency of the venous sinus system and to check for ruptures. We performed emergent IST to the patient because of the young age and rapid clinical deterioration. Our case highlights that use of IST as an early therapeutic intervention can facilitate successful clot lysis and restore neurologic deficits caused by extensive involvement of the sinuses, including deep venous systems. In a previous report, Kumar and colleagues suggested that there is no correlation between the extent of

recanalization and clinical outcome[3]. Indeed, patients with cerebral venous sinus thrombosis improved, despite the lack of angiographic recanalization[3]. However, the authors suggested that early recanalization is still of benefit for improving outcomes and for relieving symptoms in patients with extensive CVST.

IST may be associated with a higher incidence of hemorrhagic complications compared with IST and heparin. Indeed, a non-randomized retrospective study found that 10% of patients in the thrombolysis group and 0% of patients in the heparin group experienced hemorrhagic complications[7]. Despite this, patients in the thrombolysis group (who had worse neurologic function before treatment) had better neurologic function than patients in the heparin group at the time of discharge[7]. This finding is encouraging regarding the beneficial effect of IST. The link between IST and minor hemorrhage is controversial, with one study study reporting that thrombolytic infusion was safe in the context of preexisting intracerebral hemorrhage[8]. Direct IST is not of benefit for patients with large infarcts and impending herniation[9,10]. In patients with parenchymal lesions leading to herniation, lifesaving hemicraniectomy should be considered[10].

Approximately 23% of patients experience deterioration after admission, with worsening mental status, headache, focal deficits, and / or the development of new symptoms, such as seizures, in nearly one-third of patients who present with new parenchymal lesions[1,11]. Patients who experience deterioration despite adequate anticoagulant therapy without new parenchymal lesions are obvious candidates for IST. Besides recanalizing the occluded sinus or vein with IST, additional treatment is warranted to prevent propagation of the thrombus and to treat the underlying prothrombotic state. Full dose oral anticoagulants, such as warfarin (at an international normalized ratio of between two to three for 3 months if CVST was secondary to a transient risk factor or for 6 to 12 months for idiopathic CVST and for patients with "mild" thrombophilia), is recommended[1,2]. More prolonged oral anticoagulation should be reserved for patients with inherited or acquired prothrombotic disorders, such as antiphospholipid antibody syndrome[1,2].

CVST is often unrecognized at initial presentation. As was the case in our patient, headache is the first and the most frequent symptom of CVST, occurring in 75 to 95% of all cases[12]. For patients with new, atypical headache, headache progressing steadily over days to weeks despite conservative treatment, and thunderclap headache, prompt imaging studies should be performed to exclude CVST[13]. A high index of clinical suspicion is needed to diagnose this uncommon condition so that appropriate treatment can be initiated. Management of CVST includes treatment of the underlying condition, antithrombotic treatment, prevention of complications[4], and symptomatic treatment. Antiepileptic agents should be prescribed for patients with supratentorial lesions experiencing seizures[10]. Lumbar puncture can be performed to help relieve symptoms in patients with severe headache and papilledema, intracranial hypertension, or hydrocephalus[10]. Our case highlights that early IST can provide rapid symptomatic relief because the associated symptoms, such as headache, seizure, and intracranial hypertension, are primarily caused by sinus occlusion.

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