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Case Report

Effectiveness of Transvenous Aspiration Thrombectomy for Cerebral Venous Sinus Thrombosis: A Report of Three Cases

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Objective: We report three patients successfully treated by emergent transvenous thrombectomy for cerebral venous sinus thrombosis (CVST).

Case Presentation: (Case 1) A 77-year-old man presented with vomiting, dizziness, and headache. CT revealed local subarachnoid hemorrhage (l-SAH), and angiography confirmed occlusion of the right transverse sigmoid sinus and superior sagittal sinus (SSS). Emergent transvenous aspiration thrombectomy using a Penumbra catheter (PC) resulted in effective reperfusion. (Case 2) A 60-year-old man developed disorientation, sensory aphasia, and right hemiparesis. MRI demonstrated extensive cerebral edema caused by venous congestion in both thalami, and angiography revealed poor opacification of the SSS, straight sinus, and bilateral transverse sinuses. Venous sinus flow was restored by catheter aspiration using a PC and topical infusion of urokinase (UK). (Case 3) A 19-year-old man developed a headache, numbness of the right upper limb, motor paralysis, and convulsions. CT revealed l-SAH and dense clot sign in the SSS. The SSS was poorly delineated on angiography. Thrombus aspiration using a PC and topical UK administration achieved partial recanalization.

Conclusion: Transvenous aspiration thrombectomy using large lumen catheters for patients with CVST is effective and safe. In particular, this method may be a better option than anti-coagulation therapy alone for patients presenting with a severe neurological condition or intracranial hemorrhage.

Keywords ▶ cerebral venous sinus thrombosis, Penumbra catheter system, transvenous aspiration thrombectomy

Introduction

Cerebral venous sinus thrombosis (CVST) is rare and its annual incidence is reportedly 5/1000000 which accounts for 0.5–1.0% of all stroke patients. Etiological factors for CVST include hereditary or acquired coagulation disorder, surgery, trauma, and pregnancy. As symptoms, headache caused by intracranial hypertension is observed in 90% of patients and convulsion is observed in 40%. As topical focal symptoms caused by venous infarction or subcortical hemorrhage, aphasia, and hemiplegia are common.[1)] The above-mentioned symptoms slowly exacerbate over a few days to a few weeks. First-choice treatment is anticoagulant therapy. Recent studies reported favorable results of transvenous thrombectomy while its efficacy remains controversial.[1–7)] In this study, we report three patients in whom transvenous thrombectomy using a Penumbra catheter (PC) was effective for CVST, and review the literatures.

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Case Presentation

Patient 1: A 77-year-old man (heavy drinker).

Present illness: the patient developed general fatigue, vomiting, vertigo, and headache 4 days previously, and then other symptoms, such as dressing apraxia, also gradually appeared. A CT revealed local subarachnoid hemorrhage (l-SAH) involving the right temporo-parietal lobes (**Fig. 1A** and **1B**). As the patient reported a head trauma, he was admitted under a diagnosis of traumatic SAH. Laboratory data on the initial consultation demonstrated that the international normalized ratio of the prothrombin time (PT-INR),

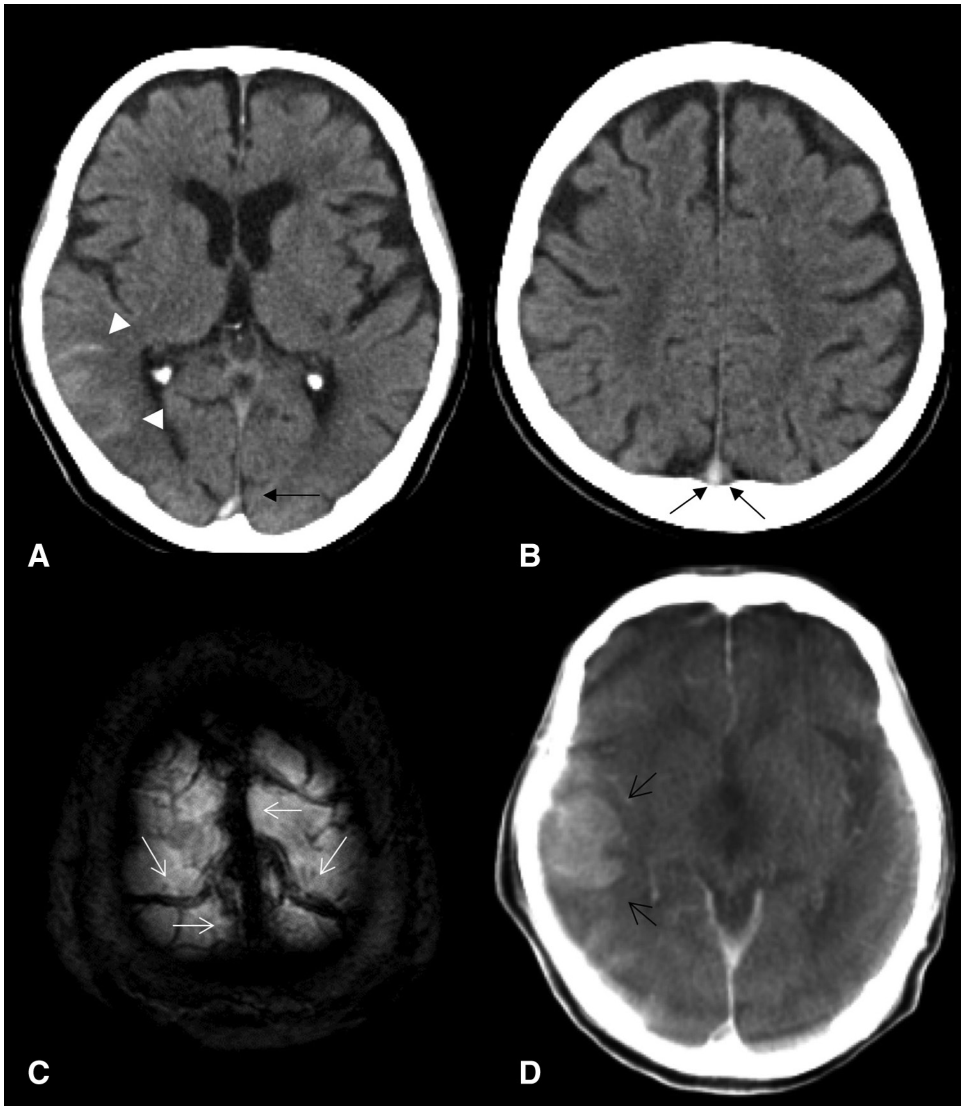

Fig. 1 (**A** and **B**) Initial CT shows L SAH in the right temporal lobe (white arrowheads) and dense clot sign in the SSS (black closed arrow). (**C**) MRI (T2*WI) reveals susceptibility vessel sign in the SSS and bilateral cortical veins (white open arrows). (**D**) Cone-beam CT just before angiography demonstrates subcortical hematoma in the right temporal lobe in addition to local SAH (black open arrows). L SAH: local subarachnoid hemorrhage; SSS: superior sagittal sinus

activated partial thromboplastin time (APTT), and D-dimer level were 1.05, 24.7 seconds, and 34.7 mg/mL, respectively. There was an increase in the D-dimer level. MRI T2*-weighted imaging (T2*WI) demonstrated low signal intensity in the superior sagittal sinus (SSS) and cortical vein (**Fig. 1C**), but this finding was not initially recognized as significant. He developed restlessness and left hemiplegia on the next day. Cone-beam CT revealed intracerebral hemorrhage in the right temporal lobe (**Fig. 1D**). Cerebral angiography demonstrated occlusion of the SSS and the right transverse sinus (**Fig. 2A** and **2B**). Emergent transvenous aspiration thrombectomy was performed. Initially, a trans-left internal jugular approach was attempted, but a guidewire could not select the SSS. Therefore, an 8Fr Roadmaster 90 cm (Goodman, Aichi, Japan) was inserted into the right internal jugular vein and a 0.035-inch Radifocus guidewire 180 cm (Terumo, Tokyo, Japan) was introduced to the right transverse sinus. Subsequently, an ACE68 (Penumbra, Alameda, CA, USA) was guided into the SSS using a Marksman as an inner catheter, and selective venography was obtained (**Fig. 2C**). After confirming the localization and extent of thrombus, aspiration thrombectomy was initiated between the intermediate point of the SSS and confluence (**Fig. 2B**). On the 3rd pass, intra-ACE68 reflux stopped and the ACE68 was slowly pulled back into the guiding catheter. Red thrombus measuring

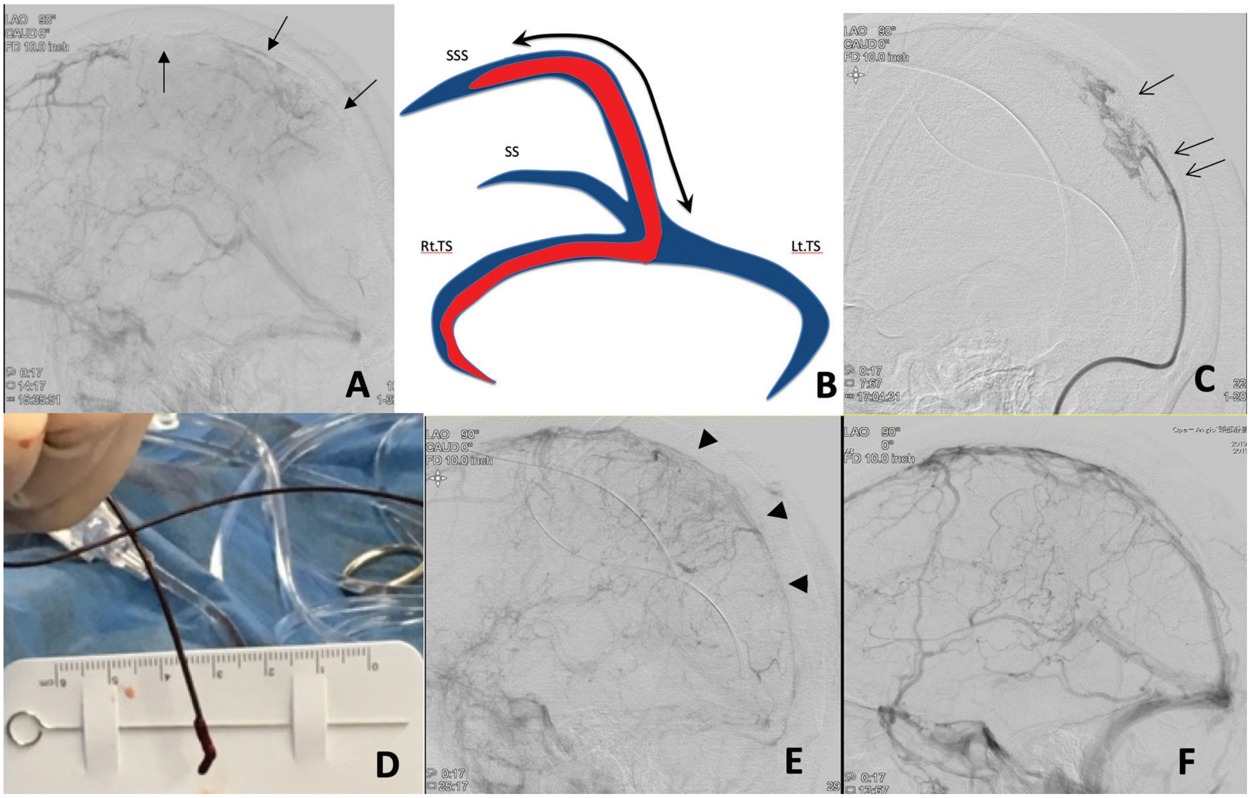

Fig. 2 **(A)** Venous phase of right carotid angiography (lateral view) discloses SSS occlusion (black closed arrows). (**B)** Schema of the sinuses: The SSS (bidirectional arrow) and right TS were occluded. (**C)** Venography through a microcatheter shows a filling defect in the SSS, indicating a large clot in the posterior part of the SSS (black open arrows). (**D)** A retrieved large clot through ADAPT. (**E)** Postoperative left carotid angiography shows improved antegrade venous outflow in the SSS (black arrowheads). (**F)** Left carotid angiography 2 months after the procedure demonstrates normal venous flow. ADAPT: direct aspiration first-pass technique; SSS: superior sagittal sinus; TS: transverse-sigmoid sinus

approximately 2 cm in length was captured through the distal end of ACE68 (direct aspiration first pass technique (ADAPT) (**Fig. 2D**). Final angiography confirmed improvement in visualization of the SSS (**Fig. 2E**). After the procedure, the activated coagulation time (ACT) was maintained at 150–200 using 10000 units/day of heparin. Heparin was converted to warfarin 10 days after the procedure after 3 days of a transition period. With consideration of his advanced age and renal dysfunction, the PT-INR was adjusted to range from 1.6 to 2.6. Detailed examination revealed decreases in the protein C antigen and its activity levels (51% and 45%, respectively), but follow-up examination confirmed normalization of these values. The above changes were considered to be transient decreases related to consumption, leading to a final diagnosis of idiopathic CVST. After the rehabilitation period, the neurological symptoms almost disappeared. After 2 months, cerebral angiography demonstrated further improvement of visualization of the sinus (**Fig. 2F**). The patient was discharged 3 months after the procedure with a modified Rankin Scale (mRS) score of 0.

Patient 2: A 60-year-old man.

Present illness: The patient developed headache and anorexia 5 days previously. He was diagnosed with a common cold at a local clinic and rested at home. His wife found him unable to move and he was brought to our hospital by ambulance. On arrival, the Glasgow Coma Scale (GCS) score was E4V3M5, and sensory aphasia, disorientation, and right hemiplegia were observed. Laboratory data demonstrated that PT-INR and APTT were 0.95 and 24.6 seconds, respectively, and the D-dimer, blood urea nitrogen (BUN), thrombin–antithrombin complex (TAT), plasmin a_2 plasmin inhibitor complex (PIC), von Willebrand activity, antigen, and lupus anticoagulant levels were 6.5 mg/mL, 22 mg/dL, 18.6 ng/mL, 3.6 mg/mL, 482%, 398%, and 1.33, respectively. A plain CT revealed high signal intensity in the straight sinus (**Fig. 3A**). MRI-fluid-attenuated inversion recovery (FLAIR) demonstrated an extensive high signal intensity area involving the bilateral thalami and peri-third ventricle (**Fig. 3B**). On T2*WI, low signal intensity in the SSS was observed (**Fig. 3C**). Under a diagnosis of CVST with thalamic congestion, administration

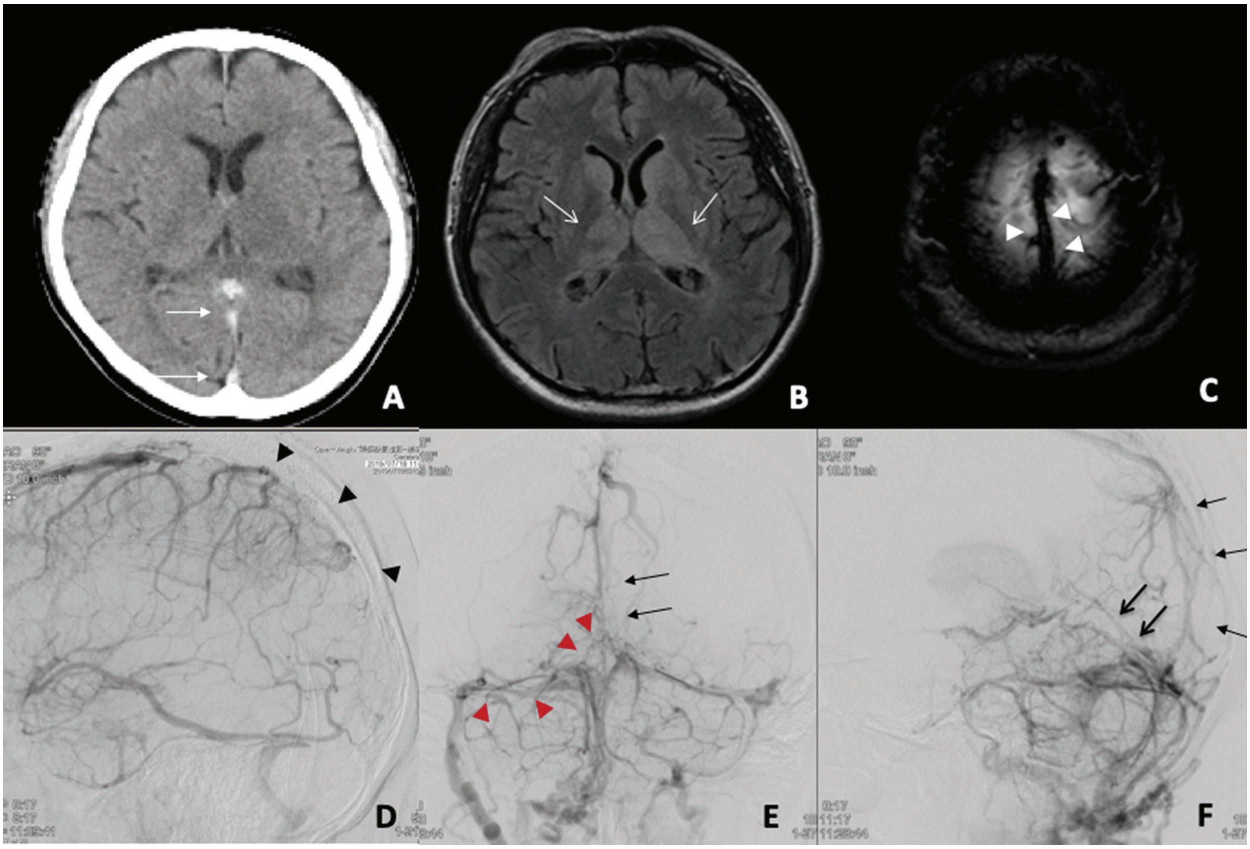

Fig. 3 **(A)** Initial Plain CT reveals abnormal high density in the straight sinus (white closed arrows). (**B**) MRI (FLAIR) shows mild signal high intensity in bilateral thalami (white open arrows). (**C**) MRI (T2*-weighted imaging) reveals longitudinal low intensity signal in the SSS, suggesting intra-sinus clot (white arrowheads). (**D**) Right CAG (lateral view) demonstrates severe stenosis of the proximal third of the SSS (black arrowheads). (**E** and **F**) Vertebral angiography demonstrates a filling defect of the SSS (black closed arrows) and faint visualization of the straight sinus (black open arrows). The left sigmoid sinus is slightly visible, whereas the transverse sinus on the right side is almost obliterated (red arrow heads). FLAIR: fluid-attenuated inversion recovery; SSS: superior sagittal sinus

of 10000 units/day of heparin was started and cerebral angiography was performed the following day. The posterior two-thirds of the SSS, bilateral transverse sinuses, right sigmoid sinus, straight sinus, left internal cerebral vein, and bilateral internal jugular veins were poorly visualized (**Fig. 3D–3F**). An emergent thrombectomy was performed. An 8Fr Roadmaster 80 cm was introduced into the left internal jugular vein and a 4Fr CeruleanG 127 cm (Medikit, Tokyo) was guided to the left transverse sinus as an intermediate catheter. Selective venography was conducted at several locations by a Headway 17 (MicroVention TERUMO, Tustin, CA, USA). The sinus was extensively occluded (**Fig. 4A**). Urokinase (UK) at 60000 units was slowly infused through the 4Fr CeruleanG 127 cm inserted into the confluence. Headway 17 was then guided to an area adjacent to the Galenic vein-straight sinus junction and 30000 units of UK was slowly infused. After guiding an ACE60 (Penumbra) + 3MAX (Penumbra) system to the center of the SSS where selective venography confirmed as the occlusion area. Under aspiration with negative pressure, running aspiration involving the sinus confluence was conducted. The Headway was guided to the distal left transverse sinus and 30000 units of UK was slowly infused (**Fig. 4B**). Finally, running aspiration was performed with ACE60 between the confluence and the left internal jugular bulb. A large amount of red and white thrombi could be retrieved from the collected blood (**Fig. 4C**), leading to improvement in visualization of the sinus (**Fig. 4D–4E**). Subsequently, anticoagulant therapy with 14400–16000 units/day of heparin in the acute phase and warfarin from the subacute phase was continued to maintain the PT-INR range from 1.8 to 2.7. The neurological symptoms gradually improved. Follow-up digital subtraction angiography (DSA) 1 week after the procedure revealed marked improvement of visualization of SSS (**Fig. 4F**). Detailed examination of coagulation factor revealed no significant abnormality except slight increase in the lupus anticoagulant level, leading to a final diagnosis

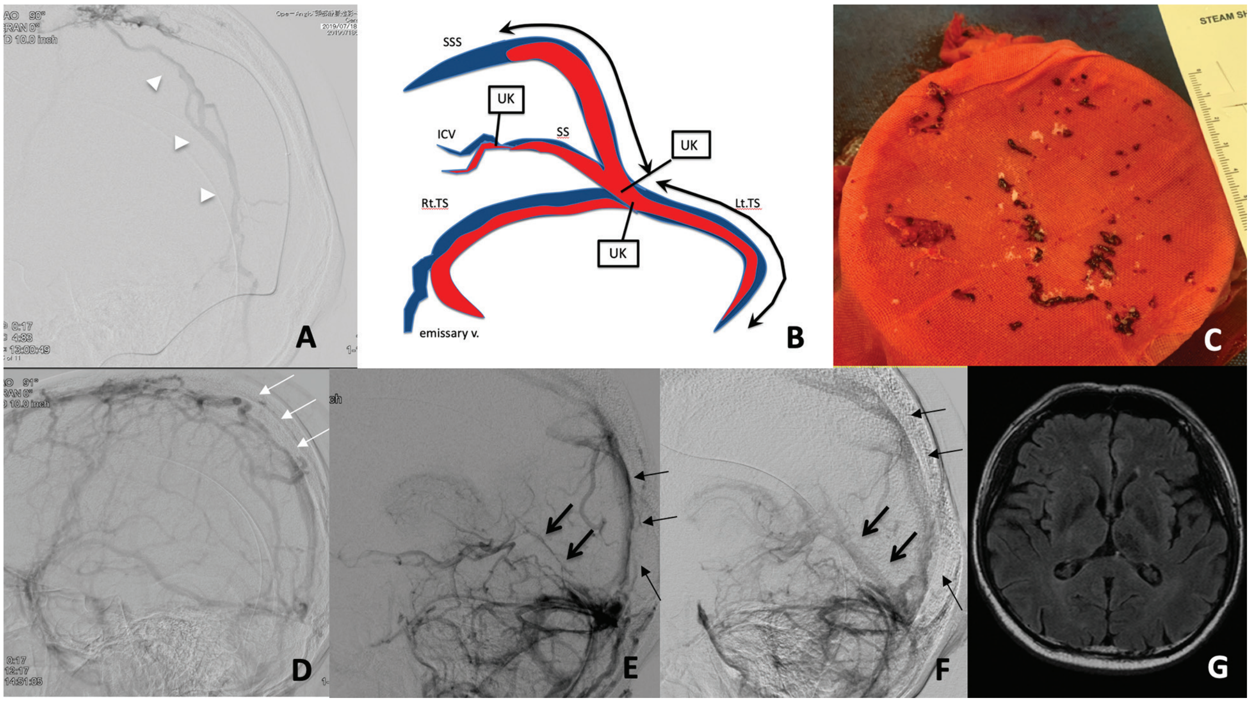

Fig. 4 **(A)** Selective venography via a microcatheter reveals near-occlusion of the proximal one-third of the SSS. White arrowheads indicate collateral flow via a diploic vein. **(B)** Schema of the sinuses during aspiration thrombectomy: Running aspiration using the PC is conducted between the SSS and left transverse sinus (bidirectional arrow) in combination with local UK thrombolysis. (**C**) Multiple red and white thrombi were harvested in the aspirated blood. (**D**) Lateral view on postoperative right carotid angiography shows partial recanalization of the proximal part of the SSS (white closed arrows). (**E**) Postoperative left vertebral angiography demonstrates good visualization of the proximal SSS (black closed arrows) and the remaining clot in the straight sinus (black open arrows). (**F**) Left VAG 1 week after the procedure shows good visualization of the straight sinus (black open arrows) and the SSS (black closed arrows). (**G**) FLAIR image of MRI 1 month after the procedure confirms the disappearance of abnormal signal intensity in the bilateral thalami. FLAIR: fluid-attenuated inversion recovery; SSS: superior sagittal sinus

of idiopathic CVST. MRI obtained 1 month after the procedure confirmed the disappearance of the high signal intensity involving the bilateral thalami on FLAIR (**Fig. 4G**). There was no neurological deficit 2 months after the procedure and the patient was discharged with a mRS score of 0.

Patient 3: A 19-year-old man.

Present illness: The patient had symptoms related common cold persisted for the past 2 weeks. He developed sudden onset of headache 3 days prior to the admission. As he had numbness and weakness of the right upper and lower limbs, he consulted a local clinic and was referred to the emergency department of our hospital. He once returned to home after examination of MRI. However, a generalized clonic seizure occurred after returning home and he was brought to our hospital by ambulance. His GCS score was E4V5M6 and he had right hemiparesis (MMT: 3/5). Laboratory findings including PT-INR, APTT, fibrinogen level, and antithrombin III level were 1.04, 25.7 seconds, 288 mg/dL, and 81.0%, respectively. CT revealed localized SAH in the bilateral frontal lobes and a dense clot sign in the SSS (**Fig. 5A**). MRI-T2*WI demonstrated low signal intensity in the SSS and cortical veins (**Fig. 5B**), and emergent cerebral angiography was performed. The cortical veins and cerebral sinus including SSS to origin of right transverse sinus were poorly visualized, leading to a diagnosis of CVST. As the left transverse sinus was patent, thrombectomy was attempted through the left transverse sinus (**Fig. 6A**). Using an 8Fr Brite tip (Cardial Health Japan, Tokyo, Japan) as a guiding catheter, Penumbra systems 054 and 032 (Penumbra) were guided to the SSS, and the localization of thrombi was confirmed using selective venography (**Fig. 6D**). 120,000 units of UK at was topically infused. Aspiration of thrombus between SSS and the confluence was conducted using the Penumbra 054. A large amount of crushed thrombi could be retrieved. 120,000 unit of UK was then topically infused. Final angiography confirmed improvement in visualization of the SSS and cortical veins (**Fig. 6E**). After the procedure, anticoagulation therapy with heparin (10000–14400 units/day) was continued. His right hemiparesis improved gradually. There were no neurological symptoms 3 months later and the patient was discharged with a mRS score of 0. Laboratory findings at admission and 12 weeks later revealed positive anti-cardiolipin antibody, suggesting that anti-phospholipid

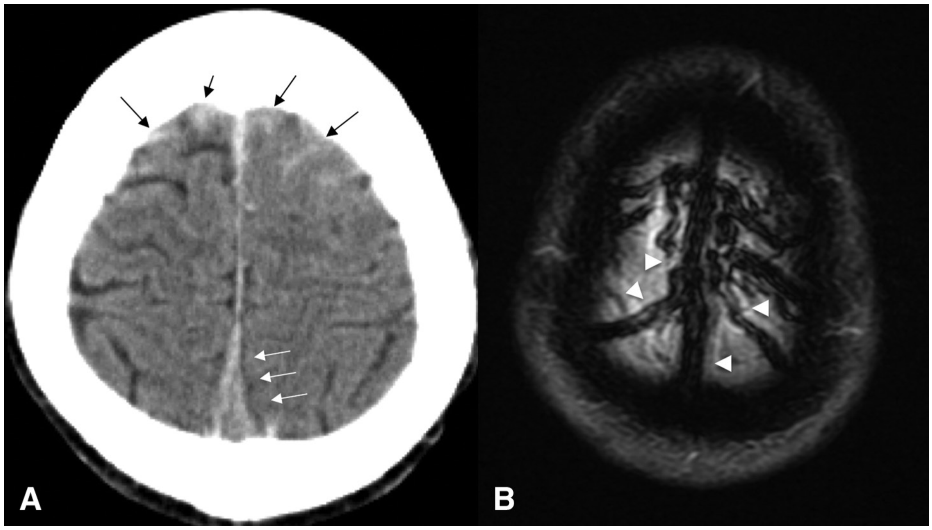

Fig. 5 **(A)** Initial CT shows local subarachnoid hemorrhage in bilateral frontal lobes (black arrows) and dense clot sign in the SSS (white arrows). (**B)** MRI (T2*WI) reveals susceptibility vessel sign of the SSS and adjacent cortical veins (white arrowheads). SSS: superior sagittal sinus

antibody syndrome affected CVST. Anticoagulation therapy has continued with PT-INR range from 2.0 to 3.0 (Patient 3 was presented on Pages 78–83 of Neurosurgery News Flash Volume 24 in 2014, and approval for publication was received from MEDICA SHUPPAN, Publishers Co., Ltd.).[8]

Discussion

A definitive diagnosis of CVST is made on the basis of cerebral angiography or MR venography (MRV) findings. CVST is suggested that imaging findings include a dense clot sign on CT, but its sensitivity is approximately 25%.[9] As T2*WI can demonstrate intra-thrombus deoxyhemoglobin as low signal intensity through magnetic susceptibility effects, T2*WI is thought to be more sensitive.[10] Cerebral sinus and cortical veins with thrombus or blood flow stasis can be demonstrated as low signal intensity with a sensitivity of 90% in the acute phase of CVST.[11]

As the first-choice treatment for CVST, anticoagulation therapy with heparin in the acute phase and warfarin in the chronic phase is administered by using an optimal range of PT-INR (2.0–3.0).[1] The recanalization rates of anti-coagulation therapy have been reported 83%–85%. Favorable outcome with mRS score of 0–2 were achieved in 86% of patients, whereas another study reported that the incidence of cerebral hemorrhage caused neurological exacerbation in 10% of patients and the mortality rate was 8–13%.[12] We adopted a treatment strategy of anti-coagulation therapy with heparin in acute phase and with Warfarin in chronic stage on the basis of PT-INR within a range of 2.0–3.0. Recent advancement of endovascular therapy provides new treatment strategy of intraluminal thrombectomy in the acute phase. According to recent several studies, endovascular thrombectomy achieved recanalization rate of 86–95% and 84–92% of patients had a favorable outcome with an mRS score of 0–2. The incidence of exacerbation caused by cerebral hemorrhage are 10%–14% and the mortality rate are 7%–12%; these results suggested endovascular thrombectomy is thought to be the same or superior to anticoagulant therapy alone.[13,14] Endovascular thrombectomy can also be adopted to heparin-resistant or severe patients, and facilitate earlier recovery. Additional topical infusion of UK or tissue plasminogen activator (tPA) may achieve synergic effects of recanalization. In patients with cerebral hemorrhage, such as Patients 1 and 3, endovascular thrombectomy can reduce the dose of a fibrinolytic drug. In patients with extensive venous congestion, such as Patient 2, prompter recanalization may be achieved by endovascular thrombectomy in combination with anti-coagulation therapy, which result in favorable outcome. Endovascular thrombectomy including topical fibrinolytic therapy, balloon angioplasty, and thrombus-capturing therapy with a microsnare, Penumbra system, Fogarty embolectomy catheter, or stent retriever have been reported.[4,6] However, a randomized study (TO-ACT) found no significant difference between the anticoagulant therapy alone and anticoagulant therapy with thrombectomy,[5] but TO-ACT study did not include thrombectomy using large-diameter catheter. TO-ACT study could

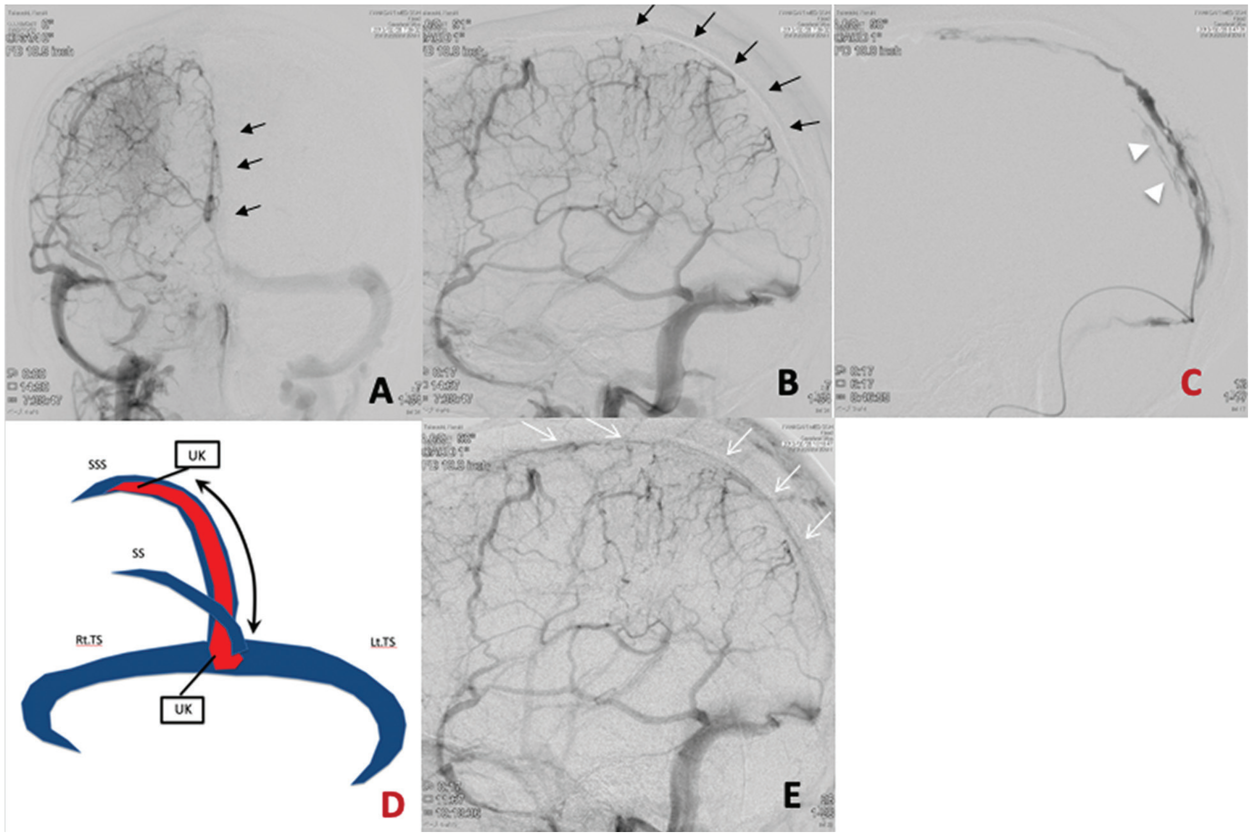

Fig. 6 (**A** and **B**) Preoperative right carotid angiography demonstrates a filling defect in the proximal half of the SSS (black closed arrows). (**C**) Selective venography through a microcatheter before thrombectomy shows the irregularly narrow lumen of the SSS (white arrowheads). (**D**) Schema of the sinuses: Clot formation is found in the SSS. Suction thrombectomy is completed using the PC (bidirectional arrow) and topical infusion of UK. (**E**) Post-procedural carotid angiography (lateral view) demonstrates partial recanalization of the SSS (white open arrows) and cortical veins. PC: Penumbra catheter; SSS: superior sagittal sinus; UK: urokinase

suggest that thrombus-crushing effects of an AngioJet or balloon catheter were limited, and a stent retriever was too small for the SSS size. In our three patients, combination of thrombus aspiration with a large-diameter catheter and topical fibrinolytic therapy was effective.[7] Most sinus thrombi were extensive and large, differing from arterial thrombi. Therefore, a method of direct aspiration of thrombi using strong aspiration force through the large lumen catheter may be efficient. The recent development of large-diameter catheters, a Sophia flow plus (MicroVention Terumo), React (Medtronic, Minneapolis, MN, USA), Penumbra JET7 (Penumbra), Catalyst 6, and Catalyst 7 (Stryker, Kalamazoo, MI, USA) may enable us more efficient thrombus aspiration. In the future, the most appropriate device for sinus aspiration thrombectomy may be clarified by examining a large number of patients.

We have three technical strategies for efficient thrombus aspiration of sinus thrombosis as follows: First, selective venography through a microcatheter or 3MAX catheter is useful for evaluating the precise location of sinus occlusion. Second, an 8Fr guiding catheter 80 cm should be selected rather than the 90 cm. This makes it possible for ACE60/68 catheters 132cm in length to reach the more distal segment of SSS or contralateral transverse/sigmoid sinuses. Third, two surgeons should carefully observe frontal/lateral views using biplane fluoroscopy in order to avoid migrations of guidewire to wrong venous systems. In particular, assistants should pay attention to guidewire motions on the frontal view during intra-SSS procedures and on the lateral view during intra-confluencial procedures.

The precise evaluation of sinus anatomy is essential for sinus thrombectomy. As the sinus is surrounded by the hard dura mater, intra-sinus guidewire or catheter operations may be relatively safe, while cortical veins are fragile and careless guidewire maneuvers may induce vessel perforations. Considering the anatomical variations of the confluence, guidewire maneuvers should be carefully conducted. The anatomy of the confluence is classified into three types, and further into a total of 15 subgroups.[15] As for the route to the SSS in type I, catheters can be guided through the left or right transverse sinus, it accounts for 55.9%. In type IIR, an approach to the SSS through the right transverse sinus is possible, it accounts for 31.7%, and in type IIL, an approach through the left transverse sinus is possible, it accounts for 12.3% (modified Gokce/Bayaro Gullan's classification[15,16]). Concerning the sinus pattern of the SSS to the transverse sinus in Japanese patients, a symmetric type accounts for 50.7% and a right-predominant type accounts for 38.0%.[17] In embryos, predominant drainage to the right transverse sinus accounts for 89%.[18] Thus, when in doubt to select an approach side for SSS occlusion, an approach through the right sigmoid sinus could be recommended. In our three patients, Patient 1 was classified as type I, and Patients 2 and 3 were classified as type IIL. Therefore, an approach through the right transverse sinus was selected in Patient 1, and an approach through the left transverse sinus was selected in Patients 2 and 3.

At present, in cases of incomplete aspiration of thrombi, combination with selective infusion of fibrinolytic drug may be necessary and post-procedural anticoagulation therapy is mandatory. In the future, further improvements of diagnostic imaging and devices may make the endovascular treatment as first-line treatment for CVST.

Conclusion

We underwent three cases of transvenous thrombus aspiration therapy using a large-lumen catheter in the acute phase, in combination with anticoagulation therapy for CVST, and obtained favorable results. This procedure is relatively simple and may be effective, especially in intracranial hemorrhage or severe-status patients.

Disclosure Statement

The authors declare no conflict of interest.

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