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Case Report

CASE REPORT

Successful endovascular recanalization of massive cerebral venous sinus thrombosis in a patient with tuberous sclerosis and protein S deficiency: a case report

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Abstract

Here, we report the case of a 27-year-old woman with tuberous sclerosis complex who underwent successful endovascular intervention for cerebral venous thrombosis at the superior sagittal sinus. She had protein S deficiency and a long-term history of anemia caused by menorrhagia from uterine fibroids, possibly leading to a hypercoagulable state. Cerebral venous sinus thrombosis accounts for ~0.5–1% of all strokes. Several cases of venous thrombosis in patients with tuberous sclerosis complex and protein S or protein C deficiency have been reported, but further studies are needed to identify whether an association of this rare combination may be explained.

INTRODUCTION

Cerebral venous sinus thrombosis is a rare and often unrecognized type of stroke, which may account for up to 0.5–1% of all strokes [1] and primarily affects young women. Cerebral venous sinus thrombosis can cause death and dependency [2] and may be provoked by prothrombic factors associated with anemia and various other clinical conditions such as protein S deficiency [2].

Systemic anticoagulation is a widely used therapy for cerebral venous thrombosis, but not all patients recover fully with this treatment. Recently, endovascular intervention for cerebral venous thrombosis has been indicated for patients who show deterioration despite systemic anticoagulation therapy.

Tuberous sclerosis complex is a rare disorder, involving seizures, characteristic skin lesions and intellectual disability [3]. Only a few cases of tuberous sclerosis complex in combination with protein S protein C deficiency have been reported [4]. Here, we present the first report of a patient with tuberous sclerosis complex who underwent successful endovascular intervention for cerebral venous thrombosis.

CASE REPORT

A 27-year-old woman presented with a severe generalized seizure followed by unconsciousness. She had been diagnosed with tuberous sclerosis complex (no family history) based on

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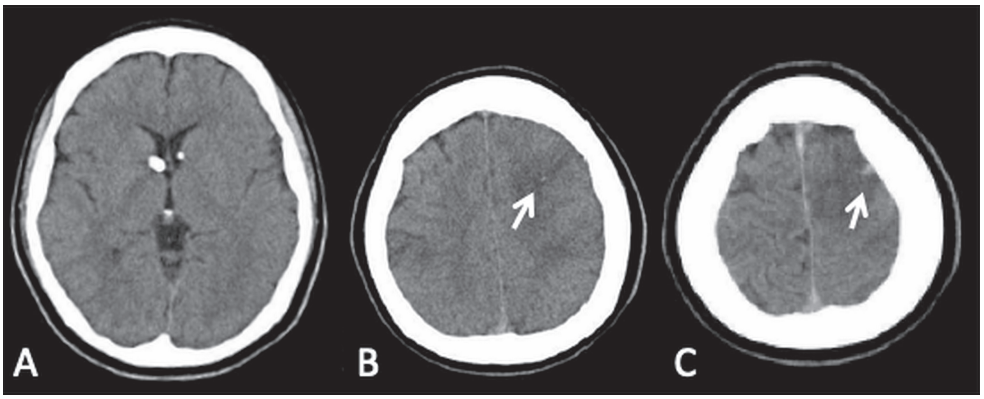

Figure 1: Brain computed tomography on admission demonstrates bilateral subependymal nodules and at caudate nucleus that are calcified (**A**) and bilateral frontal edema with a very small area of hyperdensity in the left frontal region (**B**, **C**) as congestion (arrows).

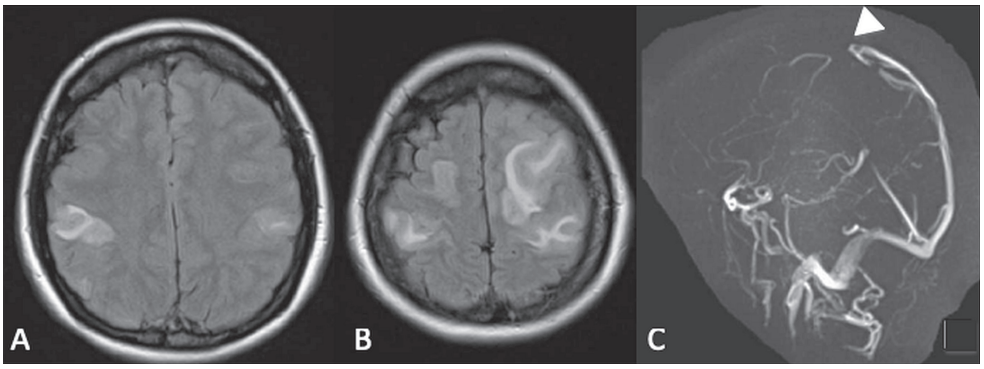

Figure 2: Brain magnetic resonance FLAIR sequence demonstrates bilateral frontoparietal edema (**A**, **B**) and magnetic resonance venography reveals an occlusion in the middle third of the superior sagittal sinus (arrowhead) on admission.

uncontrolled epileptic seizure at age 7 along with hypomelanotic patches, cortical tuber and ungual fibroma. She had also suffered from a pulmonary thromboembolism at 26 years old due to protein S deficiency.

Laboratory examination revealed that the level of protein S was normal (104% of the reference value), but its activity was below normal (43% of the reference value). Protein C concentration and activity were both normal. Therefore, the patient was diagnosed with type II protein S deficiency.

An initial non-contrast head computed tomography demonstrated low attenuation within the left frontal cortex with increased attenuation of the cortical vein (Fig. 1). Magnetic resonance fluid-attenuated inversion-recovery (FLAIR) sequence showed bilateral frontal edema with mass effect, and magnetic resonance venography revealed an occlusion within the anterior middle portion of the superior sagittal sinus (Fig. 2). Anticoagulation therapy with intravenous heparin infusion was started immediately. Over the next 24 hours, however, the patient exhibited repeated seizure episodes. The decision was made to attempt endovascular venous mechanical thrombectomy. Initial angiography revealed near-complete occlusion of the anterior half of the superior sagittal sinus and cortical veins (Fig. 3). A 90-cm 8-Fr Fubuki catheter (Asahi Intecc, Aichi, Japan) was placed in the right jugular bulb via a right trans-femoral approach. In addition, a construct consisting of a 5MAX ACE reperfusion catheter (Penumbra, Alameda, CA, USA) was navigated over a micro-catheter (Marksman; Medtronic, Irvine, CA, USA) over a 0.014″ micro-guidewire (Chikai; Asahi Intecc, Aichi, Japan), which was used to reach the middle portion of the superior sagittal sinus. Then the micro-guidewire was removed, and a Solitaire FR revascularization device (4 × 20 mm) was deployed in the anterior portion of the thrombosed superior sagittal sinus. The Solitaire FR device was then pulled into the 5MAX reperfusion catheter, which was connected to the Penumbra aspiration system. Using the same procedure, a total of three sequential passes from the distal to the proximal aspect of the superior sagittal sinus were performed, resulting in significantly improved flow and complete recanalization in the superior sagittal sinus.

After the procedure, she remained on full-dose intravenous anticoagulation throughout her hospitalization, but she experienced worsening anemia caused by metrorrhagia and uterine fibroids and subsequently received 4 units of packed red blood cells and underwent surgical hysterectomy. Pathological examination of the uterus revealed both leiomyomas and adenomyosis. Eventually, her anemia improved, and treatment with edoxaban was started. Six weeks later, the patient was completely independent, with no significant cognitive dysfunction and minimal and improving right-hand weakness (modified Rankin scale 1).

DISCUSSION

To our knowledge, this case represents the first report of a patient with tuberous sclerosis complex who underwent mechanical treatment using Solitaire FR stents and a 5MAX ACE reperfusion catheter for cerebral venous thrombosis of the superior sagittal sinus.

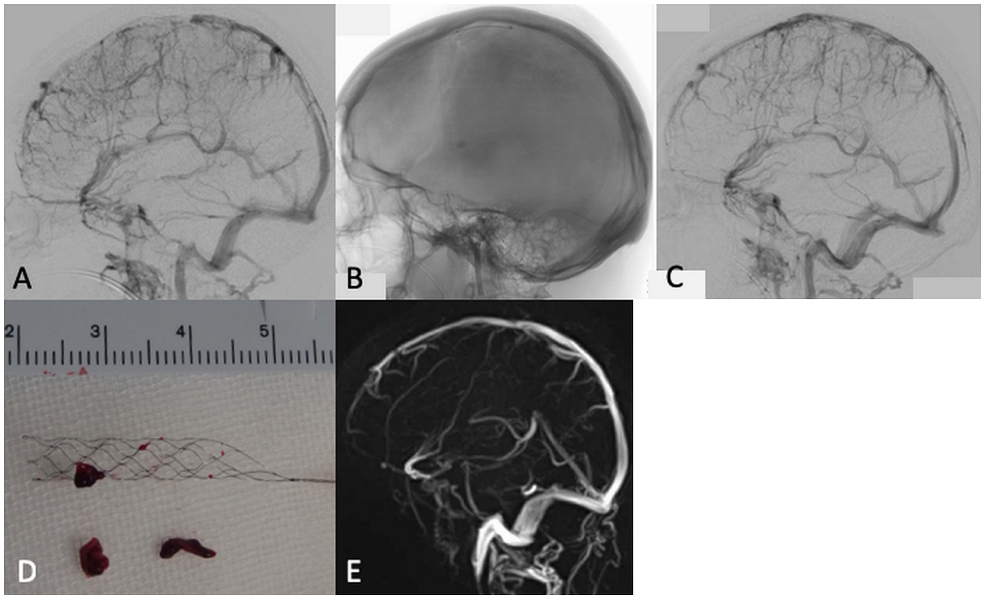

Figure 3: Lateral digital subtraction angiography of the superior sagittal sinus. (**A**) Venous-phase left internal carotid angiography reveals a thrombus in the middle third of the superior sagittal sinus. (**B**) On angiography, a 4 × 20-mm Solitaire FR revascularization device was deployed in the anterior half of the thrombosed superior sagittal sinus. (**C**) After thrombectomy, angiography shows markedly improved flow in the superior sagittal sinus. (**D**) The thrombus was entangled and removed with Solitaire FR stents. (**E**) Follow-up magnetic resonance venography 5 weeks after thrombectomy demonstrates complete patency of the previously occluded superior sagittal sinus.

Cerebral venous thrombosis is an uncommon cause of stroke with a multifactorial aetiology. It has been associated with uterine fibroids, metrorrhagia [5] and protein S and C deficiency [6]. Therefore, extensive investigations are often essential once the diagnosis is established.

Our patient demonstrated type II (qualitative) protein S deficiency. The reported prevalence of protein S deficiency is ∼2% overall (and specifically 1% for type II protein S deficiency) in a Japanese population [7] and 0.03–0.13% overall in Scotland [8].

Once the diagnosis of cerebral venous thrombosis is established, anticoagulation therapy should be started immediately, with heparin being the first-line treatment [9]. A recent systematic review suggested that patients presenting with very severe neurological deficits even after anticoagulation therapy may benefit from early and more aggressive therapies, such as mechanical treatment with or without intrasinus thrombolysis, and found that, overall, >80% of such patients had a good outcome [10].

No mechanism linking tuberous sclerosis complex and venous thrombosis has been established, although these clinical manifestations might be related. Further studies should be conducted to identify whether this is an association of this rare combination that can be explained.

CONFLICT OF INTEREST STATEMENT

None declared.

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CONSENT

Informed consent was obtained from the patient.

GUARANTOR

Yasuhiro Nishiyama, Kanako Muraga and Masayuki Ueda.

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