

Case Report

Deep Venous Thrombosis with Decreased Cerebral Blood Flow to the Thalamus was Completely Restored by Factor Xa Inhibitor

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Background: Cerebral venous thrombosis is rare and an uncommon cause of stroke and has diverse etiologies and varied clinical presentations. Here, we report 2 cases of deep cerebral venous thrombosis. **Case Description:** A 64-year-old woman presented with cerebral venous thrombosis due to a hypercoagulable state associated with ovarian tumor. On initial fluid-attenuated inversion recovery and diffusion-weighted imaging, there was a diffuse high-intensity lesion in the bilateral thalamus. Computed tomography angiography showed occlusion of the straight sinus, vein of Galen, and internal cerebral vein. Single-photon emission computed tomography showed decreased cerebral blood flow in the bilateral thalamus. After 3 weeks of factor Xa inhibitor therapy, the patient's consciousness gradually improved and eventually became clear enough to leave the hospital. She had no neurological deficit. Another patient was a 47-year-old man who presented with splitting headache and drowsiness. Magnetic resonance venography confirmed deep thrombosis of the vein of Galen. He completely recovered after 4 weeks of factor Xa inhibitor therapy. **Conclusions:** This study reports on 2 rare cases of decreased cerebral blood flow in the bilateral thalamus on single-photon emission computed tomography, which improved following the administration of factor Xa inhibitor.

Key Words: Deep venous thrombosis—single-photon emission computed tomography—cerebral blood flow—thalamus—factor Xa inhibitor

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Introduction

Acute bilateral thalamic edema may vary in clinical presentation, with symptoms such as coma, disorientation, and confusion. Venous drainage in the thalamus occurs via vessels that drain into the vein of Galen and straight

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We used heparin to control APTT in 2-2.5 times of the normal level. We used edoxaban 60 mg, because the weight of the patient exceeded 60 kg.

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sinus. We report the clinical and imaging findings of a patient with thrombosis of the vein of Galen and straight sinus, leading to a completely reversible thalamic edema, and review the literature on this rare entity. No case of deep cerebral venous thrombosis (DCVT) that presents as decreased cerebral blood flow (CBF) to the bilateral thalamus on single-photon emission computed tomography (SPECT) has been reported to date. Factor Xa inhibitor is an uncommon therapy for DCVT but was very effective in our cases.

Case Description

Case 1

A 64-year-old woman was found unconscious, requiring endotracheal intubation. On admission, neurological examination revealed that she was stuporous, with a

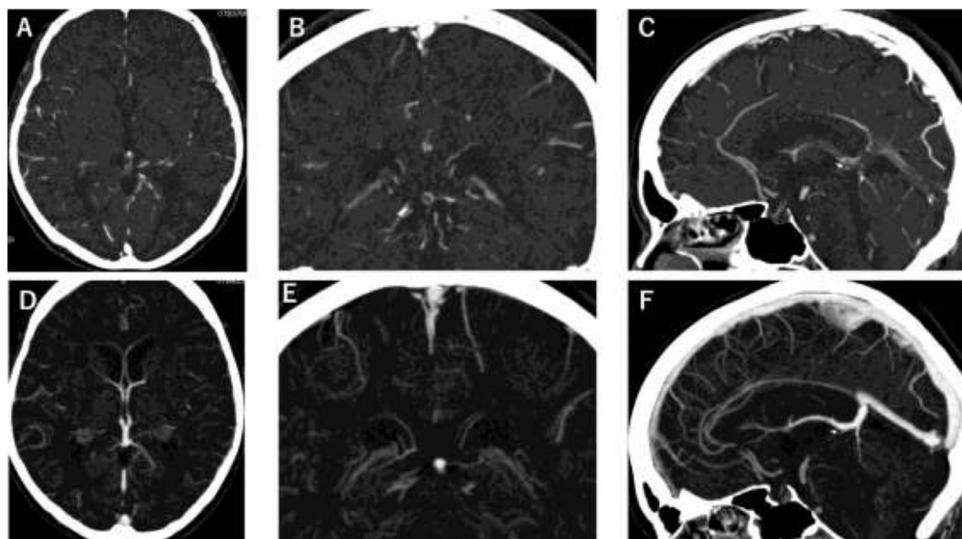


Figure 1. (A) Axial reconstruction of the CT angiography shows a filling defect on the vein of Galen and ICV. (B) Coronal section shows a filling defect of the straight sinus. It appears like a ring that is strongly indicative of an intraluminal clot. We call it the ring sign. (C) Sagittal section shows a filling defect on the straight sinus, vein of Galen, and ICV. (D-F) CT angiography images obtained 3 months after thrombosis show complete recanalization of the straight sinus, vein of Galen, and ICV.

Glasgow Coma Scale score of E2V4M6. Her cranial nerves were intact. She had no weakness, ataxia, sensory disturbance, or signs of meningeal irritation. Blood tests revealed iron deficiency anemia (hemoglobin, 11.2 g/dL; iron, 54 mg/dL), normal platelet counts ($21 \times 10^3/\mu\text{L}$), and elevated D-dimer level (2.4 $\mu\text{g}/\text{mL}$). White blood cell counts were within normal ranges. The C-reactive protein level was 1.22 mg/dL. The serum interleukin-6 level was elevated at 36.7 pg/mL (reference, <4.5 pg/mL). Results indicated that renal function, liver function, and serum electrolyte level were normal. Her medical history included benign ovarian tumor. Computed tomography (CT) showed high attenuation in the straight sinus. CT angiography revealed a filling defect in the straight sinus, vein of Galen, and internal cerebral vein (Fig 1A-C). The inferior sagittal sinus was dilated due to venous congestion. This was confirmed on magnetic resonance (MR) imaging as representing a partial dural venous sinus thrombosis with congestive thalamic edema (Fig 2). SPECT showed decreased CBF in the bilateral thalamus (Fig 3). Analysis of cerebrospinal fluid showed normal protein and glucose levels. Gram staining was negative. Heparin (15,000 U/day for 7 days) and edoxaban (60 mg/day) were administered for therapeutic efficacy. Levels of factors, including protein C, protein S, antithrombin III, and antiphospholipid antibodies that potentially cause a hypercoagulable state were within normal ranges. After a 3-week follow-up, the patient completely recovered. Findings on CT angiography 3 weeks after symptom onset revealed that the bilateral internal cerebral vein and straight sinus had regained blood flow, and SPECT findings normalized (Fig 3). She had no intracranial or other major bleeding complications and no recurrent thrombotic events during the 3-year follow-up.

Case 2

A 47-year-old man was admitted to the hospital with 1-week history of progressive headache and drowsiness. On admission, a neurological examination revealed that he was stuporous, with a Glasgow Coma Scale score of E3V4M6. His cranial nerves were intact. He had no weakness, ataxia, sensory disturbance, or signs of meningeal irritation. He had no past or family history of coagulation

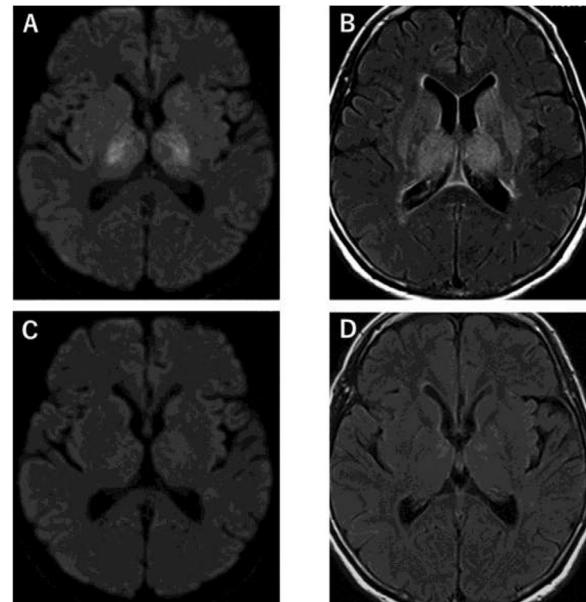


Figure 2. (A) Diffusion-weighted image (DWI) shows bilateral thalamic edema. (B) Axial fluid-attenuated inversion recovery (FLAIR) MRI depicting extensive bilateral thalamic and basal ganglia edema. (C, D) FLAIR and DWI images in the 3-month follow-up show resolution of bilateral thalamic edema and no residual parenchymal defects.

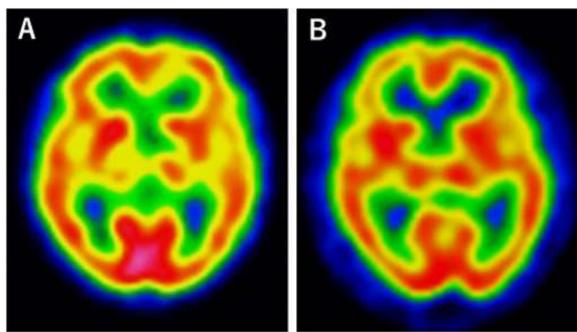


Figure 3. (A) Single-photon emission computed tomography in the 3-month follow-up shows hypoperfusion in the thalamic regions and basal ganglia similar to that in MRI (CBF: right thalamus, 31 mL/100 g/min; left thalamus, 35 mL/100 g/min; right basal ganglion, 34 mL/100 g/min; left basal ganglion, 37 mL/100 g/min). (B) After the patient's recovery showing improvement of perfusion in the bilateral thalamus and basal ganglia (CBF: right thalamus, 44 mL/100 g/min; left thalamus, 45 mL/100 g/min; right basal ganglion, 47 mL/100 g/min; left basal ganglion, 46 mL/100 g/min).

abnormalities. The results of an initial fundoscopic examination were normal. Findings on brain CT, showed no abnormal findings. A fluid attenuated inversion recovery imaging study of brain MRI showed bilateral thalamic high signal intensity, suggesting edema. MR venography (MRV) confirmed deep thrombosis of the vein of Galen. MR angiography was normal. MRV images are shown in **Figure 4**. The results of coagulation studies, including prothrombin time, platelet count, thrombin time, partial thromboplastin time, fibrinogen, antithrombin III, activated protein C resistance, antiphospholipid antibody, lupus anticoagulant, and protein C and S, were all normal. The CSF protein level was slightly elevated. Other screening investigations, including antinuclear antibodies, anti-DNA, and antineutrophil cytoplasmic antibodies, were normal, and tests for tumor markers were also

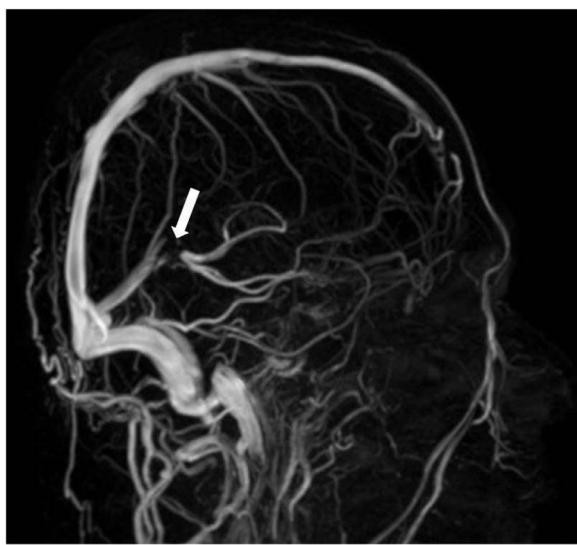


Figure 4. Filling defect consistent with thrombosis of the vein of Galen seen on MR venography (arrow).

normal. Initial anticoagulation with heparin (15,000 U/day for 7 days) was followed by edoxaban (60 mg/day). A fluid attenuated inversion recovery image of the brain MRI taken 1 month after the initial symptoms showed disappearance of pre-existing edema of the thalamus. The patient completely recovered by the end of the first month.

Discussion

Thrombosis of the deep cerebral veins develops very rarely, and approximately 6% of patients with cerebral venous thrombosis develop deep cerebral venous thrombosis.¹ DCVT often leads to death or major long-term sequelae.² It is an uncommon disease, arising from various causes, including infection, connective tissue disease, anemia, inflammatory diseases, and trauma.³ Women are affected 3 times more often than men.⁴ Clinical manifestations of DCVT, including headache, nausea, vomiting, focal neurologic deficits, hemiparesis, aphasia, seizures, coma, and death, are complex and nonspecific. In CT scans, direct and indirect signs of CVT, including the cord sign in the superior sagittal sinus or cortical vein and the empty delta sign in CT scans with contrast, are well documented. They are often not primarily identified.⁵ CT angiogram, MRI, and MRV are valid techniques in CVT diagnosis and follow-up. Thrombosis appears as an absence of flow void on spin-echo images and lack of signal in angiographic techniques.⁵ We found bilateral hyperintensities in diffusion-weighted imaging and fluid-attenuated inversion recovery sequences in the thalamus and basal ganglia.

Edema observed on imaging in cases of venous infarction is vasogenic in nature due to reduced venous drainage.⁶ An imaging study of our patient shows congestive thalamic edema and DCVT and decreased CBF in the thalamus and basal ganglia. We believe that because of the persistence of high venous and capillary pressures, ischemic change occurred in the thalamus. Like in arterial infarction, if this state continues, it might lead to complete stroke.

Of 23 patients reported in the literature (Table 1), 5 presented with mild symptoms, 7 with neurologic deficits, and 11 with decline of consciousness or seizure. In all patients with DCVT, signal intensity changes were limited to one thalamus ($n=7$) or both thalami ($n=16$). Of all patients, 5 had mild symptoms, 17 completely recovered, and 1 had persistent deficits. In 7 patients with focal neurologic symptoms, 3 recovered almost completely. Finally, of 11 patients with impairment of consciousness or coma, 1 had persistent deficits. In 22 of 23 patients treated with heparin and warfarin, 1 patient was treated with factor Xa inhibitor (edoxaban). The patients had no relevant complications or recurrent thrombotic events. Factor Xa inhibitor was an uncommon therapy for deep venous infarction but safe and effective in our case

Table 1. Patients with cerebral deep venous sinus thrombosis

Case no.	Author [reference]	Age/Sex	Symptoms	Thrombosed vein	Risk	Location	Treatment	Outcome (mRS)
1	Spearman et al ⁷	18/M	Headache, Paresis	ICV, Galen, SS	Unknown	BT	H/W	1
2		24/F	Headache, Paresis	ICV, Galen, SS	Unknown	UT, BG	H/W	1
3	Gladstone et al ⁸	24/F	Headache	ICV	Unknown	BT	H/W	0
4	M. von Mering et al ⁹	15/M	Headache, Paresis	ICV, Galen, IPS, SS, TS	Unknown	BT	H/W	0
5		56/M	Coma	ICV, Galen, IPS, SS	Unknown	BT, BG	H/W	0
6		24/F	Headache	ICV, Galen, IPS, SS	ProteinC resistance	BT	H/W	0
7		65/F	Coma, Paresis	ICV, SS	Hormonal medication	BT, BG	H/W	3
8		21/F	Coma, Headache, Seizure	Galen, SS, TS	Hormonal medication	BT	H/W	0
9		15/F	Coma, Paresis	ICV, Galen, SS	ProteinC resistance	BT	H/W	0
10		43/F	Coma, Headache, Seizure	Galen, SS	Hormonal medication	BT	H/W	0
11	Herrmann et al ¹⁰	47/F	Headache, Paresis	ICV	Unknown	UT	H/W	0
12	Prochazka et al ¹¹	24/F	Coma, Headache, Seizure	Galen, TS	Unknown	UT	H/W	0
13	Rossetti et al ¹²	18/F	Coma, Headache, Seizure	Galen	Hormonal medication	BT	H/W	0
14	Wada et al ¹³	57/M	Coma, Paresis, Headache	SS, SSS	Unknown	UT	H/W	0
15	Won Chung et al ¹⁴	36/F	Paresis	ICV	Unknown	UT	H/W	1
16	Kochanski et al ¹⁵	58/M	Coma	SS	Unknown	BT	H/W	0
17	Taniguchi et al ¹⁶	52/F	Coma	SS	Unknown	BT	H/W	0
18	Soda et al ¹⁷	69/F	Coma	Galen, SS	Cancer	BT	H/W	0
19	Wiesemann et al ¹⁸	14/F	Headache, Paresis	ICV	Factor V Leiden.	UT	H/W	1
20	Haug et al ¹⁹	12/M	Paresis	Galen, SS	Unknown	UT	H/W	0
21	Bezerra et al ²⁰	18/F	Headache	Galen, SS	Unknown	BT	H/W	0
22		49/F	Headache	Galen, SS	Unknown	BT	H/W	1
23	Amemiya et al ²¹	53/M	Headache	ICV, ISS, Galen	Unknown	BT	H/E	0

BG, basal ganglia; BT, bilateral thalamus; H/E, heparin/edoxaban; H/W, heparin/warfarin; ICV, internal cerebral vein; IPS, inferior petrosal sinus; ISS, inferior sagittal sinus; SS, straight sinus; TS, transverse sinus; UT, unilateral thalamus.

and review case. Even in DCVT, edoxaban might be a desirable treatment alternative to vitamin K antagonists because of its known application and metabolism benefits.

Conclusions

Symptoms from bilateral thalamic edema caused by increased venous hypertension can be reversed with appropriate management of the inciting vascular lesion. This case demonstrates a rare patient with decreased CBF in the thalamus in SPECT and completely recovered after factor Xa inhibitor administration. If a patient presents with focal neurological deficits, headache, and neuropsychological symptoms such as somnolence, DCVT might be the underlying condition. As in DCVT in other locations, early recognition of this clinical entity and treatment are prerequisites for a favorable outcome.²² Although this is a case report, factor Xa inhibitor may show a similar clinical benefit as vitamin K antagonist in the treatment of DCVT. Further systematic prospective evaluation is warranted.

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