Case Report

Cerebral venous thrombosis: report of 2 cases of hemorrhagic venous infarction

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\textbf{A B S T R A C T}

Cerebral venous thrombosis (CVT), a rare but potentially severe cerebrovascular disease, is defined as the thrombosis of a cortical or deep cerebral vein, or a cerebral venous sinus. This article reports 2 cases of CVT. In the first case, the patient is a 40-year-old woman with a history of 2 miscarriages, using oral contraception and presenting intense headache, cervical irradiation, and drowsiness. The second case reports a 43-year-old woman with a history of Crohn disease and daily use of oral contraception, presenting headache, neck pain, and hypersensitivity to noise and light. Noncontrast CT, CT venography, magnetic resonance imaging (MRI) and MR venography (MRV), first-line noninvasive diagnostic modalities in clinical practice, led us to the diagnosis of CVT: hypoplastic lateral sinus CVT in the first case and deep cerebral vein CVT complicated by hemorrhagic infarction in the second case. The early diagnosis of CVT is extremely important, but often a challenge due to highly variable clinical presentation and radiographic findings. MRI and MRV play a crucial role in case of anatomical variant and in better assessing the extension of thrombus, as well as parenchyma involvement and complications.

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\textbf{Introduction}

Cerebral venous thrombosis (CVT) is a rare and serious cerebrovascular condition and accounts in 0.5% of all stroke cases [1]. The prevalence of CVT in adult is estimated to be 3-4 cases per 1 million people, while in children and newborns, it is higher up to 7 cases per million [2]. This condition has a female gender predominance probably related to pregnancy, puerperium and oral contraception. CVT has a wide spectrum of clinical presentations as well as imaging findings. We report 2 cases of CVT observed in 2 young female patients.

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Case report

Patient 1

A 40-year-old woman with a history of depression disorder, 2 miscarriages, currently using oral contraceptives, who arrived at the emergency room (ER) with intense headache, cervical irradiation and drowsiness. No focal neurological deficit was found. She underwent a lumbar puncture and a cerebral contrast-enhanced CT that showed no abnormalities. She was discharged from the ER with an antalgic therapy. Seven days later, the patient came back to the ER for intense headache with nausea and vomiting this time associated with a left-sided weakness. The patient presented fever up to 39.2°C and physical examination showed a slow psychomotor retardation and a Glasgow score of 14/15, meningeal irritation signs were also found. The cerebrospinal fluid examination revealed elevated levels of protein and leukocyte (0.58 g/L and 25/mm³ respectively). The magnetic resonance imaging (MRI) showed a massive 5 cm right fronto-parieto-temporal hematoma presenting multiple fluid-fluid levels, related to active bleeding, and causing mass effect, and a 10 mm thick right subdural frontal hematoma (Fig. 1). T1-weighted images showed hypointense signal in the right lateral sinus without flow-void, as seen in the contro-lateral lateral sinus. The MR venography (MRV) after gadolinium injection showed a filling defect in the right lateral sinus, which confirmed the diagnosis of venous thrombosis (Fig. 2). The right lateral sinus was also hypoplastic with smaller diameter compared to the contro-lateral lateral sinus (Fig. 3). The patient was transferred to the operating theatre for hematoma evacuation. The surgery succeeded and no complication occurred. Afterwards, she received antithrombotic treatment with heparin followed by antivitamin K. Ten days later, when discharged from the hospital, the patient still presented a mild left sided paresis, which later improved with kinesiotherapy.

Patient 2

A 43-year-old woman with a history of Crohn disease and daily use of oral contraceptives, who arrived at the ER with headache, neck pain and hypersensitivity to noise and light, nausea and profuse vomiting. Physical examination revealed a Glasgow score of 15/15, pyramidal syndrome with diffuse deep tendon hyperactive reflex, bilateral Babinski sign and reactive dilated pupils. The patient had no convulsion or motor deficit and the cervical movements were normal with no pain on flexion and no tenderness point. A noncontrast CT (NCCT) revealed spontaneous hyperdensity and, after contrast injection, absence of opacification of the vein of Galen, the straight sinus, the torcular sinus, the proximal portion of lateral sinus and the posterior portion of superior sagittal sinus, which led to cerebral venous thrombosis diagnosis (Fig. 4). The thrombophilia investigation revealed an increased level of factor VIII up to 297%. A cerebral MRI (Fig. 5 and 6) performed 5 days later showed spontaneous hypersignal on T1-weighted and T2 FLAIR-weighted images in the vein of Galen, the straight sinus, the torcular sinus, the proximal portion of the lateral sinuses and the posterior portion of superior sagittal sinus, which confirmed cerebral venous thrombosis. MRV with gadolinium injection showed the “rail sign” and “empty delta sign,” which further strengthen the diagnosis. MRI also showed T2 and T2 FLAIR hypersignal and T1 hyposignal in the left thalamus with minimal mass effect. This lesion had a restricted diffusion, signal drop on susceptibility-weighted images and no enhancement after injection of gadolinium, suggesting a hemorrhagic venous infarction of the left thalamic region. The patient received an antithrombotic treat-
Fig. 2 – Patient 1: Sagittal T1-weighted image (A) shows spontaneous hyposignal in the right lateral sinus (red arrow). Sagittal (B) and coronal (C) postgadolinium T1-weighted images show filling defect of the right lateral sinus corresponding to thrombus (red arrow).

Fig. 3 – Patient 1: Postcontrast coronal (B and C) and axial (A) CT scan images show a hypoplastic right lateral sinus (blue arrow) but no filling defect (red arrow).

Fig. 4 – Patient 2: Precontrast axial (A) and sagittal (B) CT scan images show spontaneous hyperdensity of the vein of Galen, straight sinus and posterior portion of superior sagittal sinus (red arrows), corresponding to thrombus.
Fig. 5 – Patient 2: Postcontrast axial (A) and sagittal (B and C) T1-weighted images show filling defects of lateral sinuses (red arrows), superior sagittal sinus (blue arrow), straight sinus (green arrow), and left internal cerebral vein (yellow arrow) corresponding to thrombus.

Fig. 6 – Patient 2: The left thalamus (red arrow) shows hypersignal T2FLAIR (A), punctate diffusion restriction on diffusion-weighted image (not shown) and ADC map (B), signal drop on susceptibility-weighted image (C) and no contrast enhancement after injection (D), corresponding to a hemorrhagic venous infarction.

diagnostic accuracy by unfractionated heparin and then subcutaneous low-molecular-weight heparin for 10 days, then replaced by vitamin K antagonist. When discharged patient had no residual symptom and no focal deficit.

Discussion

CVT is a rare but serious cerebrovascular disorder, which may have severe outcome if misdiagnosed. Due to its variable clinical presentation the diagnosis is a challenge; this is the reason why, on average, a 7 days delay is estimated to occur between the onset of symptoms and the diagnosis [3]—as in the first case presented. Patients affected by CVT can present signs of intracranial hypertension as headache and vomiting, symptoms identified in our 2 patients, but also vigilance disorder, neurological deficit. Eventually CVT can lead to a coma status in most serious cases [4].

As reported by the International Study on Cerebral Vein and Dural Sinus Thrombosis by Ferro et al. [3], the mean age of CVT patient is 39.1 y/o with a female dominance of 74.5%. Prior medical conditions (thrombophilia, inflammatory bowel disease), transient situations (pregnancy, dehydration, and infection), selected medications (oral contraceptives, substance abuse), and unpredictable events (head trauma) are the identified risk factors; oral contraception, especially of third-generation [5], has been found in 54.3% of included patients. Our 2 patients belong to the demographic category at the highest risk of CVT: female, in their 40s, using oral contraception. In one case the thrombophilia investigation revealed an increased level of factor VIII.

The confirmation of the diagnosis depends on the visualization of the thrombus in the vein or in the sinus [6]. Different imaging modalities and techniques can be used for the diagnosis of CVT in adults. NCCT, CT venography, MRI, and MRV are the first-line tests in clinical practice, but each modality and technique has its advantages and disadvantages.
The NCCT is the technique of choice for screening patients with nonspecific clinical presentation and a low suspicion of CVT. Direct visualization of thrombosis in dural sinus may give the "dense clot sign" and the "cord sign" representing a thrombosed cortical vein that is seen as linear hyperdensity [6]. More often, NCCT shows the indirect signs of CVT, such as diffuse brain edema or decreased ventilar size. Venous infarction is the most specific NCCT indirect sign. When the infarction is not conforming to a major arterial vascular territory, presents multiple isolated lesions, involves subcortical region with sparing of the cortex and has an extension over more than one arterial distribution, it is likely to be a venous infarction. The infarction may be hemorrhagic or nonhemorrhagic and its location gives a hint to find out the venous structure involved. NCCT is useful as the primary imaging modality completed by CT venography that is a contrast-enhanced helical CT performed with a time-optimized contrast bolus in order to enhance the cerebral venous system. The diagnosis of CVT can be made by the evaluation of the axial thin-section contrast-enhanced source images and of 2- and 3-dimensional reformatted images. On the CT venography the "empty delta sign," which may be seen 5 days to 2 months from the onset, represents a filling defect (thrombus) in the dural sinus, with peripheral enhancement possibly due to the development of collaterals. Indirect evidence of CVT may be seen as contrast enhancement of the falx and tentorium due to venous stasis and hyperemia of the dura mater (approximately 20% of cases) [6]. CT venography was found to have a sensitivity and specificity of both 100%; however, quality of this evidence is low, since individual studies included <100 patients and were observational and suffered from a high risk of bias [7]. Furthermore, CT venography has been shown to be of limited diagnostic value for diagnosing cortical vein thrombosis (sensitivity of 6%-75%). In past years, new CT techniques have been developed that may allow better diagnosis of CVT such as multidetector row CT providing thin slices obtained with less contrast and shorter scanning time allowing better image quality without significantly increasing overall radiation dose. Furthermore, several techniques can be used for removing unwanted overlying structures (bone) from the vascular structures (venous) to improve the diagnostic accuracy of CT venography, especially for 3D interpretation.

On conventional MRI sequences, patent dural sinus is often seen as a flow void. This is particularly well seen when the imaging plane is orthogonal to the blood flow direction (e.g., coronal images are best for visualization of the superior sagittal, transverse, and sigmoid sinuses), while the effect of a flow void may be reduced in a plane parallel to the dural sinus. The abnormal signal intensity follows the signal characteristics of intracranial hemorrhage and may evolve through the stages of oxyhemoglobin, deoxyhemoglobin, methemoglobin, and hemosiderin. On T1-weighted images, thrombus with methemoglobin is hyperintense and on T2-weighted images, it has an exaggerated signal loss because of the increased susceptibility effect of deoxyhemoglobin, methemoglobin, or hemosiderin. Conventional MRI techniques have an overall sensitivity and specificity of 84%-97% and 28%-96%, respectively, for the diagnosis of CVT [7]. Indirect evidence of venous thrombosis is often secondary to parenchymal involvement such as brain swelling and hemorrhagic or nonhemorrhagic infarction. The diagnosis can then be further confirmed on MRV performed without contrast agent, time-of-flight (TOF) or the phase contrast (PC) technique, or after administration of intravenous gadolinium-based agent (contrast-enhanced MRV). TOF and PC MRV rely on MR flow phenomena and they are subject to flow-related image artifacts, contrast-enhanced MRV takes advantage of luminal filling by contrast agent and it is less likely to be affected by complex flow artifacts. TOF and PC MRV had a sensitivity of 64%-100% and 48%-100%, respectively, although with wide 95% confidence interval and are less accurate for identifying cortical vein thrombosis [7].

Lateral sinus thrombosis is usually associated with head and neck infection, particularly otitis media and mastoiditis [8]; however, our first patient did not show signs of local infection and no imaging findings suggested sinus or ear infection. The only predisposing factor was a hypoplastic lateral sinus, which in some studies is related to a higher percentage of thrombosis [9]. It is suspected that the slow or disrupted flow in a hypoplastic sinus could lead to increased intracranial pressure and development of thrombosis when other risk factors are associated. Furthermore, as mentioned above, the direct signs of the lateral sinus thrombosis are difficult to assess on CT and the congenital hypoplasia or aplasia of the lateral sinus (observed in approximately 24% of normal population on MRI [10]) is impossible to differentiate from lateral sinus thrombosis. In these cases, MRI is the imaging modality of choice to differentiate the 2 conditions with the following major therapeutic implications. The diagnosis of a lateral sinus hypoplasia is evident on MRI sagittal plane where an asymmetry in size of the transverse portion of sinus is visible without any other abnormal flow signal. In a hypoplastic lateral sinus thrombosis, the presence of abnormal signal intensity on T1- or T2-weighted images or the absence of flow void in the sinus further strengthen the hypothesis of thrombosis. The CT venography of the first patient had shown no abnormality, while the MRI performed 7 days later revealed direct signs of thrombosis in the right lateral sinus: hypointense signal on T1-weighted images with no flow-void and filling defect in MRV. At a subsequent review of the CT, a right lateral sinus hypoplasia was identified.

Thrombosis of the vein of Galen and posterior portion of superior sagittal sinus was revealed on both CT and MRI of the second patient, by direct (hyperdensity on NCCT, hyperintensity on T1-weighted images and filling defect on contrast-enhanced images) and indirect signs (edema of the left thalamus). Deep cerebral vein thrombosis represents a relatively low percentage of CVT (10.9%) according to Ferro et al. [3] and in most cases, the thalamus is affected bilaterally [11] and other structures, such as basal ganglia and mesencephalon, are involved. The unilateral thalamic venous infarction is rare and often mimics other conditions. It usually does not enhance after contrast media injection and may evolve in a hemorrhagic infarction. The differential diagnosis includes the arterial thalamic infarction, evolutive lesions—germinoma or glioma—and vascular abnormalities—cavernous hemangioma [12]. Interestingly, the left thalamus is more affected by unilateral infarction [13] and some authors suggest that the unilateral infarction of the left thalamus usually causes symptoms, while the right one does not manifest clinically [14].
The TVC management includes antithrombotic, etiological, and symptomatic treatment. In the acute phase, the intravein heparin therapy, followed by oral anticoagulation with vitamin K antagonists, plays the crucial role. The heparin followed by low-molecular-weight heparin is the first-line therapy to achieve the recanalization of sinus or veins and to prevent the spread of thrombus. Both the American Heart Association/American Stroke Association (AHA/ASA) and the European Federation of Neurological Societies recommend to start the anticoagulation therapy even if a parenchymal hemorrhage is identified [15]. If anticoagulation is contraindicated or no improvement is achieved, chemical or mechanical endovascular thrombolytic therapy can be considered even if strong evidence for endovascular treatment is yet lacking according to AHA/ASA. Most patients with TVT have a good prognosis after anticoagulation therapy; a minority of patients (nearly 5%) can have a malignant evolution with high intracranial hypertension and transtentorial herniation. In such cases, a decompressive surgery can be a lifesaving procedure allowing a better outcome and improving survival rate. That was the case of our first patient who underwent a surgical hematoma evacuation. Death or long-term sequelae are far more likely to occur in deep cerebral vein thrombosis, than in dural sinus thrombosis. Residual focal deficit could persist after a dural sinus thrombosis which later can improve with kinesiotherapy, has happened to our first patient. The second patient received unfractionated heparin (500 IU/kg/d, 25,000 IU/24 h) followed by subcutaneous low-molecular-weight heparin for 10 days, then replaced by vitamin K antagonist. Eventually, the patient recovered with no residual symptom and no focal deficit.

**Conclusion**

CVT is a rare but potentially severe cerebrovascular disease. The early diagnosis is extremely important, but often a challenge. The NCCT is the imaging modality of choice for screening patients, revealing the thrombosis by direct and indirect signs. CT venography was found to be reliable for CVT diagnosis too, even though of limited diagnostic value for cortical vein thrombosis. MRI and MRV help in case of anatomical variant, such as the hypoplastic lateral sinus in our first patient. MRI and CT play a role in the assessment of the extension of thrombus, as well as parenchyma involvement by deep cerebral vein thrombosis—as in the case of our second patient.

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