Clinical Communications

HEADACHE: CORTICAL VEIN THROMBOSIS AND RESPONSE TO ANTICOAGULATION

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Abstract—Cerebral venous thrombosis (CVT) is being diagnosed more frequently with the use of advanced radiologic imaging. The presentation of CVT includes a wide spectrum of nonspecific symptoms with headache predominating. We present a case with acute, severe headache. The evaluation included a head computed tomography (CT) scan that was normal. The presence of opacified sinuses led to treatment for sinusitis. The patient returned the following day with a generalized tonic-clonic seizure. A magnetic resonance imaging (MRI) study identified an isolated cortical venous thrombosis. This patient was treated with anticonvulsant and anticoagulation therapy. A CVT is an unusual cause of headache and should be considered in patients with atypical presentation or associated seizure, or who are refractory to current therapy. Diagnosis may be made with MRI. Resolution and complete recovery are possible with appropriate therapy. © 1999 Elsevier Science Inc.

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INTRODUCTION

Headache is a common Emergency Department (ED) complaint with a wide spectrum of etiologies, clinical manifestations, and outcomes. One uncommon cause of headache, cerebral venous thrombosis (CVT), can be diagnosed with modern imaging techniques, particularly magnetic resonance imaging (MRI) and magnetic resonance venography. A CVT is a broad term that includes thrombus in the deep cerebral venous system as well as in the cortical veins. Isolated cortical vein thrombosis is a rare entity. We present a case illustrating the nonspecific presentation of CVT, concomitant sinus opacification, and a dramatic improvement after anticoagulation. This report discusses the predisposing factors, pathophysiology, diagnosis, and management of CVT.

CASE REPORT

A 54-year-old female presented to the ED with a history of 2 days of progressive, bilateral, severe headache, unlike any prior, with radiation to the back of the neck. She noted association of nausea and productive cough of white sputum. The patient denied fever, photophobia, or post-nasal drip. She also denied any antecedent medical problems, did not take any medications, and was without allergies. Family history revealed no hypercoagulable disorders. She reported smoking one pack of cigarettes per day.

Physical examination revealed a well-developed female who was awake, alert, and holding her face in her hands. She spoke in complete sentences. Vital signs were: temperature 36.4°C tympanically, pulse 101 beats/min, respirations 16 breaths/min, blood pressure 117/75 torr., and pulse oximetry 97% on room air. The head was
normocephalic and atraumatic with bilateral tenderness over the frontal sinuses. The oropharynx was moist with a mild whitish exudate posteriorly. The neck was supple. Neurologic examination revealed no focal deficits. A computed tomography (CT) scan of the head revealed no subarachnoid hemorrhage, mass effect, or midline shift. A sinus CT scan, however, was significant for complete opacification of the right maxillary sinus without bony erosion or expansion (Figure 1). Laboratory data revealed a WBC of 8.7 with no left shift and an ESR of 12. The patient was discharged on oral antibiotics.

The following day, she experienced a generalized tonic-clonic seizure at home and presented to the ED via EMS. She was awake, alert, and completely oriented. The temperature was 36.9°C tympanically, pulse 112 beats/min, blood pressure 123/88 torr., respirations 40 breaths/min, and pulse oximetry 97% on room air. Neurologic examination revealed mild right facial droop, a Babinski reflex that was upgoing on the left and equivocal on the right. The remainder of the neurologic examination was normal. The patient was noted to have a right humerus fracture sustained during the seizure activity. A head CT scan showed a new parenchymal lesion with pectechial hemorrhage in the high right parietal lobe with surrounding vasogenic edema (Figure 2). An MRI was subsequently obtained with and without gadolinium, which revealed an abnormal enhancing lesion in the right parietal lobe (Figure 3). This was consistent with early venous infarction from an isolated cortical venous thrombosis without dural sinus thrombosis, as MR venography showed flow through a patent superior sagittal sinus.
ittal sinus. The patient was admitted to the neurosurgical service, anticoagulated with heparin, and given phenytoin. Blood cultures were drawn, and she was placed on broad-spectrum antibiotics. A lumbar puncture revealed clear cerebrospinal fluid (CSF) with 22 white blood cells (77 lymphocytes, 22 monocytes), 9 red blood cells, and the AFB smear, Gram’s stain and culture were negative. Coumadin therapy was initiated. Repeat MRI on hospital day 12 illustrated resolving right parietal cortical venous infarction. Blood cultures were negative. The patient’s neurologic deficits and headache completely resolved. She was discharged on hospital day 15 on coumadin and phenytoin.

Three days later, she suffered a recurrence of headache, and returned to the ED. She was afebrile, and neurologic examination revealed no deficits. Laboratory data showed her to have subtherapeutic anticoagulation with a prothrombin time (PT) of 13.5 and an international normalized ratio (INR) of 1.28. A head CT scan revealed right parietal cortical venous infarction. Blood cultures were negative. The patient’s neurologic deficits and headache completely resolved. She was discharged on hospital day 15 on coumadin and phenytoin.

Approximately 1 month later, the patient developed bilateral lower extremity swelling. Ultrasound evaluation revealed bilateral deep venous thromboses despite being therapeutic on coumadin with a PT of 19 and an INR of 2.7. She was admitted for an extensive evaluation for malignancy. A Bird’s nest IVC filter was placed, and her anticoagulation therapy was changed to subcutaneous heparin. Laboratory values, in search of a hypercoagulable state, were normal for: protein C, protein S, antithrombin III, factor V, anticardiolipin antibodies, ANA, and homocysteine. No evidence of malignancy was discovered.

DISCUSSION

Cerebral venous thrombosis has been a known entity since the first part of the 19th century; however, the disorder was usually diagnosed at autopsy (1–3). Isolated cortical vein thrombosis, in the absence of sagittal sinus thrombus, is rarely reported. With modern radiologic imaging techniques, visualization of the cerebral venous circulation is improving, making early diagnosis and implementation of therapy more available. The true incidence of CVT is unknown. It is thought to be higher in females and in the elderly (1). Estimates of mortality vary. Initially thought to be fatal, CVT demonstrated a mortality of 30–50% with early angiographic studies. Recent figures, however, report the mortality to be 5.5–30% (1). The prognosis for recovery in surviving patients is variable but generally good. Approximately 20% of patients suffer residual neurologic deficits (1), and about 5% have a persistent seizure disorder (3). Most seem to make a complete recovery, as in this case.

Factors contributing to the underdiagnosis of CVT are its wide variety of presenting symptoms, the nonspecific nature of these symptoms, and a variable mode of onset (4–6). Headache is by far the most common initial presentation; others may include: lethargy, confusion, seizure, focal neurologic deficit, coma, or even death (3,4,6). Headache will occur in 75–90% of patients with CVT, in stark contrast to patients with cerebral arterial ischemia (approximately 18%) (6). Seizures are also much more common in venous thrombosis when compared with arterial, occurring 49% and 4.4% of the time, respectively (6). There are thought to be larger areas of brain functionally impaired but not infarcted, which become potential foci for seizure formation (6). The onset of symptoms is also highly variable, al-
though usually more insidious than stroke presentation. The patient presented here suffered an acute onset of headache progressing to seizures and focal neurologic deficits.

There are few reports of concurrent CVT and infection of the maxillary sinus (7). Approximately 8% of patients with CVT have an infectious etiology (1). It has been well-documented that cavernous sinus thrombosis is a complication of paranasal sinusitis (9). These patients typically present with fever, proptosis, chemosis, and ptosis. Treatment may include antibiotics, surgical drainage, and possibly anticoagulation (8–10). The thrombotic process in this patient subsequently progressed from the isolated cortical vein to involve the superior sagittal sinus. As she was afebrile, had normal WBC and ESR values, and all cultures of CSF and blood were negative, direct bacterial thecal invasion was virtually excluded. The predisposition to CVT is the same as for most thrombotic diseases. Virchow’s triad of endothelial damage, venous stasis, and a hypercoagulable state are risk factors. There may be associated deep venous thrombosis or pulmonary embolus (11). Comorbid conditions such as head injury, brain tumor, malignancies, dehydration, use of oral contraceptive with or without cigarette smoking, coagulation disorders, Behçet’s syndrome, inflammatory bowel disease, and the peripartum state all may cause hypercoagulability and lead to CVT. After initial treatment, our patient did go on to suffer bilateral deep venous thromboses despite adequate anticoagulation. This suggests an underlying thrombotic disorder with the acute event triggered by dehydration. As previously mentioned, however, extensive evaluations for malignancy and coagulation disorders were negative. Approximately 30% of CVTs are idiopathic (4,12).

Radiologic investigation begins with an unenhanced CT scan of the head to exclude intracranial hemorrhage. In many cases, such as ours, the initial CT scan is normal (13). There are some rare CT signs such as the cord sign, dense triangle, and, if contrast is used, the empty delta sign, which are consistent with venous thrombosis (1,13). The cord sign is a curvilinear hyperdensity of clot in the vein, whereas the dense triangle represents a prominence of the superior sagittal sinus secondary to thrombus. The empty delta sign, seen in this patient, is observed when the dural venous sinus is filled with clot that is then outlined by a thin rim of contrast on the enhanced CT scan. Contrast-enhanced CT, however, is insensitive for both cortical venous and dural sinus thrombosis compared with MRI and may be omitted as the next study.

Computed tomography alone cannot secure the diagnosis of hemorrhagic venous infarct caused by CVT, since a number of disease processes can cause similar CT findings. The CT imaging differential diagnoses also include hemorrhage at the site of a cavernous hemangioma, an AVM, an area of focal cerebritis, and spontaneous hemorrhage in a small metastatic lesion. An MRI provides the greatest sensitivity and specificity in identifying the underlying cause of the abnormality seen on CT examination. Angiography has been held as the gold standard for cerebral venous visualization (and the lack of filling for the presence of thrombus) (1,13,14). It is somewhat less useful when examining the small and variable cortical veins (12). An MRI is the radiologic study of choice in such cases (1,5,12). The noninvasive MRI and MR venography are playing a more dominant role in the evaluation of cerebral venous disease (13,14).

Reasons to pursue an MRI would include an abnormality on the CT scan that requires further characterization, progressive neurologic deficits, papilledema, or unexplained new onset of seizure with headache. In patients predisposed to dural sinus thrombosis, an MRI should be considered early in the workup. These include patients with penetrating injuries traversing the dural sinuses, the post-partum patient with headache, patients with known jugular vein thrombosis, and patients with hypercoagulable states and undiagnosed headache. Upon this patient’s second presentation (associated with seizure), the unenhanced CT scan revealed a small petechial hemorrhage prompting MRI evaluation, which made the diagnosis. A conventional angiographic study was later performed to confirm the MRI results and to evaluate the need for thrombolysis.

The use of anticoagulants and thrombolytic therapy in treating patients with CVT has been controversial. Since many venous infarctions are associated with small hemorrhages, the risk of expanding this hemorrhagic component by using heparin seemed great. Evidence is increasing, however, to show that the severity of hemorrhage is not influenced by heparin, and that patients treated with anticoagulation clinically improve (15). This is in contradistinction to hemorrhagic arterial infarcts where bleeding occurs upon reperfusion of ischemic tissue and is exacerbated by heparin with devastating effects. In venous thrombosis, hemorrhage occurs secondary to increased capillary pressure as a result of the venous thrombus (6). Halting the thrombotic process, thereby diminishing intralumenal pressure at the capillary bed, should theoretically reduce cerebral hemorrhaging. With anticoagulation therapy, complete recovery is much more common after CVT than after a stroke, 57% vs. 6.7%, respectively (6). This is thought to be due to a larger penumbra existing in venous thrombotic disease.

Our patient illustrates well the efficacy of anticoagulation in CVT, as her symptoms recurred when subthera-
peutic on coumadin, and again resolved with heparinization. In addition, her petechial cerebral hemorrhage did not expand with heparin therapy. If the dural sinus is involved, direct i.v. thrombolysis can be performed, with the goal of reestablishing flow in the sinus (16–18). Although the superior sagittal sinus was involved in our patient, she exhibited no new neurologic deficits and, therefore, thrombolytic agents were withheld. In general, anticonvulsant therapy is continued only if the patient’s initial presentation included seizure activity. This is discontinued after approximately 1 year if the patient remains seizure-free, as the risk of residual epilepsy is low (3). In the minority of patients with suspected infectious etiology, complete cultures followed by broad-spectrum antibiotics are appropriate.

**CONCLUSION**

This case illustrates the rarely reported occurrence of isolated cortical vein thrombosis. The thrombus subsequently extended to the deep venous system and showed a favorable response to anticoagulation. A CVT, although not common, should be considered in atypical cases (patients with persistent severe headache after exclusion of usual causes, or associated seizure activity), or in patients with potential hypercoagulable states. An MRI is the diagnostic mode of choice. Anticoagulation seems to be safe and efficacious. Thrombolysis is possible if the thrombus involves the dural sinus and compromises neurologic function.

**REFERENCES**