A 42-year-old woman with a history of Crohn disease presented with left temporal headache for 1 week. On the day of presentation, she had transient word finding difficulty, lasting for 1 to 2 minutes and worsening headache. The patient reported starting prednisone 10 days earlier for a flare of Crohn’s disease associated with dehydration. She had been using the Nuva ring (ethinyl estradiol vaginal ring) for birth control. Neurological examination was significant for moderate expressive aphasia. Emergent computed tomography (CT) head revealed a hyperdense focus with surrounding hypodensity in the left temporoparietal lobe. Subsequent MRI of the brain revealed a venous infarct in the anterior left temporal lobe with surrounding edema and areas of hemorrhagic transformation. Magnetic resonance venography (MRV) showed left transverse and sigmoid thrombosis. Hypercoagulable studies were sent including Protein C & S, factor V leiden, prothrombin G20210A gene mutation, lupus anticoagulant, anticardiolipin antibody, homocysteine, and antithrombin III. Systemic anticoagulation (unfractionated heparin drip) was started immediately. Prednisone was continued for Crohn disease. For the next 2 days, her aphasia improved. At the time of discharge, she was transitioned to warfarin with low molecular weight (LMW) heparin bridge. After 1 month, the aphasia and headache completely resolved. Hypercoagulable workup revealed that she was heterozygous for prothrombin G20210A gene mutation, whereas other laboratory tests were unremarkable. Repeat MRV at 3 months showed partial recanalization of the left transverse sinus.

Cerebral venous and dural sinuses thrombosis (CVT) is an uncommon and frequently unrecognized, representing ≈0.5% to 1% of all strokes. CVT is potentially serious and life threatening.

Clinical Findings

Symptoms in CVT are usually secondary to increased intracranial pressure or focal brain injury from venous infarction or hemorrhage. Headache is often localized and is the most frequent and usually the first symptom. Isolated headache without focal neurological findings or papilledema occurs in 25% of patients with CVT and poses a significant diagnostic challenge. Other clinical symptoms are encephalopathy, focal neurological signs, and seizures. Clinical presentation depends on several factors, including location of the thrombosis, the presence of venous infarction or hemorrhage, patient’s age, and duration of CVT (acute versus chronic). Superior sagittal sinus thrombosis is the most common form and usually leads to bilateral deficits. Focal or generalized seizures are frequent, occurring in ≈40% of patients with CVT.

Risk Factors

Risk factors for CVT are those that affect blood stasis, changes in the vessel wall, and changes to the composition of blood (Virchow triad). Both genetic and acquired prothrombotic conditions can contribute to CVT. American Heart Association guidelines define antithrombin III, protein C and S deficiency, homozygosity for either factor V leiden or prothrombin G20210A mutations as high-risk thrombophilias. Antithrombin III, protein C and S testing acutely is of limited use in the acute setting and should be tested 2 to 4 weeks after anticoagulation has been stopped. Heterozygosity for factor V leiden or prothrombin G20210A mutation is considered a relatively mild thrombophilia but still carries an increased risk. More recently, an association between the JAK 2 V617F gene and an increased incidence of CVT has been reported. In addition to genetic prothrombotic states, acquired prothrombotic states should be investigated. The more common of these include oral contraceptives, pregnancy, puerperium, malignancy, infection, and trauma. In developed countries, the most common cause of CVT is pregnancy/puerperium, whereas parameningeal infections (ear, sinus, mouth, face, and neck) remain relatively common causes in developing countries. The relationship between CVT and inflammatory bowel disease is well established, although the mechanism is poorly understood. The association between the 2 entities may be secondary to dehydration, or the inflammatory state may predispose the patient to clot formation. Only ≈3% of CVT occurs in patients with inflammatory bowel disease, and it is usually associated with other risk factors. Oral contraceptives are associated with a 22-fold risk of CVT. The risk of CVT with oral contraceptive
use in women is greater among those with a hereditary prothrombotic factor. Although the risk of venous thrombosis is thought to be less with vaginal rings that release low progesterin/estrogen, a recent study found that users of vaginal rings with ethinylestradiol and etonogestrel have a 6.5-fold increase in venous thrombosis when compared with nonusers.

Importantly, CVT is often multifactorial and, therefore, every patient requires a full workup. Our patient is an excellent example of this. She has a previously unrecognized prothrombin gene mutation and had a flare of her inflammatory bowel disease. In addition, she was using a vaginal ring for contraception. Other potential triggers for CVT in patients with an underlying procoagulable predisposition include head trauma, lumbar puncture, jugular catheter placement, pregnancy, surgery, infection, or drugs.

**Neuroimaging**
CT of the head is often the first investigation performed. The primary sign of acute CVT on noncontrast CT is hyperdensity of a cortical vein or dural sinus. Thrombosis of the posterior portion of the superior sagittal sinus may appear as a dense triangle, the dense or filled delta sign. CT venography is most useful in subacute or chronic situations because of varied density in a thrombosed sinus. MRV is usually preferred to CT venography because of bone artifact and radiation exposure. MRI is more sensitive for CVT than CT at every stage of thrombosis. The characteristics of the MRI signal depend on the age of the thrombus. The principal early signs of CVT on non–contrast-enhanced MRI are the combination of absent flow voids with altered signal intensity within the dural sinus. Invasive cerebral angiographic procedures are rarely needed to establish the diagnosis of CVT, given the availability of MRV and CT venography (CTV).

**Management**
Treatment should be started as soon as the diagnosis is confirmed. Management of CVT consists of (1) identification and treatment, of the underlying cause, (2) symptomatic management, and (3) antithrombotic therapy. Underlying infection, dehydration, or other correctable precipitants should be investigated and aggressively treated to reduce the prothrombotic state. In our patient, intravenous fluids were given to treat dehydration, and her prednisone was continued to treat the underlying inflammation associated with Crohn’s disease. Seizures are a common complication of venous thrombosis and there should be a low threshold for electroencephalogram in patients with unusual behavior or reduced level of consciousness. American Heart Association guidelines recommend the use of anticonvulsants for seizures but not for prophylactic treatment. Patients may have increased intracranial pressure and treatment using standard measures may be life saving. Patients frequently have severe headache and may require analgesics, but care should be taken not to sedate the patient to the point that the examination becomes unreliable. Anticoagulation is the mainstay of acute and subacute treatment for CVT. Because heparin can influence the...
interpretation of hypercoagulable testing, blood work should be drawn for hypercoagulable studies before heparin. Initial anticoagulation is generally with adjusted-dose unfractionated heparin or weight-based low molecular weight heparin in full anticoagulant doses (Figure). Several randomized controlled clinical trials support the use of anticoagulation in CVT, even in the setting of intracranial hemorrhage. Although no trial showed clear statistical benefit, it is unlikely that additional trials will be conducted because of a lack of equipoise. A recent study suggests that low molecular weight heparin may be superior to unfractionated heparin. Patients receiving low molecular weight had a greater likelihood of full recovery and less bleeding complications, including intracerebral hemorrhage. There are little data from controlled trials to support endovascular thrombolysis, and the American Heart Association recommends it be restricted to patients with a poor prognosis who have not responded to anticoagulation. The Thrombolysis or Anticoagulation for Cerebral Venous Thrombosis (TO ACT) study is an ongoing multicenter, prospective, randomized, open-label, blinded end point trial of standard anticoagulation versus endovascular therapy in patients with CVT and a high probability of poor outcome. American Heart Association guidelines suggest that after the acute phase, treatment with vitamin K antagonists be continued for 6 to 12 months in patients with provoked CVT (associated transient risk factors) or for 3 to 6 months in patients with unprovoked CVT. Indefinite anticoagulation may be considered with recurrent CVT, venous thromboembolism after CVT, or a first CVT with severe thrombophilia (Figure). Aspirin is given indefinitely once anticoagulation is stopped.

Prognosis

CVT can result in death or permanent disability but usually has a favorable prognosis. Currently 3% to 15% of patients die in the acute phase of the disorder, and many patients make a complete recovery. Predictors of mortality at 30 days are depressed consciousness, altered mental status, thrombosis of the deep venous system, right hemisphere hemorrhage, posterior fossa lesions. Available data suggest that cerebral vein and sinus recanalization occurs in 40% to 90% of patients after CVT, usually within the first 4 months.

Disclosures

None.

References


Key Words: cerebral hemorrhage • stroke • venous thrombosis

TAKE-HOME POINTS

- Patients with lobar hemorrhage of unclear origin or with cerebral infarction that crosses typical arterial boundaries should have imaging of the cerebral venous system.
- Thrombophilic states, both genetic and acquired, should be investigated in all patients.
- Anticoagulation with adjusted-dose unfractionated heparin or weight-based low molecular weight heparin in full anticoagulant doses is reasonable in cerebral venous thrombosis, followed by vitamin K antagonists, regardless of the presence of intracranial hemorrhage.
- A follow-up cerebral venous thrombosis or MRV 3 to 6 months after diagnosis is reasonable to assess for recanalization of the occluded cortical vein/sinuses in stable patients.

Illustrative Teaching Case: CVT

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Cerebral Venous Thrombosis: Diagnosis and Management
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