



CASE REPORT

Diagnosis and Treatment of Superior Sagittal Sinus Thrombosis

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Introduction

Cerebral venous sinus thrombosis (CVST), although a common diagnosis, is missed frequently by both general practitioners and neurologists.¹ The most common presenting complaints are headache with focal neurological symptoms such as weakness, numbness, and aphasia.² CVST has a female predominance of 3:1.³ A risk factor usually is able to be determined, most common of which is oral contraceptive use.^{4,5} Other prothrombotic risk factors include antithrombin III deficiency, dehydration, factor V Leiden mutation, increased factor VIII, infection, protein C and S deficiency, pregnancy, prothrombin mutation, malignancy, and trauma.^{2,6} The superior sagittal sinus is the most common site of cerebral venous thrombosis, followed by the other sinus systems.⁷⁻¹⁰ Treatment of CVST includes anticoagulation or thrombolytics with symptomatic support, although treatment with heparin has been controversial with some physicians hesitant to administer it due to the risk of hemorrhagic infarction.^{2,11} We report the diagnosis and treatment of superior sagittal sinus thrombosis.

Case Report

A 44-year-old, gravida 2, para 2, right-handed, Caucasian female presented to the emergency department with acute symptoms of right leg, right arm, and right hand

numbness and paresthesia. Additionally, she had difficulty moving her right leg which made it hard to walk. When she could no longer stand due to right leg weakness, she was taken to the emergency department. The MRI performed at this hospital showed diffusion restriction in the right parietal cortex. Additionally, there was a well demarcated fluid signal abnormality in the right dorsal medulla and the caudal aspect of the inferior cerebral peduncle. Rostral to this, there were bilateral circinate areas of fluid signal abnormality. Suspecting an acute stroke, she was transferred to our facility.

The patient reported a history of progressive dysmotility of the right hand extending over the course of five years. Fine motor skills had degenerated to the point that the patient began to write with her non-dominant left hand. While doing this, she noted tremor-like associated movements of the right hand. Medications included atorvastatin, escitalopram, omeprazole, and trazodone. She had taken oral contraceptives in the past, but stopped approximately five years prior.

Physical exam showed reduced facial sensation in the ophthalmic, maxillary, and mandibular branches of the trigeminal nerve on the right. The patient had a modest right hemiparesis and dysmotility and a moderate ataxia in the right arm and leg. Stereognosis was reduced on the right. The patient could

not stand due to right leg weakness. Pupils were round and reactive to light bilaterally with extra ocular eye movements intact and no photophobia. She did not have nuchal rigidity. Palatal arch elevated symmetrically. Reflexes were normal and symmetric bilaterally.

An ultrasound carotid duplex study showed minimal atherosclerotic disease involving both carotid systems, but no evidence for a hemodynamically significant stenosis of the common or internal carotid arteries. An echocardiogram bubble study showed normal left ventricular systolic function and wall motion with ejection fraction estimated at 55 to 60% and no evidence of right-to-left shunting. MRI of the cervical spine showed no evidence for spinal stenosis or nerve root encroachment, but there were several sub-centimeter nodules associated with the thyroid gland. Magnetic resonance arteriogram (MRA) of the brain without contrast showed no evidence of an aneurysm of the circle of Willis and there was no hemodynamically significant stenosis identified. MRI of the brain with and without contrast showed a new para-Rolandic central and parietal high convexity cortical signal abnormality in addition to the signal abnormality seen on the right parietal cortex on previous imaging. Abnormal signal in the right inferior cerebellar peduncle and left dorsal medulla also were seen, as well as a sulcal tendril of abnormal signal flowing down from a high convexity cortical or meningeal level, indicating a possible subarachnoid bleed (Figure 1). She was admitted for further workup of the etiology of her symptoms.

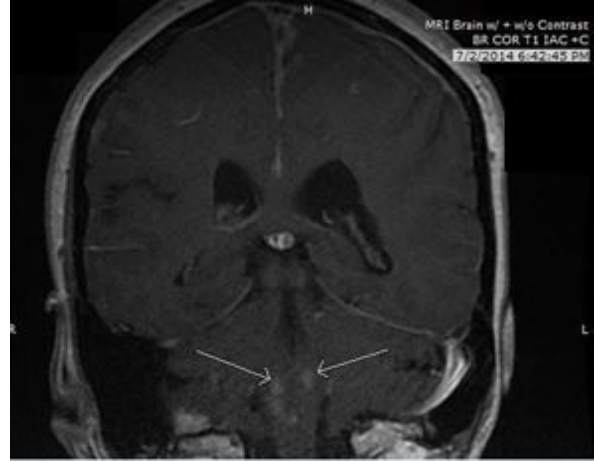


Figure 1. Coronal T1W MRI demonstrates small foci of abnormal hyperintense signal demonstrated within the dorsal medulla (arrows).

On day two post-admission, she experienced new-onset numbness on the left side of her face and the palm of her left hand that was accompanied by ataxia of her left arm and uncontrollable head bobbing. This episode lasted for approximately one minute and was not apparent on physical exam. The patient reported being able to walk with minimal assistance but dragging of her right foot was observed. These symptoms raised concerns of a new neurologic process of unclear etiology, and an extensive workup for demyelinating disease, infectious disease, or thrombotic disease was undertaken.

On day six, cerebral spinal fluid analysis showed 18 white cells (92% lymphocytes) and 253 red cells. Cerebrospinal fluid protein was 45 mg/dL and glucose 65 mg/dL (serum 113 mg/dL). No oligoclonal bands were detected. Cryptococcal antigen and VDRL titers were negative. Further infectious workup of Lyme disease, West Nile virus, and HIV were negative. Dexamethasone 2mg PO TID, divalproex sodium 500 mg PO BID, topiramate 25 mg PO daily, and minocycline 100 mg PO q12hr were started for the suspicion of a demyelinating process possibly contributing

to her symptoms. Thyroid ultrasound revealed multiple hypo-echoic lesions in each lobe which were interpreted as benign with a recommendation to repeat in six months. Thyroid stimulating hormone with reflex free T4 level was normal. Computed tomography (CT) of the chest and abdomen revealed a 4 mm right lower lobe pulmonary nodule with a recommendation to reimagine in six months to assess stability. No abnormally enlarged lymph nodes in the chest, abdomen, or pelvis were found.

Repeat MRI revealed a new abnormal high T1 signal intensity demonstrated throughout the superior sagittal sinus as well as some central low signal within the superior sagittal sinus on the gradient acquisition, suggestive of superior sagittal sinus thrombosis (Figure 2). FLAIR acquisition also demonstrated some nonspecific foci of high T2 signal demonstrated within the posterior aspect of the medulla. This appeared unchanged from previous imaging. Dexamethasone, divalproex sodium, topiramate, and minocycline were discontinued and anticoagulation started with heparin drip 18 unit/kg/hr and warfarin 5 mg PO daily with a partial thromboplastin time (PTT) goal of at least 75 and an INR goal of 2-3.

Seven days post-admission, the patient reported the abnormal movements of her right arm had improved. She was walking without assistance. She also denied symptoms of right leg or right arm weakness, but reported mild dizziness and another brief episode of left palm numbness that lasted approximately one minute. A coagulopathy workup was initiated in an attempt to determine the source of the thrombosis. Blood and urine homocysteine levels were normal. The patient was heterozygous for methylenetetrahydrofolate reductase (MTHFR) gene mutation and negative for prothrombin G20210A mutation. Coagulation studies indicated an

elevated Factor VIII of 227 (normal 50-150). Antithrombin, protein C and S, B6, folate and B12 levels were within normal ranges.

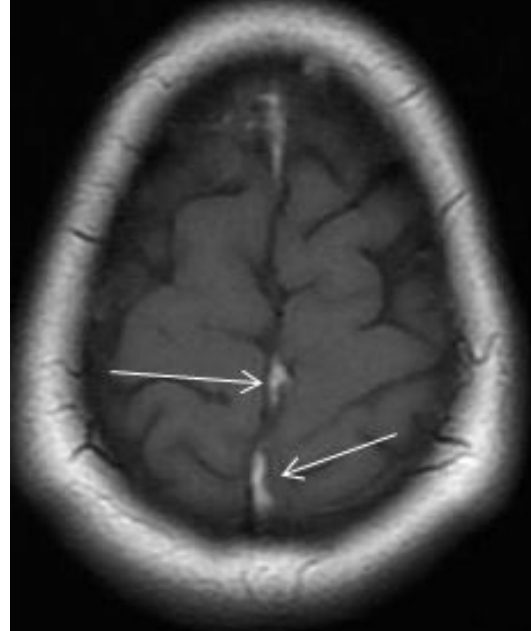


Figure 2. Axial T1W MRI demonstrates thrombosis throughout the superior sagittal sinus (arrows).

Eleven days after admission, the patient denied right leg or right arm numbness with no ataxia of her right limb. She was able to walk normally without assistance and denied dizziness or weakness. Routine CT scan of the brain revealed no intracranial hemorrhage as a result of heparin and warfarin treatment. At that time, her PTT was 91.7 and INR 1.7. Her warfarin dose was increased to 7.5 mg PO daily and heparin drip adjusted to 22.5 mL/hour. Urinalysis was negative for white cells, red cells, leukocyte esterase, glucose, or protein. Blood cultures were negative for bacterial or fungal growth.

On the sixteenth and final day of hospitalization, the patient had no symptoms of weakness, numbness, paresthesia, dizziness, or difficulty walking. On discharge, her INR was 2.1 and PTT 99.3.

Heparin was discontinued and the patient continued on 7.5 mg warfarin PO daily, with a follow up appointment scheduled in the outpatient clinic and repeat MRI to assess treatment.

Discussion

Although a common diagnosis, cerebral venous sinus thrombosis (CVST) is missed frequently by both neurologists and general practitioners.¹ The most common symptom is headache (70%), followed by focal neurologic signs such as aphasia, numbness, and weakness (29%).² A study that included 625 patients from 89 centers in Europe with CVST found the mean age of patients was 39.1 years with a 3:1 female predominance.³ In most diagnoses of CVST, there is usually a prothrombotic risk factor that is likely the etiology that predisposes to CVST, most commonly oral contraceptive use. Some studies calculate a >10-fold increase in the risk of thrombotic events in women taking oral contraceptives.^{4,5} Other prothrombotic risk factors include antithrombin III deficiency, dehydration, factor V Leiden mutation, increased factor VIII, infection, protein C and S deficiency, pregnancy, prothrombin mutation, malignancy, and trauma.^{2,6}

Hyperhomocysteinemia has been suggested as a risk factor for deep vein thrombosis and stroke, but has not been shown to cause increased risk for CVST.⁷ The heterozygous mutation of the MTHFR gene is not an independent risk factor for CVST; however, this patient's combined risk factors of elevated factor VIII, previous exposure to oral contraceptives, and prior pregnancies may be compounded further by heterozygosity of the MTHFR gene.¹² The superior sagittal sinus is the most common site of cerebral venous thrombosis. Other sinus systems can be affected, including the sigmoid and transverse sinuses.⁷⁻¹⁰

Imaging of the brain is necessary to diagnose CVST.¹³ Non-contrast computed

tomography (CT) usually is performed in the emergency department when a central neurologic process is suspected. The most common findings in CVST using this method are hyperdense foci or generalized swelling.¹⁴ However, a normal CT scan or MRI does not exclude the diagnosis of CVST. In a study where 52 patients had evidence of CVST, 9 of the 30 patients who had a CT as the first imaging study had normal findings. Of these nine, the MRIs of four of the patients were also normal. Using an MR venogram (MRV) study, evidence of CVST was revealed in two of the four patients. The authors of this study concluded that MRV is the investigation of choice for confirming CVST.¹

Treatment for CVST includes initial anticoagulation with heparin or thrombolytics, with symptomatic therapy.¹¹ The use of heparin has come into question because of its association with hemorrhagic infarction in up to 40% of CVST cases.² For this reason, physicians hesitate to administer heparin. Unfortunately, there are few controlled trials on the safety and efficacy of anticoagulation treatment for CVST. A meta-analysis of two small trials of 80 patients which compared the safety and efficacy of anticoagulation with placebo showed that the use of anticoagulation had an absolute risk reduction in death or dependency of 13% (confidence interval -30 to +3%) with a relative risk reduction of 54%.¹⁵ Intracranial hemorrhage has not been shown to be a contraindication to anticoagulation when related to CVST.¹¹ It is unclear if low molecular weight heparin (LMWH) is a better choice than dose-adjusted intravenous heparin, or vice versa. LMWH given subcutaneously increases the mobility of patients and reduces the need for laboratory monitoring and dose adjustments. However, intravenous heparin can be discontinued and an activated partial

thromboplastin time normalized within one to two hours if complications occur.

Thrombolytic therapy for the treatment of CVST is an option.¹⁶ Thrombolytic therapy with tissue plasminogen activator (tPA) after failed anticoagulation was an effective treatment in patients with severe or worsening CVST. Those who had thrombolytic treatment after worsening of symptoms survived with mild residual neurologic damage or symptom-free recovery. The same study also found that patients who had only mild symptoms or no worsening of clinical course benefited from anticoagulation therapy alone.

Other studies of thrombolytic therapy for the treatment of CVST have seen similar results, with rapid and complete recanalization achieved with full recovery. However, there were two extra-cerebral bleeding events and two patients whose pre-treatment intracranial hemorrhage worsened.^{17,18} There may be a higher risk of bleeding complications with thrombolytic treatment compared to anticoagulation therapy, particularly in patients with intracranial hemorrhage before treatment.¹⁹

Oral anticoagulation for three months with a target international normalized ratio (INR) of 2.0-3.0 has been recommended if CVST is believed to be secondary to a reversible risk factor such as oral contraceptive use, infection, or dehydration. If idiopathic, oral anticoagulation is recommended for 6-12 months.²⁰ Oral anticoagulation for 6-12 months is recommended for patients with a mild hereditary thrombophilia such as prothrombin G202A mutation, heterozygous factor V Leiden mutation, or protein C or S deficiency. More severe cases of hereditary coagulopathies with frequent recurrences such as antithrombin deficiency or homozygous factor V Leiden mutation may require oral anticoagulation indefinitely. The clinician's judgment in the severity of the

hereditary thrombophilia, if present, may decide the length of treatment. Our patient had identifiable risk factors for CVST which may warrant long-term treatment with oral anticoagulation and scrupulous monitoring for potentially fatal side effects of treatment.

The etiology of the patient's new neurologic symptoms on day 2 post-admission remained unclear. The small foci of the abnormal hyper-intense signal demonstrated within the dorsal medulla were present even when the symptoms resolved. Workup did not reveal a cause for these lesions and the patient had become asymptomatic. As such, follow-up to the neurology clinic as an outpatient was recommended to monitor the lesions for any changes.

While common, CVST is a frequently missed diagnosis. Its symptoms can present similarly to an acute stroke and should be suspected in patient populations where acute strokes are uncommon. The superior sagittal sinus is the most common site of dural sinus thrombosis, and the gold standard for diagnosis is MRV. Treatment is controversial but intravenous heparin administration with bridging to oral anticoagulation is used most commonly. More studies are needed to determine the safest and most efficacious treatment for CVST.

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