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Elevated Factor VIII Level Associated with Transverse Cerebral Venous Sinus Thrombosis

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Funds Collection G

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Conflict of interest: None declared

Patient: Female, 50
Final Diagnosis: Transverse cerebral venous sinus thrombosis
Symptoms: Headache, diplopia, nausea, vomiting
Medication: —
Clinical Procedure: —
Specialty: Neurology

Objective: Rare disease

Background: Cerebral venous sinus thrombosis (CVST) is an uncommon cause of stroke. CVST can be caused by systemic conditions as well as mechanical factors that reduce blood flow to promote thrombosis. These can include hormonal therapies, pregnancy, malignancy, genetic conditions. trauma, neurosurgical procedures, and adjacent infections (mostly mastoiditis). This case report describes a patient with right transverse sinus thrombosis with no prior risk factors.

Case Report: A 50-year-old female with no risk factors presented with complaints of headache associated with diplopia for 2 weeks. She did not have any other neurologic signs or symptoms. The patient initially underwent a cerebral magnetic resonance imaging that revealed right transverse sinus thrombosis. She underwent an extensive procoagulant workup and was found to have an increased factor VIII level. All other workups were negative. The patient was started on heparin infusion and bridged to coumadin to achieve a therapeutic international normalized ratio. The patient had improvement in her headache symptoms and was discharged to be followed as an outpatient.

Conclusions: We report a case of right transverse sinus thrombosis in a patient with increased factor VIII levels. It is prudent to promptly diagnose cerebral sinus venous thrombosis and start antithrombotic treatment for complete resolution of symptoms.

MeSH Keywords: Cranial Sinuses • Factor VIII • Venous Thrombosis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/913917

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Background

Venous thromboembolism of the cerebral veins and dural sinuses is a rare condition which is often overlooked, but is a cerebrovascular emergency. The clinical diagnosis of cerebral venous sinus thrombosis (CVST) is difficult and requires a low clinical threshold in children and adults as the exact prevalence of the disease is unknown. The usual manifestations include headache, focal or generalized seizures, altered mental status, or signs of intracranial hypertension. CVST is more common in women due to pregnancy, oral contraceptive use, and puerperium. It largely affects superior sagittal and lateral sinuses [1]. We report a patient with headaches who was diagnosed with transverse venous sinus thrombosis secondary to elevated factor VIII levels.

Case Report

A 50-year-old female with no significant past medical or surgical history presented to our hospital with the complain of sudden onset headache and occipital pain that started 2 weeks earlier. Her headaches were exacerbated by sitting and standing and were relieved on lying down supine. Her headaches were associated with nausea, vomiting, and diplopia. She did not take any medicines at home.

On presentation, the patient was afebrile, respiratory rate was 19 breaths per minute, heart rate was 80 beats per minute, blood pressure was 120/65 mmHg, with 100% oxygen saturation on room air. On physical examination, her pupils were equally round, reactive to light and accommodation. Nystagmus was absent. Furthermore, her mental status was normal, and her cranial nerve, motor, and sensory examinations and her reflexes were also normal. Laboratory workups done on admission were normal (Table 1). Magnetic resonance imaging (MRI) of the brain was done, and revealed bilateral balance subdural collections. Meningitis was ruled out by the absence of fever, leukocytosis, and the lack of elevated sedimentation rate and C reactive protein. Contrast magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) were done, and revealed right transverse venous thrombosis (Figures 1, 2). The patient was started on a heparin drip and was subsequently transitioned to oral coumadin with international normalized ratio (INR) goal of 2 to 3. A pro-coagulant workup was done; a summary of findings is shown in Table 2.

Neurosurgery and Endovascular Neurology Departments were consulted; however, no operative intervention was recommended. The patient was discharged on oral coumadin; the patient was scheduled for follow-up in the clinic with no further events reported.

Table 1. Initial laboratory workup at time of admission.

Laboratory variable	Value	Reference value
Lactic acid	1.6 mmol/L	0.5–2 mmol/L
Glucose	106 mg/dL	65–110 mg/dL
Sodium	141 mmol/L	135–145 mmol/L
Potassium	4.0 mmol/L	3.5–5 mmol/L
Chloride	107 mmol/L	95–105 mmol/L
Bicarbonate	29 mmol/L	18–22 mmol/L
Blood urea nitrogen	20 mg/dL	8–21 mg/dL
Creatinine	0.7 mg/dL	0.8–1.3 mg/dL
Prothrombin time	10.3 seconds	11–14 seconds
Internalized normal ratio (INR)	1.01	0.9–1.2
Hemoglobin	15.4 gm/dL	12–15 gm/dL
Hematocrit	45.1%	36%–47%
Platelets	207 000/mm^3	150 000–400 000/mm^3
Erythrocyte sedimentation rate	7 mm/hour	<Age/2 mm/hour
C-reactive peptide	3.9 mg/L	<5 mg/L

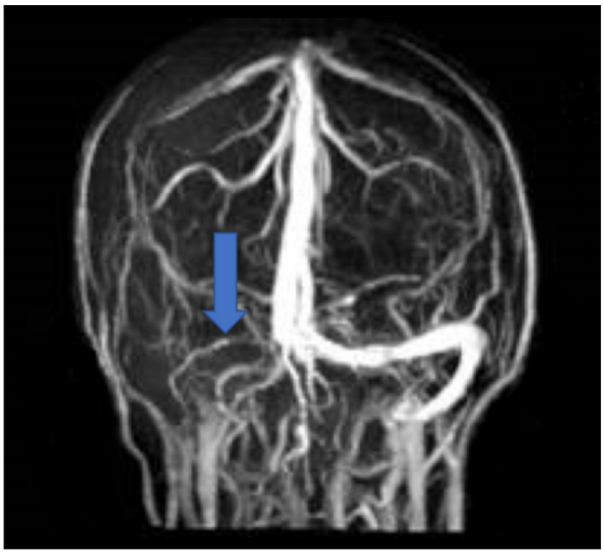

Figure 1. Coronal view of magnetic resonance venogram (MRV) demonstrating no contrast within the right transverse sinus (arrow) compatible with thrombosis.

Discussion

The first detailed report of CVST published by Ribes in 1825 described a 45-year-old patient who died after 6 months of

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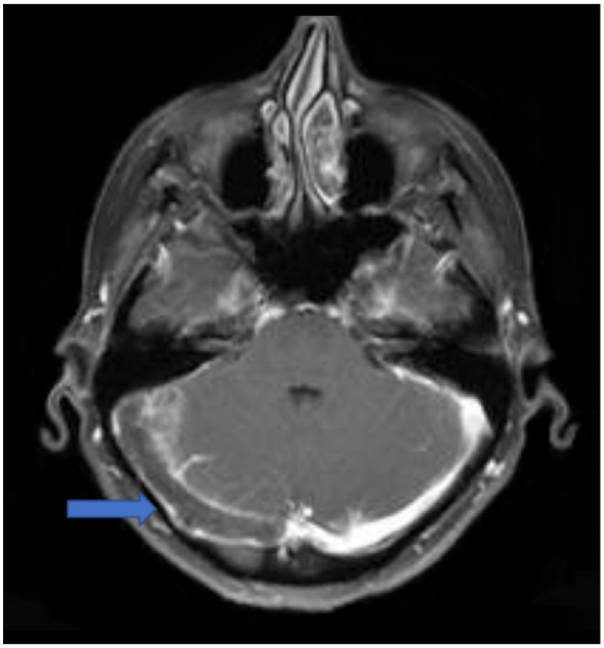

Figure 2. Axial view of contrast-enhanced magnetic resonance imaging (MRI) identifying no contrast within the transverse sinus (arrow) compatible with occlusion or thrombus.

Table 2. Laboratory values for hemophilic workup.

Pro-coagulant Factor	Values	Reference Values
Factor VIII	215.6%	50–150%
Factor V Leiden mutation	Negative	Present in positive cases
Protein C	126.8%	70–180%
Protein S	56.6%	60–140%
Antithrombin III	102%	80–120%
Lupus anticoagulant	Negative	Present in positive cases
Antiphospholipid antibodies	Negative	Present in positive cases
Fibrinogen	249 mg/dl	149–353 mg/dL
Thrombin time	18 seconds	13–19 seconds
Homocysteine	10.5 µmol/L	<10.4 µmol/L
Prothrombin time	10.3 seconds	11–14 seconds

headaches, delirium, and seizures. Autopsy findings revealed superior sagittal sinus, left lateral sinus, and parietal cortical vein thrombosis [2]. Since then, literature has reported that CVST is a disease with variable presentations, which include headaches, strokes, seizures, and signs of intracranial hypertension. Results of the International Study on Cerebral Vein and Dural Sinus Thrombosis demonstrated that the median delay from onset of the symptoms to admission was 4 days and from onset of symptoms to diagnosis was 7 days [3].

CVST generally occurs in children and young adults and accounts for less than 1% of all strokes. The peak incidence rate in adults occurs in the third decade of life with the incidence rate is higher in women compared to men [4]. Approximately 57% to 86% of patients have functional recovery [5–7]; the mortality rate is 5.5% to 18% [1,5,6]. Headache is the most common manifestation and presents as thunder clap headache. Patients can also present with focal or generalized seizures, focal central nervous system (CNS) deficits (hemianopsia, aphasia, motor or sensory defects), and coma. The risk factors associated with poor outcomes include age greater than 37 years, male sex, altered mental status on presentation, coma, cerebral hemorrhage, cancer, CNS infection, and deep venous thrombosis [3].

CVST can be caused by reversible factors like infection and malignancy, or irreversible factors such as prothrombotic mutations [8]. One study showed that factor VIII levels greater than 150 mcg/L are associated with a 5-fold risk for venous thrombosis [9]. Our patient had elevated factor VIII levels, which predisposed her to develop CVST in the absence of any other etiology. Another reported prothrombotic risk factor is elevated vWF (von Willebrand factor), however, it is possible that this effect may be mediated by factor VIII as vWF was found to be elevated simultaneously with factor VIII [10].

CVST on non-contrast computed tomography (CT) of the head appears as a “cord sign”, which is basically thrombosed cortical veins [11]. This may provide a clue to clinicians of a potential diagnosis of CVST. The best test for diagnosis, however, is MRI and MRV of the brain. Treatment modalities include anticoagulation with either unfractionated heparin (UFH) or subcutaneous low molecular weight heparin (LMWH) [12–14]. The data regarding the duration of therapy with oral anticoagulation are unclear, however, guidelines recommend at least 3 months of therapy if CVST is secondary to transient risk factors. If CVST is deemed to be idiopathic, the duration of therapy should be extended to be 6 to 12 months. In patients with recurrent CVST or CVST associated with a prothrombotic condition, indefinite oral anticoagulation is recommended [15,16]. Prophylactic antiepileptic therapy is recommended for patients with focal neurological deficits and supratentorial lesions on admissions, however, the optimal duration is unknown.

Conclusions

CVST involving the transverse sinus is an uncommon disease with good prognosis if the diagnosis is made early. It requires

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a high level of clinical suspicion and involves imaging studies using MRV in order to make prompt diagnosis so that treatment can start immediately. Early treatment can have a good prognosis. The workup for CVST should also include measuring factor VIII levels, as factor VIII can be a contributing indicator for initial as well as recurrent CVST. Long-term management of CVST involves anticoagulation and anti-seizure medication.

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Conflict of interests

None.

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