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An Unusual Cause of Cerebral Venous Thrombosis

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Abstract
Cerebral vein and dural sinus thrombosis is quite an uncommon phenomenon. Symptoms range from headache, vomiting, visual disturbances, stupor, focal deficits, seizures and multiple cranial nerve palsies. Further evaluation of the cause is deemed in unprovoked cases. Treatment includes anti oedema measures, seizure prophylaxis and anticoagulation. We report a 30 year old male who presented to us with a headache and blurring of vision, found to have Protein S deficiency and moderate hyper-homocysteinemia.
Keywords: *Cerebral vein thrombosis, Protein S deficiency, Homocysteinemia.*

Introduction

Patients with cerebral venous thrombosis (CVT) have a highly variable presentation. Symptoms range from headache, vomiting, visual disturbances, stupor, focal deficits, seizures and multiple cranial nerve palsies. Frequent causes are CNS infections, sinusitis, head injury, inflammatory diseases and acquired or genetic prothrombotic states.

Inherited thrombophilias should be suspected in patients presenting with recurrent venous thromboembolism (VTE), young age, unusual sites like portal, mesenteric and cerebral veins and strong family history. The incidence ranges from 0.22 to 1.57 per 100,000, female to male ratio of 3:1 and the mean age of patients being 39 years[1][2][3][4][5].

In 2013, the Multiple Environmental and Genetic Assessment of risk factors for venous thrombosis (MEGA study) studied 2331 adults with VTE and 2872 controls. Protein S deficiency (described as <33 units/dL) was found to be 0.9% Only 10 out of these individuals had *PROS1* mutation.[9]

Case Report

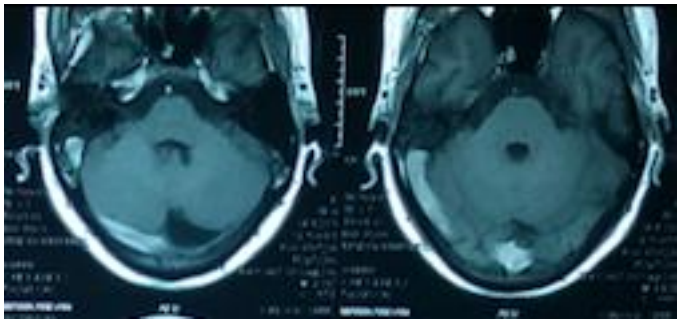
30 year old male presented with complaints of headache and giddiness for four days. The headache was insidious in onset, present over the frontal and temporal aspects associated with nausea and vomiting which was non projectile in nature. He also complained of right ear fullness, tinnitus and giddiness. On closer questioning he also revealed complaints of blurring of vision and diplopia for the past two days. He had no complaints of fever, neck stiffness or any head trauma. He had no previous known comorbidities and no similar previous

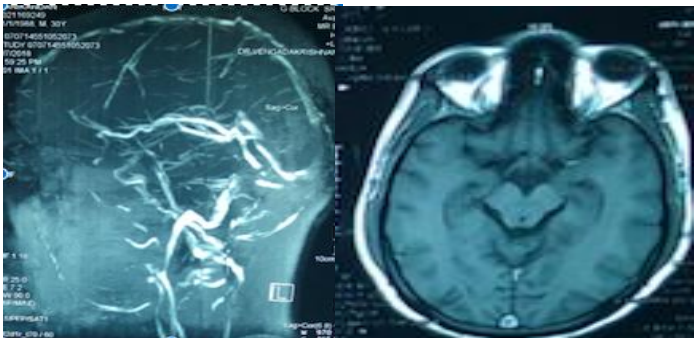
episodes. He gave no history of drug abuse, smoking or alcohol consumption.

On physical examination he was conscious but irritable and disoriented to time, place and person. There was no neck muscle stiffness, no skin excoriations or rash. Frontal and maxillary sinus tenderness was present Vitals were stable and CNS examination revealed nystagmus and right lateral rectus palsy. Fundus showed blurring of disc margins, B/L papilledema. Motor and sensory systems were intact.

Labs revealed Hb-16.5, PCV-46.2. MRI with MR venogram showed thrombosis of bilateral transverse and superior sagittal sinus, right sigmoid sinus and right internal jugular vein with right otomastoiditis and features of intracranial hypertension. Hyper coagulable workup showed moderate hyper-homocysteinemia- 30.27mcgmol/L (N-5-15mcgmol/L) and Protein S deficiency- 23% (N-77-143). ANA was negative and found to have normal Protein C, Antithrombin III levels and Factor V levels.

Patient was treated with Inj Vancomycin 15mg/kg Q8H and Inj Ceftriaxone 2g IV Q12H in view of the otomastoiditis. In view of increased intracranial tension, Inj Mannitol 25% 100ml Q8H and Inj Dexamethasone 4mg Q8H was started and prophylactic anti epileptics, T.Levetiracetam 500mg Q8H. He was started on Inj Enoxaparin 60mg S/C Q12H bridged with oral acenocoumarol 3mg to maintain a target INR of 2-3. Patient was also started on multivitamin formulation containing folic acid, cyanocobalamin and pyridoxine in view of moderate hyper-homocysteinemia. He improved symptomatically, no longer complained of diplopia, headache or blurring of vision. He was counselled about the need for lifelong anticoagulation and discharged.





Discussion

Patients with CVT at a young age, family history or absence of any risk factors should be subjected to evaluation of thrombophilic state, ideally after the acute phase of six weeks, which includes Anti Thrombin III, Protein C, Protein S, Factor V Leiden, Prothrombin G20210A mutation, Lupus anticoagulant, anticardiolipin, and anti-beta2 glycoprotein-I antibodies. Two mechanisms contribute to the clinical features. of CVT. Thrombosis of cerebral veins or dural sinuses obstructs blood drainage from the brain, leading to cerebral parenchymal dysfunction and to increased venous pressures with disruption of the blood-brain barrier. Occlusion of dural sinus also results in a decrease of cerebrospinal fluid absorption and thus elevated intracranial pressures.

Protein **S**, originally purified and discovered in **S**eattle, where it gets its name from, is a Vitamin K dependent glycoprotein. It is a co-factor for activated Protein C. Activated protein C is involved in inactivating factor Va and factor VIIIa thereby reducing thrombin generation, enhancing fibrinolysis and inhibiting prothrombin activation. Therefore Protein S deficiency increases the risk of thrombosis. Protein S deficiency is an autosomal dominant condition caused by mutations in the *PROS1* gene on chromosome 3. Majority are heterozygous for *PROS1* mutation Some manifesta-tions of protein S deficiency include VTE (Deep vein thrombosis, pulmonary embolism, cerebral and mesenteric veins) arterial thrombosis, neonatal purpura fulminansand obstetric complications.

Treatment of CVT however, regardless of etiology, revolves around the same concepts. Anti-edema measures like mannitol, hypertonic saline, diuretics-

acetazolamide and furosemide, glucocorticoids like dexamethasone and in some cases repeated lumbar punctures. Antiepileptics for patients who have seizures and focal cerebral supratentorial lesions such as edema or infarction. Anticoagulation is the mainstay, LMWH bridged with oral Vitamin K antagonists to maintain a target INR of 2-3.[6] Duration of anticoagulation is still one under debate. The usual norms being, in provoked CVT 3-6months, unprovoked CVT 6-12months, recurrent CVT or severe thrombophilia (homozygous prothrombin G20210A mutation, homozygous factor V Leiden mutation, protein C, protein S, or antithrombin deficiencies, combined thrombophilia defects, or antiphospholipid syndrome), anticoagulation to be continued indefinitely.[7][8]

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