Case Report

Cerebral venous sinus thrombosis–A primer for emergency physician

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Abstract

Cerebral venous sinus thrombosis (CVT) is notoriously known for its varied presentations and extremely high risk of mortality, if remains undetected and untreated. On the other hand, life can be saved with full functional recovery if CVT can be identified with high index of clinical suspicion with supportive imaging and treatment with appropriate anticoagulation. It is important for clinicians to be meticulous to screen for both the potential reversible and heritable causes of CVT so that appropriate measures can be taken to prevent such catastrophe. Here we report a case of CVT involving right sigmoid and transverse sinuses presenting with acute onset left sided hemiplegic without antecedent headache or seizures. Patient was successfully treated with anticoagulants with nearly full functional recovery. Multiple predisposing factors were identified. As per our knowledge, this is the first case of CVT with underlying conglomeration of multiple acquired (lactation, folate deficiency, hyperhomocysteinemia, depot medroxyprogesterone acetate injection) and hereditary risk factors (deficiency of protein C, protein S and antithrombin-III) in a single patient.

Keywords: Anticoagulation, cerebral venous sinus thrombosis, neuroimaging

Introduction

Cerebral venous sinus thrombosis (CVT) is notoriously well-known for its rarity, myriad etiological risk factors, diverse, and masquerading clinical presentations and very high mortality, if not timely diagnosed and treated aggressively on urgent basis.[1] Nowadays with highly advanced diagnostic imaging modality the incidence of CVT has been found to be more common than previously thought.[2] Although it may occur across all range of populations, it is more common among females of child-bearing age and pediatric patients, with superior sagittal sinus and transverse sinus being most commonly involved.[1] Female-specific conditions (pregnancy, lactation, hormonal contraception, etc), malignancy, dehydration, infection (particularly of ears), head injury, myeloproliferation and autoimmune disorders are common underlying risk factors. In total 18% patients with CVT have hereditary thrombophilic risk factors, with nearly in 25% cases no etiological risk factor might be identified.[1,3] Although overall CVT as a cause of hemiplegic stroke is rare entity, 24% patients with CVT might have hemiplegia as found in classical intracerebral hemorrhages or infarct.[4] Here, we present a case of young female presented initially with isolated hemiplegia and upper motor neuron (UMN) type facial palsy, who was ultimately diagnosed to be suffering from CVT with multiple hereditary and acquired thrombophilic risk factors.

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Case Report

A 18-year-old lactating mother, with last child birth 10 months ago presented to the emergency department with complain of sudden onset left sided weakness and slurring of speech since early morning. There was no prior history of headache, convulsions and visual difficulty. There was no similar history in the past. Dietary history, family history, menstrual history, drug history, immunization or vaccination history were non-contributory on the day of admission. On examination she was pale, normotensive, adequately hydrated and had Glasgow Coma Scale (GCS) score of 15/15. The patient had left sided complete uncrossed hemiplegia with left sided UMN type facial weakness. Power of left upper limb was 2/5, left lower limb was 1/5, left sided plantar reflex was mute and deep tendon reflexes were normal. Rest of the systemic examination was normal except systolic murmur in mitral area. An urgent non-contrast computed tomography (NCCT) scan brain was advised keeping provisional clinical diagnosis of stroke in mind. It revealed right parietal lobe hemorrhage with surrounding edema [Figure 1]. Conservative management was started with intracerebral edema or pressure reducing therapies (mannitol, glyecerol) and prophylactic anti-convulsant therapy (levetiracetam). Further investigations were planned to establish the etiology of this "lobar bleed in young female".

The patients became progressively restless and started complaining of severe intractable headache and relentless vomiting from night. Headache was not responsive to paracetamol, dexamethasone or tramadol. Vomiting was also not responsive to intravenous anti-emetics. On the second day fundoscopic examination revealed mild blurring of right optic disc. By second day evening we had few basic reports in our hands. Hemoglobin was 4.8 gm/dl, mean corpuscular volume (MCV) was 105 fl and rest of the reports (total count, differential count, platelets, liver function test, renal function test, random blood sugar, serum electrolytes, PT-INR, aPTT, BT, CT, TFT, lipid profile, HIV, HBsAg, anti-HCV) came out to be normal. Cardiac evaluation (ECG 12 leads and 2D-Echocardiography) was within normal limit. CT angiography of brain was done and found no arterial abnormalities (aneurysm or arteriovenous malformations). Magnetic Resonance Imaging (MRI) brain showed an ill-defined lesion in right parietal lobe which was hyperintense on T1-weighted, heterointense on T2-weighted, heterointense on diffusion-weighted with blooming on gradient recalled echo (GRE) images suggestive of hemorrhage with moderate perilesional low signal intensity which was hyper on fluid attenuation inversion recovery (FLAIR) images suggestive of edema. Effacement of right lateral ventricle was noted with midline shift of 8.8 mm towards left [Figure 2]. Contrast enhanced MR venography (MRV) was done and revealed narrow lumen of right sigmoid sinus, right transverse sinus and right internal jugular vein along with fillings defects [Figure 3]. Thus, a final diagnosis of CVT involving right sigmoid and transverse sinuses was made. Patient was anticoagulated with injection enoxaparin 0.6 ml for 7 days. It was followed by introduction

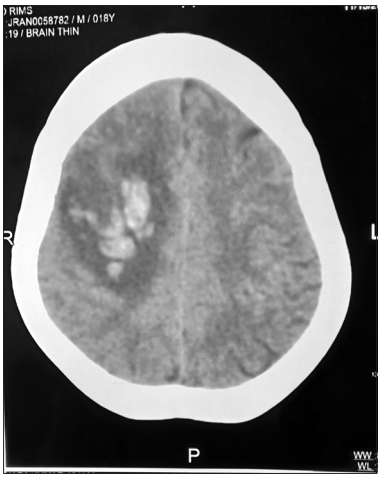

Figure 1: NCCT scan brain showing parietal lobe hemorrhage with extensive perilesional edema

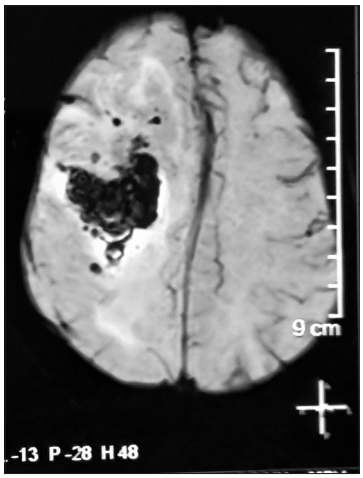

Figure 2: MRI brain (GRE sequence) showing blooming suggestive of haemorrhage

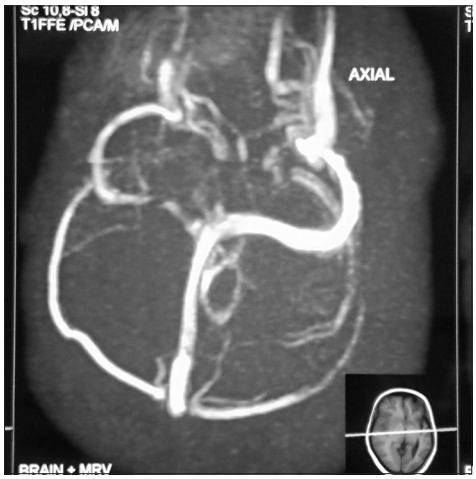

Figure 3: Contrast enhanced MRV showing narrow lumen of right sigmoid sinus, right transverse sinus and right internal jugular vein along with fillings defects

of warfarin 1 mg with gradual tapering dose of enoxaparin. Dose of warfarin was gradually increased based on PT-INR

monitoring (target 2–3). By 2 weeks eoxaparin was stopped and warfarin was continued on maintenance dose of 4 mg/day. The patient responded well, headache was abolished by two days of initiation of enoxaparin.

On further interrogation to probe the reasons of thrombosis, we retook the contraceptive history again and again. Patient and her attendants repeatedly denied use of oral contraceptive pills (OCP); but her husband later gave the history of taking injection of depot medroxyprogesterone acetate (DMPA) injection every three months from nearest primary health centre. Complete thrombophilia screening [serum vitamin B_{12}, folate, homocysteine, anti-nuclear antibody profile, cytoplasmic anti-neutrophil cytoplasmic antibody, perinuclear anti-neutrophil cytoplasmic antibody, anti-phospholipid antibodies, protein C, protein S, anti-thrombin III (AT-III), factor V Leiden, hemoglobin electrophoresis) was carried out. Blood sample for thrombophilia screening was sent just before the start of anticoagulation therapy. Serum folate came out to be low (1.40 ng/ml) with marginal hyperhomocysteinemia (13.70 μmol/l). Protein C activity (34.8% of normal), protein S activity (35.9% of normal) and AT-III activity (67% of normal) were low. We ruled out decreased production or increased renal loss of protein C, S, and AT-III by excluding chronic liver disease and protein losing nephropathy respectively by relevant investigations. Although we could not perform genetic studies for protein C, protein S and AT-III, decreased activity of those three natural anticoagulants was probably attributable to genetic mutations. On the basis of the above findings, folate supplementation was started.

Patient and her attendants were counseled about the inherent thrombophilic risk in this patient (AT-III, protein C and S deficiency) and acquired factors (folate deficiency, hyperhomocysteinemia, DMPA injection, lactation) leading to such a catastrophe. Patient and her husband had also been specifically advised to use non-hormonal contraceptives.

At the time of discharge patient was completely headache and vomiting free, power of both upper and lower left limbs improved significantly (4/5 in both left limbs) and facial paralysis was improved as well. Patient and her attendants were taught neuro-rehabilitation techniques. Patient was discharged with the advice of dabigatran 150 mg twice a day, levetiracetam 500 mg twice a day and folic acid 5 mg once daily.

Discussion

This case was peculiar in the view that it presented with only complete hemiplegia without antecedent complain of headache or seizure. As a routine protocol of the evaluation of acute onset hemiplegia, we performed NCCT brain. Features on CT brain which might provide clues towards CVT in our case were lobar location of the bleed which did not follow the arterial territory, heterogeneity of the core lesion and extensive perilesional edemain appropriate to the size of the bleed.[5] NCCT features of CVT should be kept in mind by the emergency phyisicians as more often than not this is the only investigation available in most of the resource poor health centers. Clinically strong suspicion of CVT should be borne in mind when the patient with stroke complains of headache which is an early and typical manifestation of CVT unlike arterial obstruction. As in our case, although patient did not had complain of headache or vomiting initially, she developed progressively increasing intense headache associated with vomiting from the second day of admission. This prompted us to make an urgent arrangement for MRV which ultimately proved to be diagnostic. Concomitant internal jugular vein thrombosis was there in our case, which might be found among 11.9% cases as per previous report.[6]

While searching for cause of CVT, history remains of paramount importance. In our case on the day of admission the patient and her attendants repeatedly denied history of OCP intake. On further probing, history of DMPA injection was revealed in the second week of hospital stay. This underscores the importance of taking much detailed history regarding all kinds of hormonal contraceptives when a diagnosis of CVT is strongly suspected among patients of child-bearing age.[7-9] Before delving into the costly investigations to screen for hereditary thrombophilic states (mostly unavailable in resource poor settings), clinicians must target to search for the correctable risk factors.[10] In our case use of injectable hormonal contraceptive preparation, folic acid deficiency and hyperhomocysteinemia were correctable risk factors. Hyperhomocysteinemia was thought to be due to nutritional folic acid deficiency, a fairly common comorbidity among lactating mothers.[11] We could not screen for 5-methyltetrahydrofolate reductase gene mutation due to non-availability of the facility. We screened for hereditary thrombophilic risk factors available in our setup. The patient was counselled for being extra-cautious during future pregnancy, post-operative period or any conditions which would make her bed-bound.

The prognosis of CVT has been grossly improved over last few decades due to increasing awareness among clinicians, detection rate by advanced imaging and prompt treatment initiation.[6] Anticoagulation with unfractioned heparin or low molecular weight heparin followed by vitamin K antagonist is the treatment of choice in acute phase of CVT irrespective of the presence of intraparenchymal hemorrhage.[12] As per the latest guideline, we initiated anticoagulation with enoxaparin, followed by warfarin on maintenance targeting PT-INR of 2-3 in our case. Duration of treatment depends on the underlying disorder; varying from 6 to 12 months.[12] One particular point to mention is that 3 before days before discharge we switched the patient to dabigatran. Although novel or newer oral anticoagulants are still not recommended by the guidelines and several randomized control trials [13-15] are still ongoing, multiple anecdotal evidences have shown encouraging results.[16-19] The reason we shifted to dabigatran from warfarin was that as the patient was from area with extremely resource poor health-care setting, regular monitoring of PT-INR might not have been possible jeopardizing the proper monitoring of the case and anticoagulant

dose adjustment. Recommendations regarding recanalization therapies using fibrinolytics or mechanical thrombectomy are still unclear. It is recommended that recanalization therapy may be used if the patient deteriorates despite adequate anticoagulation, or there is an absolute contraindication to anticoagulation.[12]

Conclusion

Our case underpins the fact that heightened awareness of this "not-so-rare" diagnosis, having knowledge about its various clinical presentations, and taking through history will help to clinch the diagnosis.[20] Although MRV and thrombophilia screening should be done to diagnose CVT, strong clinical suspicion remains the key. CVT can be devastatingly fatal; but with prompt recognition and aggressive treatment excellent functional recovery is possible.[21] Both reversible and hereditary thrombophilic risk factors should be identified and treated accordingly to minimize the chance of recurrence. As per our knowledge, this is the first case of CVT with underlying conglomeration of multiple acquired (lactation, folate deficiency, hyperhomocysteinemia and use of DMPA injection as contraceptive measure) and hereditary risk factors (deficiency of protein C, protein S, and AT-III) in a single patient.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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