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Anaemia with neuro ophthalmic symptoms as a manifestation of cerebral venous thrombosis

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Abstract
Aim: To study the ocular manifestations in cerebral venous thrombosis.
Materials and Methods: We report a case of a 25-year- old married woman who presented to medical emergency with frank per rectal bleeding and later after two days complained of blurring of vision in both eyes and binocular diplopia. On probing the patient, she also gave history of on and off headache since 6 months.
Results: MRI Brain with Venogram was suggestive of intracranial hypertension and non-occlusive thrombus in bilateral transverse and sigmoid sinuses.
Conclusion: CVT should be kept in mind in any patient with acute onset of diplopia with papilledema or cranial nerve involvement. Acute blood loss with severe anaemia can precipitate CVT. Imaging modalities like MRI with venogram should be the investigation of choice in all cases of CVT.

Keywords: Cerebral venous thrombosis, Diplopia, Papilloedema, Transverse sinus, Sigmoid sinus and intracranial hypertension.

Introduction
Cerebral venous sinus thrombosis (CVT), a form of stroke often occurs in young women and very remains undiagnosed at initial presentation. CVT though common in pregnancy and puerperium, there have been several other risk factors that have been identified that have contributed significantly to the pathogenesis of CVT. Cerebral venous thrombosis is potentially life threatening disease that often occurs in young women. Its incidence ranges from 0.22 to 1.32/1,00,000 person- years.[1] Its varied etiology, clinical manifestations and outcomes has aroused interest in several authors for further study. The various clinical patterns of CVT are focal deficits associated with headache, seizures, altered sensorium, others being isolated intracranial hypertension with features of headache, nausea, vomiting, papilledema and eventually sixth nerve involvement. Painful ophthalmoplegia has also been reported.[2]

Etiology can be divided into pregnancy and non pregnancy related risk factors. Pregnancy brings about changes in the coagulation system and persists even during the early postpartum period making them more vulnerable to venous thromboembolic events. The nonpregnancy risk factors include oral contraceptive use, vasculitis, thrombhophilia, dehydration, infection, trauma, malignancy, haematological conditions like polycythemia, thrombocytopenia, anaemia. Some cases have also been reported as idiopathic. Patients with CVT often present with altered sensorium, multiple cranial nerve involvement and sometimes with unconscious state. Very rarely they present to Ophthalmic OPD. This case gives us insight about ocular involvement in CVT. We have made an attempt to review ocular manifestations in CVT with various studies.

Case Report
A 25 year old married female patient presented to medical outpatient department with complaints of giddiness since 1 day, frank per rectal bleed since 10 days, headache on and off since 6 months. There was no history of fever, tinnitus, hearing loss, trauma, any drug intake. There was no other significant medical history. At presentation her blood pressure was 150/90 mm Hg, pulse rate was 98 bpm, patient was afebrile. Systemic examination was within normal limits except for pallor 2+ and multiple sentinel tags and sphincter tone being increased on per rectal examination and provisional diagnosis was anaemia secondary to haemorrhoids. Baseline investigations were as follows: Haemoglobin (Hb) 3g/dl, rest of the blood components were normal. ECG, liver function tests, renal function tests, urine routine were normal. In view of anaemia two pints of packed cell volume were transfused, injection tranexamic acid and sitz bath were advised.

Two days after admission patient developed blurring of vision in both eyes, double vision when looking through both eyes and inward deviation in the right eye (Fig. 1). On examination head posture was normal, ocular posture showed right sided inward deviation of 15° esotropia, extraocular muscle movements showed limitation of abduction in the right eye (Fig. 2). Distant visual acuity in right eye was 6/24 improving to 6/12 with pinhole and in left eye was 6/36 with 6/12 on pinhole improvement. Retinoscopy showed improvement to 6/6 in both eyes at follow up. Anterior segment examination was normal. Diplopia charting showed uncrossed diplopia. Colour vision was normal with ishihara chart.

Fundoscopy showed bilateral papilledema of both eyes (Fig. 3). Sixth cranial nerve palsy was seen with all the other cranial nerves were normal. The diagnosis was bilateral

advanced papilledema with sixth cranial nerve palsy (false localizing sign).

MRI Brain plain with venogram was done after obtaining consent from the patient that showed significant narrowing of the left transverse and bilateral sigmoid dural venous sinuses suggestive of intracranial hypertension and Linear filling defects in bilateral transverse and sigmoid sinuses - likely non occlusive thrombus (Fig. 4,5). Coagulation profile showed values of Prothrombin time - 12.5 seconds, International normalized ratio (INR) – 1.0, Activated partial thromboplastin time that was increased to 82.40 seconds, prothrombin time ratio that was decreased to 0.90. Protein C, protein S, antithrombin III levels, homocysteine were normal. ESR and CRP were normal. Patient was started on low molecular weight heparin (LMWH) 0.4 mg with acenocoumarol 1 mg. Patient improved symptomatically and was discharged. Patient is on regular monthly follow up with vision regained to 6/6 in both eyes, Hb improved to 9.5 g/dl and acenocoumarol is being continued.

Fig. 1

Fig. 2: Showing limitation of abduction of right eye on dextroversion

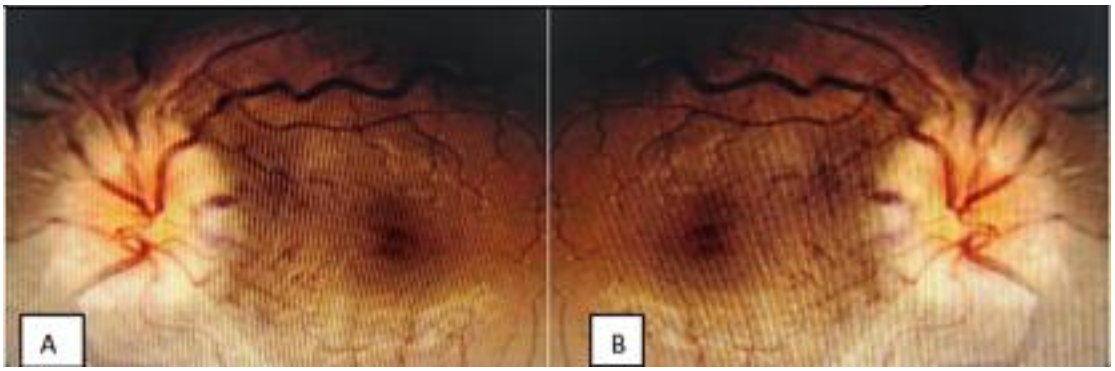

Fig. 3: Showing bilateral advanced papilledema. A: Right eye; B: Lefty eye

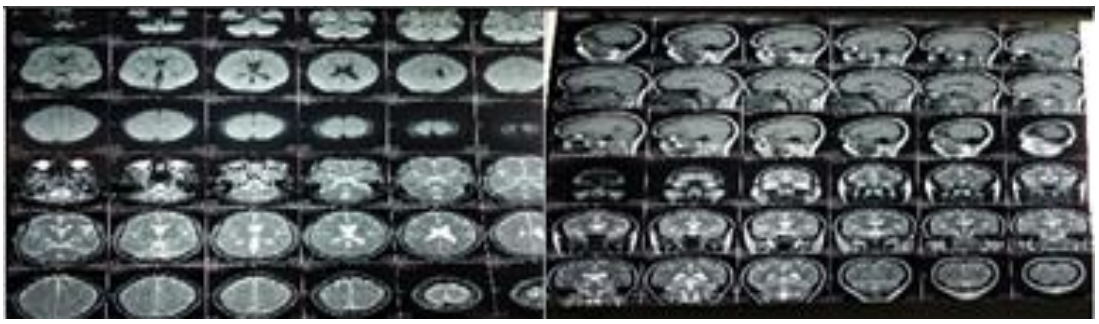

Fig. 4: MRI images

Fig. 5: MR venogram showing oclusion of transverse and sigmoid sinus

Discussion

CVT should be considered as differential diagnosis in any case of neurological involvement. A high index of suspicion and prompt treatment would reduce neurologic damage and mortality. MRI with venography is mandatory in all cases of CVT. We reviewed several journals and headache was the most common presenting symptom.[1-4] In our case giddiness and acute blood loss were the presenting features In contrast our patient presented with Hb of 3g/dl that was the precipitating factor for CVT, and on probing the patient gave history of headache on and off since 6 months. Iron is an important regulator of thrombopoiesis, low iron levels disinhibhit this regulation causing secondary thrombocytosis and thus a hypercoagulable state. Secondarily, anaemic hypoxia causes turbulent flow and platelet aggregation causing thrombosis.[5] The diagnosis of CVT is usually made on the basis of clinical presentation and imaging studies where, as clinical laboratory studies are useful for determining the possible causes of CVT. Complete blood count is done to rule out anaemia, thrombocytopenia, leucocytosis, malignancy. Antiphospholipid and anticardiolipin antibodies to evaluate for antiphospholipid syndrome. Tests for hypercoagulable states include Protein C, Protein S, Antithrombin III, lupus anticoagulant, Factor V leiden mutation. Erythrocyte sedimentation rate and C- reactive protein to rule out systemic vasculitis and urine routine to rule out nephrotic syndrome, Liver function tests and renal function tests to rule out cirrhosis and renal damage. In our patient laboratory investigations pointing towards CVT were Hb 3g/dl, aPTT 82.40 seconds, PT Ratio 0.90. Protein C, Protein S, Antithrombin III levels, homocysteine were normal. ESR and CRP were normal. Thus, any case with high index of suspicion should be further investigated to rule out the appropriate cause of CVT and hence treat the same.

The International study on cerebral vein and dural sinus thrombosis showed superior sagittal sinus involvement to be the most common followed by left and right transverse sinus and then the straight sinus, deep venous system, cortical veins, jugular veins, cavernous sinus.[3] This was similar to a study by Hossein Azin.[2] Superior sagittal sinus was the most common site of thrombosis followed by sigmoid and transverse sinuses.[1] In a study by Borhani Haghighi et al superior sagittal sinus involvement was followed by transverse and sigmoid sinuses.[6] In our study, significant narrowing of the left transverse and bilateral sigmoid dural venous sinuses were suggestive of intracranial hypertension and Linear filling defects in bilateral transverse and sigmoid sinuses - likely non occlusive thrombus. On examination second and sixth cranial nerves were involved without any other neurological deficits.

According to the European stroke Organization guidelines 2017,[7] MRI or CT angiography is recommended for confirming the diagnosis and not routinely screening for thrombophilia or cancer.

In acute CVT, parenteral anticoagulation and decompressive surgery are required to prevent death due to brain herniation. Low molecular weight heparin is recommended and not oral anti coagulants. Antiepileptics are to be given to prevent seizures. Steroids should not be given as they enhance hypercoagulability and increases the mortality rate subsequently. It is also recommended that contraceptives containing estrogen must be avoided in women who have suffered previous CVT and on prophylactic LMWH treatment should be given throughout pregnancy and puerperium. Treatment of CVT includes mainly to reduce intracranial tension, headache, seizures and to avoid increase in thrombus. The mainstay of treatment with heparin avoids the thrombus extension, prevent pulmonary embolism and the chances of spontaneous resolution are high. Low molecular heparin is the treatment of choice in most patients.[7]

Heparin increases the action of antithrombin III, leading to inactivation of coagulation enzymes thrombin, factor Xa and factor IX a. LMWH also has the same action but it is preferred due to more bioavailability, lack of need for laboratory monitoring and continuous infusion, all of which increases mobility of patients and less chances of intracranial or extra cranial bleeding. Heparin is given as initial infusion of 18U/Kg/h and dose is adjusted according to aPTT that is checked every 6 hours.

Thrombolytic therapy will give faster relief in deteriorating patients by recanalizing of veins. Thrombolytic agents like urokinase, recombinant tissue plasminogen activator (rtPA) can be used, but there is no sufficient evidence to use these drugs. After an acute attack, vitamin K antagonist like warfarin can be used as maintenance therapy. The dose of which should be adjusted so to maintain INR of 2.5 to 3. According to the American Heart Association/American Stroke Association (AHA/ASA)[8,9] recommends anticoagulation therapy for 3 months in patients with CSVT secondary to transient risk factor, 6-12 months for patients with idiopathic CSVT and indefinite period in patients with recurring episodes of CSVT or one episode with severe thrombophlia or other cause like Protein C deficiency or antithrombin III deficiency. Vitamin K (Vit K) antagonists, Warfarin and acenocoumarol will inhibit hepatic synthesis of Vit k – dependent coagulation factors II, VII, IX, X. Both have same mechanism of action but acenocoumarol has advantages over warfarin like rapid onset of action, better stability of prothrombin time, rapid reversal of anticoagulant action with smaller dose of Vit k. The dose of oral warfarin is 5 mg QID, dose adjusted according to INR. Acenocoumarol is available as 0.5 mg – 4mg. Dose titration is done according to INR.

Anti-edema measures include intravenous osmotic diuretics like mannitol. Lumbar puncture, ventriculostomy or optic nerve decompression are other modalities of treatment in patients with increased intracranial pressure and visual involvement. A Neurosurgical intervention may be required for hemorrhagic infarction or decompressive craniectomy in some cases of CSVT. Anticoagulation therapy to be resumed as soon as possible following surgery.

Our patient was started on LMWH 0.4 mg and switched to oral acenocoumarol 1mg on discharge.

Conclusion

CVT should be kept in mind in any patient with acute onset of diplopia with papilledema or cranial nerve involvement. Acute blood loss with severe anaemia can precipitate CVT. Imaging modalities like MRI with venogram should be the investigation of choice in all cases of CVT.

Conflict of Interest: None.

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