ORIGINAL RESEARCH PAPER

Internal Medicine

CEREBRAL VENOUS THROMBOSIS IN A YOUNG MALE SECONDARY TO POLYCYTHAEMIA

KEY WORDS:

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ABSTRACT

Cerebral venous thrombosis (CVT) is a rare cause of venous thromboembolism, a challenge to diagnose and treat. Here we present, a 32-year-old man with long-standing smoking and alcohol consumption presented with holocranial headache, projectile emesis, blurring of vision, and diplopia. Imaging demonstrated extensive cerebral venous sinus thrombosis (CVST) of the superior sagittal, bilateral transverse, and sigmoid sinuses. Work-up for aetiology was negative apart from borderline SS-A and Mi-2 positivity. Polycythaemia due to smoking and alcohol was the suspected cause. Management was anticoagulation, venesection, and anti-oedema treatment. Vision worsened to loss of perception during hospital stay and patient was taken up for placement of ventriculo-peritoneal shunt. The case brings out CVT as a possible complication of secondary polycythaemia.

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a rare but potentially life-threatening neurological disorder caused by dural venous sinus and/or cortical vein thrombosis [1-2] .CVST constitutes less than 1% of all strokes and most commonly involves young adults [3] .The clinical picture can be very nonspecific and variable and therefore presents a diagnostic challenge of great magnitude. Patients can present with isolated headaches, focal neurological signs, seizures, or evidence of raised intracranial pressure such as vomiting, diplopia, or papilledema [4].Although CVST is generally associated with hereditary or systemic disorders, lifestyle elements such as cigarette smoking and can lead to secondary polycythaemia, although less frequently noted but can also provide a considerable thrombotic risk.

CASE PRESENTATION

32 year old male with no known comorbidities, alcoholic and smoker for the last 15 years with smoking index of over 30 pack-years , presented with complaints of headache, was apparently normal till one week back, then he developed complaints of headache, throbbing in nature, holo-cranial, associated with projectile vomiting. Patient also had complaints of blurring of vision and diplopia. There was no history of fever, altered sensorium, weakness of limbs, seizures or sensory disturbances.

On examination, patient was hemodynamically stable and conscious, oriented to time, place and person. Examination of cranial nerves revealed restriction of abduction in both eyes, decreased visual acuity with the patient able to appreciate hand movements and perception of light in both eyes. Other aspects of central nervous system examination were normal. External markers of atherosclerosis were absent.

Computed Tomographic venogram showed dural venous thrombosis in the superior sagittal bilateral transverse sinus and sigmoid sinus. Computed Tomographic Angiogram of neck and intracranial vessels showed no significant major arterial occlusion.

Magnetic Resonance Imaging of the brain with Magnetic Resonance Venogram showed no infarct or bleed with dural venous thrombosis in the superior sagittal, bilateral transverse sinus and sigmoid sinus.

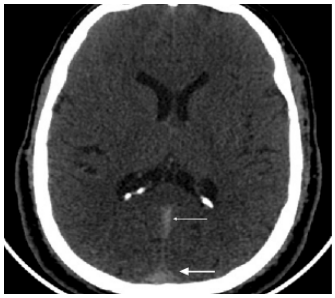

Figure 1: Axial non contrast CT showing hyperdense and thickened Straight (thin arrow) and Superior Sagittal Sinus (thick arrow)

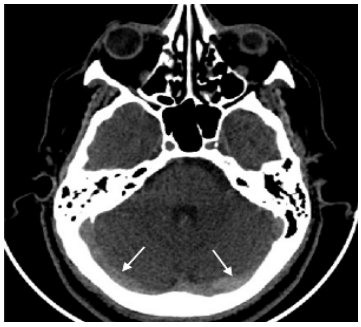

Figure 2: Axial non contrast CT showing hyperdense and thickened bilateral Transverse Sinuses (thick arrows)

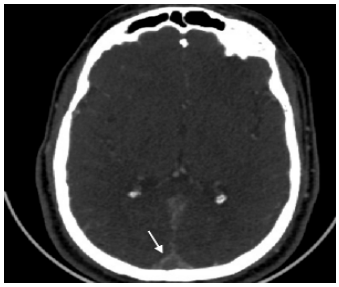

Figure 3: Axial contrast scan showing a central filling defect defect in the Superior Sagittal Sinus (thick arrow)

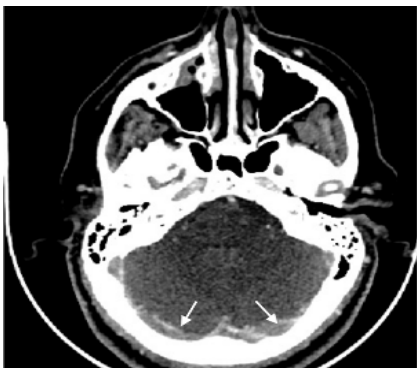

Figure 4: Axial contrast scan showing filling defects in bilateral Transverse Sinuses (thick arrows)

Baseline laboratory investigations revealed haemoglobin 18.6 g/dL, haematocrit of 53.2%, Red Blood Cell count 5.68 million/ L, White Blood Cell count 19700 cells/ L, Platelet count was 3.48 lakh/ L. Other parameters including kidney function test, liver function test and glycated haemoglobin were within normal limits.

Electrocardiography showed sinus bradycardia. Two dimensional echocardiography showed normal chamber dimensions, no regional wall abnormality, ejection fraction 62%,normal left ventricular systolic function. Cardiac biomarkers done showed CKMB <1.0 (Creatine Kinase - MB), TN -I < 0.01 (Troponin- I), BNP -88.6 (Brain Natriuretic Peptide). Chest X-ray showed normal lung fields.

On admission, Workup was done to determine a possible aetiology for hypercoagulable state- Serum Homocysteine levels 14. Anti-nuclear antibodies by Immunofluorescence-negative, Line immunoassay-23 showed borderline positivity for SS-A and Mi -2 beta. Serology for Retrovirus, Hepatitis A and Hepatitis B was negative. Anti cardiolipin IgG and IgM was negative. Lupus Anticoagulant was negative. Beta-2 microglobulin was negative. Perinuclear and Cytoplasmic Antineutrophil Cytoplasmic Antibody (ANCA) by enzyme-linked immunosorbent assay was negative. Erythropoietin - 7.25. JAK 2-V617F mutation was negative. Bone Marrow examination done showed erythroid hyperplasia. Thrombophilia panel was negative for Protein C, Protein S and Factor V. HLA B51 was sent in in view of borderline positivity for SS-A and Mi -2 beta in concurrence with Rheumatology department which was negative.

Patient was treated with Inj. Unfractionated Heparin, Inj. Levetiracetam, Inj. Thiamine and anti-oedema measures in the form of Hypertonic saline and Acetazolamide. In view of polycythaemia, patient underwent venesection twice during hospital stay.

Ophthalmology opinion was obtained in view of gaze restriction with blurring of vision and found the presence of bilateral papilledema and need of optic nerve fenestration if symptoms worsen over the period of time. During the course in the hospital, vision worsened to inability to perceive light. Ophthalmology review obtained and found the presence of fulminant papilledema with post papilledema optic atrophy. Optic Coherence Tomography Retinal Nerve Fibre Layer was done which showed peripapillary oedema and Optic Coherence Tomography Ganglion Cell Layer was within normal limits.

Repeat neuroimaging done during stay in hospital showed reduced flow related signal intensities seen involving superior sagittal sinus, straight sinus and bilateral transverse, sigmoid sinuses-corresponding to the region of old cerebral venous thrombosis however faint flow related signal intensities are present along the dural venous sinuses-likely due to recanalization. Optic nerve sheath thickening and posterior sclera flattening was noted on bilateral aspect.

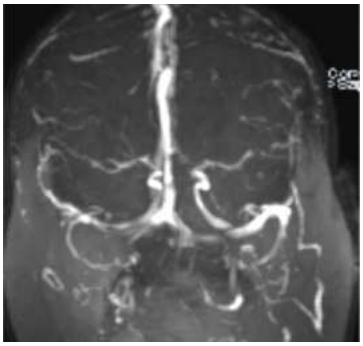

Figure 5: Reduced flow related signal intensities seen involving Superior Sagittal Sinus, Straight Sinus and Bilateral Transverse, Sigmoid Sinuses---corresponding to the region of old CVT, however faint flow related signal intensities are present along the dural venous sinuses.

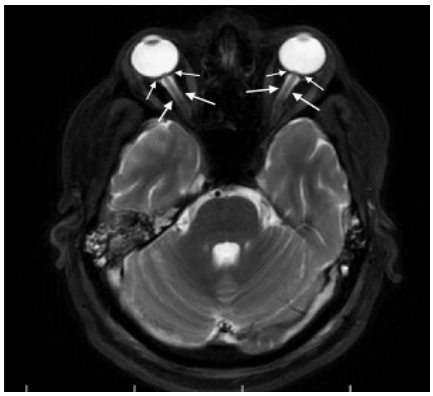

Figure 6: Axial T2 weighted MRI showing flattening of bilateral posterior Sclera (thin arrows) and Optic Nerve Sheath thickening (thick arrows) suggestive of raised Intracranial Pressure Anti-oedema measures were up titrated. Pulsing of steroids was initiated. Neurosurgery opinion was obtained and guarded lumbar puncture was done, 30 ml of cerebrospinal fluid was removed and with an opening of more than 30cm H20. Patient was taken up for ventriculo-peritoneal shunting under department of Neurosurgery.

Patient had no further deterioration from his baseline neurological status, gradually tapered off hypertonic saline and was discharged on anticoagulation in the form of Rivaroxaban, T.Levitiracetam and T.Acetazolamide. Vision gradually improved to perception of light in both eyes.

DISCUSSION

With an incidence rate of about 0.2-0.5 per 100,000 population per year, CVT is much less common than arterial stroke and represents no more than 0.5% of all strokes [4]. The clinical course of CVT varies widely, from full recovery to chronic disability-e.g., hemiparesis-or even death in fatal cases [5]. In spite of the progress made in imaging and treatment, the multifactorial aetiology of CVT renders it challenging to define precipitators of long-term prognosis clearly, which are still ill-defined.

CVT may be caused by many factors, and in developed nations, about 80-85% of cases have an identifiable underlying direct cause or risk factor. In individuals with risk factors, precipitating events such as childbirth, dehydration, infection, or trauma can trigger CVT [5]. While CVST is most

commonly associated with inherited thrombophilia, autoimmune conditions, malignancies, and endocrinological causes, it can also arise as a consequence of acquired illnesses predisposing to hypercoagulability. Lifestyle factors like cigarette smoking, resulting in secondary polycythaemia, are less commonly described but can be a major source of thrombotic risk [4].

The underlying mechanisms in the patients with cerebral venous thrombosis often involve a hypercoagulable state, reduced fibrinolysis, impaired blood flow, endothelial damage, and other unexplained factors. Polycythaemia is one among the hypercoagulable states. An increase in haemoglobin level, or polycythaemia, may be caused by a reduction in plasma volume or an increase in red cell mass [6]. Thrombosis is a sinister complication of polycythaemia and is the cause of death in 8.3% of patients as reported by Ferro et al [7].

Based on the World Health Organization (WHO) 2016 criteria, a diagnosis of polycythaemia vera necessitates a B-haemoglobin and haematocrit cut-offs of 16.5 g/ dL and 49% in men and 16.0 g/dL and 48% in women, respectively [7].

It can be classified as primary and secondary where in primary polycythaemia, increased RBC production occurs independently of erythropoietin levels as in the case of myeloproliferative neoplasms, as in polycythaemia vera. Secondary polycythaemia vera occurs when RBC production is induced by increased levels of circulating erythropoietin [7].

Several aetiologies lead to secondary polycythaemia [7]. Chronic hypoxia is one of the more important causes of the same. It is usually believed that secondary polycythaemia is a non-malignant disease and rates of thrombotic were lower than in myeloproliferative neoplasms [6].

Erythropoietin, released when oxygen-deprived blood flows past the kidney, increases the number of erythrocytes and helps the body cope with acute hypoxia. But persistent hypoxia causes an overabundance of erythrocytes, which results in secondary polycythaemia [2] .

This leads to pooling of blood which leads to increased viscosity and eventually thrombosis. Pressure gradually builds in the venous system and thus decreasing perfusion leading to cerebral oedema. Increased intracranial pressure results from impaired CSF absorption caused by cerebral sinus thrombosis leading to haemorrhage and cerebral oedema [6].

Smokers' polycythaemia is a hybrid type with features of relative polycythaemia (from reduced plasma volume) and secondary polycythaemia (secondary to chronic hypoxemia from carbon monoxide [CO] in cigarette smoke) [7].

Viscosity is raised non-linearly with haematocrit so that at high levels of haematocrit, small rises produce proportionally large increases in viscosity. This produces a threshold beyond which there is an abrupt increase in the risk of vaso-occlusion and stroke. In smoker's polycythaemia, the optimal haematocrit is less well established, as erythrocytosis can be a hypoxemic response [7]. Additionally, the results for JAK2 mutation may be negative but primary polycythaemia cannot be excluded since 20% of polycythaemia vera cases have no JAK2 mutation and normal erythropoietin levels [6].

Smoker's polycythaemia manifesting as CVT is rare, and there is limited evidence for such a connection. Diagnosis of Smoker's polycythaemia is made following exclusion of other aetiologies for primary polycythaemia, including JAK2 mutation and erythropoietin level [6].

CVT has a good prognosis with early diagnosis and management. There are, however, bad outcomes ; factors which include high age, altered mentation, focal neurological deficit, frequent seizure, and haemorrhagic infarct. Trans tentorial herniation is the most frequent cause of death. Endovascular therapy is quite safe and may be attempted in severe cases that do not respond to anticoagulation. However, impending herniation is not aided by endovascular thrombolysis and needs surgery [6].

Occasionally, cerebral venous sinus thrombosis advances to a highly elevated intracranial pressure resulting in papilledema and visual disturbances. Neurosurgical procedure in the shape of sequential drainage through repeated lumbar punctures or then insertion of a lumbo-peritoneal or ventriculo-peritoneal shunt must be done. A shunt insertion in a patient with severe papilledema, especially with superior sagittal sinus thrombosis can stop disease progression, save vision and aid re-canalisation. This spares multiple lumbar punctures and reduces the risk of major visual complications in patients who do not follow up regularly [8-9].

CONCLUSIONS

Cerebral venous thrombosis (CVT) is an uncommon but dangerous condition with varied clinical presentation and aetiology. Although polycythaemia vera is a classical prothrombotic condition, secondary causes like smoker's polycythaemia are less commonly involved. Smoker's polycythaemia due to coexistence of hypoxia-induced erythrocytosis and haemoconcentration raises blood viscosity and renders it prone to thrombosis. Though the combination of smoker's polycythaemia with CVT is rare and poorly documented, the case reinforces the requirement of increased clinical suspicion in smokers with neurological manifestations. Exclusion of primary polycythaemia by negative JAK2 mutation and normal erythropoietin is necessary for diagnosis. Early diagnosis and quick intervention continue to be important in minimizing morbidity and mortality from CVT, particularly in unusual or unsuspected risk contexts such as smoker's polycythaemia.

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