STUDY OF CLINICAL PROFILE OF CEREBRAL VENOUS SINUS THROMBOSIS

Manavalla Subrahmanyam[1], Y. Ramesh Naidu[2], V. Satya Prasad[3]

[1]Associate Professor, Department of Medicine, Rangaraya Medical College.
[2]Associate Professor, Department of Medicine, Rangaraya Medical College.
[3]Associate Professor, Department of Medicine, Rangaraya Medical College.

ABSTRACT: The syndrome of intracranial venous sinus thrombosis termed as cerebral venous thrombosis is a distinctive cause of cerebrovascular disease in the young. CVT has been diagnosed almost exclusively at autopsy. However, with the advent of modern neuroimaging techniques, the quantum of CVT cases being diagnosed has increased significantly when compared to previous years. The annual incidence is currently estimated to be 3-4 cases for one million people. It accounts for 10% to 20% of the etiology of young stroke in India.[1] CVT is now typically recognized as a disorder with various clinical presentations and usually favorable outcome. Magnetic resonance imaging and magnetic resonance angiography are the best diagnostic methods available for diagnosis of CVT, and heparin is the first line treatment. But as the symptoms, modes of onset, and neuroimaging methods are diverse, the diagnosis of CVT is commonly overlooked. Pathological hallmark of CVT is hemorrhagic infarction. CVT is primarily a disease of a young man, can present in protean ways with a wide spectrum of clinical manifestations. These include headache, altered sensorium, seizures, focal neurological deficits, papilledema and cranial nerve palsies. The commonest dural venous sinuses involved are superior sagittal sinus and transverse sinus. Nearly 20% of cases of CVT are idiopathic in origin. However, in the Asian Studies, infectious puerperium seems to be the commonest cause of CVST. Though stroke due to arterial thrombosis is more common, cerebral venous sinus thrombosis especially in young strokes. The clinical and neurological presentation can be variable, hence there needs to be a high index of suspicion for venous sinus thrombosis in order to diagnose this entity clinically. There is a wide spectrum of underlying causes of this condition. The prognosis is good, especially when the diagnosis is prompt and treatment initiated. The aim of this study is to study the clinical profile of cerebral venous sinus thrombosis, to study the etiology factors of cerebral venous sinus thrombosis, to correlate the severity and clinical presentation with imaging studies to study the outcome at discharge and at follow-up if possible.

KEYWORDS: Thrombosis, Infarction, CVST, MRI, CT, Headache, Seizures, Heparin.

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INTRODUCTION: The clinical spectrum of CVST closely mimics that of idiopathic intracranial hypertension (IIH). IIH is mainly a diagnosis of exclusion based on Dandy's criteria, presence of elevated intracranial pressure (ICP) on lumbar puncture, normal cerebral spinal fluid (CSF) biochemistry and microbiology, no localizing sign with the exception of abducens nerve palsy and normal neuroimaging as depicted by computed tomography (CT) scan. Since Dandy's criteria were formulated prior to the MRI era, CT scan alone may be an insufficient tool for accurate diagnosis of IIH. MRI along with MRV wherever necessary should be the modality of neuroimaging for accurate diagnosis.

Risk factors for cerebral venous sinus thrombosis (CVST) may not be apparent in all the cases, hence it is difficult to exclude CVST clinically in these patients. Magnetic resonance imaging (MRI) in combination with Magnetic Resonance Venography (MRV) is recommended to correctly diagnose CVST in these patients.

We report the rate of occurrence of CVST in patients with presumed IIH as well as the associated risk factor profile, which prompted subsequent MRV.

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Corresponding Author:
Dr. Manavalla Subrahmanyam,
B-207, Jeevan Visakha Apts,
M. M.T. C. Colony, Vizag.
E-mail: smanavalla@gmail.com
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MATERIALS AND METHODS: We have done a prospective observational study and data was collected from January 2013 to April 2015. Study population consisted of patients with cerebral venous sinus thrombosis satisfying the inclusion criteria coming to the outpatient department as well as those admitted in medical and neurology wards during study period. Inclusion Criteria: Any patient admitted or attended OPD with the diagnosis of cerebral venous sinus thrombosis proved on CT or MRI, presence of clinical features suggestive of CVT and confirmed by neuroimaging findings diagnostic of CVT. Age more than 16 years. Diagnostic Criteria: Neuroimaging findings used for diagnosis of CVT were based on either presence of direct signs on CT brain or classical features of CVT on MRI brain or MRV brain. Exclusion Criteria: CVT secondary to trauma/injury, neurosurgical procedures. Methods of Collection of Data: Patients with CVT satisfying inclusion criteria were enrolled for the study with consent, detailed history of etiology including obstetric history is

taken. After the history patients were subjected to general examination which included pulse, blood pressure, respiratory rate, temperature, pallor and icterus, raised ICT, edema, thrombosis at any other side evidence of other comorbid conditions like malignancies, vasculitis, and signs of dehydration. A detailed neurological examination, investigation such as CT, MRI/MRV are done and diagnosis is confirmed based on clinical features and investigations. Apart from these routine investigations such as Haemogram, LFT, RFT, Blood sugar levels, ECG, Chest x-ray, HIV, HBsAg, CSF analysis, B12/homocysteine levels, APLA profile are also done. Further workup such as protein C/S deficiency, Antithrombin III deficiency, Factor V Leiden mutation, Prothrombin gene mutation were done after a 3-6 month followup.

OBSERVATIONS: In present study, 50 patients with cerebral venous thrombosis satisfying the inclusion criteria were studied. The observations made in the study are presented below with an analysis of the same. The study population consists of 24 females (48%) and 26 males (52%). Thus gender distribution is almost equal in our study. Mean age of presentation was 34.7+/-10.06 years, maximum incidence was amongst 21-40 years. In which maximum cases in males is in the age group of 31-40 years and in females were in the age group of 21-30 years. Mean age of presentation for males and females is 38.5, 30.62 respectively.

Clinical profile of CVT (Table 1.1). Commonest presentation was headache (88%) followed by altered sensorium (60%), seizures (56%), visual deficit (42%), coma/impaired consciousness (22%). Papilledema was an important clinical sign present in 68% of patients. However, no statistically significant correlation could be found between clinical presentation and MRI findings. Out of the patients with focal neuro deficit 11 had hemiparesis and 4 had monoparesis. Patients with death as outcome had extensive hemorrhagic infarct and had early seizures, coma and papilledema (raised ICT) as clinical manifestations. Majority of the patients had more than one sinus involvement (88%). Commonest involved sinuses are transverse sinus (72%) followed by superior sagittal sinus (60%), and sigmoid sinus (46%). Cortical veins were found to be involved in 16% of the patients. Puerperal CVST showed predominant involvement of superior sagittal sinuses. Etiology of CVT (Table 1.2). The disease is found to be multifactorial as many patients had more than one etiology (22 patients) and lesser patients had only one etiology (21 patients), most common combination being hyperhomocysteinemia and dehydration; 4 patients had a combination of 4 etiologies. Outcome of the patients was studied at the time of discharge and on followup and classified as complete recovery (76%), morbidity (18%) and death (6%). Patients died mostly due to complications of CVST. Neuroimaging Findings: MR venography was most commonly used, CVST was predominant finding in MRI seen in 50% of the patients, 48% had infarction. Cavernous sinus thrombosis is seen in one patient with uncontrolled diabetes mellitus with mucormycosis.

Clinical profile of CVT patients (n=50)		
Clinical Feature	**No. of Patients**	**% of Patients**
Headache	44	88
Altered sensorium	30	60
Seizures	28	56
Visual deficit	21	42
Motor deficit	15	30
Impaired consciousness	11	22
Cranial nerve Palsy	7	14
Papilledema	34	68
TIA	1	2
Sensory deficit	1	2
Fever	4	8

Table 1

Etiological Finding	**No. of Patients**	**% of Patients**
Hyperhomocysteinemia	27	54
CNS Infection	5	10
OC Pills	10	20
APLA	2	4
ANA/dsDNA	2	4
Dehydration	14	28
JAK-2	1	2
HIV Infection	7	14
Alcoholism	4	8
Hypercoagulable State	3	6
Puerperium	2	4
General Infection	2	4
Idiopathic	3	6

Table 2

DISCUSSION: Cerebral venous thrombosis in recent times has been recognized as a distinctive cause of cerebrovascular disease in the young. The reported incidence of CVT in India is much higher compared to that of Western literature amounting to nearly 20% of the young strokes. Our study was conducted to study clinical profile of cerebral venous sinus thrombosis. There was an equal gender distribution in our study with ratio of 1.08:1, which was comparable to Khealani et al.,[1] and Tharaknath et al.[2] The mean age of presentation in our study population of 50 patients was 34.7+/–10.6. Maximum number of patients were in the age group of 21 to 40 years, which was in concordance to Khealani et al.,[1] and Diaf et al.,[3] (3rd to 4th decade). Mean age group of CVT was 38.5 years for males and 30.62 for females. This finding was significant as this show earlier age of presentation in women. Clinical presentation was varied. The commonest presenting symptom was headache which was recent onset (2 months), progressive, continuous, and refractory to medical treatment, increasing in intensity and when subjected to MRI brain revealed a CVST. It was observed in

most (88%) of cases followed by altered sensorium (60%) and seizures (56%), motor neuro deficit (30%) which was similar to the study done by Biousse et al.,[4] and Katrak et al.,[5] papilloedema was the most common presenting sign and was observed in 68% of patients which was in concordance to Biousse et al.,[4] and Katrak et al.,[5] Cranial nerve palsies were observed in (14%) of study patients similar to Agnello and Paciani et al.,[6] (12%). The cranial nerves that have been described to be involved are III, IV, V, VI, VII, VIII, IX, X, XI. Visual disturbances were noted in 42% of patients; 2% of patients had TIA, 2% of the patients had sensory deficit with persistent hemisensory burning pain, 8% of the patients had high-grade fever due to TB meningitis (6%) and P. falciparum (2%). The commonest cerebral venous sinus involved was transverse sinus (72%) followed by superior sagittal sinus (60%), sigmoid sinus (46%), cortical veins were involved in 16% of study patients. Majority of the patients (88%) had involvement of more than one cortical venous sinus. In our study we noted that maximum patients 25 (50%) had involvement of 2 venous sinuses; 12 patients (24%) had involvement of 3 sinuses; 3 patients (6%) had involvement of 5 sinuses; 2 patients (4%) had involvement of 4 sinuses; 1 patient (2%) had involvement of 6 sinuses and 1 patient (2%) had involvement of 7 sinuses. Transverse sinus has been reported as the commonest involved sinus in CVT (72%) followed by superior sagittal sinus (53%) by Christo et al.,[7] in their study. Similar findings were also reported by Wysokinska et al.,[8] in their study. The commonest neuroimaging modality used for diagnosis was MRI brain with MRV122. Etiological profile of CVT in our study was found to be hyperhomocysteinemia (54%), dehydration (28%), OC pills (20%), HIV positive status (14%), CNS infection (tubercular meningitis) (10%), alcoholism (8%), APLA positive state 4%, Factor V Leiden mutation 4%, Factor VIII elevation 4%, puerperium (4%), JAK-2 positive polycythemia vera 2%. Considerable proportion of patients (54%) had multifactorial etiology of CVST, no cause could be ascertained in 6% patients. The most common MRI findings was CVST without infarct followed by CVST with venous hemorrhagic infarction and cavernous sinus thrombosis; 2% which was in concordance to Khealani et al.[1] Outcome was studied at the time of discharge and follow up and was graded as complete recovery (76%), residual neuro deficit (18%) and death (6%). Complete recovery was seen in maximum number of patients. Recurrence was seen in 2 patients. On followup, both of them had underlying hypercoagulable factors. These patients are treated with a lifelong anticoagulation. This was in concordance with Middle East Study.,[9] ISCVT et al.,[10] Srinivas et al.,[11] Banerjee et al., Chopra et al.,[12] also stated that 85-90% of the patients recover completely without any residual deficit. All patients in our study were treated with anticoagulation and the cause of the disease was also treated definitively or symptomatically; 60% patients received LMWH and 40% received UFH during acute phase as an anticoagulation followed by oral anticoagulation. Symptomatic management of CVT included treatment of Seizures, Metabolic derangements, Cerebral Edema, Elevated ICT as dictated by the clinical situation. Anticonvulsant measures were given to patients having early seizures, imaging suggestive of hemorrhagic lesion with focal neuro deficit and supratentorial lesion on admission. A hemorrhagic lesion in acute brain scan is the strongest predictor of post-acute seizures; 4% required decompressive craniotomy as a measure to reduce ICT, but death supervened which was mostly due to natural course of the disease. Large hemorrhagic infarct, early seizures and deeply comatose state is an indicator of poor prognosis; 4% of our study patients had recurrence, both of them had underlying hypercoagulable states (Factor V Leiden Mutation, Factor VIII elevation) and were treated with lifelong anticoagulation.

CONCLUSIONS: The present study emphasizes that CVS is not an uncommon condition. It is an important cause of stroke, especially one of the common causes of stroke in young people. Clinical presentation is extremely varied and symptoms may evolve over hours to few weeks. Commonest age group affected is 21 to 40 years. Headache though nonspecific is the commonest presenting symptom. Other common presenting symptoms include seizures, altered sensorium, transient focal neurological deficits, and visual disturbances. Papilloedema and raised ICT is the most common presenting sign. A diagnosis of CVT should be considered in young patient presenting with the above combination of clinical features. The commonest dural venous sinus involved in our study cohort is transverse sinus followed closely by superior sagittal sinus. The most common etiological abnormalities in our study included hyperhomocysteinemia due to Vitamin B12 deficiency, Dehydration, CNS infection, intake of OC pills, Factor VIII elevation, and APLA syndrome and Factor V Leiden mutation. Though in Western countries thrombophilia was a major cause of CVST. Percentage of genetic thrombophilia was low in our study due to lack of workup for complete thrombophilia study in a resource limited setup. As a complete prothrombotic workup is expensive, it can be stratified based on common etiological states in a given population to minimize the cost. In our population homocysteine account for majority of cases could be the initial workup. For evaluation of causes of CVST, detailed clinical evaluation such as history of OC pills, fever, past history of Koch's disease, DVT elsewhere, dehydration, anemia, HIV status, signs of Vitamin deficiency, DM should be evaluated. After ruling out the above factors, it is advisable to do coagulation profile. If no cause could be found after extensive thrombophilia workup, Factor VIII levels should be done before starting OCP screening, for common prothrombotic state could prevent serious complications like CVT. For evaluation of CVST, routine CSF analysis is advisable since 5 of our patients had TB meningitis as underlying cause. Puerperal CVST was less common in our study, probable cause of which is better OBGY services, better ANC care in a big urban city. HIV status of the patient is also essential for

complete evaluation regarding etiology. Better antenatal care such as control of anemia, folic acid and B12 supplementation, control of PIH, delivery and hygienic environment has led to decrease in incidence of beautiful CBT in our study cohort; 60% patients of our study cohort were treated with LMWH, 40% were treated with UFH. This was followed by oral anticoagulation, antiedema measures, anticonvulsant measures. Complete recovery remains the rule. Patient with recurrence were treated with lifelong anticoagulation.

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