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Original Research Article

Etiology, clinical profile in cortical venous thrombosis

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ABSTRACT

Background: Cerebral venous sinus thrombosis (CVST) is increasingly recognized entity in young patients due to the widespread availability of MRI and rising clinical awareness. CVST is a multifactorial condition with a wide clinical presentation, variable etiologies and prognosis and it requires high index of suspicion for diagnosis.
Methods: It is an observational prospective study conducted in 57 patients. Patients above 12 years of age with a diagnosis of cerebral venous sinus thrombosis were included in the study to know aetiology, risk factors, clinical presentation and prognosis.
Results: Mean age for males was 40 years and for females it was 36.5 and male to female ratio was 3:2. Headache was the most common symptom (89.47%) followed by convulsions, vomiting, focal neurological deficit, altered sensorium, fever and papilloedema. Superior Sagittal Sinus was the most common sinus involved followed by transverse sinus. Common risk factors were Hyperhomocysteinemia, alcohol, tobacco, APLA syndrome. 52.63% of patients had complete neurological recovery.
Conclusions: CVST is uncommon condition and it is more common in neonates, children and females. The major risk factors for CVT in adults are prothrombotic (hypercoagulable) conditions, oral contraceptives, pregnancy and the puerperium, malignancy, infection, head injury. Headache is the most common symptom may be accompanied by focal neurologic deficits, seizures, and encephalopathy. It carries 5% mortality in the acute phase and 10% over a long-term follow up.

Keywords: Headache, Magnetic resonance imaging, Prothrombotic conditions

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is increasingly recognised entity in young patients due to the widespread availability of MRI and rising clinical awareness. CVST is a multifactorial condition with a wide clinical presentation, variable etiologies and prognosis and it requires high index of suspicion for diagnosis.

The annual incidence ranges from 0.22 to 1.57 per 100,000 and is more common in female compared to male with the ratio of 3:1. It is mainly due to pregnancy, puerperium and use of oral contraceptives. The mean age of patients with CVT was 39 years as per International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT).[1,2]

The pathogenesis of CVT remains incompletely understood because of the high variability in the anatomy of the venous system, and the paucity of experiments in animal models of CVT. However, there are at least two different mechanisms that may contribute to the clinical features of CVT. Thrombosis of cerebral veins or dural sinus obstructs blood drainage from brain tissue, leading to cerebral parenchymal lesions or dysfunction. And it

increases venous and capillary pressure with disruption of the blood-brain barrier. It is responsible for vasogenic edema, with leakage of blood plasma into the interstitial space. As intravenous pressure continues to increase, severe cerebral edema and venous haemorrhage may develop.

Occlusion of dural sinus will results in decreased cerebrospinal fluid absorption and elevated intracranial pressure. Obstruction of the venous structures results in increased venous pressure, decreased capillary perfusion pressure, and increased cerebral blood volume. Advances in understanding the pathophysiology of venous occlusion have been aided by using MRI methods, mainly diffusion-weighted MRI and perfusion-weighted MRI. These techniques have demonstrated the coexistence of both cytotoxic and vasogenic edema in patients with CVT.

The other effect of venous thrombosis is impairment of CSF absorption. Normally, CSF absorption occurs in the arachnoid granulations, which drain CSF into the superior sagittal sinus. Thrombosis of the dural sinuses leads to increased venous pressure, impaired CSF absorption, and consequently elevated intracranial pressure. Elevated intracranial pressure is more frequent with superior sagittal sinus thrombosis but may also occur with thrombosis of the jugular or lateral sinus. There are various risk factors for CVT such as age, gender, pregnancy, puerperium, OC pills, deficiency of protein S, C, anti- thrombin III.

Heparin or low molecular weight heparin (LMWH) is used for opening of sinuses or vein. Both heparin has almost same efficacy. And there is a limited data suggest that LMWH is more effective and more safe than unfractionated heparin.[3]

Endovascular treatment is another option, but its use is typically restricted to patients with a poor prognosis who have not responded to anticoagulation with heparin or LMWH. Urokinase or rt-PA may be used as direct thrombolysis to dissolve the venous clot by delivering a thrombolytic substance within the occluded sinus through an intravenous catheter. Another method involves mechanical endovascular disruption of the thrombus. But there are no randomized controlled trials have evaluated endovascular interventions for the treatment of CVT.[4-6] In view of above findings, we wanted to conduct study the aetiology and clinical profile in a patient of cortical venous thrombosis at our institute.

METHODS

It is an observational prospective study conducted at tertiary care centre in western Maharashtra. Study was conducted for 1½ years after approval of study by institutional review board. Sample size was calculated, and it was 57 taking into consideration of prevalence of CVST. End point of study was death of the patient or discharge of the patients from the hospital.

Inclusion criteria

- Admitted patients in Medical wards with a diagnosis of with CVST
- Age >12 years
- Patient and/or relative willing to give consent.

Exclusion criteria

- Patients with simultaneous arterial and venous sinus thrombosis
- Patients already started on anticoagulation
- Old cases of cerebral venous thrombosis/deep vein thrombosis.

All consecutive patients of CVST meeting inclusion and exclusion criteria were included in the study. Individual patient will be asked detailed personal demographic data (age, sex, physical activity etc.), family history of CVST and other risk factors pertaining to the study using a case record form. Detailed physical examination including Anthropometric measurements (weight, height and waist circumference) and other relevant general (vital signs) and systemic examination (RS/CVS/PA/CNS) was carried out in this study.

Investigations like Hb%, CBC, Blood sugar, kidney and liver function test, lipid profile, ECG, Chest X-ray, CT chest and/or MRI were performed in all the patients. Anti-phospholipid antibody, Protein S deficiency, Protein C deficiency, Factor V Leiden mutation, Packed cell volume, Antithrombin III deficiency, sucrose lysis test and ANCA test was performed in all the patients

Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS). Multiple logistic regression analysis done using variables such as age, gender and other risk factors. Calculations of odds ratios (ORs), relative risk ratios (RRRs) and 95% confidence intervals (CIs) for CVST with respect to risk factors was done with binary logistic regression and multinomial logistic regression.

RESULTS

Age of the patients ranges from 12-70 years. Mean age for males was 40 years and for females it was 36.5 and male to female ratio was 3:2.

Headache was the most common symptom (89.47%) and it was the only symptom in 14.03% of patients. Other sign and symptoms were convulsions (63.15%), vomiting (71.92%), focal neurological deficit (63.15%), altered sensorium (26.31%), fever (14.3%) and papilloedema (31.57%). Other clinical features are summarised in Table 1.

Table 1: Frequency of various clinical features.

Clinical feature	No. of patients N = 57	Percentage of patients
Headache	51	89.47
Vomiting	41	71.92
Convulsions	36	63.15
Focal neurological deficit	36	63.15
Giddiness	18	31.57
Papilloedema	18	31.57
Altered sensorium	15	26.31
Fever	8	14.03

Table 2: Frequency of different sinuses involved.

Venous sinus	Number of patients, N = 57	Percentage
Superior sagittal sinus + 1 or more sinus	33	57.89
Transverse sinus+ 1 or more sinus other than SSS	10	17.54
Superior sagittal sinus alone	10	17.54
Straight sinus + 1 or more sinus other than SSS or TS	3	5.26
Transverse sinus alon	1	1.75
Straight sinus alone	0	0
Sigmoid sinus alone	0	0
Inferior Sagittal Sinus alone	0	0

Table 3: Frequency of risk factors in CVST.

Risk factors	No. of patients N = 57	Percentage
Hyperhomocysteinemia	38	66.66
Tobacco only	9	15.78
Alcohol only	8	14.03
Tobacco + Alcohol	6	10.52
Alcohol + Smoking	6	10.52
Smoking only	5	8.77
Tobacco + Smoking	4	7.01
Alcohol + Tobacco+ Smoking	2	3.50
Prothrombotic conditions other than hyperhomocysteinemia	15	26.31
Others	8	14.03

Superior sagittal sinus was the most common sinus involved (80.76%) followed by transverse sinus (61.40%). Table 2 shows a frequency of different sinuses involved. Risk factors in a patient of CVST are summarised in Table 3. Prothrombotic Conditions in Patients with CVST are summarised in Table 4.

Table 4: Prothrombotic conditions in patients with CVST.

Prothrombotic condition	No. of patients n=15	Percentage
APLA syndrome	5	33.33
Protein C deficiency	3	20
Factor V leiden mutation	3	20
Protein S deficiency	2	13.33
Polycythemia vera	2	13.33
PNH	0	0
Antithrombin III deficiency	0	0
ANCA positivity	0	0

52.63% of patients had complete neurological recovery whereas 33.33% of patients had residual neurological deficits at the time of discharge.

DISCUSSION

CVTS, in recent times, has been recognized as a distinctive cause of cerebrovascular disease in the young. According to western literature, CVT constitutes 0.5% of all strokes. Hereditary thrombophilic states constitute 22.4% of all cases of CVST when compared with acquired prothrombotic state and it is 17% cases as per the I SCVT (International Study on Cerebral Venous Thrombosis) study.[1,7]

Cerebral venous thrombosis can present with a varied manifestation. Headache was the most common symptom in our study (89.47%) which is almost similar to the study by Biousse et al, (82%) and 73% in study done by Tharaknath et al.[2,8] Headache was the only symptom in 14.03% of patients in the present study and 23% in study done by Cumurciuc R, et al.[9] In the present study, convulsions were present in 63.15% of the patients, which is similar in the study conducted by Kumar S et al i.e. 69%.[10]

In the present study, there was significant correlation between convulsions at initial presentation and presence of venous infarct on imaging and also with focal neurological deficit. This observation has been confirmed in the studies by Ferro JM, et al.[11]

Altered sensorium was found to be the presenting symptom in 26.31% of patients in the present study, which is in concordance with a study published before by Bousser et al (26%), but it appears to be substantially less common as compared to other studies. Nagaraja et al reported an incidence of altered sensorium of 50%.[12,13] 31.57% of patients in the present study had papilledema which is less

than the studies done by Bousser et al in which the incidence of papilledema was 45%.[2]

Focal neurologic deficits (FND) were observed in 63.15% of patients in the present study. Study by Kumar S et al shows incidence of FND was 66%.[10] It is quite higher than other study conducted by Daif et al (27%).[13] In the present study, Superior Sagittal Sinus (SSS) was most common sinus involved. (77.19%) It is similar to the observation in the study of Daif et al. In present study haemorrhagic infarct was noted in 54.38% of patients which is quite higher than other studies.[13]

The most common risk factors were hyperhomocysteinemia (66.67%) followed by tobacco chewing (38.59%) and smoking (36.84%), but prothrombotic conditions are not too uncommon. In males the most common risk factor was hyperhomocysteinemia (74.28%) followed by alcohol consumption (51.42%). In females the most common risk factor was hyperhomocysteinemia (54.54%) followed by tobacco consumption (40.90%).[14]

In the present study 26.31% of patients had prothrombotic condition. And it was lower (15%) in the study by Deschiens MA et al. In the present study the most common inherited prothrombotic condition was Protein C deficiency and Factor V Leiden mutation (both 20%) and the most common acquired prothrombotic state was APLA syndrome present in 33.33% of all prothrombotic conditions. In the present study polycythemia vera was found in 2 patients (3.50%). Despite screening of all patients of study group no patient was found to have PNH or antithrombin III deficiency.[15,16]

In the present study, mortality was 14.03% (8 out of total 57 patients) and majority (52.63%) of the survived patients had complete recovery whereas 33.33% of patients had residual neurological deficits. The mortality rate in our study is comparable to the study by Daif et al in which mortality was 10%.[13]

CONCLUSION

Cerebral venous thrombosis (CVT) is uncommon, with an estimated incidence of <1.5 per 100,000 annually. The disorder is more common in neonates and children than in adults. And it is more common in women than men. The mean age of onset is 39 years. The major risk factors for CVT in adults are prothrombotic (hypercoagulable) conditions, oral contraceptives, pregnancy and the puerperium, malignancy, infection, head injury, and mechanical precipitants.

The clinical presentation of CVT is highly variable. The onset can be acute, subacute, or chronic. Headache is the most common symptom, occurring in 90% of patients and it may be accompanied by focal neurologic deficits, focal or generalized seizures, and encephalopathy with altered mental status or coma. Brain MRI venography is the most sensitive investigation to diagnose CVT. There is a 5% mortality in the acute phase and 10% over a long-term.

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