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A PROSPECTIVE STUDY ON CVT IN YOUNG MALES

Neurology

Dr C. Kanaga Raju M.D.,DM,Professor Of Neurology Karpagam Faculty Of Medical Sciences And Research Othakkalmandapam Coimbatore –32.

Dr.G.Shakthi Raja Guru * M.D,Asst.professor Of Medicine Government Medical College And Esi Hospital, Coimbatore *Corresponding Author

Dr. T. Ravikumar M.D.,Professor Of Medicine , Government Medical College And Esi Hospital, Coimbatore

Dr. K. Govindarajan M.D.D.M,Professor Of Neurology (rtd) Coimbatore Medical College And Hospital, Coimbatore

ABSTRACT

Background : Cerebral venous thrombosis (CVT) is one of the common causes of stroke in young people. CVT is a disease with potentially serious consequences and usually affecting young to middle-aged people. Strokes in the young account for nearly 30% of all cases of stroke in India and cerebral venous thrombosis (CVT) accounts for 10-20% of these cases Accurate and prompt diagnosis of CVT is crucial because timely and appropriate therapy can reverse the disease process and significantly reduce the risk of acute complications and long-term squelae.

CVT can be caused by a number of prothrombotic states and disorders of clotting system such as inherited causes like Protein C resistance secondary to Factor V Leiden polymorphism, Protein C and S resistance, and antithrombin III deficiency. Many other etiological factors like drugs ,infections,etc.

Aim: To analyse the clinical profile and the outcome of young males with CVT.

Methodology: This prospective study was carried out over a period of one year in the Neurology department in whom the diagnosis were confirmed by magnetic resonance imaging (MRI), MRV venogram , plain/contrast CT were included in the study. A total of 42 patients were enrolled for the study in the period of one year. The patients demographic details including the diabetic and hypertensive status along with their family history was obtained by using a detailed questionnaire.

Results: Majority of them were between the age group of 18 - 35 years. Headache was found to be the most common symptom followed by nausea vomiting and seizures. Majority of the patients with CVT had a history of alcoholism in this study. In our study exactly 33% were unknown factors, 32% Alcohol, 28% Dehydration, 7% infections.

Conclusion: . Accurate and prompt diagnosis of CVT is crucial because timely and appropriate therapy can reverse the disease process and significantly reduce the risk of acute complications and long-term sequelae.

KEYWORDS

Anticoagulation; causes; cerebral venous thrombosis; India; neuroimaging

INTRODUCTION

Cerebral venous thrombosis (CVT) is an uncommon cause of stroke with extremely varied clinical presentations, predisposing factors, imaging findings, and outcomes The first description of CVT, appearing in the French literature in 1825, was by Ribes, in a 45-year old man who died after a 6-month history of severe headache, epilepsy, and delirium.

In 1957, Padmavati *et al*., for the first time from India, reported 15 cases of CVT in puerperium in an epidemiological study evaluating the causes of hemiplegia in 44 women.

With the advent of sophisticated imaging techniques prompt diagnosis of CVT with appropriate therapy can reverse the disease process and significantly reduce the risk of acute complications and long-term sequelae.

MATERIALS AND METHODS

This prospective study was carried out over a period of one year in the Neurology departments in various tertiary care medical college hospitals in Tamil Nadu.This was a prospective, observational, and non interventional study.. The study was approved by the ethical committee.

All the patients included in the current study have documented CVT on magnetic resonance imaging (MRI) venogram. The information of all the patients fulfilling the criteria of CVT of was entered in a data entry sheet. All the patients were treated in the intensive care unit under standard guidelines and protocols. Patients with diagnosis of CVT were treated in intensive care unit. Patients with diagnosis of CVT were treated with intravenous fluids to correct dehydration, decongestive agents, anticonvulsant drugs, antibiotics, low–molecular weight heparin (LMWH) (if not contraindicated), decompressive craniotomy, methylcobalamin and folic acid supplementations, and so on.

All 42 Male patients in whom the diagnosis of CVT was confirmed by computed tomography/MRI brain venogram were included in this study. All patients underwent basic investigations, such as hemogram, electrolytes, blood sugar levels, renal function tests, and chest radiographs. Liver function tests, coagulation studies, inflammatory markers, and homocysteine levels were done in selected patients because of financial constraints.

Cerebral venous system was classified into two major groups: (1) Sagittal sinuses and cortical veins draining superficial surfaces of both cerebral hemispheres. (2) Deep system comprises lateral sinus, straight sinus, and sigmoid sinus along with draining deeper cortical veins. We excluded the trauma as a factor for development of CVT from history.

The following guidelines for CVT have been provided by the American Heart Association and the American Stroke Association[1]:

- In patients with suspected CVT, routine blood studies consisting of a complete blood count, chemistry panel, prothrombin time, and activated partial thromboplastin time should be performed.
- Screening for potential prothrombotic conditions that may predispose a person to CVT (eg, use of contraceptives, underlying inflammatory disease, infectious process) is recommended in the initial clinical assessment.
- Testing for prothrombotic conditions (including protein C, protein S,or antithrombin deficiency), antiphospholipid syndrome, prothrombin G20210A mutation, and factor V Leiden can be beneficial for the management of patients with CVT. Testing for protein C, protein S, and antithrombin deficiency is generally indicated 2-4 weeks after completion of anticoagulation. There is a very limited value of testing in the acute setting or in patients taking warfarin.
- In patients with provoked CVT (associated with a transient risk factor), vitamin K antagonists may be continued for 3-6 months, with a target international normalized ratio of 2.0-3.0.
- In patients with unprovoked CVT, vitamin K antagonists may be

continued for 6-12 months, with a target international normalized ratio of 2.0-3.0.

- For patients with recurrent CVT, venous thromboembolism (VTE) after CVT, or first CVT with severe thrombophilia (ie, homozygous prothrombin G20210A; homozygous factor V Leiden; deficiencies of protein C, protein S, or antithrombin; combined thrombophilia defects; or antiphospholipid syndrome), indefinite anticoagulation may be considered, with a target international normalized ratio of 2.0-3.0.
- For women with CVT during pregnancy, low-molecular-weight heparin (LMWH) in full anticoagulant doses should be continued throughout pregnancy, and LMWH or vitamin K antagonist with a target international normalized ratio of 2.0-3.0 should be continued for ≥6 weeks postpartum (for a total minimum duration of therapy of 6 months).
- It is reasonable to advise women with a history of CVT that future pregnancy is not contraindicated. Further investigations regarding the underlying cause and a formal consultation with a hematologist or maternal fetal medicine specialist are reasonable.
- It is reasonable to treat acute CVT during pregnancy with full-dose LMWH rather than unfractionated heparin.
- For women with a history of CVT, prophylaxis with LMWH during future pregnancies and the postpartum period is reasonable.

Magnitude of the Problem in India

The literature search yielded no population-based study from India exploring the exact incidence of the disease. In the late 1970's, hospital-based series from Northern India documented CVT in a frequency of 4.5/1000 obstetric admissions.

Another population-based study from Southern India in the late 1960's found that 25% of stroke patients were less than (<) 40 years of age and were primarily young women having a CVT that had occurred in the postpartum stage.

Banerjee *et al.*, in an autopsy series in late 1980's found that CVT accounted for almost 10% of all strokes in India. In a hospital-based study from South India in the 1980's, 15% of strokes were in individuals <40 years of age and CVT accounted for 15-20% of these cases. In a prospective hospital-based study, Dr Govindarajan and Dr Ravikumar evaluated 102 cases of CVT in pregnancy and puerperium,in this study, approximately 25% of young patients hospitalized with a stroke had CVT as the etiological factor and pregnancy induced hypertension and or pre existing hypertension as co factor.

It has been thought that the incidence of CVT may be more in India compared to the western countries. This was probably due to the reporting of many large series of puerperal CVT from India in the 70's and 80's. [2] But, due to the lack of any population-based study or nationwide multicentric hospitajl-based studies, the exact incidence of CVT in India is still not known and also the incidence of CVT in males has less data.

Etiology

Etiological factors are usually divided into acquired risks (e.g. surgery, trauma, pregnancy, puerperium, antiphospholipid syndrome, cancer, exogenous hormones) and genetic risks (inherited thrombophilia). Drugs like oral contraceptives (OCs), steroids, hormone replacement therapy, and oncological treatments have been implicated in the causation of CVT. In tropical countires like india dehydration ,alcoholism and infections play a major role.

The most common risk factor identified for CVT throughout the world is often a prothrombotic condition. In the ISCVT cohort, a prothrombotic condition was found in 34% of all patients, and a genetic prothrombotic condition was found in 22% of all patients. [1]

Almost all the large series from the western literature have a large proportion of patients having a prothrombotic condition as a risk factor

Most of the earlier published studies from India did not have information regarding these inherited prothrombotic states due to lack of laboratory facilities and resources to conduct these tests. But in recent times, Pai *et al.* recruited 612 consecutive patients from various hospitals of Bombay over a period of 9 years and tested them for the common thrombophilia markers (protein C [PC], protein S, antithrombin and factor V Leiden [FVL] mutation).

18% of the patients were positive for the thrombophilia markers studied. PC deficiency was the most common thrombophilia marker followed by a deficiency of protein S, FVL mutation, and AT deficiency

Pai *et al*. reported associated tuberculosis as an etiological factor for CVT in 14.3% of patients. . The postulated mechanisms of CVT in tuberculosis are: Endothelial injury due to the inflammatory response, sluggish venous flow, increased platelet aggregation and release of procoagulant factors.

Despite the continuous description of new causes, in about 30% of patients, no etiology can be found, therefore, the search for an etiology remains a difficult problem in CVT. It requires an extensive initial workup and when no cause is found, a long term follow-up with repeated investigations.

Many causative conditions have been described in cerebral venous thrombosis (CVT). These may be seen alone or in combination. For example, a prothrombin gene mutation in association with oral contraceptive use raises the odds ratio for developing CVT.Rarely, sphenoid sinusitis may be associated with cavernous sinus thrombosis.
Many medical conditions have been associated with CVT. For example, hypercoagulable states associated with the antiphospholipid syndrome, protein S and C deficiencies, antithrombin III deficiency, lupus anticoagulant, and the Leiden factor V mutation may result in CVT. Pregnancy also is associated with a hypercoagulable tendency. Malignancies may be associated with hypercoagulable states as well, and therefore may be risk factors.

Isolated cortical venous thrombosis has been associated with intracranial hypotension syndrome, but only rarely. In a study, Schievink and Maya found that CVT was present in only 3 (2.1%) out of 141 patients with spontaneous intracranial hypotension.[3]

A few cases of CVT have been reported after lumbar puncture (LP), suggesting a causal association. In a study by Canhao et al, LP induced a sustained decrease in mean blood flow velocity (BFV) in the straight sinus (SS), suggesting that the decrease in venous blood flow is a possible mechanism contributing to the occurrence of CVT.

Inflammatory bowel diseases, such as Crohn disease and ulcerative colitis, are described as risk factors for venous thrombosis [5] .Hyperhomocysteinemia is a strong and independent risk factor for CVT, being present in 27-43% of patients with CVT but in only 8-10% of the general population. Hyperhomocysteinemia is a strong and independent risk factor for CVT, being present in 27-43% of patients with CVT but in only 8-10% of the general population; whether treatment with folate, pyridoxine, and/or cobalamin reduces the risk of CVT is unclear.

Clinical findings in CVT fall into two major categories:

Those related to increased intracranial pressure due to impaired venous drainage; and, those related to focal brain injury from venous ischemia/infarction or hemorrhage.

Headache is the most frequent and most of the times, the earliest symptom of CVT. In the NIVSR cohort, 88.3% patients had headache as the presenting complaint with CVT.

If the thrombosis extends to the jugular vein, the patient may develop involvement of cranial nerves IX, X, XI, and XII (jugular foramen syndrome). Cavernous sinus thrombosis may lead to III, IV, and VI cranial nerve palsies.

Seizures are far more frequently seen in CVT than in arterial stroke with a frequency of 35-50% of all patients suffering from it, with an even higher incidence in peripartum CVT (76%). [5] Kalita *et al.* conducted a retrospective study to evaluate the frequency and predicting factors responsible for seizures as the predominant presentation in patients with CVT. Of the 90 patients, 42 patients presented with seizures, of whom 10 had status epilepticus. On multivariate analysis, only the presence of a supratentorial parenchymal lesion on magnetic resonance imaging (MRI) was independently associated with a higher risk of presenting seizures. [2]

The mental status may be quite variable, with patients showing no change in alertness, developing mild confusion or progressing to coma. Earlier case series from India reported that 43% to 93% of patients had an altered sensorium at presentation., [3], .[4] Recent studies show a lower proportion of patients having changes in sensorium ,at presentation. [2]

Focal neurological deficit may occur depending on the area involved. Thus, hemiparesis may be encountered, and in some cases of sagittal sinus thrombosis, there is involvement of bilateral lower extremities. Papilledema may be seen on fundoscopy in chronic cases or those with a delayed presentation but is less common in acute cases. In the NIVSR cohort, a stroke-like presentation was present in 28.5% patients, isolated seizures in 29.4%, benign intracranial hypertension-like presentation in 18.2%, encephalopathy in 25.2%, and psychosis was observed in 1.8% patients. [1]

How to Make the Diagnosis of Cerebral Venous Thrombosis?

The diagnosis of CVT is based on a high degree of clinical suspicion followed by imaging confirmation. The imaging findings of CVT can be categorized as direct, as when there is a visualization of cortical or dural sinus thrombus; or, indirect, as when there are ischemic changes related to the venous outflow disturbance.

In about one-third of cases, the CT demonstrates direct signs of CVT, which are as follows: The cord sign, usually seen on head CT with contrast, is the visualization of the hyperdense thrombosed cortical vein the dense triangle sign, seen on noncontrast head CT, is the visualization of a fresh thrombus in the posterior part of the sagittal sinus; and, the most frequent direct sign is the "empty triangle" or delta sign, seen as non-filling of the confluence of sinuses after contrast injection. In the NIVSR cohort, only 11.2% patients demonstrated an empty delta sign.

More frequently, the contrast-enhanced CT scan reveals indirect signs such as local or generalized brain swelling, contrast enhancement of the falx and tentorium, and localized hypodense or hyperdense areas reflecting hemorrhagic transformation.

In a suspicious case, the diagnosis may be confirmed by more sensitive imaging techniques such as an MRI and MRV. The conventional MR sequences show patent dural sinuses as flow voids. The coronal images are best suited for visualization of the superior sagittal, transverse, and sigmoid sinuses. A plane parallel to the dural sinus offers better depiction of the extent of the thrombus within them. In the acute stage, the thrombus may be seen as iso-intense on T1W but hypointense on T2W MRI sequences. In such a situation, either a gradient sequence or an MRV is warranted, the latter being the investigation of choice.

The vascular imaging includes MRV and conventional angiography. MRV is most commonly used to confirm the diagnosis of CVT in a suspected case especially in the acute stage, as direct visualization of the thrombus may be difficult on MR (as it is isointense on T2). Contrast MRV is preferred although MRV may also be performed without the use of a contrast agent using the time-of-flight technique or the phase contrast technique. Because these techniques use MR flow phenomena for contrast generation, they are subject to flow-related image artifacts. depicts a case of superior sagittal sinus thrombosis.

A 64-slice multi-detector row CT and CT venogram have been used in some centers for the diagnosis of venous sinus thrombosis and has been found to be 100% sensitive and specific. Cerebral catheter angiography is rarely used for the diagnosis of CVT because of the invasive nature of this diagnostic modality; although conventional angiography best demonstrates the dynamics of the intracranial circulation. The venous collateral circulation is also best appreciated on the conventional angiography. Dilated tortuous collateral veins develop in the setting of chronic venous hypertension related to the veno-occlusive disease. This constellation of findings on the venous phase of the angiogram has been referred to as the "pseudophlebitic pattern." The ability to develop venous collateral circulation accounts for the variable clinical presentations and the unpredictable outcome of CVT.

According to the Indian guidelines for stroke management, patients suspected to be having a stroke due to CVT should be investigated by MRI/MRV/CTV only if the CVT is not diagnosed by a CT scan. [2] In a statement issued by the American Heart Association/American Stroke Association in 2011, a negative plain CT or MRI does not rule out the presence of a CVT. They recommend a venographic study (either CTV or MRV) in suspected CVT if the plain CT or MRI is negative. The venography was also recommended in order to define the extent of CVT if the plain CT or MRI suggests the presence of a CVT (Class I; Level of Evidence C). [1]

Laboratory Tests

There is no confirmatory laboratory test that can confidently rule out CVT in the acute phase of the disease. Routine blood studies consisting of a complete blood count, chemistry panel, prothrombin time, and activated partial thromboplastin time (PTT) are recommended for patients with suspected CVT. The results from these tests may suggest the presence of conditions that contribute to the development of CVT such as an underlying hypercoagulable state, an infection, or an inflammatory process. Screening for potential prothrombotic conditions that may predispose to CVT is recommended

The D-dimer measurement is a diagnostic screening tool for the assessment of patients with possible CVT. However, a normal D-dimer value cannot exclude the presence of CVT, especially in patients with isolated headache or with thrombosis of a single sinus.

Anticoagulation

The immediate goals of anticoagulant (AC) therapy are to recanalize the occluded sinus, prevent propagation of the thrombus and to treat the underlying prothrombotic state. Heparin is the obvious therapy for any venous thrombosis yet AC therapy has been controversial, due to the high incidence of spontaneous hemorrhagic infarcts in patients with CVT.

Guidelines from India, Europe and America recommend that patients with CVT without contraindications for AC should be treated either with activated partial thromboplastin time adjusted IV heparin or body-weight-adjusted LMWH. The presence of concomitant intra-cranial hemorrhage related to CVT is not a contraindication for heparin therapy. The optimal duration of heparin is not established. As for deep vein thrombosis of the leg, after a few days of heparin, once the patient is stabilized, oral ACs are started to reduce the risk of heparin-induced thrombocytopenia. Warfarin is usually adjusted to obtain an International Normalized Ratio between 2 and 3. The usually recommended duration of treatment is 3-6 months, particularly when there is a known acute cause for CVT, such as minor head trauma, postpartum state, or local infection. In contrast, prolonged treatment is warranted whenever there is a continuing risk of thrombosis, such as lengthy immobilization, malignant disease, inflammatory disease such as systemic lupus erythematosus or Behcet's disease, inherited thrombophilia .

TABLE 1 : Age wise distribution of the study population

Age group	Frequency	Percentage
18 – 20	01	2%
21 – 23	15	37%
24 – 26	19	45%
27 – 29	06	14.%
>29	01	2%
Total	42	100%

Mean age 23.5±3.5

TABLE 2 : Symptom wise distribution of the study population

Symptom (n=42 Percentage	Number	Percentage
Headache	35	84%
Seizures	24	59%
Neurological deficit	10	26%
Nausea/Vomitting	29	70%
Visual disburbance/papilloedema	09	23%

TABLE 3:MRI findings of the patients with CVT

MRI findings	Frequency	Percentage
Hemorrhagic Infarct	26	60%
Non Hemorrhagic Infarct	12	30%
ICH	04	10%
Unilateral lesion	28	67%
Bilateral lesion	12	33%

DISCUSSION

CVST is reported to be more common in developing countries, and has been linked to pregnancy, multiparity, dehydration, and infection. Developments in imaging, diagnostic laboratory investigations, and genetics have provided valuable information about risk factors and clinical spectrum of CVST. We compared our experience of CVT, highlighting its diverse clinical presentations, predisposing factors, and neuroimaging with other studies from India and abroad. In our study exactly 33% unknown factors, 32% alcohol, 28% Dehydration, 7% infections. Around 96% of age group in our study presents in third

decade .Headache is the predominant presenting feature followed by nausea and vomiting then seizures.60 % of our study population showed Hemorrahagic Infarct in MRI findings . Asymptomatic CVT with hypoplasia and aplasia of venous sinus are also seen during routine radiological investigations for other symptoms. Heparin bridge while initiating warfarin is recommended for two reasons, the delayed onset of action of warfarin and the initial prothrombotic state created by warfarin use due to decrease in natural anticoagulants. Rivaroxaban with its factor Xa inhibition and rapidonset of action may be initiated directly. However taking food with rivaroxaban is essential for the optimal absorption of the drug . In clinically stable CVT rivaroxaban is safe and effective and may be used without previous heparin therapy. This can shorten the duration of hospitalization thereby decreasing the costs of treatment. [6]

CONCLUSION

We concluded that the treatment of CVT has to be aggressive as morbidity and mortality is relatively minimal. The present study revealed significant number of patients affected by CVST in 2nd and 3rd decade of life, Most common sinus affected in male was sigmoid and transverse sinus thrombosis. Sagittal sinus was most commonly affected in female population. Affections of sigmoid, transverse, and multiple sinus thrombosis had more mortality and morbidity with longer duration of stay and residual significant neurodeficit. Headache and vomiting were the most common presenting symptoms and next was seizure. Significant proportion of individual with CVT had hyperhomocysteinemia. Alcoholism,Acute gastro-enteritis, fluid loss, and presence of infection were the precipitating factors for development of CVT.

REFERENCES

1. Saposnik G, Barinagarrementeria F, Brown RD, Jr, Bushnell CD, Cucchiara B, Cushman M, et al. American Heart Association Stroke Council and the Council on Epidemiology and Prevention. Diagnosis and management of cerebral venous thrombosis: A statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2011;42:1158–92.
2. Prakash C, Bansal BC. Cerebral venous thrombosis. J Indian Acad Clin Med. 2000;5:55–61.
3. Nagaraja D, Kruthika-Vinod TP, Christopher R. The prothrombin gene G20210A variant and puerperal cerebral venous and sinus thrombosis in South Indian women. J Clin Neurosci. 2007;14:635–8.
4. Pfefferkorn T, Crassard I, Linn J, Dichgans M, Boukobza M, Bousser MG. Clinical features, course and outcome in deep cerebral venous system thrombosis: An analysis of 32 cases. J Neurol. 2009;256:1839–45.
5 Dr T Ravikumar , Dr J A vasanthakumar , Dr K Govindarajan , Dr Chetan Bharadwaj , Dr P Prasannakumar , 6Dr Shankar R . Association of Hypertension and Cerebral Venous Thrombosis amongthe Women in the Puerperal Period – A Prospective Study Indian Journal of Basic and Applied Medical Research; March 2016: Vol.-5, Issue- 2, P. 472-480
6 Dr Rajesh Shankar Iyer, Dr Ramakrishnan TCR, Dr Saleem Akhtar, Dr Karunakaran Dr Muthukalathi, Dr Praveen Kumar, Dr Kumar Muthukumar. Is it safe to treat cerebral venous thrombosis with oral rivaroxaban without heparin? A preliminary study from 20 patients. Clinical Neurology and Neurosurgery 175 (2018) 108–111.