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Review Article

Cerebral venous thrombosis: a changing landscape

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ABSTRACT

Cerebral venous thrombosis (CVT) is an uncommon cause of stroke and is mainly a disease of the young. The aims of the study were to summarize the change in the clinical profile of CVT and provide an update regarding the current management of the same. A literature search was conducted using Pubmed and Google scholar using the desired terms. Studies were analysed and review was formulated. The median age of CVT in most studies was 32 years. There has been a shift from female preponderence to equal gender predilection. Several studies are confirming the efficacy of D-dimer as a diagnostic marker of CVT. Newer oral anticoagulants have been found to be as efficient as warfarin. There have been several cases of CVT reported in association with COVID-19. This review confirmed the traditional understanding of age and risk factors of CVT. It also noted a change from the female preponderence. NOACS are emerging as the preferred drug for the long-term management of CVT.

Keywords: Cerebral venous thrombosis, Clinical profile, Biomarkers, NOACS

INTRODUCTION

Cerebral venous thrombosis (CVT) is a disease mainly seen in young adults which occurs secondary to occlusion in the venous drainage of the brain.1 Despite the fact that CVT contributes to less than 1% of all strokes its can be debilitating, with significant morbidity and mortality, especially if detected late.2 The clinical manifestations are highly heterogeneous and range from florid symptoms such as hemiplegia and generalized tonic clonic seizures to persistent and non-specific headache.3

While traditionally described in post-partum women, there has been a change in the clinical profile of patients with some studies showing male preponderance as compared to previous documented literature in recent times. Additionally, with the emergence of COVID the incidence of CVT has increased secondary to the procoagulant nature of the disease.4,5

The aim of the study was to provide an update on the current clinical profile of CVT in our country.

METHODS

This article was intended to be a review of the current clinical profile of CVT in our country and an update on recent therapeutic strategies. Literature searches were conducted in Pubmed, google scholar combining the terms cerebral venous thrombosis, epidemiology clinical profile and management.

DISCUSSION

Anatomy and pathophysiology

The venous system of the brain runs in the subarachnoid space and does not strictly follow the arterial pattern.

The superficial system consists of three groups i.e.; superior, middle and inferior cerebral signs, based on the area they drain while the deep system consists of the deep middle cerebral and internal cerebral vein. In brief, the superficial and deep veins progressively drain into the transverse, sigmoid sinus and ends as the internal jugular vein.1,2
CVT is divided into dural venous sinus thrombosis, deep vein thrombosis and superficial or cortical vein thrombosis. Like thrombosis elsewhere in the body, they are caused by any disruption in the Virchow’s triad i.e.; changes in blood stasis, vessel wall abnormalities or the composition of the blood. Obstruction of venous vessels induces increased venous pressure, vasogenic edema, reduced capillary perfusion leading to decrease in cerebral perfusion and tissue infarction. 

Clinical profile

CVT is a disease with a highly variable clinical presentation. CVT is a disease of the young with a global prevalence of 32 years. Most studies show a strict female preponderance. However a recent study conducted in 2020 India showed an equal gender distribution. This study concluded that CVT is a disease that affects both sexes equally in contrast to the previous understanding of the disease. Additionally, two other studies conducted in India showed a male preponderance with a male: female ratio of 1.1:7:1 and 1.5:1 respectively. 

Most studies report headache among their patients with an average range of 80-96%. The second common presenting symptom is nausea and vomiting. Studies have shown that patients with CVT can present with isolated headache without features of raised ICT. In most studies the location of the headache is holocranial in location and the nature is throbbing. Hence in any young patient, irrespective of gender, if there is a new onset of headache, we must perform an active survey for other clinical signs of CVT.

Seizures are another clinical presentation of CVT and incidence is around 48%. CVT can be associated with status epilepticus and usually likelihood of seizures increase with the presence of a neuro-parenchymal lesion, more so in supratentorial locations.

The most common neurological deficit observed in patients with CVT is motor weakness, however rarely sensory symptoms have also been documented. Very rarely patients can present with TIA like features as well.

Additionally, patients can present with a diffuse alteration in sensorium in the absence of seizures in 21% of the cases, mimicking an acute confessional state. This is a scenario more commonly encountered in elderly patients with CVT.

Risk factors

Historically the most common risk factors associated with CVT were anemia and the post-partum state. A study that included 465 women found that 65% of cases had some form of risk factors like pregnancy, puerperium, oral contraceptive pill (OCP) use, and hormonal replacement therapy associated with CVT. Hyperhomocysteinemia has also been incriminated as a risk factor and three studies conducted in India confirmed the same. This has also been noted in the context of vitamin B12 deficiency especially in alcoholics.

Other risk factors include excessive alcohol intake, dehydration, hyperglycemia, inherited prothrombotic states.

Biomarkers

A recently published study which included 383 patients CVT concluded that adding d-dimer values to a prediction model increased the likelihood of a diagnosis. Other studies on CVT have also recognized the valued of d-dimer assessment in the diagnosis of CVT. This is a significant finding since d-dimer is not an established biomarker in the diagnosis of CVT and would have tremendous value in evaluating patients with low risk headache is the sensitivity and specificity are definitely established.

Imaging

Imaging findings among CVT patients include evidence of the thrombus with or without involvement of the parenchyma. The direct signs of the thrombus include the dense clot sign, cord sign and empty delta sign along with loss of normal flow void on MRI. The parenchymal signs include evidence of venous infarction, lobar hemorrhage or diffuse cerebral edema. The MRI appearances in CVT are secondary to an increased amount of deoxyhemoglobin and methemoglobin in the thrombus in the acute and sub-acute forms respectively.

Prognosis

A study conducted in 2018 formulated a prognostic score to assess outcomes in CVT. This included size of parenchymal lesion if present, presence of bilateral Babinski’s signs, level of consciousness, involvement of the deep system and hemorrhage. Moreover, male gender also scored a point. Higher the score, poorer the prognosis. This study concluded that a score of more than 8 was associated with the worse outcomes. Other studies have also shown the that patients with deep venous thrombosis are more likely to have a poor prognosis. A multinational study including 624 patients with CVT documented a 4.3% mortality rate. This study also showed that emergent initiation of treatment in CVT is associated with better outcomes.

CVT and newer oral anticoagulants (NOACS)

The management of CVT entails anticoagulation and anti-edema measures. Traditionally warfarin has been used for the long term anticoagulation. A recently published systematic review comparing the efficacy of warfarin and newer oral anticoagulants has concluded that NOACS are as efficacious as warfarin in the management of CVT.
of drugs recruited 120 patients of CVT and concluded that both were equally effective in preventing recurrence of CVT. Hence further larger multicentric studies are required to firmly establish criteria for usage of NOACS in CVT.

**CVT and COVID-19**

With the emergence of the COVID-19 pandemic, globally there have been a number of cases of CVT being reported in these patients. The clinical profile of these patients is similar to other patients with CVT. The proposed pathophysiological mechanisms that have been proposed in addition to the procoagulant state induced by the virus include vascular endothelial dysfunction and altered flow dynamics. Additionally some cases of CVT have also been reported as part of the vaccine induced thrombotic thrombocytopenic purpura seen in association with a COVID vaccine.

**CONCLUSION**

CVT is a disease disproportionately represented among the younger population with stroke. The peculiarity about this disease is that the diagnosis is not always straight forward and often can be quite heterogenous. CVT has a favourable outcome when detected and treated early. A delay in diagnosis can be lethal or lead to a lot of co-morbidity. Since it was pre-dominantly a disease of the young, there is an additional economical strain on the patient and family in addition to the psychological and physical burden. It was hence of paramount importance to keeping a low threshold for work up in a young patient with new onset headache and a background of risk factors. Risk factors should be limited not just to the traditional ones of post-partum state and anemia, but should also focus on alcoholism, dehydration and procoagulant states. Papilledema should be considered a leading clue. Additionally, the usage of NOACS should be considered in patients.

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