ORIGINAL RESEARCH ARTICLE

Role of Magnetic Resonance Venography in Clinically Suspected Cases of Cerebral Venous Thrombosis

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A B S T R A C T

Introduction: Cerebral venous thrombosis (CVT) is the most common venous infarcts in young population, but it is completely reversible in most of the patients without any residual deficits. Initially CVT was diagnosed during post-mortem, later on it was diagnosed through Digital Subtraction Angiography (DSA) which was an invasive procedure. With the advancement in imaging techniques like screening MRI (Magnetic Resonance Imaging) brain which includes Fluid-attenuated inversion (FLAIR) sequence and Diffusion weighted Imaging (DWI) and Time of Flight (TOF), Phase Contrast (PC) sequences in MR venogram (MRV), most of the CVT cases can be diagnosed without any invasive techniques and radiation issues.

Materials and methods: 100 cases who had clinical suspicion of CVT underwent both screening MRI brain (FLAIR & DWI) and MR Venogram (MRV) of which 46 patients were diagnosed to have CVT, 42 cases were picked on routine MRV, 4 patients were diagnosed on Contrast enhanced MRI brain

Results: 46 cases out of 100 cases had CVT, of which the most common sinus to be involved in thrombosis was Superior sagittal sinus (SSS) (n=34). Venous infarcts were found in 23 cases, of which 10 cases had both superior sagittal sinus and transverse sinus thrombosis. The most common aetiology was found to be hyperhomocysteinemia in males and puerperium in females, followed by DM in both sexes. 3 patients underwent contrast enhanced MRI(CE-MRI) brain among the NON-CVT cases which turned out to be negative. Hence the sensitivity and specificity of CE-MRI brain in our study was found to be 100%.

Conclusion: TOF and PC of MRV are the most sensitive imaging sequences in diagnosing thrombosis as they have 100% and 91% sensitivity respectively and 100 % specificity. Conventional MRI brain FLAIR sequence can be strongly recommended in CVT cases to know the parenchymal changes. To diagnose venous sinus thrombosis the sensitivity of FLAIR sequence is low. If needed CE MRI brain would solve the problem in diagnostic dilemma.

Keywords: Magnetic Resonance Venography, Clinically Suspected Cases, Cerebral Venous Thrombosis

INTRODUCTION

Cerebral venous thrombosis has been documented since the early 19th century, however it still relics as a diagnostic encounter for the treating physician. In comparison to arterial stroke, cerebral venous thrombosis is unusual and often seen to occur in early age individuals. CVT can transpire at any age group ranging from infancy to old age with a female predilection particularly in the course of the puerperium phase.[1,2]

The clinical symptoms vary from acute to the chronic phase. Further, CVT causes venous infarction which is time and again multifocal as well as bilateral affecting both gray and white matter. CVT customarily manifests itself with headache, visual disturbances, seizures, papilledema, altered sensorium and focal deficits due to thrombosis of intracranial veins and sinuses instigating as raised intracranial tension besides haemorrhagic infarctions.[1,2]

CVT is one of the leading causes of mortality during the reproductive age group in the Indian population. Post-partum period shows the preponderance of cases, whereas alcoholism is a major risk aspect seen among males.[1,2]

Cerebral venous thrombosis is a moderately unusual disorder, with an estimated annual incidence of between 2-7 cases per million in the general population.[1]

As early as the 18th century, CVT was acknowledged during an autopsy consequently which was assumed to be fatal.[2] With the introduction of imaging modalities like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) and Magnetic Resonance Venography (MRV) the diagnosis of CVT has improved significantly.

Aims and objectives

- To determine the ability to detect Cerebral Venous

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Thrombosis in Time of Flight, Phase Contrast and FLAIR sequences individually and in combinations.
- To correlate the findings in MRV with FLAIR/ Diffusion weighted imaging sequences of brain.
- To correlate the extent of venous thrombosis with clinical presentation and etiology.

MATERIALS AND METHODS

It was a hospital based prospective descriptive study carried out on 100 patients who underwent MR Venogram and MRI brain (FLAIR and DWI) sequences in the department of Radio-diagnosis, M. S. Ramaiah Hospitals, Bengaluru that had suspicion of cerebral venous thrombosis during a period of 20 months from November 2018 to June 2020.

A detailed case history as well as medical history of the patient was recorded as and when possible depending on the condition of the patient. Emergency cases were dealt swiftly with utmost care to stabilize the patient's condition initially. Later, consent was obtained from the patient in respect to the participation in the study. All ethical protocols were followed as per the approval by the ethical committee.

Inclusion criteria

Patients of all ages and both sexes presenting with clinically suspected CVT who undergo MRV and MRI Brain sequences (FLAIR and DWI).

Exclusion criteria

- Known patients of previous CVT on follow up
- Any absolute contraindication for MRI
- Technically inadequate studies, hindering inappropriate data collection

All subjects underwent conventional MRI brain scan with a 1.5 Tesla, 18 channel MR Scanner (Magnetom Avanto TIM, Siemens, Erlangen, Germany) with a standard head coil. MR evaluation included screening brain sequences like FLAIR, DWI and ADC (Apparent Diffusion Coefficient) maps with MR venogram sequences like 2D TOF and 3D PC including Maximum Intensity Projection(MIP) of 2D TOF images in axial, sagittal and coronal planes.

MRI brain contrast images were obtained using Gadolinium intravenous contrast when there was doubt of CVT on routine MRV images.

Technique of examination

All subjects were screened before entry into the MRI scanning room for ferromangentic objects, cardiac pacemakers, aneurysmal clips etc.

Subjects were examined in the supine position on the MRI table for proper positioning and immobilization of the head. The standard head coil was used for the scan.

Imaging protocol and interpretations

Conventional screening MRI –These included FLAIR, DWI and ADC maps.

The images obtained were assessed to look for:

Venous sinus thrombosis

Loss of flow void within the thrombosed venous sinuses in FLAIR sequences.

Parenchymal changes

Flair

Change in signal intensity in the cerebral parenchyma due to hemorrhage or infarct or edema (vasogenic or cytotoxic edema).

DWI

To look for high signal intensity within lesion or in perilesional edema that corresponds to low signal intensity on ADC maps and the ADC values are recorded. It is mainly used to differentiate cytotoxic edema from vasogenic edema.

DWI Protocol

The diffusion measurements were done using echo planar imaging (EPI) sequence in axial plane modified by addition of bipolar gradient on both sides of the refocusing radiofrequency pulse. Three different magnitudes of diffusion encoding gradients with a b value of 0 and 1000 mm^2/sec in x, y and z direction. Post processing, ADC values were calculated automatically and expressed in $10^{-3}mm^2$/sec.

ADC values were recorded from the ADC maps by drawing the circular region of interest (ROI) manually in the region which appears more hypo-intense avoiding hemorrhagic areas, on all axial ADC maps, using the manufacturer's software and contralateral normal area. The minimum ADC values were obtained in $10^{-3}mm^2$/sec. The ROIs measurements varied from 8 to 20 mm^2.

MR Venogram

2D TOF and 3D PC images with MIP in axial, sagittal and coronal planes.

2D TOF

Loss of signal intensity or irregular signal intensity within the thrombosed sinus or vein.

3D PC

Change in signal intensity within the venous sinuses and loss of signal intensity.

When there is a suspicion of CVT on routine MRV images contrast enhanced MRI brain using non –ionic intravenous contrast gadolinium was used at the dose of 0.1mg/kg.

Before administering the contrast the patient's renal functional status any contraindication toward the contrast medium was noted. The imaging procedure was completed within 45mins to 1 hour of injection of contrast.

Contrast enhanced MRI brain

Loss of enhancement within the venous sinuses.

The entire qualitative variable was expressed in term of frequency and percentage. Sensitivity, specificity, positive predictive value and negative predictive value were calculated between MRV and MRI brain. McNemar's test was used to compare the MRV and MRI brain findings. P value <0.05 was considered statistically significant. SPSS 17 version was used for the analysis.

RESULTS

Out of 100 clinical suspicion subjects who underwent screening MRI and MRV only 46 subjects had cerebral venous thrombosis while the remaining had other causes (by ruling out the etiological causes for CVT).[Table 1]

The age range for patients with cerebral venous thrombosis in our study on MRI brain and MRV was observed to be

Clinically suspected CVT	Number of patients	Percentage (%)
Subjects with CVT	46	46%
Subjects without CVT	54	54%

Table-1: Frequency and percentages of cases with / without CVT

Age	Male	Female	Total (%)
<20 yrs	2	5	15%
21-30 yrs	11	6	37%
31-40 yrs	3	3	13%
41-50 yrs	1	5	13%
> 50 yrs	5	5	22%

Table-2: Age and Gender distribution in CVT

between 13 and 77 years.

The most common age range for presentation of cerebral venous thrombosis (CVT) in this study was 21 to 30 years (36.9%).

It was observed that among the CVT cases 22 were males (50%) and 24 were females (50%) out of 46 patients. There was no difference in the gender distribution in both CVT positive and CVT negative cases. Female patients were commonly involved in the age group < 40 years, due to use of OCP's and puerperium, however due to systemic causes there has been increased incidence of CVT in elderly age group also.

Male patients are commonly seen in the age group 21-30 years mainly due to increased influence of smoking, which is a risk factor for CVT.[Table 2]

Sequences	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value	P Value
PC	91%	100%	100%	93%	0.125
FLAIR	78%	100%	100%	84%	0.002
TOF, PC & FLAIR	78%	100%	100%	84%	0.002
The sensitivity and specificity of PC in diagnosing CVT considering TOF as gold standard as it picked up in 45 cases was calculated to be sensitivity of 91% with specificity of 100% with the P value of 0.12(not significant).					

Table-3: Sensitivity and specificity of PC, FLAIR and in Combinations in diagnosing CVT

Sinus	Frequency
Superior sagittal sinus(SSS)	34
Transverse sinus(TS)	33
Sigmoid sinus(SS)	28
Straight sinus(STS)	6
Cortical veins(CO)	4
Internal jugular vein(IJV)	10

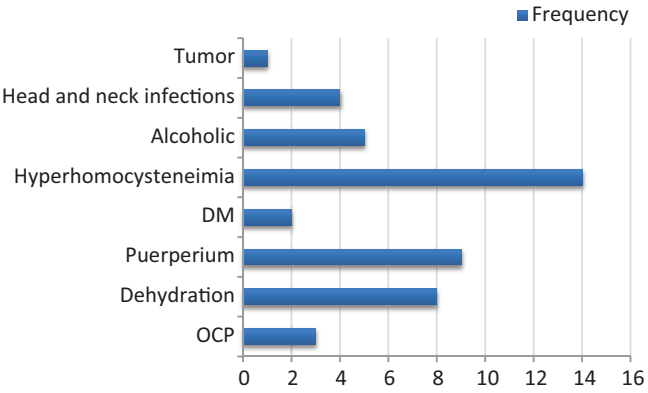
Table-4: Frequency of various venous sinuses involved in CVT

SINUSES	INFARCT +	INFARCT-
SSS	15	18
TS	15	16
SS	13	15
STS	2	4
IJV	6	4
CO	3	1
Deep cerebral vein	1	-

Table-5: Frequency of various thrombosed sinuses with/without infarct

	Infarct	No infarct
CVT Positive	23	23
CVT Negative	11	43
From the above table venous infarct was present in 23 cases and 11 cases had arterial infarct. The P value was found to 0.03(significant). Hence there is significant difference between the venous and arterial infarct in clinically suspected cases of CVT.		

Table-6: Frequency of infarct in CVT +/- cases



From the above table we have arrived at a conclusion in our study that among the CVT female patients puerperium is a major etiology followed by OCP accounting for 20 % and 7 % respectively.

Figure-1: Bar graph showing frequency of various etiologies in CVT

DISCUSSION

The verdict of CVT has customarily been made with conventional angiography (DSA).[3] Lately, MR imaging techniques have superseded DSA as the optimal technique. MR imaging with venography is currently considered as the non-invasive "gold standard" in establishing thrombosis of the cerebral venous sinuses.[2,4]

Diagnosis of CVT is challenging due to wide-range spectrum of clinical presentations, compound predisposing factors, and it distresses people of all ages. Impersonations of CVT are demonstrated as arterial stroke, tumor, encephalitis, abscess and idiopathic intracranial hypertension. Hence, diagnosis

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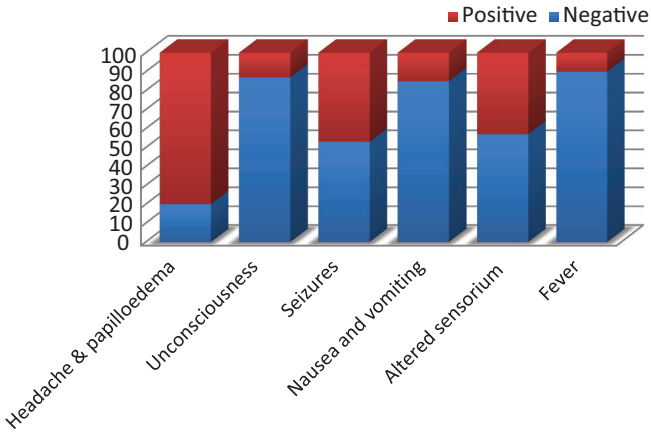
Sinuses	Frontal	Temporal	Parietal	Gangliocapsular region	Cerebellum
SSS	5	2	5	0	0
SSS+TS+SS+IJV	0	2	2	0	0
SSS+SS+TS+STS+DV	0	0	0	1	0
TS+SS	0	3	1	0	0
TS+SS+IJV	0	2	2	0	0
SS	0	1	0	0	2

Table-7: Parenchymal location with the various sinus thrombosis and extension



From the above-obtained data headache with papilloedema was the most common clinical symptom followed by seizures and altered sensorium. The least common presenting symptoms were fever and unconsciousness.

Figure-2: Bar graph showing various clinical features in CVT

is by elimination of the differential diagnosis along with supportive imaging investigations.

Imaging modalities which includes, but are not limited in the diagnosis of cerebral venous thrombosis (CVT) are DSA, CT, CTV and MRV. However, their limitations as well as diagnostic potential along with their advantages and disadvantages should always be taken into consideration.

In our study, 46 positive CVT cases and 54 cases without CVT was observed, with a female predominance by about 6%. Similarly, analysis of data across various studies showed to have more female preponderance than males.[5,6,7]

Out of 46 CVT patients, 24 patients were of the age group less than 30 years, 6 patients between 30 - 40 years and 6 patients within 50 years and 10 patients were >50 years. From our study it is evident that patients in the age group less than 30 years are commonly affected and are more prone to a high risk for CVT. In a study done by Sanchette and Dhamija in 1992 concluded that young to middle age is the most common age group in CVT patients.[8]

In our study, female population less than 30 years constituted 24 % of CVT cases and in male population 28%. Initial studies had higher incidence in female population but now due to increased incidence of smoking causing hyper-homocystenemia there has been increased incidence even in male population which is in agreement with a study by VC Patil, Kushal C, Desai Neeraj and Sumith A in 2014.[9]

The most common etiology detected in female patients less than 30 years was found to be puerperium followed by OCP's. This causes young female patients to be more prone to CVT in a very young age. In a similar study done by Nagaraj et al found that 200 out of 230 cases (86%), had OCP and puerperium as a predisposing factor in female population.[10]

Narayan et al in his study 2012 also reported similar findings that female on OCP's were at higher risk for CVT and in his study it accounted for nearly 11.5%.[11] Puerperal CVT is more common in Indian population than in the western population because of associated predisposing factors like anemia, increased coagulability of blood, slowing of blood stream and dehydration aggravated by local custom of withholding fluid intake and sepsis.

The etiology associated with male were found to be hyper-homocysteinemia followed by alcoholism, hence most of the CVT are common in young age group due to early exposure to smoking and alcoholism. Further, increased incidence of CVT due to dehydration was noted across both the genders. [Figure 1]

In our study CVT due to dehydration in both sexes accounted for 17% of cases due to hypercoaguable state.

Narayan et al, 2012 in his study showed results which was in concordance with our findings that alcohol in males was a major risk factor for CVT in about 15.6% cases.[11]

According to recent studies there is an increase in incidence in male population.[9,12] who are diagnosed as CVT because of modern diagnostic modalities like CT and MRI, and due to reduction in puerperal sepsis rates because of recent medical advances and awareness in general population. Congenital or acquired coagulation abnormalities also make another important risk factor for development, management and prognosis of CVT.

The clinical features are variable depending on the site, extent, type and duration of the thrombosis. When the thrombosis affects the cortical veins leading to an infarct, it results in seizures and paralysis, and if the thrombosis is limited to superior sagittal sinus and lateral sinuses it may present with symptoms of increased intracranial hypertension.[13]

Unlike the arterial stroke the presentation of CVT can vary from acute to chronic. The clinical features may range from headache, papilledema, seizures, altered sensorium, fever and unconsciousness.

In our study the spectrum of clinical features seen were headache and papilledema being the most common and earliest complaint with which the patients presented. Around 38 out of 46 positive CVT cases headache constitutes for 80%, which is significant.[Figure 2]

Nagaraj et al.[10] and Ameri and Baussser[14] in their study on CVT reported that 75% of the 110 cases had their main complaint as headache, which is again in accordance with the current study. Similarly, Einhaupl et al[15] has reported

similar findings in 1990 when they observed that 91% of the patients presented with headache and 45% with seizures.

The next most common symptom was seizures which accounts for 47% and altered sensorium 45%. Katrak et al[13] in his study accounts the same for about 68% and 60% and Nagaraj reports for about 63% and 34 %.[10] Narayan et al in their study found that 40-45% cases had seizures as clinical presentation.[11]

Other clinical features such as nausea, vomiting (15%), fever (10%) and unconsciousness (13%) are noted in our study. These findings seem to vary and differ with each literature and other studies.

MRI brain was done in 100 cases of clinical suspicion of which 46 were found to have CVT positive and the remaining 54 had no CVT. among the positive cases 23 had infarct and 23 had no infarct. Hemorrhagic infarct was found in19 cases out 23 constituting for about 83%.

In our study single and multiple sinuses were involved in patients undergoing MRI brain with MRV having CVT. Out of 46 patients who had CVT single sinus involvement was found in 13 cases and multiple sinuses was found in 33 cases. The sinuses that were involved in CVT are Superior sagittal sinus, transverse sinus, sigmoid sinus, straight sinus, cortical veins, and internal jugular veins.

The predominant and most commonly involved sinus was Superior sagittal sinus, which accounted for about 73% in our study. Literature also reports that Superior sagittal sinus was most commonly involved accounting for 86.7% and this is seen again in agreement with Ameri and Bousser[14] who reported in their study of 110 cases that SSS accounts for 72%. Other sinuses that were involved are transverse sinus (32), sigmoid sinus (28), straight sinus (6), cortical veins (4), internal jugular vein (10) and deep cerebral vein (1).[14]

Incidence of superior sagittal sinus thrombosis is higher, because the lumen of superior sinus with luminal and fibrous trabeculae favors thrombosis. Cantu et a1[16] have reported similar findings.

It is hence seen that even if multiple sinuses are involved in MRV, SSS is the most commonly affected and usually these patients have headache as the earliest complaint.

Variants of venous anatomy are commonly seen which include hypoplastic sinus or prominent arachnoid granulations. The thrombus in methemoglobin stage can present with increased signal and falsely stimulate blood flow in the 2D TOF MRV techniques, hence with the use of phase contrast MRV it can be avoided.

The transverse sinus is the most common sinus to have hypoplasia, which are the normal anatomical variants that can stimulate CVT. In plane flow-induced signal loss in 2D TOF MRV may also mimic CVT. Prominent arachnoid granulations can also stimulate thrombus. Hence careful review of the MRV images and conventional MRI leads to correct diagnosis.

In our study 7 patients underwent CE MRI brain and MRV of which 4 had CVT and 3 required other MRI brain imaging findings. In our study 28 patients had FLAIR hyper-intensity of which 23 patients had venous infarcts, 3 had vasogenic edema and 2 had only hematoma.

DWI sequence helps us in differentiating cytotoxic edema from vasogenic edema with the ADC values that are generated on ADC maps automatically with the advent of newer software. The minimum ADC values were calculated for these areas and was concluded that lower ADC values were seen in cytotoxic edema and higher ADC values were seen in vasogenic edema. This was in agreement with the literature and by Lovblad KO et al[17] because venous infarct has only vasogenic edema due to breakdown of blood brain barrier later on cytotoxic edema supersedes due to involvement of Na- K+ATPase pump disruption.[17]

Among the other causes that are found in NON-CVT cases in our study, most common being hypertension in males and head and neck infections like sinusitis/ mastoiditis/ encephalitis in females. As CVT has varieties of clinical presentation it needs to be suspected in cases that have occipital headache or new onset of headache with visual disturbance, young patients with hemiplegia, seizures following pregnancy, few other acquired conditions because CVT when compared to arterial stoke can be reversible in many cases without deficits.

Hence radiologist in emergency department needs to aware of the imaging features of CVT and if suspected MRV with MRI brain should be recommended, as they are safe, non-invasive, non-ionizing and has accurate results. Also phase contrast has the ability to differentiate thrombosed sinuses from other variants and pitfalls.

CVT is more commonly found in India when compared to the western countries however the exact prevalence remains unknown with the need for studies with a higher sample size.

CONCLUSION

We conclude that TOF and PC of MRV are the most sensitive imaging sequences in diagnosing thrombosis as they have high sensitivity and specificity. Conventional MRI brain FLAIR sequence can be strongly recommended in CVT cases to know the parenchymal changes. To diagnose venous sinus thrombosis the sensitivity of FLAIR sequence is low. If needed CE MRI brain would solve the problem in diagnostic dilemma.

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