RESEARCH ARTICLE

A STUDY OF 25 CASES OF CEREBRAL VENOUS SINUS THROMBOSIS

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DOI: 10.5455/ijmsph.2014.210220144 **Received Date: 09.02.2014** **Accepted Date: 21.04.2014**

ABSTRACT

Background: Cerebral venous sinus thrombosis is a rare but dangerous condition, occurring with an incidence of 3-4 cases/ million/ year. It has a higher frequency among patients younger than 40 years of age. Cerebral venous thrombosis occurs 3 times as frequently in women. The symptoms and signs associated with cerebral venous thrombosis (CVT) are relatively nonspecific.

Aims & Objective: To study the demographic profile, identify various etiologies different mode of onset and presentations, identify common sites of occlusion and outcome of the patients with CVST.

Materials and Methods: Total 25 patients admitted in medical wards with MR venography suggestive of CVST were enrolled. Detailed medical history with general and systemic examination done. Routine and specific investigations carried out. Patients treated with anticoagulation therapy. At time of discharge recovery is graded in form of Modified Rankin Score.

Results: Higher incidence in young female of 21 – 30 age group. Male to female Ratio was 1:3.167. Pregnency and puerperium accounts for 36%of total cases. Headache was presenting symptom in all patients. CSF was abnormal in 17 patients. Superior sagittal sinus alone or in combination affected in 72% of cases.52% of patients had complete recovery. Death occurred in 20% of cases.

Conclusion: Sinus thrombosis remains a diagnostic challenge and a potentially disabling or lethal disease, but improved diagnosis by recent advances and treatment now result in an excellent outcome for most patients.

Key Words: Cerebral Venous Sinus Thrombosis; Pregnency and Puerperium; Superior Sagittal Sinus

Introduction

Cerebral venous thrombosis, thrombosis of cerebral veins and major dural sinuses, is an uncommon disorder in the general population. In 1825, Ribes described first detailed description of cerebral venous thrombosis (CVT) in 45 year old man who died of headache, epilepsy, and delirium and post mortem report was suggestive of cerebral venous sinus thrombosis. Since then, numerous case reports and series have been published.

Cerebral venous sinus thrombosis is a rare but dangerous condition, occurring with an incidence of 3-4 cases/ million/ year.[1] CVST represents 0.5 to 1% of all strokes. The ratio of venous to arterial strokes has been found to be 1:62.5. However, it has a higher frequency among patients younger than 40 years of age. Cerebral venous thrombosis occurs 3 times as frequently in women, likely because of increased risk during pregnancy and with hormonal contraceptive use.[1]

The symptoms and signs associated with cerebral venous thrombosis (CVT) are relatively nonspecific. These include headache, papilledema, vomiting, seizures, and focal neurological deficits. CVT may be difficult to diagnose clinically because of its various and nonspecific presentation.[2] Hypercoagulable states associated with peripartum period as well as infectious diseases are believed to be the major causes in the third world, but these are less significant in western countries. Other causes includes trauma, Hematologic conditions including paroxysmal nocturnal hemoglobinuria, thrombotic thrombocytopenic purpura, sickle cell disease and polycythemia, Collagen-vascular diseases such as systemic lupus erythematosus, Wegener granulomatosis, and Behçet syndrome, Nephrotic syndrome, dehydration, hepatic cirrhosis, and sarcoidosis.[2] Mortality varies from 6 to 15%.

In this study, 25 cases of CVT are reported. The features of this condition, including frequency, clinical patterns, etiologies and outcomes are described with the objectives: (1) To study the demographic profile of patients of cerebral venous sinus thrombosis; (2) To identify various etiologies of cerebral venous sinus thrombosis; (3) To observe different mode of onset and presentations of cerebral venous sinus thrombosis; (4) To identify common sites of occlusion of cerebral venous system; (5) To study outcome of the patients with cerebral venous sinus thrombosis.

Materials and Methods

This open labelled study of 25 cases of cerebral venous sinus thrombosis was conducted during period from December 2012 to November 2013. Patients were enrolled from medical wards of general hospital. We have enrolled 25 patients in this one year with these inclusion criteria: (i)

MR Venography showing cerebral venous sinus thrombosis; (ii) Age > 13 years. Informed consent was taken from them. Detailed medical history including: Chief complaints, Origin, duration and progress, Past history particularly hypertension, IHD, DM and stroke and other, Family history, Personal history, menstrual history and obstetric history for women, Drug history – particularly in women for consumption of oral contraceptive pills taken. In all patients apart from vital data and detailed systemic examinations particularly of cardiovascular and central nervous system including fundus examinations done systematically.

Routine blood investigations like Complete Blood count, Random blood sugar, urea, serum creatinine, SGPT, Serum Bilirubin and serum electrolytes were done on enrollment. Other specific investigations like PT with INR and aPTT, 24 hr urinary protein, Chest X-Ray and X-Ray paranasal sinuses, ECG standard 12 leads, 2D Echo with colour Doppler, USG abdomen and pelvis, EEG in patients with seizures, Factor V leiden, Antithrombin III, Protein C and Protein S, Serum Homocysteine, Anti-phospholipids antibodies, ANA, Neuroimaging in form of MR Venography for confirmation of diagnosis and for etiological evaluation carried out.

All the patients were given supportive as well as specific medications. *(a) Supportive Treatment:* (i) To reduce intra cranial tension head elevation 30^{o} to 40^{o} and IV mannitol was given. (ii) Appropriate antibiotics were given to control infection if any. (iii) Seizures were controlled with appropriate anti epileptics. *(b) Anti Coagulation:* (i) IV Heparin was given in 15 patients. Rest of the patients were given low molecular weight heparin S/C as an anticoagulant therapy. (ii) Maintenance anticoagulation was provided with Warfarin.

Patients were followed up and outcome on discharge was assessed according to modified Rankin scale.

Table-1: Modified Rankin Scale

0	No symptoms at all
1	No significant disability despite symptoms; able to carry out all usual duties and activities.
2	Slight disability; unable to carry out all previous activities but able to look after own affairs without assistance.
3	Moderate disability requiring some help, but able to walk without assistance
4	Moderate severe disability; unable to walk without assistance and unable to attend to won bodily needs without assistance.
5	Severe disability; bedridden, incontinent, and requiring constant nursing care and attention.

Results

This study shows incidence of cerebral venous sinus thrombosis were higher among age group 21 to 30 years. In male no characteristic age distribution was found. While majority of female belong to age group of 21 to 30 years (Table 2). This study shows incidence of cerebral venous sinus thrombosis were higher in females as compared to male with male to female ratio of 1: 3.167 (Table 3). In this study group puerperium was the most common cause of cerebral venous sinus thrombosis and multipara women are more commonly affected then primipara.

Antiphospholipid antibodies were found positive in four cases (16%) and repeat titer on follow up after 12 weeks were also positive. Two patients with cerebral venous sinus thrombosis had serum homocysteine value 80 µM/L and 60 µM/L (Normal adult value 5- 15 µM/L). Four patients with cerebral venous sinus thrombosis had meningitis out of which three were pyogenic and one was tuberculous. Among pyogenic meningitis one was secondary to skin infection of dangerous area of face and in the others primary site of infection was not found. In this study three cases with cerebral venous sinus thrombosis had history of oral contraceptive pills ingestion. Due to any reason the cause was not identified in two cases (Table 4). This study shows that subacute and chronic mode of onset of cerebral venous sinus thrombosis was found in 40 % each, while 20 % of cases had acute onset (Table 5).

The most common symptom of cerebral venous sinus thrombosis was headache found in all the patients, while visual disturbances (excluding diplopia) and diplopia were found in 56 % and 25 % cases respectively. Partial seizures and / or generalized seizures had occurred in 44% of patients. Behavioural symptom like delirium was found in one case (4%). One patient with intracranial hypertension (headache and papilledema) had bilateral extensor planter response without any focal deficits/ seizures and three patients had neck rigidity. Both to these were included in other cortical signs. Headache was the most frequent and often the earliest presentation. Thus, in all the series the most frequent manifestations of cerebral venous sinus thrombosis is headache. (Table 6)

D. Dimer level was done in 10 patients, out of which 60 % had elevated D. Dimer level, while 40 % patients level was normal (Table 7). In this study only 8 patients had normal CSF (CSF pressure not measured). Total protein was increased (> 45 mg/100ml) in 68 % of cases. Cell count was increased (> 5/cumm) in 32 % patients. It was in 12 % cases predominantly neutrophilic and 20 % cases predominantly lymphocytic. Three patients with low glucose, with predominantly CSF neutrophilic pleocytosis, were diagnosed to have pyogenic meningitis, while one patient with lymphocytic pleocytosis was diagnosed to have tuberculous meningitis (Table 8).

In this study the most common site of sinovenous occlusion was in superior sagittal sinus. One patient had cavernous sinus thrombosis secondary to skin infection of dangerous area of face. In 36 % of cases only single sinus is involved while in majority of cases more than one sinus is involved (Table 9). In this study 52 % of patients had complete recovery [Modified Rankin Scale (MRS): 0-1] on discharge. About 12 % of patients were partially recovered and independent (MRS: 2), while 16 % of patients had partial recovery but with dependence (MRS: 3-5). Death had occurred in 20 % of cases (Table 10).

Table-2: Incidence of cerebral venous sinus thrombosis according to age group

Age Group (Years)	Number of Cases			Percentage
	Male	Female	Total	
Up to 20	0	3	3	12
21 - 30	1	10	11	44
31 - 40	0	5	5	20
41 – 50	2	0	2	8
51 – 60	1	0	1	4
> 61	2	1	3	12

Table-3: Incidence of cerebral venous sinus thrombosis according to Sex

Sex	Number of Cases	Incidence	Male: Female
Male	6	24	1 : 3.167
Female	19	76	

Table-4: Incidence of different Etiologies

Etiology	No. of Cases	%
Puerperium	7	28
Multipara	6	24
Primipara	1	4
Pregnancy	2	8
Antiphospholipid syndrome	4	16
Hyperhomocysteinemia	2	8
Pyogenic Meningitis	2	8
Tuberculous Meningitis	1	4
O. C. Pills	3	12
Skin infection of dangerous area of face	1	4
Cause not identified	3	12

Table-5: Mode of onset in cerebral venous sinus thrombosis

Mode of Onset	No. of Cases	%
Acute (< 48 hours)	5	20
Subacute (> 48 hours to 1 month)	10	40
Chronic (> one month)	10	40

Table-6: Incidence of Neurological symptoms and signs in the patients of this study

Neurological Symptoms and Signs	No. of Cases	%
Headache	25	100
Visual disturbance (excluding diplopia)	14	56
Diplopia	5	25
Generalized Seizures	6	24
Partial Seizures	1	4
Partial seizures and secondary generalization	4	16
Behavioral disorders	1	4
Sensory symptoms	0	0
Stupor or coma	10	40
Dysphasia	8	32
Papilledema	13	52
Rt. Hemiparesis/plegia	4	16
Lt. Hemiparasis/plegia	4	16
Other cortical signs	4	16

Table-7: Incidence of elevated D. Dimer level in this study Group

D. Dimer	No. of Cases	%
Normal	4	40
Elevated	6	60

Reference range: Normal value less or equal to 500 ng/ml

Table-8: Incidence of CSF changes in cerebral venous sinus thrombosis

CSF Picture	No. of Cases	%
Normal	8	32
Elevated protein	17	68
Reduced glucose	4	16
Leucocytosis	8	32
Polymorphonuclear leucocytris	3	12
Lymphocytic leukocytosis	5	20

Table-9: MR Venography site of occlusion in patient with cerebral venous sinus thrombosis

Sinus involved in MR Venography		No. of Cases	%
SSS	Overall	18	72
	Alone	3	12
	With LS	10	40
	With SS	0	0
	With LS + SS	3	12
	With Cortical Veins	2	8
LS	Overall	15	60
	Alone	5	20
	With SS	1	4
	With Cortical Veins	0	0
SS	Overall	4	16
	Alone	0	0
	With cortical veins	0	0
Cavernous sinus		1	4
Others		0	0

Table-10: Outcome of the patient on discharge according to Modified Rankin Scale

Modified Rankin Scale	No. of Cases	%
0	5	20
1	8	32
2	3	12
3	2	8
4	2	8
5	0	0
Death	5	20

Discussion

Women tend to be at an increased risk particularly between the ages of 20 - 35, mainly due to the use of the oral contraceptive pill and the post-partum state.[1] Cerebral venous thrombosis occurs 3 times as frequently in women, likely because of increased risk during pregnancy and with hormonal contraceptive use The higher incidence in female reflects the overall greater incidence of thrombo-embolic diseases in this category.[1] Pregnancy and pueperium are common causes of transient prothrombotic states. Approximately 2% of pregnancy associated strokes are attributed to cerebral venous sinus thrombosis.[3] The incidence of CVST is 12/100000 deliveries. Mostly occur in 3rd trimester or pueperium.[3]

A survey in the US based on data from the 1993–4 Healthcare Cost and Utilization project, Laska DJ et al. study, identified a number of independent risk factors for

CVST occurring in the peripartum period. Increased risk was associated with caesarian delivery, increasing maternal age and the presence of several co-morbid conditions including hyperemesis, intercurrent infection and maternal hypertension. There may be a cumulative effect of resistance to activated protein C during pregnancy together with decreased protein C levels following surgery. Predisposing risk factors can be identified in up to 80% of patients.[1] Thus pregnancy and post-partum period has recognized as period of increase susceptibility for cerebral venous sinus thrombosis. Headache is most common symptoms in >90% of patients and suggestive of raised intracranial pressure. Headache is very severe and progress gradually over days.[3]

Clinical manifestation depends on location of thrombosis. Superior sagittal sinus is most commonly affected and leads to headache papilloedema, and raised intracranial tension. Seizure and motor symptoms may occur.[3] Unless there is suspicion of meningitis, examination of CSF is not helpful for diagnosis of CVST. Elevated opening pressure is most common finding and found in >80 % of cases. Elevated cell count and protein usually found but their absence does not rule out diagnosis.[3] In lateral sinus thrombosis constitutional symptoms, ear discharge, mastoid tenderness, and signs and symptoms suggestive of raised intracranial tension found. Presence of hemianopia, aphasia and hemiparesis suggestive of cortical involvement.[3]

D-dimer is the final product of degradation of fibrin-rich thrombi that can be used in diagnostic algorithms for the exclusion of venous thromboembolism. D-dimer is an acute-phase reactant hemostatic marker.[4] Several factors may account for discrepant findings in D dimer. D dimer is an acute-phase reactant hemostatic marker so it decline from time of onset which suggest that in patient with subacute and chronic presentation it may be negative.[3] The anatomic extent of of thrombosed sinus may correlate with D dimer level so patient with lesser clot burden may have false negative D dimer.[3]

Conclusion

Cerebral venous sinus thrombosis is a rare condition but commonly affecting young female of age group 21 – 30 years. Peurperium and pregnancy are the most common cause of cerebral venous sinus thrombosis in this study. Cerebral venous sinus thrombosis is 3.5 times more common in peurperium than in pregnancy. Headache is present in all the patients with cerebral venous sinus thrombosis. MR venography in most of the patient thrombosis was suggestive of more than one sinus. Involvement of superior sagital sinus is most common either alone or along with other sinuses. In this study, majority of patients had complete recovery on discharge with anticoagulant therapy. Death had occurred in 20% of cases. In summary, Sinus thrombosis remains a diagnostic challenge and a potentially disabling or lethal disease, but improved diagnosis by recent advances and treatment now result in an excellent outcome for most patients.

ABBREVIATONS

%: Percentage;
APC: Absolute platelet count;
aPTT: Activated partial thromboplastin time;
BP: Blood pressure;
CBC: Complete blood count;
CSF: Cerebro spinal fluid;
CT: Scan: Computed tomography;
CVT: Cerebral venous thrombosis;
DC: Differential count;
DM: Diabetes mellitus:
ECG: Electrocardiogram;
EEG: Electroencephalography;
ESR: Erythrocyte sedimentation rate;
F: Female;
Hb: Hemoglobin;
IHD: Ischemic heart disease;
IV: Intravenous;
L: Liter:
LMWH: Low molecular weight heparin;
LS: Lateral sinus;
M: Male;
mg: Miligrams;
MRI: Magnetic resonance imaging;
MRV: MR Venography;
N: Normal;
No.: Number;
NSAIDs: Nonsteroidal antiinflammatory drugs;
O.C. Pill: Oral contraceptive pills;
PT: Prothrombin time;
RBS: Random Blood sugar;
S.: Serum;
SAH: Subarachnoid hemorrhage;
SC: Subcutaneous;
SSS: Superior sagittal sinus;
TC: Total count;
USG: Ultra sonography;
Yrs: Years

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Cite this article as: Darji Z, Dabhi L. A study of 25 cases of cerebral venous sinus thrombosis. Int J Med Sci Public Health 2014;3:581-584.
Source of Support: Nil
Conflict of interest: None declared