

A Study of Clinical Profile, Risk Factors and Outcome in Patients of Cerebral Venous Sinus Thrombosis

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Abstract

Background: Cerebral venous sinus thrombosis (CVST) is an uncommon cause of stroke with extremely varied clinical features, predisposing factors and outcomes. With the widespread use of neuroimaging and hematological work up more and more patients are being confidently diagnosed.

Objective: To study the clinical profile, risk factors, radiological findings and outcome in patients of CVST at tertiary care center in Haryana.

Study Design: Prospective study.

Materials and Methods: Thirty patients with radiologically proven CVST were studied over a period of 12 months. The demographical, clinical, radiological and laboratory data was recorded and analyzed. Follow up was done for a period of 6 months.

Results: Of the 30 patients, 23 (76.7%) were female and the mean age was 29.1 years (range 14-52 years). Most common presenting features were headache (73.3%), focal deficit (56.7%) and seizures (46.7%). Stroke like presentation was seen in 11 patients (36.7%), benign intracranial hypertension was seen in 2 patients (6.7%) and isolated headache was seen in 2 patients (6.7%). Papilledema was most common neurological sign seen in 14 patients (46.7%). Common risk factors were puerperium (33.3%), hyperhomocysteinemia (13.3%), infections (10%). Mortality was noted in 3 patients (10%). Good outcome (modified Rankin Scale 0-2) at 6 months was observed in 22 patients (88%) out of 25 patients available for follow up.

Conclusion: CVST can affect all age groups, particularly women of child bearing age. Puerperium, hyperhomocysteinemia and infection were the most common risk factors. Overall prognosis was good, but a small percentage of patients died.

I. INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a rare type of cerebrovascular disease that affects about 5 people per million.¹ It often affects young to middle-aged patients and more commonly women. Clinical features of CVST are very variable and depend on the site, extent and rate of thrombosis. Headache is the most frequent and often the earliest manifestation.² The diagnosis of CVST requires high index of suspicion because of its varied presentation. Neuroimaging is the corner stone in the diagnosis of cerebral venous sinus thrombosis. CVST has an acute case fatality of less than 5% and almost 80% of patients recover without sequelae.³ It has been found that early diagnosis of cerebral venous thrombosis is essential because early treatment decreases morbidity and mortality. The aim of the present study was to investigate the clinical profile, risk factors, radiological findings and outcome in patients of CVST in a prospective manner.

II. MATERIALS AND METHODS

The present study was conducted on 30 cases of CVST, which were admitted in Post Graduate Institute of Medical Sciences, Rohtak, Haryana, during a span of 12 months. Patients with arterial ischemic and hemorrhagic stroke were not included in the study.

All the patients suspected to have CVST were subjected to thorough clinical evaluation. The clinical diagnosis was confirmed by one or more of the following radiological investigations: brain computed tomography (CT) scan, brain magnetic resonance imaging (MRI) and brain magnetic resonance venography (MRV). The diagnosis was based on established radiological criteria. All the confirmed cases of CVST were investigated with complete blood count, renal function tests, liver function tests, prothrombin time, activated partial prothrombin time, antinuclear antibodies, antiphospholipid antibodies, procoagulant states like protein C, protein S, antithrombin III and serum homocysteine with an aim to detect underlying etiology.

Patients were treated as per available guidelines. Follow up visits were done at 3 months and 6 months. Data recorded during follow up were disability according to modified Rankin Scale (mRS), death, any recurrence of thrombosis, seizures. Outcome was dichotomized as good (mRS score 0-2) and poor (mRS \geq 3).

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) window software. Continuous variables were presented in titer of mean and \pm SD. Categorical variables were expressed as proportions and chi square test was used to study the associations. P value \leq 0.05 was considered statistically significant.

III. RESULTS

A total of 30 patients (23 females and 7 males) were included in the study. The mean age was 29.1 years with a range from 14 to 52 years. Majority (57%) were in the age group of 20-30 years.

Presentation was acute in 14 (46.7%), subacute in 10 (33.3%) and chronic in 6 (20%). Neurological symptoms and signs are summarized in Table 1. Headache was the most common symptom, present in 22 (73.3%) patients. Papilloedema was the most common neurological sign, seen in 14 (46.7%) patients. Risk factors are shown in Table 2. Puerperium was the most common identified risk factor seen in 10 (33.3%). No possible cause could be found in 5 (16.7%) patients. Brain imaging was done in all patients. Most common CT finding was hemorrhagic infarcts seen in 15 (50%) patients. Delta sign and cord sign was seen in 4 (13%) and 2 (7%), respectively. Frequency of brain parenchymal lesions and sinus involvement is summarized in Table 3. Transverse sinus was the most common sinus involved in our study, in 20 (66.7%) patients.

Table 1: Symptoms and Signs at the Time of Presentation

Symptom and Sign	N	%
Headache	22	73.3
Focal deficit	17	56.7
Altered sensorium	17	56.7
Convulsions	14	46.7
Fever	8	26.7
Diplopia	7	23.3
Papilloedema	14	46.7
Pallor	13	43.3
Cranial nerve involvement	9	30

Dehydration	5	16.7
Dysphasia	3	10

Table 2: Predisposing Conditions

Predisposing condition	N	%
Puerperium	10	33.3
Infection	3	10
Hyperhomocysteine	4	13.3
Protein C deficiency	2	6.7
Protein S deficiency	1	3.3
APLA	1	3.3
OCP	2	6.7
Recent Surgery	1	3.3
PNH	1	3.3
No cause	5	16.7

Table 3: CT Brain and MRI Brain Findings

Location of brain parenchymal lesion (In Imaging)	N	%
No lesion	7	23.3
Parietal	4	13.3
Fronto-parietal	4	13.3
Frontal	3	10
Temporoparietal	3	10
Fronto-temporo-parietal	3	10
Temporo-parieto-occipital	3	10
Temporo-occipital	1	3.3
Occipital	1	3.3
Diffuse	1	3.3
Sinus involved		
Transverse sinus	20	66.7
Superior sagittal sinus	19	63.3
Sigmoid sinus	10	33.3
Jugular sinus	3	10
Straight sinus	3	10
Internal cerebral vein	2	6.7
Cavernous sinus	1	3.3
Cortical vein(Vein of labbe)	1	3.3

An attempt was made to correlate clinical profile with the site of venous occlusion but no significant clinical pattern was found with mode of onset, clinical parameters and outcome whether sinuses alone, deep sinuses and combination of sinuses and veins.

All 30 patients were given anticoagulation, initially with LMWH followed by OAC. Additional treatment included antiepileptics in 15 (50%) patients and antiedema measures in 18 (60%) patients and decompressive craniotomy was done in 1 patient.

Information on outcome was available for all patients at the time of discharge. In hospital mortality (mRS=6) was noted in 3 (10%) patients and 5 patients had disability (mRS≥3) at the time of discharge. At the end of 3 months, information for outcome was available in 29 patients, out of them 7 had poor prognosis (mRS≥3;

including 3 deaths). At the end of 6 months, outcome information was available for 28 patients, out of them poor prognosis (mRS≥3) was seen in 6 cases.

On multivariate analysis, focal neurological deficit (p=0.007), altered sensorium (p=0.007) and fever (p=0.008) at the time of presentation were associated with poor outcome on follow up. No significant association was found with age, sex, seizure at presentation, papilloedema, number of sinuses involved, and parenchymal lesions in brain imaging (Table 4). Isolated headache at the time of presentation was associated with good prognosis (p<0.05). During the follow up period of 6 months, none of the patients had any repeat thrombotic event while 1 patient had seizure recurrence.

Table 4: Prognostic Factors On Follow Up

Prognostic variables		3 months follow up (n=29)				6 months follow up (n=28)			
		No.	Poor outcome n=7	Good outcome n=22	P-Value	No.	Poor outcome n=6	Good outcome n=22	P-Value
Age	<30	20	4	16	0.369	19	3	16	0.28
	>30	9	3	6		9	3	6	
Sex	Male	7	2	5	0.556	7	1	6	0.522
	Female	22	5	17		21	5	16	
FND	Present	16	7	9	0.007	15	6	9	0.013
	Absent	13	0	13		13	0	13	
Papilledema	Present	17	6	11	0.108	17	5	12	0.214
	Absent	12	1	11		11	1	10	
Seizure	Present	14	3	11	0.542	14	2	12	0.324
	Absent	15	4	11		14	4	10	
Altered sensorium	Present	16	7	9	0.007	15	6	9	0.013
	Absent	13	0	13		13	0	13	
Headache	Present	22	3	19	0.038	22	3	19	0.091
	Absent	7	4	3		6	3	3	
No. of venous sinuses	1	11	3	8	0.547	10	3	7	0.358
	>1	18	4	14		18	3	15	
Parenchymal lesion	Present	22	7	15	0.109	21	6	15	0.144
	Absent	7	0	7		7	0	7	
Fever	Present	8	5	3	0.008	8	5	3	0.0009
	Absent	21	2	19		20	2	18	

IV. DISCUSSION

The clinical presentation of CVST is extremely variable ranging from isolated headache to focal deficit to encephalopathy to coma.¹ Headache was the most common symptom at presentation as in other studies.^{2,3}

Our study had 23 females and 7 males, with a M:F ratio of 1:3.3. International Study of Cerebral Vein and Dural Sinus Thrombosis (ISCVT)³ reported a M:F

ratio of 1:2.9. Puerperal state was seen in 33% of patients, it was the most common cause of CVST in females. Puerperium as a cause of CVST has been reported in lesser frequencies in western studies,^{3,4,5} however a very high proportion of puerperal CVST was seen in Indian studies done in past.^{6,7,8} The decrease in puerperal CVST in our study reflects improved obstetric care in India. In our study, only 8.7% (2 out of 23) of females were taking OCP's in contrast to western studies where OCP's is implicated in 54-77% of CVST cases.^{3,4,5} Hyperhomocysteinemia was seen in 13.3% of

patients. In 2004 Cantu et al⁹ reported a correlation of high plasma concentrations of homocysteine and low plasma folate levels and CVST in increased frequency in Mexican population owing to low socioeconomic conditions and deficient nutritional status. Infection accounted for 10% of CVST cases in our study similar to 12% seen in ISCVT. We could not find any cause for CVST in 17% of our patients.

Presence of empty delta sign and cord sign on CT scan brain suggests the diagnosis of CVST, but these were found only in 13% and 7% patients, respectively. Indirect CT abnormalities were more frequent, seen in 77% patients. MRI was found to be better than CT in identification of these findings. Areas of increased density in CT which corresponds to hemorrhagic infarcts was most common CT finding, seen in half of the patients. No parenchymal lesion was found in 23% patients. The diagnosis of CVST in these patients was made on the basis of direct visualization of thrombus in MR venography, which was found to be the most effective non invasive technique to confirm the diagnosis of CVST.

The present study like other studies^{3,10,11} confirms that superior sagittal sinus(63%) and transverse sinus (67%), with or without involvement of other sinuses, are most common sinus involved. Isolated sinus involvement (27%) is much less common than multiple sinus involvement. Most frequently involved isolated sinuses were superior sagittal sinus (20%) and transverse sinus(6.7%). There was no correlation between clinical profile and topographic radiological findings, like involvement of superficial/deep venous system or the pattern of infarction, to evolve a pattern of diagnostic significance. As most of the patients had extensive involvement of cerebral sinovenous system, contribution of degree of involvement of anatomical structures to a particular clinical profile cannot be reliably predicted.

In majority of the patients, outcome was good. At the end of 6 months, 73% of patients were functionally independent (mRS 0-2). However 10% mortality was still noted, similar to other studies.^{3,10,11} We noticed that factors associated with poor outcome were fever, altered sensorium and focal neurological deficit at the time of presentation. In ISCVT³ age >37 years, male sex, any malignancy, CNS infection, seizures, mental status disorders, intra cerebral haemorrhage and deep venous system thrombosis were associated with poor prognosis. Coma and intra cerebral haemorrhage were associated with poor prognosis in a study by Bruijn et al.⁴ Identification of high risk patient

is important because they can be benefited by more aggressive therapeutic interventions.

V. CONCLUSION

CVST is an important and treatable cause of stroke with extremely diverse clinical features, risk factors, brain imaging findings and outcome. The post partum state, hyperhomocysteinemia and infections are common risk factors. Fever, altered sensorium and focal neurological deficit at the time of presentation are associated with poor outcome.

REFERENCES

- [1] Boussier MG, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol* 2007; 6:162–70.
- [2] Boussier MG, Chiras J, Bories J, Castagne P. Cerebral venous thrombosis: A review of 38 cases. *Stroke* 1985; 16:199–213.
- [3] Ferro JM, Canhao P, Stam J, Boussier MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke* 2004; 35:664-70.
- [4] De Bruijn SFTM, de Haan RJ, Stam J. Clinical features and prognostic factors of cerebral venous sinus thrombosis in a prospective series of 59 patients. *J Neurol Neurosurg Psychiatry* 2001; 70:105–8.
- [5] Deschiens M, Conard J, Horellou M, Ameri A, Preter M, Chedu F. Coagulation studies, factor V Leiden and anticardiolipin antibodies in 40 cases of cerebral venous sinus thrombosis. *Stroke* 1996; 27:1724–30.
- [6] Nagaraja D, Sarma GR. Treatment of cerebral sinus/venous thrombosis. *Neurol India* 2002; 50:114
- [7] Nagpal RD. Dural sinus and cerebral venous thrombosis. *Neurosurg Review* 1983; 6:155-60.
- [8] Bansal BC, Gupta RR, Prakash C. Stroke during pregnancy and puerperium in young females below the age of 40 years as a result of cerebral venous/venous sinus thrombosis. *Jpn Heart J* 1980; 21:171-83.
- [9] Cantu C, Alonso E, Jara A, Martinez L, Rios C, Fernandez MA et al. Hyperhomocysteinemia, low Folate and vitamin B12 concentrations, and methylene tetrahydrofolate reductase mutation in cerebral venous thrombosis. *Stroke* 2004; 35:1790-94.
- [10] Daif A, Awada A, Al-Rajeh S, Abduljabbar M, Al Tahan AR, Obeid T. Cerebral venous thrombosis in adults. A study of 40 cases from Saudi Arabia. *Stroke* 1995; 26:1193–95.
- [11] Narayan D, Kaul S, Ravishankar K, Suryaprabha T, Bandaru VS, Mridula KR, et al. Risk factors, clinical profile, and long-term outcome of 428 patients of cerebral sinus venous thrombosis. *Neurol India* 2012; 60:154-59.