Original Article

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Clinical Syndromes of Cerebral Venous Thrombosis: An Institutional Study

Internal Medicine Section

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ABSTRACT

Introduction: Cerebral Venous Sinus Thrombosis (CVST) is a neurovascular syndrome in contrast to more common arterial disease. Despite advances in the recognition of CVST in recent years, diagnosis and management can be difficult because of the diversity of underlying risk factors and the absence of a uniform treatment approach.

Aim: To evaluate the syndromes associated with the CVST spectrum and its association with veins with detailed prognostication.

Materials and Methods: The present hospital-based, observational study was conducted in the Department of Neurology, Sri Ramachandra Bhanja Medical College and Hospital, Cuttack, Odisha, India. A total of 52 patients of age >14 years, who presented with radiological confirmation of venous sinus thrombosis were included in the study. All their clinical and epidemiological parameters were tabulated. They were classified into four clinical syndromes namely syndrome of raised intracranial hypertension without focal deficit, syndrome of the focal neurological deficit with or without raised intracranial hypertension, syndrome of cavernous thrombosis and syndrome of early altered consciousness with involuntary movements/diffuse encephalopathy. Clinical parameters were analysed according to syndromic presentation. Statistical analysis was done using Statistical Package for the Social Sciences (SPSS) software version 24.0.

Results: A total of 52 patients with radiological confirmation of CVST were evaluated over a period of two years. The mean age of presentation was 31.8±12.3 years. The mean duration of symptoms prior to hospitalisation was 13.6±11.9 days. Sensorium was normal in most of the admitted patients. In the present study, syndrome-2 (syndrome of focal neurological deficit) was the most common syndrome reported (n=32, 61.6%).

Conclusion: Cerebral venous sinus thrombosis should be classified according to the syndromic association of clinical features. It will help in easy diagnosis based only on assessment of the clinical features.

Keywords: Encephalopathy, Fundus, Headache

INTRODUCTION

The Cerebral Venous Sinus Thrombosis (CVST) is one of the commonest causes of hospitalisation in neurology indoors. It is a disease with potentially serious consequences and usually affects children and young people [1]. 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. One of the commonest time of presentation is the postpartum period [1,2]. There has been a drastic reduction of infection as a causative agent for CVST in recent years [1-3]. CVST may occur at any time from infancy to old age and symptoms can be acute, sub-acute or chronic [4-6]. A syndromic approach to CVST was described by Nagaraja D et al., and Nagaraja D and Taly AB, who had classified CVST into four distinctive clinical syndromes [7,8]:

Syndrome-1 (Syndrome of raised intracranial hypertension without focal deficit): It is found in 20% of all CVTs. It's usually associated with isolated or predominant thrombosis of the Superior Sagittal Sinus (SSS) or lateral sinus. In this clinical syndrome, headache is bilateral, and progressive with or without vomiting. The examination may reveal papilloedema and brisk reflexes. Progression is slow and may cause visual impairment in long-standing or severe cases. Anticoagulant therapy may provide the best outcome. Some patients might need decompressive craniotomy or optic nerve fenestration.

Syndrome-2 (Syndrome of the focal neurological deficit with or without raised intracranial hypertension): It is the most common presentation of CVST after the postpartum period. Patients present with short-term headaches with abrupt generalised or focal motor seizures or hemiparesis or monoparesis or cranial neuropathy other than isolated 6th cranial nerve palsy. The SSS is commonly involved. Papilloedema is very common.

Syndrome-3 (Syndrome of cavernous thrombosis): It is seen primarily in nasal and sinus infections. There is progressive swelling and oedema of the conjunctiva. The congestion starts with one eye and later spreads to another eye. The eye protrudes with redness and congestion of the conjunctiva. Eye movements are restricted due to cranial nerve involvement.

Syndrome-4 (Syndrome of early altered consciousness with involuntary movements/Diffuse encephalopathy): Deep vein involvement is a rare presentation. It is often associated with the involvement of the superficial venous system. Consciousness is altered in the early course. Eyes are depressed and involuntary movements may be present. The prognosis is usually worse.

The primary aim of present study was to classify the CVST cohort into syndromes, which was rarely done previously in India [7,8]. The classification is much important for early diagnosis and treatment. The secondary aim of the study was to isolate the most common vein involvement in a specific syndrome with prognostication.

MATERIALS AND METHODS

The present hospital-based, observational study was conducted in the Department of Neurology, Sri Ramachandra Bhanja Medical College and Hospital, Cuttack, Odisha, India. A total of 52 patients >14 years age with radiological confirmation of CVT were evaluated and followed-up for a minimum of three years, from 2018 to 2020. Patients were included in the study after obtaining informed written consent. All study related pieces of information were anonymised,

kept confidential and used only for addressing the study objectives. The eligible participants were included by consecutive enumeration.

Inclusion criteria: Patients with a diagnosis of CVST, confirmed by imaging of the brain with Magnetic Resonance Imaging (MRI)/ Magnetic Resonance Venography (MRV) scan of the brain, who gave consent to participate were included in the study.

Exclusion criteria: Patients who were clinically diagnosed as having CVST, but had normal imaging of the brain in MRI/MRV scans of brain, patients below 14 years of age and who were lost to follow-up were excluded from the study.

Study Procedure

Patients who were admitted to the In Patient Department (IPD) and were fitting to the inclusion criteria were enrolled in the study. All the epidemiological data, as well as clinical manifestations, were enlisted in a previously structured format. The patients were categorised as per the clinical manifestations and were grouped into four CVST syndromes for the purpose of comparison of various parameters [7]. Types of syndrome are:

- Syndrome-1: Syndrome of raised intracranial pressure
- Syndrome-2: Syndrome of focal neurologic deficit with/without raised intracranial pressure
- Syndrome-3: Syndrome of cavernous sinus thrombosis
- Syndrome-4: Syndrome of unspecific diffuse encephalopathy.

STATISTICAL ANALYSIS

The study data was entered into Microsoft excel spreadsheet. Categorical data were expressed as numbers and percentages. Continuous data were expressed as numbers, mean and standard deviation depending on the distribution. Statistical significance was tested at 5% using the Statistical Package for the Social Sciences (SPSS) software version 24.0. Fisher's-exact probability test was used for assessing the association of categorical factors with the dichotomous outcome (mRS ≤2 and mRS >2). A p-value <0.05 was considered statistically significant.

RESULTS

A total of 52 patients with radiological confirmation of CVT were evaluated. The minimum age of presentation was 15 years and maximum was 69 years. The mean age of presentation was 31.8±12.3 years. The transverse sinus was the most common sinus involved in 42 (80.7%) patients [Table/Fig-1].

Type of syndrome	n (%)
Syndrome-1	17 (32.7)
Syndrome-2	32 (61.6)
Syndrome-3	1 (1.9)
Syndrome-4	2 (3.8)

[Table/Fig-1]: Distribution of patients according to clinical syndromes (N=52).

The majority of patients with CVST had diverse types of symptoms and signs, found on clinical examination. The patients with these different clinical manifestations were grouped into four CVST clinical syndromes. On grouping, 17 (32.7%) patients could be classified into the syndrome of raised intracranial pressure and 32 (61.6%) patients into the syndrome of the focal neurologic deficit with/without raised ICP. Only one patient could be categorised into syndrome of cavernous sinus thrombosis and two patients into syndrome of unspecific diffuse encephalopathy. After syndromic classification from the clinical pictures, the sinus involvement was analysed.

Syndrome of raised intracranial pressure (n=17): The majority of patients (82.3%) had normal brain parenchyma. Multiple brain area involvement was absent. Most of these patients had slowly progressive or uncommonly intermittent progressive headaches associated with vomiting or diminution of vision. The majority of patients had papilloedema on examination [Table/Fig-2a,b].

Site of parenchyma	Number of patients	Percentage out of similar clinical symptoms
Occipital	1	5.9
Frontal	1	5.9
Basal ganglia calcification	1	5.9
Normal brain parenchyma	14	82.3
Total	17	100

[Table/Fig-2a]: Distribution of site of brain parenchyma involved (n=17).

Sinus/vein	As individual sinus involvement	Part of multisinus involvement	Total number of patient	Percentage out of total number of similar patients (n=17)
SSS	2	10	12	70.6
TS	3	12	15	88.2
Straight sinus	0	1	1	5.8
Sigmoid sinus	0	7	7	41.2
Trocula	0	1	1	5.8
Cavernous sinus	0	1	1	5.8
IJV	0	1	1	5.8

[Table/Fig-2b]: Pattern of individual sinus/vein involvment (n=17).
SSS: Superior sagittal sinus; TS: Transverse sinus; IJV: Internal jugular vein

Syndrome of focal neurologic deficit with/without raised ICP (n=32): Hemiparesis with or without a seizure was the most common presentation overall, found in 37.5% of patients with this clinical syndrome. Seizure, as an isolated clinical manifestation, was a common presentation found in 28.1% of these patients. Among the patients of this syndrome, normal brain parenchyma was found in 14 patients after neuroimaging. Out of these 14 patients, four patients had 6th cranial nerve involvement and four patients had seizures as the only major manifestation. Hemiparesis was present in two patients. With 7th cranial nerve palsy (1/14), Monoparesis (1/14), Aphasia with headache (1/14), and seizure with monoparesis (1/14) as individual major manifestations were also found. Among the patients of this syndrome, brain parenchyma involvement was found in 18 patients after neuroimaging. Out of these 18 patients, hemiparesis with or without seizure was the commonest presentation found in 10 patients. Sixth nerve palsy was found in one patient and seizure as the dominant clinical presentation was seen in five out of a total of 18 patients. One patient had quadriparesis with seizure and 3rd nerve palsy. One patient presented with hemisensory loss and 7th, 9th, and 11th cranial neuropathy with cerebellar symptoms. Among the 32 patients with the syndrome of the focal neurologic deficit with/without raised ICP, major symptoms of swallowing difficulty and dysphasia were present in 4 and 5 patients, respectively [Table/Fig-3a-c].

Site of involvement	As single area involvement	As part of multilobar involvement	Total number of patients	Percentage out of total number of similar patients (n=32)
Frontal lobe	0	9	9	28.1
Parietal lobe	2	13	15	46.9
Temporal lobe	0	9	9	28.1
Occipital lobe	1	9	10	31.3
Brainstem	0	1	1	3.1
Basal ganglia	0	1	1	3.1

[Table/Fig-3a]: Distribution of site of brain parenchyma involvement.
SSS: Superior sagittal sinus; TS: Transverse sinus; IJV: Internal jugular vein; ISS: Interstitial system

Syndrome of cavernous sinus thrombosis (n=1): One patient was categorised into the syndrome of cavernous sinus thrombosis. He presented to the hospital with progressive headache, swelling of the eyelid with conjunctival redness, ophthalmoplegia and blurriness of

Sinus/vein involved	As individual sinus involvement	As part of multisinus involvement	Total number of patients	Percentage out of total number of similar patients (n=32)
SSS	3	14	17	53.1
TS	3	23	26	81.2
Sigmoid sinus	0	17	17	53.1
Torcula	1	7	8	25
IJV	0	4	4	12.5
SUP.COT. vein	0	3	3	9.8
PAN SINUS INV (LT.)	0	1	1	3.1
ISS	0	1	1	3.1
Straight sinus	0	1	1	3.1
Vein of Labbe	0	1	1	3.1

[Table/Fig-3b]: Distribution of site of sinus/venous involvement.

Major symptoms/ signs	Number of patients with normal brain parenchyma (n=14)	Number of patients with brain parenchyma involvement (n=18)	Total number of patients (n=32)	Percentage out of total number patients with syndrome focal deficit (n=32)
Hemiparesis	2	5	7	21.8
Hemiparesis+seizure	0	5	5	15.6
Seizure	4	5	9	28.1
Quadriparesis+Seizure+ 3rd nerve palsy	0	1	1	3.1
Brainstem syndrome	0	1	1	3.1
Seizure+monoparesis	1	0	1	3.1
Monoparesis	1	0	1	3.1
Aphasia, headache	1	0	1	3.1
6th nerve palsy	4	1	5	15.6
7th nerve palsy	1	0	1	3.1

[Table/Fig-3c]: Clinical spectrum of syndrome of focal neurologic deficit with/without raised icp (n=32).

vision for a few days. Patient had thrombosis of cavernous sinus, torcula and transverse sinus but with normal brain parenchyma. He improved completely with treatment without any sequelae.

Syndrome of unspecific diffuse encephalopathy (n=2): Two patients were categorised into the syndrome of unspecific diffuse encephalopathy. One patient presented to the hospital with a history of sudden onset headache and drowsiness followed by altered sensorium with intermittent decerebrate posturing. The patient had an infarction of the brain involving the bilateral thalamus. He had thrombosis of straight sinus and deep veins. Another patient with a similar presentation had a haemorrhagic infarct of the fronto-parietal-thalamic area with oedema. He had involvement of SSS, Inferior Sagittal Sinus (ISS), sigmoid sinus, superficial cortical vein. One patient died during the treatment and one patient left the hospital and lost to follow-up.

DISCUSSION

In the present series, 51.9% of patients were female. It has been suggested that the incidence of CVST was higher in females. Most of the earlier case series from India have reported a higher proportion of females suffering from CVST than males [8-10].

In this series, most (63.5%) patients presented subacutely. Most of the patients with chronic or subacute presentation had a slowly progressive or uncommonly intermittent headache, vomiting and blurriness of vision indicating intracranial hypertension. The acute presentation was found in 21.2% of patients and the duration of symptoms was <48 hours. Sudden onset of focal deficits simulating arterial strokes was present in 13.5% patients and six patients presented acutely with seizure. This type of presentation of CVST was also observed earlier by Bousser MG and Ross Russel RW, as per their series, the symptom onset in CVST was usually subacute (two days to one month) in 50-80% of patients and acute (two days or less) in 20-30% and many patients who presented in acute condition simulated arterial stroke [12]. Chronic presentation (>2 months) was seen in 10-20% of patients predominantly presenting as isolated intracranial hypertension [13].

Most CVST patients had multiple clinical presentations, which were categorised into various clinical syndromes for comparison. On grouping, the patients into four clinical syndromes, out of 52 patients, 17 (32.7%) patients could be classified into the syndrome of raised intracranial pressure (Syndrome-1). This is the most homogeneous group among the CVST clinical syndromes in the present series, in which, the majority of patients had a progressive onset of symptoms and signs due to intracranial hypertension, presenting with headache, papilloedema with/without vomiting. This type of clinical presentation mimicked benign intracranial hypertension or pseudotumour cerebri syndromes to a great extent. As the majority of these patients (82.3%) had normal brain parenchyma on neuroimaging, it is necessary for all the neurophysicians to rule out the possibility of CVST before putting a diagnosis of benign intracranial hypertension. This type of presentation was described in various studies. In the NIVSR cohort, the benign intracranial hypertension like presentation was seen in 18.2% of patients [11].

About 61.5% of total patients were categorised into the syndrome of the focal neurologic deficit with/without raised ICP. It was the most common type of clinical syndrome in the present series, but also the clinical syndrome with the most heterogeneous presentation. About 43.7 % patients of with this syndrome had normal brain parenchyma on neuroimaging and 56.3% of patients had some parenchymal involvement. Overall, hemiparesis with or without seizure was the most common presentation, found in 37.5% of patients in this clinical syndrome. Although it is an uncommon association similar condition was described by Straub J et al., [14]. Among the patients of this syndrome with brain parenchyma involvement, hemiparesis with or without seizure was the commonest presentation followed by an isolated seizure.

It represents 1.3% of all CVST syndromes. Cavernous sinus thrombosis was described in 2.4% of cases in the NIVSR cohort [11]. Similar presentation was seen in the present series, but as only one patient had cavernous sinus syndrome in our series, it was difficult to assess its true frequency from this small series. About 3.8% of the total patients in the series were categorised into the syndrome of unspecific diffuse encephalopathy. One patient had an infarction involving the bilateral thalamus. He had thrombosis of straight sinus and deep veins. Patients of CVST presenting as a generalised encephalopathic illness without localising signs is not a very rare presentation, but it was described in various series in varying proportions 6-29% [7,13].

Limitation(s)

The duration of follow-up was limited and also the sample size of the present study was small.

CONCLUSION(S)

Venous thrombosis is a disease in young people, especially females. It is one of the most common neurovascular syndromes. The presentation is subacute most of the time. All the CVST clinical spectrums can be divided into four syndromes. The syndrome with raised intracranial pressure was the commonest. Syndromic classification will help to know the typical clinical

presentation of the disease. Early diagnosis by MR venogram with prompt anticoagulation can limit morbidity. Several catastrophic complications can be avoided by appropriate treatment. The present study was a small study in the Southeast Asia region, and there is need of more studies in future from the present study area to delineate the exact demographic parameters along with risk factors for early diagnosis and better treatment of CVT.

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