Analysis of Clinical Features, Risk Factors and Laboratory Parameters in Cerebral Venous Thrombosis: A Study of 70 Cases

Kedariprasad Shripad Kulkarni[1], Mugdha Pradeep Kulkarni[2]

ABSTRACT

Introduction: Cerebral venous thrombosis (CVT) has variable clinical presentations mimicking other neurological disorders. There is variation in risk factors for CVT in different areas. Study was done with the aim of analyzing the clinical features, risk factors and laboratory parameters on patients diagnosed with CVT on Magnetic Resonance Venography (MRV) and MRI.

Material and Methods: In this retrospective study, data of 70 consecutive patients attending a private neurology center with CVT confirmed on MRV and MRI from May 2016 to April 2019 was analyzed. Laboratory parameters emphasized were hemoglobin content, serum homocysteine level and lipid profile.

Results: Out of 70 patients, 48 were men and 22 women in the age range of 14 to 71 years. Most common presenting symptom was progressive headache (63 cases,90%) alone or in combination with other symptoms like vomiting (22 cases, 31.42%), hemiparesis (17 cases, 24.28%), ataxia (17 cases, 24.28%) and seizures (15 cases, 21.42%). Hyperhomocysteinemia was seen in 15 cases (21.42%), anemia in total 30 cases (42.85%), and alcoholism in seven cases (10%). Twenty four patients (34.28%) had high density lipoprotein (HDL) level of less than 40mg/dl, five patients (7.14%) had total cholesterol more than 200mg/dl and three patients (4.28%) had triglycerides more than 200mg/dl. One patient (1.42%) had protein S deficiency.

Conclusion: CVT is an uncommon but treatable cause of stroke in young patients. Due to variety of clinical presentation, a high degree of clinical suspicion is neccessory for correct diagnosis and early treatment.

Keywords: Cerebral Venous Thrombosis, Hyperhomocysteinemia, Prothrombotic State, Superior Sagittal Sinus

INTRODUCTION

Cerebral Venous Thrombosis (CVT) is a distinct cerebrovascular disorder commonly affecting young adults and children.[1] It has extremely wide spectrum of clinical manifestations. Hence high degree of clinical suspicion is necessary for early and correct diagnosis as the outcome in most of the patients is excellent if treated early. The causes and risk factors of CVT include genetic and acquired prothrombotic disorders, pregnancy, oral contraceptive pills (OCP), deep vein thrombosis (DVT) and central nervous system infections. There is geographic variation in the causes of CVT.[2] Hence a retrospective study was undertaken on 70 patients diagnosed with CVT on Magnetic Resonance Venography (MRV) and MRI at a private neurology center in Western Maharashtra with the aim of analyzing their clinical features, risk factors and laboratory parameters.

MATERIAL AND METHODS

The study included 70 patients attending a private neurology center with a diagnosis of CVT on MR venogram and MRI between a three year period from May 2016 to April 2019. It was a retrospective study. Data was collected from patient's records and analysed for history, clinical features and laboratory investigations which included complete blood count (CBC), HIV status, lipid profile, blood urea, serum creatinine, blood sugar, prothrombin time and serum homocysteine. Assay for antiphospholipid antibody, antinuclear antibody, protein C, protein S and antithrombin III was also done. Hyperhomocysteinemia was defined as serum homocysteine level more than 15mg/100ml in less than 60 year old patients and more than 20mg/100 ml in more than 60 year old patients.[3,4] Anemia was defined as hemoglobin level of less than 13gm/dl in men and 12gm/dl in women as per World Health Organisation (WHO) guidelines.[5] Genetic studies for mutations were, however not done due to economic constraints.

RESULTS

Total 70 patients, 48 men and 22 women diagnosed as CVT on MRI and MR Venogram were included in the study. The age ranged from 14 years to 71 years (Table 1). In all, 44 patients were less than 40 years of age. As depicted in Table 2, 63 patients (90%) presented with progressively increasing headache either alone or in combination with other complaints. Twenty two patients (31.42%) had projectile vomiting while 17 patients each (24.28%) had ataxia and hemiparesis. Fifteen patients (21.42%) presented with seizures. Less common presentations included dysarthria in eight (11.42%), vertigo and blackouts in five patients each (7.14%) and insomnia in two patients. Three patients had Idiopathic Intracranial Hypertension (IIH) and complained

[1]Consultant, Department of Neurology, Samvedana Neurological Hospital, Sangli, [2]Observer, Samvedana Neurological Hospital, Sangli, India

Corresponding author: Dr. Mugdha Pradeep Kulkarni, 'Parijat', Vidyanagar, Lane 6, Warnali Road, Vishrambag, Sangli 416415. Maharashtra, India

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Age groups	Male	Female
11-20	2	4
21-30	12	6
31-40	17	4
41-50	8	6
51-60	5	1
61-70	3	1
71-80	1	_
Total	48	22

Table-1: Showing age distribution of patients

Serial no.	Symptom	No. of patients
1	Headache alone or in combination	63 (90%)
2	Projectile vomiting	22 (31.42%)
3	Hemiparesis	17 (24.28%)
4	Ataxia	17 (24.28%)
5	Seizures	15 (21.42%)
6	Dysarthria	8 (11.42%)
7	Blackouts	5 (7.14%)
8	Vertigo	5 (7.14%)
9	Insomnia	2 (2.85%)

Table-2: Showing distribution of symptoms

Serial No.	Risk factors	No. of patients
1	Anemia	30 (42.85%)
2	Hyperhomocysteinemia	15 (21.42%)
3	Oral Contraceptive Pills	4 (5.71%)
4	Deep vein thrombosis	2 (2.85%)
5	Puerperium	1 (1.42%)
6	Protein C deficiency	1 (1.42%)
7	Protein S deficiency	1 (1.42%)
8	No risk factor	28 (40%)

Table-3: Showing prevalence of risk factors

of diplopia.

History revealed OCP use in four women. Two patients had Deep Vein Thrombosis (DVT). One woman was postpartum and one was hypothyroid (TSH 19.1).

Examination showed papilledema in seven patients (10%). Fifteen patients (21.42%) were hypertensive, two (2.85%) were diabetic and three (4.28%) had both hypertension and diabetes.

On MR Venography, superior sagittal sinus was most commonly involved accounting for 32 (45.71%) cases while other sinuses were also involved either alone or in combination. Multiple sinuses were involved in five (7.14%) cases. Venous hemorrhagic infarcts were seen in 23 (32.85%) cases.

Hyperhomocysteinemia was observed in 15 patients (21.42%). In lipid profile, total 24 patients (34.28%) had HDL less than 40, five patients (7.14%) had total cholesterol more than 200 mg/dl and three patients (4.28%) had triglycerides more than 200mg/dl. One patient (1.42%) had protein S deficiency.

Anemia was seen in total 30 patients including 14 out of 48 men (29.16%) and16 out of 22 (68.18%) women. In men, the anemia was microcytic in five, normocytic in five and macrocytic in four cases. In women, 15 had microcytic and only one had macrocytic anemia.

DISCUSSION

This retrospective study was carried out on 70 patients over a period of three years. There were 48 men and 22 women with a male to female ratio of 2.18:1. Forty four patients (62.85%) were less than 40 years old emphasizing the fact that CVT is a disease affecting the young. Many previous studies from India[6,7,8] have reported a high prevalence of CVT in women and association with postpartum state in a significant number of patients. However, these studies have been carried out almost two to three decades ago when MRI or MR Venography were not widely available. Currently, combination of MRI which visualizes the thrombus and MR Venography which shows the nonvisualization of the vessel is the gold standard for diagnosis of CVT.[2] In our study, all the cases were diagnosed by both MRI and MR Venography. In the NIVSR cohort, Narayan D et al have reported on a study of 428 patients of CVT out of which 230 (53.7%) were men. The mean age in their study was 31.3 years.[9] Pai et al in a large study on 612 patients with CVT have also reported male to female ratio of 3:2.[10] Although our sample size is small, we also have observed more males affected by CVT than females in keeping with other studies.[9,10] The plausible reason for this change in gender trends over the last two decades could be the improvement in obstetric care.

The commonest presentation in our study was progressively increasing headache affecting 63 (90%) patients either alone or in combination with other symptoms. The mechanism of the headache remains unknown in most cases. The two plausible hypotheses are i) stretching of the nerve fibres in the walls of the occluded sinus and ii) local inflammation as suggested by the evidence of contrast enhancement of the sinus wall surrounding the clot.[11] Other symptoms included projectile vomiting (22 cases, 31.42%), ataxia (17 cases, 24.28%), hemiparesis (17 cases, 24.28%), seizures (15 cases, 21.42%), dysarthria (eight cases, 11.42%), vertigo and blackouts (five each, 7.14%) and insomnia (2 cases, 2.85%). Stroke-like presentation was seen in 17 patients (24.28%) while focal or generalized seizures were seen in 15 cases (21.42%), two of which presented with status epilepticus. In the NIVSR cohort, headache was observed in 378 patients (88.3%), vomiting in 298 (69.6%) and seizures in 171 (39.9%) patients with CVT. Stroke like presentation was observed in 122 (28.5%) while isolated seizures were noted in 126 (29.4%) cases.[9] Other studies have also reported headache as the commonest presenting symptom of CVT.[6,7,12]

On MR Venography, superior sagittal sinus was most commonly involved (32 patients, 45.71%), left transverse sinus alone and combined with left sigmoid sinus in seven patients each (10%), right sigmoid and right transverse sinus together in four cases (5.71%) while straight sinus, right transverse sinus and left sigmoid sinus were involved in three cases (4.28%) each. One case (1.42%) each of right and left cavernous sinus thrombosis was noted. Involvement of

more than two sinuses was observed in five (7.14%) patients. Similar observations have been reported by Narayana D *et al* and Patil *et al*.[9,12] Idiopathic intracranial hypertension (IIH) was seen in three patients (4.28%). Twenty three (32.85%) patients showed venous hemorrhagic infarcts on MRI.

Table 3 shows the distribution of risk factors in our study. Some patients had more than one risk factors. Hyperhomocysteinemia is an independent and strong risk factor for CVT. It was seen in 15 patients (21.42%), 13 men and two women.

Use of OCP is associated with an increased risk of CVT. The risk of CVT with OCP use is more in women with a hereditary prothrombotic factor.[5] In developed countries, OCP as a risk factor for CVT has been more commonly reported compared to the developing countries. In the prospective International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) cohort of 624 adults with CVT, 46% of women were on OCP. Narayan D et al have reported only 11.4% prevalence of OCP in their study.[9] Many other series from India have also shown a much lower proportion of OCP usage as a risk factor for CVT compared to series from west. This could be due to different sociocultural environment of our patients and western patients.[13] We had only four women (5.71%) on OCP in our study.

Pregnancy and puerperium are well known risk factors for CVT. Most of the pregnancy related CVTs occur in third trimester or in puerperium.[5] We had a single woman three weeks postpartum and we did not encounter any pregnant patient. The NIVSR study and the study by Pai et al have reported 9.8% and 8% prevalence of patients with CVT in the postpartum or pregnant state respectively.[9,10]

Antithrombin (or antithrombin III) is the major plasma protease inhibitor of thrombin and the other clotting factors in coagulation. Inherited quantitative or qualitative deficiencies of antithrombin lead to a lifelong predisposition to venous thromboembolism. Protein C is a plasma glycoprotein that becomes an anticoagulant when activated by thrombin. Protein S is also a glycoprotein that acts as cofactor of protein C. Quantitative or qualitative deficiencies of protein C or S or resistence to the action of activated protein C by a specific mutation at its target cleavage site in factor V (factor V Leiden) lead to hypercoagulable states.[5]

We had a single (1.42%) case of protein S deficiency. Narayan et al have reported protein S deficiency in 53 (12.3%) out of 428 patients while Pai et al have quoted the prevalence of thrombophilia markers to be 18% in their study.[9,10] The proportion of CVT patients with prothrombotic condition in India has been under reported in the earlier studies probably due to lack of facilities for protein C or S estimations as well as imaging.

Abnormal lipid profile was seen in total 29 patients. Twenty four had HDL level less than 40 mg/dl, five had total cholesterol more than 200mg/dl and three patients had triglycerides more than 200mg/dl.

History of alcoholism was obtained in six males. Alcohol contributes to thrombosis by dehydration, hypercoagulability and reactive thrombocytosis.[9]

One female was hypothyroid (TSH of 19.1) while one male was diagnosed with carcinoma of prostate with extensive skeletal metastases.

CONCLUSION

CVT is an uncommon but treatable cause of stroke in young patients, both men and women. Although the clinical presentation is variable, a high degree of clinical suspicion especially in cases with risk factors like use of OCP, hyperhomocysteinemia or a procoagulant state aids in correct diagnosis and early treatment.

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