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Cerebral venous thrombosis and the eye: the neuro-ophthalmology of cerebral venous blood clot

Ashutosh Kumar Mishra[1], Ruchi Shukla[2], Archana Verma[3], Rameswar Nath Chaurasia[4]

[1] Assistant professor, Department of Neurology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India -229405

[2] Assistant professor, Department of Ophthalmology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India -229405.

[3]Professor, Department of Neurology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India -229405

[4] Professor, Department of Neurology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, Uttar Pradesh 221005, India.

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Abstract

Introduction: Cerebral venous thrombosis (CVT) is a form of venous thromboembolism which has varied clinical presentation. Ocular clinical features are quite common in CVT and may be the sole presenting feature and often tend to get misdiagnosed. This study was conducted to analyse clinical features especially neuro ophthalmological manifestations in CVT patients.
Materials and Methods: In this prospective study 60 patients were enrolled in a study period of 3 years at tertiary care hospital. Follow up visits were performed at 1 month, 3 months, 6 months and 12 months after the initial diagnosis. We analysed the clinical features as well as aetiology of CVT, special focus was on the ocular symptoms and signs.
Results: Headache was the most common clinical symptom with 93.33% patients. Among ocular symptoms 43.33 % patients presented with complaint of blurring of vision. Among ophthalmological signs papilledema was reported in 40.0 % patients, cranial nerve involvement in 10.0 % patients, diplopia was seen in 6.66 % patients. In patients with papilledema the intensity reduced as time progressed. Vision loss was seen in 2 patients who had secondary optic atrophy.
Conclusion: To avoid misdiagnosis and for the prevention of vision deterioration the ophthalmologist must pay attention to CVT symptoms and signs when patients present with ocular symptoms as the initial manifestation.

Keywords: Cerebral Venous Thrombosis, Ocular symptoms, Optic atrophy, Papilledema

Introduction

Cerebral venous thrombosis (CVT) is an uncommon form of venous thromboembolism (VTE). CVT is a multifactorial condition with specific sex-related specific causes.[1] The disease is observed in 0.5–3% of all cases of stroke.[2]

CVT has a varied presentation, making it very difficult to diagnose unless a high degree of suspicion is present. The presentation can be acute, subacute, or chronic. The various signs and symptoms at presentation are headaches, which are the most common and present in >80% of cases. seizures, present in 35%–40% of cases; focal neurological signs, 30%–35%; altered sensorium, 30%; blurred vision; and vomiting.[3] Neuroimaging is the cornerstone of the diagnosis of CVT. The imaging modalities of choice in CVT are computed tomography (CT) scans and magnetic resonance imaging (MRI) with a magnetic resonance venogram (MRV).

Neuro-ophthalmological symptoms are related to intracranial hypertension leading to papilledema.[4]
Papilledema (optic disc swelling) is the most common ocular manifestation of increased intracranial pressure (ICP). Papilledema often produces brief episodes of monocular or binocular visual loss, called transient visual obscuration's (TVOs).

Untreated papilledema can lead to progressive, irreversible visual loss and secondary optic atrophy in up to 31% of patients.
There are many mechanisms suggested for visual impairment in CVT: (1) Optic nerve dysfunction secondary to raised ICP:

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Address for correspondence:
Dr. Ruchi Shukla, MS (Ophthalmology),
Assistant professor, Department of Ophthalmology, All India Institute of Medical Sciences, Raebareli, Uttar Pradesh, India -229405
Email id: ruchi.shukla05@gmail.com

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benign intracranial hypertension (2) Venous infarcts in the occipital cortex; (3) Raised ICP on the optic nerve following the development of a secondary Dural AV fistula following the CVT (4) Bilateral or unilateral arterial occipital infarcts due to posterior cerebral artery compression in survivors of uncal herniation in large venous infarcts.[5]

Therefore, early diagnosis and treatment of patients with visual symptoms and signs in cases of CVT significantly improves the outcome of the disorder.

The present study was conducted to analyse clinical as well as neuroimaging features, with a special focus on ocular manifestations in CVT patients.

Materials and Methods

In this study, 60 patients were enrolled for a study period of 3 years at a tertiary care hospital. A valid informed consent was taken from all patients with suspected clinical features of having CVT. Ethical approval was given by Institute Ethical Committee, Institute of medical sciences, BHU (Dean/2016-17/EC/724). Patients satisfying the inclusion and exclusion criteria were selected from the OPD during the study period and subjected to a detailed clinical history, laboratory investigations, and ocular, neurological, and radiological examination (including CT scan and MRI/MRV) as per the standard protocol.

Inclusion criteria: patients diagnosed with CVT during the study period; any age group presenting with CVT; patients who gave consent for the prospective study.

Exclusion criteria: patients unwilling to participate in the study; patients whose radiological workup did not confirm CVT.

Based on the time from symptom onset to hospital admission, mode of onset was categorized as acute (0–48 hrs.), subacute (48 hrs.–30 days), or chronic (>30 days).

Ocular examination included visual acuity, pupillary examination, fundus photograph, extraocular movements for cranial nerve palsies, and automated perimetry at the time of presentation and follow-up. Visual acuity was recorded using the electronic Snellen visual acuity charts and converted to log MAR.

Papilledema was graded clinically based on fundus photographs using Friesen's grading :

Grade 0: There is no halo of obscuration of the peripapillary nerve fibre layer.

Grade 1: There is a C-shaped halo of retinal nerve fibre layer oedema obscuring the peripapillary retina.

Grade 2: The halo is now circumferential; there is no temporal gap and no vessel obscuration.

Grade 3: Major vessels are obscured by oedema as they leave the disc.

Grade 4: Major vessels are now obscured by oedema on the optic disc.

Grade 5: All vessels are at least partially obscured by oedema.

Automated perimetry was done using Humphrey visual field analyser (Carl Zeiss Meditec, Inc, Jena Germany) at presentation and follow-up visits was analysed to look for patterns of visual field defects. Visual fields had been performed using the 24-2 Swedish Interactive Threshold Algorithm (SITA) FAST testing strategy wherever possible. Observations were recorded, and analysis was done using Statistical Package for Social Sciences (SPSS) window software v. 16. A P-value of 0.05 is considered statistically significant. Follow-up visits were performed at 1 month, 3 months, 6 months, and 12 months.

Results

In this study, 60 patients were diagnosed with CVT, of whom 41 (68.33%) were in the age group of 21–40 years. The male: female ratio was 0.875:1 (28/32). Out of 60 patients, headache was the most common clinical symptom in 93.33% (56 patients).

Ophthalmological signs Papilledema was reported in 40.0% (24) patients; cranial nerve involvement was seen in 10.0% (6) patients; and diplopia was seen in 6.66% (4) patients. Considering the aetiology of CVT, a high percentage of patients (61.66%) had anaemia at presentation. Oral contraceptive pill (OCP) use and protein C deficiency were identified as risk factors in 12.5% of CVT patients.

The majority (63.33%) of patients had a presenting BCVA less than or equal to 0.5 log MAR.

At presentation, formal visual fields were performed or were possible in only 44 patients. The most common visual field defect was enlargement of the blind spot in 22.72% of patients, but in a significant number of cases, i.e., 54.54%, the visual field pattern was completely normal. [Table 1]

Table 1: Visual acuity and patterns of the visual field in CVT patients

Visual acuity (logMAR)	Number of patients (%)	Visual field patterns	Number of patients (%)
0-0.5	38(63.33)	Normal	24(54.54)
0.6-1.0	8(13.33)	Enlarged blind spot	10(22.72)
>1.0	12(20.0)	Nasal/temporal depression	6(13.63)
PL absent	2(3.33%)	Central field defects	2(4.54)
		Advanced field loss	2(4.54)

Categorizing the patients on the Friesen's grading scale of papilledema, among 24 patients (40.0%) who presented with papilledema, 6 patients presented with grade 1, 5 patients presented with grade 2, 6 patients with grade 3, 4 patients with grade 4, and 3 patients with grade 5.

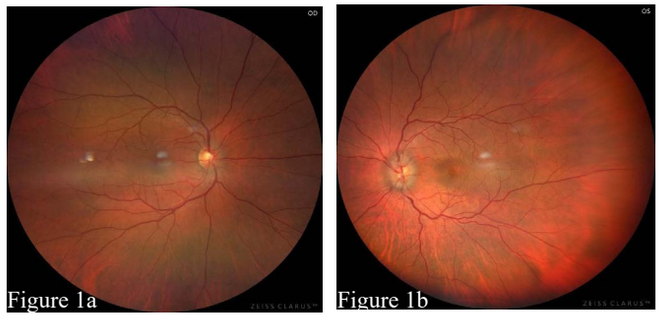

Figure 1a Figure 1b

Fundus photograph showing Grade 1 papilledema in right eye [Figure 1 (a)] and Grade 3 papilledema in left eye [Figure 1(b)] in a patient of Cerebral venous thrombosis

In terms of progression or regression in papilledema, patients were followed up at 1 month, 3 months, 6 months, and 12 months. In this study, the severity of papilledema decreased as time progressed. [Table 2]

Table 2: Changes in grades of papilledema on subsequent follow-up visits

	None	Grade1	Grade 2	Grade 3	Grade 4	Grade 5
	Number of patients (%)	Number of patients (%)	Number of patients (%)	Number of patients (%)	Number of patients (%)	Number of patients (%)
Initial presentation	34(56.67)	6(10.0)	5(8.33)	6(10.0)	4(6.67)	3(5.0)
At 1 month	34(56.67)	4(6.67)	7(11.67)	4(6.67)	6(10.0)	3(5.0)
At 3 months	35(58.33)	6(10.0)	5(8.33)	4(6.67)	5(8.33)	3(5.0)
At 6 months	40(66.67)	10(16.67)	4(6.67)	2(3.33)	1(1.67)	1(1.67)
At 12 months	42(70.0)	9(15.0)	6(10.0)	1(1.67)	0(0)	0(0)

Based on Table 3, the most common sinuses involved were the sigmoid sinus with or without other sinuses (43.33%). In Table 3, the frequency distribution of the type of involved sinus based on papilledema and lack of papilledema is shown. Results show that the most common sinus involved in papilledema patients is the superior sagittal sinus, with or without other sinuses (37.5%). However, the most common sinus involved in patients without papilledema is the sigmoid sinus, with or without other sinuses (55.56%).

Table 3: Sinus Involvement and Its Relation to the Presence of Papilledema

Sinus Involved	Patients		Papilledema Present		Papilledema Absent	
	Number	Percentage	Number	Percentage	Number	Percentage
SSS with or without other sinuses	24	40	9	37.5	15	41.67
Right transverse sinus with or without other sinuses	14	23.33	3	12.5	11	30.5
Left transverse sinus with or without other sinuses	22	36.67	4	16.67	18	50
Sigmoid sinus with or without other sinuses	26	43.33	6	25	20	55.56
Straight sinus with or without other sinuses	2	3.33	0	0	2	5.56
Isolated SSS	10	16.67	1	4.16	9	25
Isolated right transverse sinus	6	10	0	0	6	16.66
Isolated left transverse sinus	7	11.67	1	4.16	6	16.66
Cortical veins	5	8.33	0	0	5	13.88

Discussion

Cerebral venous thrombosis is an uncommon but treatable cause of stroke. Most of the previous literature on CVT is regarding the etiology, clinical profile, mortality, recurrence, and treatment; however, studies on ophthalmological manifestations are quite limited in numbers.

Most authors agree on the predominance of CVT in young subjects; this was also revealed in this study. In this series, 68.13% of the patients had the onset of CVT between 21 and 40 years of age. 15.62% of the patients had onset <20 years. In the present study, the male: female ratio was 0.875:1. Female preponderance across all age groups was also reported by The International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT).[7] The main reason for this is believed to be the high prevalence of postpartum hypercoagulable states, precipitated by dehydration and consumption of high-fat foods in developing countries during the peripartum period.

CVT has a varied pattern of presentation, and it may be difficult to diagnose it on clinical grounds alone.
Considering the risk factors, 61.66% of patients had anaemia. 25% of patients were in the postpartum phase. OCP use and protein C deficiency risk factors identified were present in 12.5% of each of the CVT patients. In a study by Sachdeva et al., 4/9 (44%) patients had multiple prothrombotic risk factors.6 Therefore, a comprehensive thrombotic risk factor evaluation is advisable, along with consultation with a haematologist.

According to previously published literature, headache is the most frequent and, most of the time, the earliest symptom of cerebral venous thrombosis. In this study on analysis of clinical symptoms, 93.33% of patients with CVT presented with headaches. Our results were comparable with those of a study done by Ferro et al., in which 92% of patients presented with headaches.7 The mechanism of headache is postulated to be the stretching of nerve fibres in the walls of the occluded sinus and local inflammation, as suggested by the evidence of contrast enhancement of the sinus wall surrounding the clot.

In a study by Ibrahim EAA, blurring of vision was present in 67.6% of patients.8 In this study, 43.33 percent of patients with CVT presented with blurred vision, and 7.69 percent presented with blurred vision at acute onset. Therefore, to avoid misdiagnosis, the ophthalmologist must pay sincere attention to CVT symptoms and signs when patients present with blurred vision as the initial symptom.

Although there can be a multitude of visual field defects detected on subjective visual field testing, the most common defect is the concentric enlargement of the physiologic blind spot.

In this study, an enlarged blind spot (10/44) was detected in 22.72% of patients. The main cause behind the enlargement of the physiological blind spot is secondary to two proposed mechanisms: compression and lateral displacement of the peripapillary retinal nerve fibre layer or acquired peripapillary hyperopia induced by the elevation of the retina with subretinal fluid. [9]

The disc oedema in papilledema is primarily caused by axoplasmic flow stasis in the optic nerve fibres in the surface nerve fibre layer and prelaminar region of the optic nerve head due to a rise in intracranial pressure (ICP). Visual loss from papilledema can occur even in cases of mild ICP elevation. In early papilledema, vision is usually not affected unless macular oedema, retinal haemorrhage, or exudation occur. With the advent of newer diagnostic modalities like optical coherence tomography (OCT), it has become possible to detect early subclinical cases of papilledema. Hence, OCT should be performed in all cases of CVT to detect subclinical papilledema, thereby preventing the progression of nerve fibre layer loss and visual impairment.

Raised ICP can cause numerous effects on the visual system, the most severe being optic nerve fibre dysfunction as in established papilledema, which leads to progressive diminution of vision and progressive loss of retinal ganglion cells, which can lead to optic atrophy and subsequent vision loss.[10]

In two patients, papilledema progressed to optic atrophy, which led to vision loss. As the prognosis of long-term papilledema is very poor, it is very important to diagnose and treat patients as early as possible to prevent vision loss.

A few studies have reported papilledema in 27–68.7% of CVT cases.11 Papilledema was present in 24 (40%) cases, which was found to be the most common ocular sign.

This result is in correlation with a study done by Saadatnia M et al., in which out of 65 patients, 30 (46.2%) suffered papilledema, with severe oedema in seven patients (23.3%).[12]

Regarding onset of disease, only 2 patients showed papilledema in acute onset, 14 patients had papilledema in subacute onset, and 8 patients showed papilledema in chronic onset. Subacute and chronic CVT patients may seek ophthalmology clinics, as there is a significant presentation of papilledema in subacute and chronic cases. As in this study, 30.76% of patients with chronic CVT presented with blurred vision.

When papilledema was assessed using Friesen's grading, only 29.16% of patients belonged to grade 5. These results are in correlation with a study done by Saadatnia M et al., in which out of 65 patients, 30 (46.2%) suffered papilledema, with severe oedema in seven patients (23.3%).[12]

Cranial nerve involvement was found in 6 (10%) patients, while in a study by Ibrahim EAA et al., cranial nerve involvement was present in only 5.4% of the patients.[8] and this cranial nerve involvement can be attributed to the elevated intracranial pressure, the extension of thrombosis to venous channels, or direct pressure from the clot itself. [12]

In this study, diplopia was present in 4 (6.66%) patients, which commonly occurs due to sixth nerve palsy, which is most vulnerable to increased intracranial pressure due to its extended route to the orbit.

Regarding the progression or regression of papilledema with subsequent follow-ups in our study, papilledema regressed in intensity from its initial presentation. A few studies have also shown a regression in the intensity of papilledema with time.[14]

But by the results, it is clear that even after 1 year, papilledema still exists; hence, the study needs a longer study period to find out the papilledema resolution time.

Cerebral venous sinus thrombosis involving multiple sinuses is frequently reported, but the distribution varies. In the International Study on Cerebral Vein and Dural Sinus Thrombosis, the sagittal sinus was more frequently involved (62%), followed by the transverse sinuses (left: 44.7%, right: 41.2%) and the straight sinus (18%).[7]

Whereas in this study, the most common site of thrombosis was the sigmoid sinus with or without other sinuses in 26 patients (43.33%).

In this study, the most involved sinus in patients with papilledema was the superior sagittal sinus with or without other sinuses in 9 (37.5%), while the most involved sinus in patients without papilledema was the sigmoid sinus with or without other sinuses in 20 (55.56%). The association of papilledema with involvement of the superior sagittal sinus may be due to an increased incidence of raised intracranial pressure with thrombosis of this sinus.

Further studies with a larger sample size are needed to establish this correlation between papilledema and involved sinuses.

Conclusion

CVT, although an uncommon form of stroke, can have varied clinical presentations, of which the ocular manifestations are quite common and are usually overlooked. The most common ocular sign is papilledema, which, if not diagnosed and treated early, may lead to permanent visual loss. In this study, papilledema was found in a high number of cases of superior sagittal sinus thrombosis. Although papilledema regressed in most patients, it remained in some for a period longer than a year. Therefore, we suggest that all diagnosed cases of CVT on MRV should have an early and complete ophthalmological examination at presentation, along with serial monitoring of ophthalmological features, to detect any presence of delayed onset or progression of papilledema.

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