

Cerebral Venous Thrombosis - Clinical Presentations

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Abstract

Cerebral venous thrombosis (CVT) is an under diagnosed condition for acute or slowly progressive neurological deficit. CVT is less frequent than arterial thrombosis. CVT has a wide spectrum of signs and symptoms, which may evolve suddenly or over the weeks. It is clinically challenging and mimics many neurological conditions such as, meningitis, encephalopathy, benign intracranial hypertension, and stroke. With increasing awareness, CVT cases are now being diagnosed more frequently. Newer imaging procedures have led to easier recognition of venous sinus thrombosis, offering the opportunity for early therapeutic measures. It may be difficult to diagnose it on clinical grounds alone. Headache is the most frequent symptom in patients with CVT, present in about 80% of cases. Most common pattern of presentation is with a benign intracranial hypertension-like syndrome. The prognosis of CVT is worse in elderly subjects. The shorter the history the more likely is the presence of focal signs. Sixth cranial nerve palsy usually manifests as false localizing sign. Subarachnoid haemorrhage (SAH) has been described, as the presenting event with CVT. Patients may have seizures that can be recurrent. Cranial nerve syndromes are seen with venous sinus thrombosis. Psychiatric disturbances are sometimes the presenting symptoms. CVT, an important cause of stroke in puerperium, is frequently observed in India. We have seen 6 patients of CVT out of 490 stroke registry. Of these 6, four were females and two were males. The mean age among females was 27.75 years and among males was 41.5 years. Of the 4 females two were postpartum; one was on oral contraceptive and in one Antiphospholipid antibodies (APLA) were positive. Amongst two males one had hyperhomocysteinemia and one had hyperlipidemia.

Introduction

Cerebral venous thrombosis (CVT) is often an under diagnosed cause for acute or slowly progressive neurological deficit. It was recognized more than 150 years back, but on autopsies and was therefore always considered lethal. CVT is less frequent than arterial thrombosis, but may leave a sequel or may be fatal if not recognized and treated early.¹ CVT has wide spectrum of signs and symptoms, which may

evolve suddenly or over weeks. It is clinically challenging and mimics practically all-neurological conditions such as, meningitis, encephalopathy, benign intracranial hypertension, and stroke. It can affect all age groups with unpredictable outcome but it is not as fatal as was presumed in the past.² With increasing awareness of this entity and easy accessibility to non invasive tests like CT and MRI scans, CVT cases are now being diagnosed more frequently and it is now thought to occur more commonly than previously assumed. It is also probably true that this condition is more frequent in the underdeveloped countries.^{3,4} Thrombosis of the venous channels in the brain is an uncommon cause of cerebral infarction relative to arterial disease. Venous thrombosis may present with headache and cranial nerve palsies. Newer imaging procedures have led to easier recognition of venous sinus thrombosis, offering the opportunity for early therapeutic measures. Venous thrombosis may be associated with other medical complications that require therapeutic intervention.¹

Anatomy

Venous blood from the brain flows via the superficial (cortical) and the deep cerebral veins into the venous dural sinuses. There are numerous connections between the cortical veins and dural sinuses, and also with the venous system of the meninges, scalp and nasal sinuses. This facilitates the spread of thrombus or infection via the emissary veins to the intracranial venous system and adjacent brain parenchyma. The communication between the intracranial and extracranial venous system also may allow the opening of collateral draining vessels in the event of an occlusion.⁵

Pathology

Pathological findings have been extensively studied.⁶ These vary according to the site of thrombosis and the interval between the onset of symptoms and death. The thrombus itself is like other venous thrombi elsewhere in the body. When it is fresh, it is rich in RBCs and fibrin and poor in platelets; when it is old, it is replaced by fibrous tissue, sometimes showing recanalization. Its formation is due to the usual pathogenetic factors- mostly venous stasis, increased clotting tendency (Thrombophilia), and changes in the vessel wall. Its location and extension are variable.⁶

Pathogenesis

To understand the symptoms and signs of sinus thrombosis, two different mechanisms should be distinguished: thrombosis of the cerebral veins, with local effects caused by venous obstruction, and thrombosis of the major sinuses, which causes intracranial hypertension.⁷ In the majority of patients, these two processes occur simultaneously. The first mechanism, occlusion of the cerebral veins, can cause localized oedema of the brain and venous infarction. Pathological examination shows enlarged, swollen veins, oedema, ischaemic neuronal damage, and petechial haemorrhages. Two different kinds of cerebral oedema can develop. Cytotoxic oedema is caused by ischaemia, which damages the energy-dependent cellular membrane pumps, leading to intracellular swelling. The second type, vasogenic oedema, is caused by a disruption in the blood-brain barrier and leakage of blood plasma into the interstitial space. The second mechanism leads to the development of intracranial hypertension as a result of occlusion of the major venous sinuses.⁷ Normally, the cerebrospinal fluid is transported from the cerebral ventricles through the subarachnoid spaces at the base and surface of the brain to the arachnoid villi, where it is absorbed and drained into the superior sagittal sinus. Thrombosis of the sinuses leads to increased venous pressure, impaired absorption of cerebrospinal fluid, and consequently, increased intracranial pressure. The obstruction to the drainage of cerebrospinal fluid is located at the end of its transport pathway, and no pressure gradient develops between the subarachnoid spaces at the surface of the brain and the ventricles. Hence, the ventricles do not dilate, and hydrocephalus does not normally complicate venous sinus thrombosis. About one fifth of patients with venous sinus thrombosis have intracranial hypertension only, without signs of cortical vein thrombosis.⁸

Clinical Aspects

CVT presents with a remarkably wide spectrum of symptoms.⁶ In contrast to the arterial stroke, which can be easily diagnosed clinically in majority of cases, CVT has no single pattern of presentation and it may be difficult to diagnose it on clinical grounds alone. Headache is the most frequent symptom in patients with CVT, present in about 80% of cases.⁶ However, headache presenting as the only symptom of CVT is rare⁹⁻¹¹ and it is usually seen in combination with other neurological signs and symptoms (seizures, focal neurological deficit and signs of intracranial hypertension.). It may have acute, subacute, or chronic presentation. In a study of 48 subjects Terazzi et al reported that onset was acute in 44%, subacute in 35% and chronic in 21%.¹²

The most common pattern of presentation is with a

benign intracranial hypertension-like syndrome especially in patients with a history extending over several weeks. Elderly patients with CVT have a distinctive clinical presentation: isolated intracranial hypertension is uncommon, whereas mental status and alertness disturbances are common. The prognosis of CVT is worse in elderly subjects.¹³ The shorter the history the more likely is the presence of focal signs. Sixth nerve palsy usually manifests as a false localizing sign, but it may be the result of extension of thrombus into the inferior petrosal sinus. Subarachnoid Haemorrhage (SAH) has been described, as the presenting event with CVT. CVT should be considered in the workup of SAH, especially when the basilar cisterns are not involved.¹⁴ Patients with lateral sinus thrombosis may present with a pseudotumor cerebri-like syndrome. Farb et al found that 27 of 29 patients with idiopathic intracranial hypertension had bilateral sinovenous stenosis.¹⁵

Patients may have seizures that can be recurrent. Seizures are inaugural in 12% to 15% of cases and are present at some time during the course of CVT in about 40% of cases.⁶ Both focal and generalized seizures are almost equally common. Status epilepticus may occur and can be difficult to control. Seizures are particularly common in children, especially neonates. Mental status may be quite variable, with patients showing no change in alertness, developing mild confusion, or progressing to coma. Focal neurological deficit may occur depending on the area involved, hemiparesis may be encountered, and in some cases of sagittal sinus thrombosis, there is involvement of bilateral lower extremities. Aphasia, ataxia, dizziness, chorea, and hemianopia have been described in CVT.¹

Cranial nerve syndromes are seen with venous sinus thrombosis. These may include vestibular neuronopathy, pulsatile tinnitus, unilateral deafness, double vision, facial weakness, and obscuration of vision.¹ If the thrombosis extends to the jugular vein, the patient may develop involvement of cranial nerves IX, X, XI, and XII (jugular foramen syndrome). Cavernous sinus thrombosis may lead to III, IV and VI cranial nerve palsies. Cavernous sinus thrombosis with obstruction of the ophthalmic veins may be associated with proptosis and ipsilateral periorbital oedema. Retinal haemorrhages and papilloedema may be present. Paralysis of extraocular movements, ptosis, and decreased sensation in the first division of the trigeminal nerve are often observed and add onto varied presentations of CVT. Psychiatric disturbances (irritability, lack of interest, anxiety, depression) are sometimes the prevailing symptoms. The symptoms can be particularly misleading during the postpartum period and may raise the possibility of postpartum psychosis. Two case-control studies have shown an increased risk of sinus thrombosis in women who use oral contraceptives.^{16,17} Until the mid-1970s, men and women

were equally affected.¹⁸ More recently, there has been a significant female predominance among young adults with sinus thrombosis (70 to 80 percent of cases are in women of childbearing age) but not among children or elderly persons.¹⁹ Cerebral venous thrombosis (CVT), an important cause of stroke in puerperium, is frequently observed in India.^{3,4} In one prospective study of cerebrovascular accidents, 64 cases of cerebral venous thrombosis (CVT) were evaluated in pregnancy and puerperium. CVT made up approximately half of the young strokes and 40% of strokes occurring in females. Majority of them were below 25 years of age.²⁰ Post gestational and post puerperal CVT has been described more often from the Indian subcontinent with post puerperal occurring more commonly rather than due to use of oral contraceptive (OC) pills [38.4%].² We have recruited 490 stroke patients in the Stroke Registry from April 2001-April 2005 at G.B. Pant Hospital (a tertiary care referral hospital) out of which only 6 (1.3%) patients were confirmed to have CVT. This may not reflect the true occurrence of CVT out of total number of strokes, but this is still an uncommon disease. Out of 6, four were females and two were males. The mean age in females was 27.75 years and 41.5 years in males. Of the 4 females, two were postpartum, one was on oral contraceptives in one Antiphospholipid antibodies were significantly raised. Amongst two males one had hyperhomocysteinaemia and one had hyperlipidaemia.

With such a wide spectrum of neurological signs and mode of onset the clinical presentation of CVT is mainly divided into the five following patterns:

1. Isolated Intracranial Hypertension
2. Focal Cerebral Signs
3. Cavernous Sinus Thrombosis
4. Subacute Encephalopathy
5. Unusual Presentations

Diagnosis

The confirmation of diagnosis of dural venous sinus thrombosis is reliant on demonstration of the thrombus by neuroimaging. Non-invasive imaging by magnetic resonance venography is used in preference to cerebral angiography, although CT contrast venography remains popular in some centers, and may be a superior technique in certain cases. The 'typical' empty delta sign seen on contrast CT scanning is present only in 20% of cases. This is seen on axial CT images, and represents enhancement with intravenous contrast of the wall of the posterior sagittal sinus, outlining the clot within the lumen anteriorly. In most centers however, MRV is usually the investigation of choice for demonstrating dural sinus thrombosis, as it may exclude

significant alternative diagnoses and will also demonstrate cerebral venous infarction complicating cerebral venous occlusion. Difficulties in diagnosis arise due to unusual normal anatomical variants and cases where there is near-occlusion of the venous sinus.

Lumbar puncture (LP) is usually not helpful in establishing the diagnosis of dural sinus thrombosis, although abnormalities are commonly found.⁵ It may show raised pressure, pleocytosis, increased red cells or elevated CSF protein. Conversely, LP may be required in severely ill patients with venous sinus thrombosis to exclude other treatable diagnoses within relevant clinical settings such as subarachnoid haemorrhage and bacterial meningitis. Also, in patients with an isolated intracranial hypertension (BIH) presentation, an abnormal LP may suggest the diagnosis.

Appropriate investigation towards possible etiology (Table) in each case should also be conducted.

Table. List of various factors known to cause CVT.

<p>* Endocrine disorders</p> <ol style="list-style-type: none"> 1) Oral contraceptive 2) Pregnancy/puerperium. Symptoms usually occur in puerperium 3) Androgen therapy <p>* Haematological/Immunological</p> <ol style="list-style-type: none"> 1) Antiphospholipid antibody syndrome. 2) Anaemia 3) Prothrombotic states: antithrombin III deficiency, protein S & C deficiency 4) Leukaemia 5) Lymphoma 6) Myeloproliferative disorders 7) Paroxysmal nocturnal haemoglobinuria 8) Sickle cell disease 9) TTP <p>* Connective tissue and other inflammatory conditions</p> <ol style="list-style-type: none"> 1) Behcet's 2) Temporal arteritis 3) Inflammatory bowel disease 4) Sarcoid 5) SLE 	<p>* Infective</p> <ol style="list-style-type: none"> 1) Abscess 2) Subdural empyema 3) Meningitis 4) Sinusitis 5) Suppurative otitis media 6) Septicaemia 7) Endocarditis <p>* Neoplastic</p> <ol style="list-style-type: none"> 1) Cerebral metastases 2) Disseminated malignancy 3) Glomus tumor 4) Meningioma 5) Visceral malignancy. associated with CVT in the absence of macroscopic cerebral metastases <p>* Miscellaneous</p> <ol style="list-style-type: none"> 1) Cardiac failure 2) Jugular vein thrombosis/ligation
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Treatment

The priority of treatment in the acute phase is to stabilize the patient's condition and to prevent or reverse cerebral herniation, which may require the administration of intravenous mannitol, surgical removal of the haemorrhagic

infarct, or decompressive hemicraniectomy. Possible causes of sinus thrombosis, such as infections, should be searched for and treated.

The most obvious treatment option is anticoagulation with heparin to arrest the thrombotic process and to prevent pulmonary embolism, which may complicate sinus thrombosis. However, anticoagulant treatment has raised much controversy because of the tendency of venous infarcts to become haemorrhagic. Most neurologists now start treatment with heparin as soon as the diagnosis is confirmed, even in the presence of haemorrhagic infarcts.

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