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Complications associated with Cerebral Venous Thrombosis

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Abstract

Although CVT is associated with a good outcome in the majority of cases, it may be complicated by numerous unique and sometimes rare complications. The purpose of this review is to discuss the acute and chronic complications of CVT in greater detail. Awareness may lead to a more aggressive approach in those in which these complications are anticipated and perhaps avoided.

The complications of CVT may be temporally divided into those unique to the acute stage and those that are associated with the chronic stage of CVT. They are venous infarction and haemorrhage, subarachnoid haemorrhage, a rapid progression and pulmonary embolism. In the chronic stages of CVT, one may encounter dural AV - fistula, progressive psychiatric disease, residual epilepsy and recurrence. Cerebral venous sinus thrombosis is associated with unique acute and chronic complications, some of them may be avoidable e.g. pulmonary embolism. The chronic complications are rare but are potentially treatable e.g. dural AVFistula nidus obliteration with intervention.

Acute Complications

Venous infarction and haemorrhage is the most common and well-recognized complication of sinovenous thrombosis.

Venous infarction and haemorrhage

Parenchymal oedema with venous infarction and haemorrhage, complicates about 10-50% of cases, principally affecting the cortex and adjacent white matter.¹ Haemorrhagic infarcts are included in bad prognostic indicators of CVST by 'International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT)'.²

The Pathophysiology of venous infarction is thought to be primarily due to elevated venous and capillary pressure caused by the persistence of thrombosis.³ Extensive collateral circulation within the cerebral venous system allows for a significant degree of compensation in the early stages of venous occlusion. Elevated cerebral venous pressure due to cerebral venous occlusion can result in a spectrum of phenomena including a dilated venous and capillary bed, development of interstitial oedema, increased cerebrospinal fluid production, decreased cerebrospinal fluid absorption and rupture of venous structures (haematoma). All of these pathophysiological changes may explain the clinical observation that cerebral venous occlu-

sion, if promptly diagnosed and adequately managed, contains reversible alterations and need not always lead to venous infarction.

The rate of thrombosis is also an important factor in the evolution of venous infarction.⁴ It may be acute and stroke-like or it may be gradual, allowing time for the development of collateral venous circulation, which may protect against venous infarction or limit its extension.

The infarction due to CVST is frequently haemorrhagic with accompanied bleeding in subarachnoid and subdural spaces as discussed in detail later. The reason behind this haemorrhagic predisposition is probably the same elevated venous and capillary pressure due to persistent thrombus. Pale venous infarcts may occur, which do not conform to an arterial territory. Because of the increased venous pressure, there is early swelling of the infarct and adjacent brain.

CVST particularly thrombosis of internal cerebral veins is also a potential risk factor for neonatal intraventricular haemorrhage and periventricular leukomalacia, particularly when the infant is near term and has bilateral haemorrhagic lesions as described by Ehlers H, Courville CB (1936).⁵

The treatment of venous haemorrhagic infarct differs from its arterial counterpart over the issue of the use of anticoagulants.

After the separate trials conducted by Einhaupl⁶ and De Bruijn⁷ there is general agreement that intravenous heparin should be the first-line treatment of CVST, even in the presence of haemorrhagic infarction, provided there are no general contraindications to its use.

Subarachnoid Haemorrhage

The presentation of CVST sometimes greatly mimics subarachnoid haemorrhage. Thunderclap headache, typical of subarachnoid haemorrhage is reported in more than 10% of cases. Seizures and hemi-paresis, possible manifestations of subarachnoid haemorrhage, occur in about one third of cases with CVST. Rarely, CTscan may show a subarachnoid haemorrhage and patients with CVST may present with both clinical and radiologic features which mimic an acute subarachnoid haemorrhage from a bleeding aneurysm. It is important to establish whether subarachnoid haemorrhage is due to CVST, as this requires a completely different treatment from subarachnoid haemorrhage due to a leaking aneurysm.

The pathophysiology is similar to venous infarction with raised venous pressure due to persistent thrombus leading to rupture of a dilated tributary vein of an involved sinus.⁸ As superior Sagittal sinus is the most frequent involvement in CVST, so Sylvian vein is the usual culprit. Oppenheim et al.⁹ Zare et al.¹⁰, Shukla et al. (JAPI 2006).¹¹ The result is the involvement of sulci of the convexity and sparing of the basal cisterns. The irritative effect of blood in sulci leads to the symptoms of focal seizure and hemiparesis. There is only one case report published on the involvement of posterior circulation.¹²

As in case of venous haemorrhagic infarction, although the literature is sparse, there are reports of the use of heparin in this situation with relative safety.^{8,10,12} There is a special condition pointed out in a Japanese case report when SAH occurs in a patient of CVST complicated with multiple aneurysms and it becomes quite confusing to decide the cause of haemorrhage as well as the timing of surgery for aneurysms.¹¹ They recommend that in SAH cases, the venous phase should be examined at least in one side of the carotid arteries to avoid such confusion.

Pulmonary Embolism

It is an uncommon complication but has poor prognostic implication as described by 2ISCVT. A review of literature between 1942 and 1990 by Diaz et al.¹³ revealed that in 11.3% cases CVST was associated with pulmonary embolism and in these cases the overall mortality rate was 95.6%, far higher than in those without embolism. They found out that even in the absence of systemic thromboses, the occurrence of pulmonary embolism strongly suggests dislodgment from cerebral venous sinus system. Superior Sagittal sinus appeared to be the most important source.

Other thrombotic events like involvement of calf veins, pelvic veins, hepatic veins, and/or extra cranial veins also occur. According to Bousser in his follow up of 77 patients, proven thrombotic events other than sinovenous thrombosis occurred in 14% of CVST patients.¹⁴ This systemic thrombosis can be an independent source of pulmonary embolism. Thus, the prevention of pulmonary embolism is probably an important ancillary benefit of anticoagulation in patients with CVST, particularly patients with an identified predisposition to thrombus formation.

Rapidly Progressive Illness and coma

This is a very rare occurrence, usually associated

with the extensive involvement of deep cerebral venous system.¹⁵ The classic picture is that of a child with an acute coma associated with decerebrate decortication, extrapyramidal hypertonia, signs of raised intracranial pressure, papillary changes, and rise in blood pressure leading to death in a few hours or days. Similar cases are reported in adults. When patients survive, severe sequelae, such as akinetic mutism, mental retardation, dementia, bilateral athetoid movement, hemiparesis, vertical gaze palsy, and dystonia are common.

Rapidly progressive state can also arise due to extension of thrombosis leading to complete occlusion of the superior sagittal sinus (SSS) and right transverse/sigmoid sinus complex.¹⁶ The presentation is usually a history of several days of illness with severe headache and photophobia that changes its course to a rapid deterioration and coma.

If large unilateral infarcts or haemorrhages compress the diencephalons and brain stem; patients may become comatose or die from cerebral herniation if untreated. Other causes of coma are involvement of the thalamus and generalized seizures.¹⁷

ISCVT regards coma as one of the poor prognostic indicators and involvement of deep cerebral veins as variable indicating dependency and increase risk of death.²

Due to poor prognosis, aggressive measures are favoured in this setting. In the rare patient who develops coma, fixed and dilated pupils, and brain herniation, early intervention by emergency decompressive craniectomy may be helpful.¹⁸

Surgical thrombectomy or microsurgical revascularization with venous bypass for aseptic lateral sinus thrombosis and superior sagittal sinus thrombosis may be considered in patients with a rapidly progressive course despite appropriate medical therapy. Use of attractive techniques like Microsnare, AngioJet, intravascular laser and intravascular ultrasound for thrombus disruption are still experimental.⁴

One additional method of clot disruption is to perform balloon angioplasty within the clot to disrupt it and facilitate the effect of the thrombolytic agent.^{4,16} This technique may be helpful in patients with rapid clinical worsening and extensive thrombosis. The balloon may also be inflated in the clot and used to pull the clot into the jugular vein, such as is done in peripheral vascular diseases (Fogarty technique).

Complications due to cavernous involvement

There are certain complications specific for cavernous sinus thrombosis. A Korsakoff-like amnesic syndrome with confabulation has been described with bilateral mesial temporal lobe infarction following bilateral cavernous sinus thrombosis.⁴ Furthermore, thrombosis of the cavernous sinus may be associated with the syndrome of inappropriate antidiuretic hormone secretion (SIADH) from effects on the nearby pituitary and in extreme cases can lead to hypopituitarism.¹⁹ Ocular oedema and/or compression of optic nerve may result in blindness.⁴ Inter-cavernous internal carotid artery may be involved leading to hemiparesis.⁴ Early institution of antibiotics is mandatory for minimizing complications, as the usual cause of cavernous sinus thrombosis is infection.⁴

Other rare acute complications

Other rare acute complications of CVST include bilateral subdural effusion as reported in three cases by Marquardt et al.²¹, and intracranial hypotension in cases of extended dural sinus thrombosis.

Mosa et al.²² describe a rare syndrome called Syndrome of blindness, ophthalmoplegia and extensive radiculopathy in two cases characterized by acute bilateral visual loss, complete internal and external ophthalmoplegia, and areflexic flaccid quadriplegia with normal sensorium along with raised ICP. The possible cause is raised intracranial pressure due to CVST. Early and aggressive measures to decrease ICP led to marked recovery in both cases.

Chronic Complications

Development of AV fistula

Development of AV fistula is the most interesting though rare chronic complication of CVST.²³ There is a clear-cut association between CVST and dural arteriovenous fistulas, although it may be difficult in some cases to ascertain if the thrombosis was a primary or secondary event. According to Tripathi et al.²⁴, DAVFs can be classified into two major groups: cavernous sinus DAVFs (CS-DAVFs) and noncavernous sinus DAVFs (NCS-DAVFs). Approximately 30% of symptomatic intracranial DAVFs involve the transverse and sigmoid sinuses. Tsai et al.²³ in his analysis of 69 patients of DAVFs states that out of 69, the most frequent location of Dural AVF was the cavernous sinus (21 (30%)), followed by the skull base (13 (19%)), transverse sinus (12 (17%)), Dural convexity (8 (12%)), sigmoid sinus (7 (10%)), torcular Herophili (5 (7%)), and superior sagittal sinus (3 (4%)). Symptoms depend upon the location of AV fistulas.

DAVFs due to CVST are uncommon in young children with atypical clinical presentation representing with prematurity and delayed milestones with childhood hemiplegia as described by Tripathi in a case report. Confusion can be created by the possibility of a sequel of hypoxic-ischemic encephalopathy or a TORCH infection.²⁴

Two hypotheses have been proposed for the pathogenesis of Dural AVF.²³ The first is based on the physiological arteriovenous shunts between the meningeal arterial networks and the dural venous sinuses. An increase in sinus and venous pressure—for example, by the obstruction of venous outflow by CVST, may open these channels to create Dural AVFs. The second hypothesis, as shown in the rat model, suggests that venous hypertension induced by an obstruction to venous outflow may reduce cerebral perfusion and lead to ischemia, followed by angiogenesis. The aberrant angiogenic activity of the Dural blood vessels would then result in arteriovenous shunting. In both, CVST may be the primary event that caused the venous hypertension. The occurrence of secondary thrombotic event is also a possibility probably because of the turbulent flow into the venous sinus due to DAVFs.

Hung-Yi et al. in a case study described Serial Venous Transcranial Color-Coded Sonography as a useful technique for detecting disturbance of cerebral venous circulation and for follow-up of patients with cerebral venous sinus thrombosis.²⁵ Valuable information such as flow direction and changes in the Doppler flow waveform, which cannot be routinely obtained by time-of-flight MR angiography, can be recorded easily and noninvasively with venous TCCS. Although TCCS cannot examine all the intracranial venous structures, it can serve as a complementary examination technique, providing hemodynamic information on venous circulation.

Regarding treatment of DAVFs, it is a highly challenging subject. Intrasinus stenting can be helpful for relieving elevated sinus pressure but may lead to a greater arteriovenous pressure gradient and shunt flow. Arterial embolization of a DAVF without relief of venous hypertension can give rise to another fistula.

Techniques like, intermittent carotid arterial compression²⁵, Percutaneous intraarterial embolization using detachable balloons²⁶, isobutylcyanoacrylate, or polyvinyl alcohol particles, transvenous embolization with coils or liquid adhesives²⁷, and surgeries like venous bypass using saphenous vein²⁸ and gamma knife stereotactic surgery²⁵ are used in different cases.

Controlled hypotension can also become an alternative for treatment of DAVF in high-risk patients or when there is no chance for embolization.²⁹

Residual epilepsy

Seizures are observed only in patients who had seizures and focal signs in the acute stage, and only in a minority. It has been reported in 10% to 30% of patients who had seizures during the acute stage. Out of a follow up of 77 patients, 4 had residual epilepsy in Preter et al. analysis while 7 out of 57 patients suffered recurrences in a French study.³⁰

Seizures usually occur in the first year and are easily controlled with antiepileptic drugs. Preter et al. recommend that due to low occurrence of seizures it is appropriate to maintain anticonvulsant therapy for a year and to taper off gradually thereafter. If seizures recur, anticonvulsants should be given on a long-term basis.

Psychiatric complications

Psychiatric complications are rare and depend upon the area of involvement. There can be an acute presentation like Korsakoff-like amnesic syndrome with confabulation in bilateral mesial temporal lobe infarction following bilateral cavernous sinus thrombosis or there may be long-term deterioration in behavioral and cognitive functioning. Data on this subject is extremely varied with a Dutch study²⁰ group stating cognitive impairment in 35% of their patients while a Portugal study group³¹ argues that cognitive impairment is not that frequent. However, both acknowledge that despite the functional recovery, more than half of the patients still feel unwell depressive and anxiety symptoms.

Interesting cases of catatonia³² and dementia syndrome³³ are described in separate case reports, making CVST a constant headache for researchers and physicians.

Other rare long-term complications

Other rare long-term complications like progressive diskinesia, spasmodic torticollis with multiple cranial involvements, visual impairment and other residual neurologic deficits are reported in different parts of the world.¹⁵ It is interesting that there is no significant effect of treatment on these long-term outcomes.²⁰

CVST recurrence

Recurrence of CVT is infrequent. Preter et al¹⁵ reported only 12% recurrence in a series of 77 patients followed for a mean of 78 months. Recurrences have been mostly reported in hospitalized -patients, or in patients with an underlying prothrombotic condition.

Amberger et al. describe a unique case in which third occurrence of CVST took place in a short span of time.³⁵ The underlying cause was thrombophilia due to antiphospholipid syndrome.

Most authors recommend using oral anticoagulation for 3 to 6 months at which time they should be reevaluated with MRI/MRV. Prolonged anticoagulation may be required for refractory cases or for patients with an identified prothrombotic state. In the above-described case life long anticoagulation was started.

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