

Cerebral Venous Sinus Thrombosis- An Update

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Introduction:

Cerebral venous sinus thrombosis (CVST) is a rare form of stroke that results from thrombosis (a blood clot) of the dural venous sinuses, which drain blood from the brain. Cerebral venous sinus thrombosis is not common. In adult estimated annual incidence is 3-4 cases per million. It is most common in the third decade. Among all patients 75% are female. It has been suggested that the use of oral contraceptives in women is behind the higher incidence in female.¹ CVST is more common in the Middle East due to high prevalence of Behçet's disease in these area.¹⁻³ A Canadian study reported that In children CVST occurs in 6.7 per million annually, 43% occur in the newborn (less than one month old), and a further 10% in the first year of life.⁴

Pathogenesis:

The superficial and the deep vein, empty into the dural venous sinuses, which carry blood to the jugular vein and then to the heart. In cerebral venous sinus thrombosis, blood clots usually form both in the veins of the brain and the venous sinuses. The thrombosis of the veins themselves causes venous infarction. This results in both vasogenic and cytotoxic cerebral edema, and leads to small petechial haemorrhage that may coalesce into large haematomas. Thrombosis of the sinuses is the main mechanism behind the increase in intracranial pressure due to decreased resorption of cerebrospinal fluid (CSF).^{1,5}

The three major mechanisms for the formation of a blood clot are enumerated in Virchow's triad: alterations in normal blood flow, injury to the blood vessel wall, and alterations in the constitution of blood (hypercoagulability). Blood clot forms due to an imbalance between coagulation (the formation of the insoluble blood protein fibrin) and fibrinolysis. Most cases of cerebral venous sinus thrombosis are due to hypercoagulability.^{1,6,7}

Symptoms:

Headache ; Nine in ten people with sinus thrombosis have a headache; this tends to worsen over the period of several days, but may also develop suddenly (thunderclap headache).¹

Abnormal vision: The intracranial pressure (pressure around the brain) may rise, causing papilloedema (swelling of the optic disc) which may be experienced as visual obscurations. In severely raised intracranial pressure, the level of consciousness is decreased, the blood pressure rises, the heart rate falls and the patient may assume an abnormal posture.^{1,7}

Stroke : such as weakness of the face and limbs on one side of the body, This does not necessarily affect one side of the body as in the more common "arterial" stroke.^{1,6}

Seizures : These are mostly seizures affecting only one part of the body and unilateral (occurring on one side), but occasionally the seizures are generalized and rarely they lead to status epilepticus.¹

Other common symptoms in the elderly with this condition are otherwise unexplained changes in mental status and a depressed level of consciousness.^{5,6,8}

Causes: Cerebral venous sinus thrombosis is more common in particular situations. 85% of patients have at least one of these risk factors.^{1,8-10}

• Congenital:

Thrombophilia, a tendency to develop blood clots due to abnormalities in coagulation, e.g. factor V Leiden, deficiency of protein C, protein S or antithrombin, or related problems.

• Acquired

1. Nephrotic syndrome, a kidney problem causing protein loss in the urine.

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2. Chronic inflammatory diseases, such as inflammatory bowel disease, lupus and Behçet's disease.
3. Pregnancy and puerperium (the period after giving birth).
4. Polycythemia vera and paroxysmal nocturnal hemoglobinuria
5. Use of estrogen-containing forms of hormonal contraception
6. Meningitis and infections of the ear, nose and throat area such as mastoiditis and sinusitis
7. Direct injury to the venous sinuses
8. Medical procedures in the head and neck area

Table-I*Causes of Cerebral Venous Sinus Thrombosis⁹***Predisposing Systemic causes**

Dehydration
 Pregnancy
 Behçet's disease
 Thrombophilia
 Hypotension
 Oral contraceptive

Local Causes

Paranasal Sinusitis
 Meningitis, subdural empyema
 Penetrating head and eye wound
 Facial skin infection
 Otitis media, mastoiditis
 Skull fracture

Investigations**Neuroimaging****• Computed tomography (CT) and Magnetic resonance imaging (MRI):**

Both uses various types of radiocontrast to perform a venogram and visualise the veins around the brain.^{11,12}

• Computed tomography with radio contrast

Uses radio contrast in the venous phase (CT venography or CTV), has a detection rate that in some regards exceeds that of MRI. The test involves injection into a vein (usually in the arm) of a radio opaque substance, and time is allowed for the bloodstream to carry it to the cerebral veins - at which point the scan is performed. It has a sensitivity of 75-100% and a specificity of 81-100%. In the first two weeks, the "empty delta sign" may be observed (in later stages, this sign may disappear).^{6, 12,13}

• Magnetic resonance venography

Employs the same principles, but uses MRI as a scanning modality. MRI has the advantage of being better at detecting damage to the brain itself as a result of the increased pressure on the obstructed veins.^{6, 12,13}

• Cerebral angiography

May demonstrate smaller clots than CT or MRI. This, however, requires puncture of the femoral artery with a sheath and advancing a thin tube through the blood vessels to the brain where radio contrast is injected before X-ray images are obtained. It is therefore only performed if all other tests give unclear results or when other treatments may be administered during the same procedure.^{6, 12,13}

• Other investigations:**D-dimer**

D-dimer blood test, already in use for the diagnosis of other forms of thrombosis, with cerebral sinus thrombosis, has a sensitivity of 97.1%, a negative predictive value of 99.6%, a specificity of 91.2%, and a positive predictive value of 55.7%. Furthermore, the level of the D-dimer correlated with the extent of the thrombosis.¹⁴

In most patients, the direct cause for the cerebral sinus thrombosis is not readily apparent. Identifying a source of infection is crucial; it is common practice to screen for various forms of thrombophilia (a propensity to form blood clots protein c, protein s measurement).¹

Treatment**Anticoagulation**

Heparin or low molecular weight heparin is the initial treatment, followed by Warfarin, provided there are no other bleeding risks that would make these treatments unsuitable.^{3,15,16}

In case of extensive hemorrhage anticoagulation is not recommended, in that case, recommendation is to repeat the imaging after 7–10 days. If the hemorrhage has decreased in size, anticoagulants are commenced, while no anticoagulants are given if there is no reduction.¹⁰

The duration of Warfarin treatment depends on the circumstances and underlying causes of the condition.

- a) If the thrombosis developed under temporary circumstances (e.g. pregnancy); Warfarin is given for 3 months.
- b) If the condition was unprovoked but there are no clear causes or a "mild" form of thrombophilia; Warfarin is given for 6 to 12 months.
- c) If there is a severe underlying thrombosis disorder, Warfarin treatment may need to continue indefinitely.³

Thrombolysis: (removal of the blood clot with medication)

- a) Either systemically by injection into a vein or
- b) Directly into the clot during angiography.

The 2006 European Federation of Neurological Societies guideline recommends that thrombolysis is only used in patients who deteriorate despite adequate treatment, and other causes of deterioration have been eliminated. Bleeding into the brain and in other sites of the body is a major concern in the use of thrombolysis.^{3,14,15}

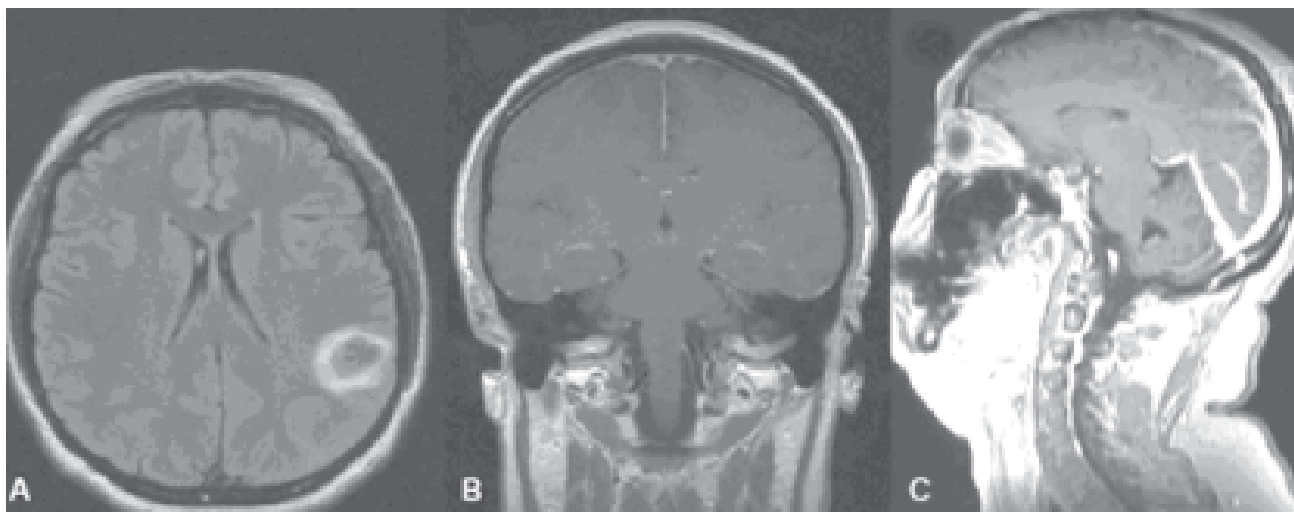


Figure-1: **Fig.-A;** MRI of brain, FLAIR image; of a young women presented with sudden onset of focal seizure, showed a resolving hematoma in left parietal region. **Fig.-B;** MRI with contrast (Coronal); showing empty delta sign . (Contrast is not taken by clot) **Fig.-C;** MRV showing poor visualization of anterior part of superior sagittal sinus

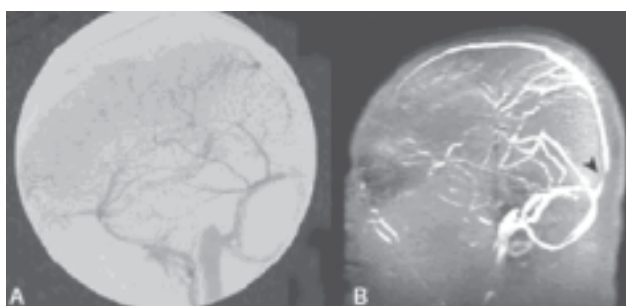


Figure 2: A) Cerebral angiogram (lateral view) showing non visualization of Superior sagittal sinus B) After treatment with Heparin & Warfarin MRV showing recanalization of sinuses with persistant filling defect in straight sinus (arrow).

Prognosis

Bad prognostic factors are

1. Aged over 37 years
2. Male,
3. Affected by coma,
4. Mental status disorder,
5. Intracerebral hemorrhage,
6. Thrombosis of the deep cerebral venous system,
7. Central nervous system infection
8. Cancer.

These were the findings of large scale study on the natural history and long-term prognosis of CVST with 16 months follow-up, 57.1% of patients had full recovery, 29.5%/2.9%/

2.2% had respectively minor/moderate/severe symptoms or impairments, and 8.3% had died. The rate of recurrence was low (2.8%).^{18,19}

Conclusion:

Wide variability of presentation has made the clinical diagnosis of CVST a challenging one. Increased awareness and availability of better non invasive diagnostic techniques in recent days helped in diagnosing the condition. Simple antithrombotic treatment strategies provide a favorable long term outcome, keeping the more aggressive and potentially dangerous intervention procedures reserved for the high risk group. The disease being first detailed in 1825 by Ribes, the clinical recognition still remains a challenge for physicians.

Conflict of Interest: None

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