CEREBRAL VENOUS SINUS THROMBOSIS

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From time immemorial, cerebral thrombosis used to be synonymous with arterial thrombosis. But, cerebral venous thrombosis was not uncommon but neurologists and pathologists were not properly oriented regarding cerebral venous thrombosis (CVT) specially because the anatomical knowledge were not updated and nobody actually believed that thrombosis can occur in low velocity capacitance vessels as opposed to the conducting vessels like cerebral arteries. Since the advent of modern investigative modalities like magnetic resonance Imaging (MRI), Computerised Tomography Angiography (CTA) and Magnetic Resonance Venography (MRV) more and more patients are being confidently diagnosed.

Occlusions of veins that drain were first published in 1820s. Ribes from France described the first case of dural sinus thrombosis. A 45 year old man developed seizures, headache and delirium who died 6 months later and on autopsy he showed superior sagittal and lateral sinus were thrombosed and the brain showed carcinomatous metastasis. In 1828, Abercrombie described the first case of puerperal sinus thrombosis. Tonelle published a review on the subject in 1829 which was strengthened by monographs of Kalbag and Woolf in 1967, whose contribution on the subject led to dramatic increase in knowledge on the subject. Sir Charles Symonds brought to our knowledge the relation between benign intracranial hypertension and cerebral venous sinus thrombosis and with it described the phenomenology of otitic hydrocephalus.

Puerperal CVT may account for about 15-20% of stroke victims of younger age. Although Western studies have shown relative rarity of puerperal CVT e.g. about 1 in 2500 deliveries as shown by Carroll et al and this rarity was also confirmed by Cross et al. But, different studies have shown CVT to be the commonest cause of stroke in young women in India. Chopra and Banerjee have reported 72 cases of CVT in India out of which 51 were related to pregnancy and puerperium. 12 of them died and on autopsy 9 of them showed evidence of CVT.

AETIOLOGY

Although aetiology varies from one anatomical region to other as also from geographical region to region there are definitely some generalization.

Primary or Idiopathic CVT are mainly caused by hypercoagulable state commonly from puerperium or from dehydration, mainly in children. Coagulation cascade is initiated by thromboplastic agents and platelet adhesion.

There has been a drastic reduction of infection as a causative agent for CVT in recent years. Still then infection is still the commonest cause of cavernous sinus thrombosis and an important cause of lateral sinus thrombosis. Septic cavernous sinus thrombosis originates from hematogenous spread of infection from face, nose, orbit and paranasal sinuses or through lateral sinus from ears. Staph. aureus and less commonly streptococci are common pathogens although Gram negative bacteria from dental infection may also be responsible. Fungal infection to cavernous sinus may occur from sinuses and even lungs, specially in diabetic patients. Septic thrombosis of superior sagittal sinus may occur from nose or paranasal sinuses, from osteomyelitis of overlying skull bone or from retrograde extension of infection from cavernous or transverse sinus. Common organisms are Gram positive e.g. S. aureus...
Cerebral Venous Sinus Thrombosis

Cerebral Venous Sinus Thrombosis (CVT) can be caused by a number of prothrombotic states and disorders of clotting system. Most important inherited cause is Protein C resistance secondary to Factor V Leiden polymorphism. Other important factors are Protein C & S resistance and Antithrombin III deficiency. Protein C & S levels may be reduced due to thrombosis itself and it is mandatory to retest them after the acute state is over.

Behcet’s disease is an important cause of CVT specially in Turkish population. Other vasculitis like SLE and PAN are also relevant specially in young adults.

Both penetrating and Non-penetrating injuries of brain can cause CVT as also implantation of cardiac pacemakers and insertion of venous lines.

Haematological malignancies like leukemias and lymphomas can cause CVT by direct invasion of sinuses, anaemia, polycythaemia, heparin induced thrombocytopenia and related to therapy e.g. L-asparaginase or Tamoxifen.

Keeping all these causes in mind, puerperal CVT and dehydration in children still comprises most of the CVTs in our country.

ANATOMY OF CEREBRAL VEINS AND SINUSES

Venous Drainage of brain is composed of Cerebral Veins and the Venous Sinuses into which the veins drain.

<table>
<thead>
<tr>
<th>Table 1: Common causes of cerebral venous thrombosis</th>
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<tr>
<td><strong>INFECTIVE</strong></td>
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<td>Bacterial infection</td>
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<td>Fungal infection</td>
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<td><strong>NON INFECTIVE</strong></td>
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<td>• Haemodynamic States</td>
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<td>Congestive Cardiac Failure</td>
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<td>Nephrotic Syndrome</td>
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<td>• Haematological disorders</td>
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<td>Activated protein C resistance-factor V Leiden poly</td>
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<td>Antithrombin III deficiency</td>
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<td>Protein C &amp; S deficiency</td>
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<td>Lupus anticoagulant</td>
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<tr>
<td>Sickle Cell anaemia and Polycythaemia</td>
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<tr>
<td>Oral Contraceptives</td>
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<td>• Inflammatory vasculitis</td>
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<tr>
<td>Behcet’s syndrome</td>
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<td>Ulcerative colitis &amp; Crohn’s disease</td>
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<td>Systemic Lupus Erythematous</td>
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<td>Polyarteritis Nodosa</td>
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<td>• Homocystinuria</td>
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<tr>
<td>Neoplasia</td>
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<tr>
<td>Haematological malignancies &amp; their treatment</td>
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<tr>
<td>Local tumours (meningioma)</td>
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<tr>
<td>• Head Injury</td>
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<td>• Idiopathic</td>
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Cerebral Veins are divisible into external and internal groups, which drain the surfaces or the inner region of the hemispheres into the venous sinuses.

The external cerebral veins drain the superficial part of cerebral hemispheres, with the superior cerebral veins draining the medial aspect of hemispheres into the superior sagittal sinus, the middle cerebral veins drain into the cavernous sinuses and the inferior cerebral veins into lateral sinuses.

The internal cerebral veins drain blood from the deeper part of cerebral hemispheres into the great cerebral veins of Galen. The basal veins of Rosenthal drain part of lower frontal lobe and insula and are joined by inferior striatal veins and terminate either in the internal cerebral veins or directly into great cerebral vein. The two internal cerebral veins drain mainly the basal ganglia, thalamus and hypothalamus to unite to form the great cerebral vein, which joins the inferior sagittal sinus to form the straight sinus.

Connections exist between external and internal venous system, which allows blood to take alternative route, if needed.

Cerebral Venous Sinuses are situated between two layers of dura. They are devoid of muscle tissue, are trabeculated and have no valve. Connection exists between venous sinuses and the veins of scalp face and neck. They not only provide alternate route but also a path by which infection can spread to venous sinuses from this area to cause CVT.

**SUPERIOR SAGITTAL SINUS**

It is situated in the attached margin of falx cerebri. It commences at crystal galli and end posteriorly into one (usually the right) transverse sinus. They are occupied by arachnoid granulations for CSF absorption.

**INFERIOR SAGITTAL SINUS**

It is situated in the free margin of falx cerebri. It passes posteriorly and drains into the straight sinus.

**STRAIGHT SINUS**

It is situated at the junction of falx cerebri and tentorium. It runs posteriorly and drains into the transverse sinus in the side opposite to which the superior sagittal sinus has drained. It is formed by the junction of great cerebral vein of Galen and inferior sagittal sinus.

**TRANSVERSE SINUSES**

These begin at internal occipital protuberances to lie in the attached margin of tentorium and pass anteromedially to continue as sigmoid sinuses. The right transverse sinus is usually bigger than the left one. In about 4% cases the left sinus may be absent and superior and straight sinuses, both drain into one transverse sinus, usually the right.
SIGMOID SINUSES
They continue anteriorly over the mastoid part of temporal bone to continue as internal jugular vein at jugular foramen.

CAVERNOUS SINUSES
They lie on each side of the sphenoid bone. They receive blood from ophthalmic veins, several of the anterior inferior cerebral veins, the sphenoparietal sinus and the pituitary vein. They are traversed by number of structures, involvement of which causes clinical consequences of cavernous sinus thrombosis. The Internal carotid artery wrapped by sympathetic plexus passes through it while abducent nerve lies inferolaterally. The oculomotor and trochlear nerves and the first and second division of trigeminal nerve lies in the lateral wall of the sinus. The two sinuses are connected by valveless circular sinus.

PATHOLOGY OF CVT
Pathology depends on the veins or sinuses affected severity of affection and duration.

Macroscopically, it is swollen, oedematous, having a bluish hue. Infarction is usually associated with extension of thrombosis into superficial cerebral veins –resulting in haemorrhagic infarct.

Microscopy does not show any inflammatory change around thrombus, there is oedema and haemorrhage .If long standing it may show cystic encephalomalacia.

CLINICAL FEATURES
Some clinical findings are related to occlusion of intracranial venous structures in general, while others are relatively specific for location of pathology. We plan to discuss the first at onset.

ONSET & TEMPORAL PROFILE
Presentation may be acute (within 48 hrs), subacute (bt. 2 days and one month) and chronic (>30days).Subacute or chronic presentation are commoner than in arterial stroke and progress in gradual or stepwise fashion is common.

Acute presentation is commoner in puerperal cases than in non puerperal patients. Gradual increase in symptoms and a fluctuating course is commoner in CVT due to other causes. Patients presenting with acute onset commonly present with focal signs while others commonly present with intractable headache, leading to delay in taking medical advice. Among 102 patients of angiographically proved CVT, mean day of admission after onset was 5 days whereas average was 14 days. The slow and gradual onset can be explained by relatively slow propagation of thrombus and development of good collaterals.

HEADACHE
Headache is the most common presenting feature and the sole feature in some. It is common in both puerperal and non puerperal cases but it is relatively more common in the first group of patients. The nature of headache is usually diffuse but in some of the patients there is complaints of thunderclap headache.

The presence of headache can be explained by:
1. Local process within the vein and dural sinuses :
   The dura and the walls of veins and sinuses are rich in pain sensitive nerve endings which when stimulated by inflammation gives rise to acute pain.
2. Development of raised intracranial pressure(ICP) :
   Thrombosis causes obstruction to venous drainage causing increased ICP, oedema, haemorrhage and infarction as also obstruction to CSF drainage resulting in headache, often with papilloedema, which was observed in about 35% patients.
   In some series, features simulating Benign Intracranial Hypertension (BIH) were more common characterized by headache, papilloedema and sixth nerve palsy. In fact in all patients of BIH due to other causes we should exclude CVT by all possible means. This type of presentation is more common in lateral sinus thrombosis caused by ear infection (otitic hydrocephalus).

FOCAL DEFICITS
When draining venous sinuses are occluded pressure must build up in feeding arteries to maintain perfusion and this results in oedema, infarct and haemorrhage leading to different focal neurological signs like hemiparesis, aphasia, ataxia, hemianopia, neglect etc. Haemorrhage may be bilateral if obstruction is in Superior sagittal sinus (SSS). Diffuse brain oedema resulting from bilateral and symmetrical involvement may cause diffuse headache and slit like ventricles on imaging.

SEIZURES
In comparison with arterial thrombosis where seizures are not common in acute phase (Except in cortical infarcts) seizures are common in CVT, about 7% to 15 % during presentation and in about 40% during the course of illness. Seizures may be generalized or focal in almost equal proportion. It is the potential reversibility of the pathology that makes the seizures more common as oedematous and partially damaged neurons produce more seizures than dead neurons.

ALTERED SENSORIUM
Incidence of diminished consciousness in CVT varies from 28% to 93% from series to series but its incidence is definitely higher than in arterial thrombosis keeping aside extensive basilar artery thrombosis and large cerebellar infarct. The pathogenetic mechanism of reduced sensorium is mainly oedema resulting in raised ICP and in cases of deep
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vein thrombosis bilateral involvement of thalamus may also be a factor. With proper management, altered sensorium is reversible except in bilateral internal jugular vein obstruction in extensive CVT.

FINDINGS RELATED TO INVOLVEMENT AT SPECIFIC SITES

Of the sinuses involved most common is involvement of Superior Sagittal Sinus (SSS) and lateral sinus (LS) as 54%, 36% and 69% in combined SSS and LS involvement. Occlusion of deep venous system is much less common than venous sinuses. Cerebral cortical veins are involved but usually in combination with SSS. Multiple venous involvement is commoner. Puerperal CVT commonly involves SSS while involvement of LS is usually a sequela of infection in ear and paranasal structures.

CAVERNOUS SINUS THROMBOSIS (CST)

Thrombosis of CS is usually infective having high mortality. Source is medial face, orbit, nose and nasal sinuses. CS drains into petrosal sinuses and then to LS and ultimately to Internal Jugular Vein (IJV). Causative pathogens are Staph. aureus, Pneumococcus, Streptococcus, Gram negatives and fungi like Aspergillus and Mucormyces.

Presenting features are headache, facial pain and fever. Eyelids and eyes are red and eyes show proptosis. Face is congested. There may be partial or total ophthalmoplegia and involvement of structures passing via CS e.g. 1st and 2nd division of trigeminal nerve and Sympathetic plexus leading to loss of sensation over part of face and partial Horner’s syndrome. The 3rd and 4th Cranial nerves are involved. It may be unilateral to start with but rapidly becomes bilateral.

In rare nonseptic causes like facial surgery or prothrombotic states the process may be indolent and symptoms less severe.

SAGITTAL SINUS THROMBOSIS (SST)

Commonest cause is puerperal thrombosis but Behcet’s disease, Parasagittal meningiomas, and prothrombotic states are also common. Clinical features may be summarized as:

1. Headache due to raised ICT
2. Extension to Rolandic veins may cause focal motor or sensory signs and seizures.
3. Signs are usually bilateral c.f. arterial stroke
4. Altered sensorium indicates high ICP
5. Those due to associated involvement of other sinuses.

LATERAL SINUS THROMBOSIS (LST)

Now becoming commoner than SST. Causes are mainly spread of infection from ear and mastoid through emissary veins and thin bone plate of sinus. Coagulopathies and other systemic causes are not very uncommon.

Presenting features comprise:

1. H/O draining ears.
2. Fever, Diffuse headache, Neck pain and tenderness are common.
3. Tenderness along anterior border of sternomastoid and over mastoid.
5. Vertigo, nausea and vomiting may be present.
6. Gradenigo’s Syndrome ; 5th & 6th nerve involvement near Dorello’s canal at Apex of petrous bone.
7. Inferior portion of temporal lobe & part of cerebellum drain into LS So :
   a. Aphasia, agitation and Right homonymous hemianopia in Lt. temporal
   b. Agitation and Left homonymous hemianopia in Rt. temporal
   c. Gait ataxia and Nystagmus in cerebellar affection.

DEEP VENOUS SYSTEM OCCLUSION

Causes may be Sepsis, dehydration in children and Systemic vasculitis, Sickle Cell disease and Oral pills in adults. They are relatively rare.

Clinically present as;

1. Headache and altered sensorium.
2. Decerebrate rigidity, Coma vertical gaze palsy are due to thalamic & Basal Ganglia involvement.
3. Some present with apathy and abulia

DIAGNOSIS

Recognition of CVT requires highest degree of suspicion and orientation of their clinical profile and radiologic findings.

A. Stroke pattern with absence of risk factors of arterial stroke.
B. Positive background factors of CVT e.g.
   Ear and paranasal infection, puerperium, dehydration in children, CNS cancers
   And anticancer therapy, sepsis, vasculitis, past h/o peripheral venous thrombosis, Head injury etc.
C. Screening with D-dimer test: Negative D-dimer (550ng/ml) has high negative predictive value but normal value does not go against CVT.
D. Investigation to confirm CVT:
a. CT scan of Brain with contrast and coronal reconstruction:
   1. To look for bony abnormalities, PN sinuses and mastoid
   2. Dense triangle sign- dural sinuses or deep vein can show as hyperdense, round or triangular structures on noncontrast axial cuts showing presence of thrombus within. It is rarely seen.
   3. Cord sign-Cerebral cortical vein is seen as high density, thin, linear structure. This sign is rare but specific.
   4. Empty delta sign; seen in contrast CT in SSS on coronal cuts- contrast enhances walls but middle lumen with thrombus does not enhance.
   5. Associated parenchymatous findings like: Infarction, oedema, haemorrhages and chinked ventricles. Deep venous system occlusion shows infarct, oedema and haemorrhages in thalamus and basal ganglia.
   6. CT angiograms may show dilated collateral veins.

b. MRI Brain:
   Usually more sensitive than CCT in locating and defining venous channels and parenchymatous changes. MRI helps in studying patients at various stages. In first week occluded sinuses are isointense in T1 and hypointense on T2. In next weeks it is hyperintense in all the sequences. After a month it is isointense in T1 and hyperintense on T2

c. MRI angiogram:
   Very useful in documenting CVT. With nonvisualisation (signal void), in later parts it becomes hypointense in all sequences. And with chronicity it becomes inhomogeneous.

d. MR Venogram:
   Highly useful modality- it can visualize all venous structures including deep veins and has made the study of CVT very easy.

   These modern developments in imaging have made the previous conventional angiograms almost redundant in investigating CVT.

e. Trans Cranial Doppler: (TCD)
   TCD in CVT is in its early phases but the present status is in monitoring the effect of treatment in CVT

E. Determination of aetiology of CVT:
   Investigations are to be tailor-made and planned according to clinical background and possibilities: investigation for prothrombotic states, coagulopathies, vasculitis and other biochemical parameters like serum homocysteine are indicated.

TREATMENT OF CVT

Treatment of CVT can be discussed under different subheadings:

A. Treatment of clinical ancilliary features;
B. Treatment of CVT
   A. Supportive and symptomatic treatment;
      a. Antibiotics and surgical drainage of ear and paranasal infections
      b. Anticonvulsants for seizure control will depend on type of seizure and comorbid conditions.
      c. Reduce raised ICT by osmotic diuretics like Mannitol, Glycerol. In BIH steroids may be tried provided infections are being managed with antibiotics, temporary ventricular drains and shunts are rarely necessary.

B. Treatment of CVT
   Mainstay of treatment of CVT are anticoagulants, keeping in mind all its proponents and opponents. Stansfield first used anticoagulants in CVT in 1940. Since then many study have shown its efficacy- not only in CVT but also to prevent dreadful pulmonary embolism associated with jugular bulb thrombosis. Some studies have been challenged with haemorrhages. But, today’s consensus is that unless there is absolute contraindication anticoagulant is to be used. European Federation of Neurological Societies in 2005 commented that when there are “no contraindication for anticoagulation- body weighted SC low molecular weight heparin in full therapeutic doses or APPT (2X normal) dose adjusted IV heparin- be given”

   Trials for thrombolytic therapy are still in preliminary stage. Using urokinase and rTPA has shown good results in one study. But it was not a controlled study and all the patients received heparin after thrombolysis.

   Yasargill and others did surgery specially in injury patients with encouraging results. Other modes of surgery includes venous bypass, jugular vein ligation with mixed results.

OUTCOME

The patients of CVT either recover totally or become...
dependent or die. In one study the figures were 79% and 13.4% respectively. 22

Outcome determining factors were:
1. extent of the disease
2. Jugular occlusion
3. Spread to deep or cortical veins
4. Level of sensorium at onset
5. Background factors
6. Presence of ICP

REFERENCES
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