

# **Cerebral Venous Thrombosis: recent advances and need for an Asian Registry**

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We congratulate and are grateful to JPMA for publishing a whole issue dedicated to cerebral venous sinus thrombosis. This is a unique collaborative effort of clinicians and researchers from Saudi Arabia, Qatar, India, Turkey, USA, and Pakistan. This issue contains more than twenty review articles related to various aspects of CVT in addition to one original article and 4 case reports.

The impetus for this effort is clear. Cerebral venous sinus thrombosis appears to be a problem which is more common in the Asian region than the West. Recently Panagariya et al from India reported that CVT accounts for half of all young strokes and 40% of strokes in women.<sup>1,2</sup> Thus, it is an important disease in the local context and needs to be picked up with a high index of suspicion. The prognosis of this disease is excellent with early diagnosis and institution of therapy. In the recent years, markers of those patients that will do poorly on presentation have become available from large international trials. Mortality usually ranges from 6-15% and transtentorial herniation is the major cause of death. Approximately 80% of patients are functionally independent in the long term.<sup>3</sup>

Older age (>37 years in ISCVT), male sex, seizures at admission, rapid evolution of thrombosis, the presence of focal deficits and CNS infection and cancer as the underlying cause also predict poor outcome.<sup>4</sup> ISCVT found involvement of cortical veins, deep cerebral veins and superior sagittal sinus, intracerebral haemorrhage on right side, posterior fossa lesions and parenchymal lesions especially ones >5 cm in their larger diameter to be poor prognostic factors.<sup>4</sup> The clinical setting affects outcome, infections, cancer patients may do poorly, contrary to that, obstetric CVT may have a good outcome.

The etiology of CVST is diverse and profound, and must be suspected in settings of inflammatory disease, malignancy, oral contraceptive use, and even as a complication post lumbar puncture for other reasons.<sup>5,6</sup> Up to 40% cases remain to be idiopathic. We believe a large number of these cases in future will turn out to be genetically predisposed. The article from Arsalan<sup>7</sup> discusses this increasingly recognized factor related to CVT. Almost 25% cases of CVT are due to known inherited causes of venous thrombosis.

The presenting symptoms include headache, focal seizures and papilloedema. Importantly, headache can be

the sole presenting symptom in about 80% of patients, and can vary from a non specific headache to an acute thunder-clap headache.<sup>8</sup> In addition, this must be suspected in patients with isolated pseudotumor cerebri and an MRV must be obtained.<sup>9</sup> Ravishankar<sup>10</sup> has discussed incidence and pattern of headache in CVT and headache profile related to CVT in this issue.

The diagnostic armamentarium consists of CT brain with and without contrast, MRI/ MRV and angiography. The sensitivity and specificity of CT scan in the diagnosis of CVT is 68% and 52%, respectively. It may be totally normal in up to 26% of patients with proven CVT.<sup>11</sup> In the first two weeks, thrombotic blood is usually hyperdense on an unenhanced CT scan compared to the brain parenchyma; therefore, acutely dense cord sign, dense jugular vein, dense triangle or dense delta sign, dense dural sinuses, these signs are usually present during the first two weeks only. After two weeks, a thrombus will become isointense to brain parenchyma and therefore will only be visible on a post-contrast CT scan. In addition parasagittal haemorrhage not respecting arterial territories may be seen.<sup>12</sup> The newer generation CT scanners allow venography with a resolution comparable to MRI in minutes.

MRI allows delineation of pathology via non invasive imaging and allows distinction via functional MRI techniques like diffusion weighted imaging of patients with cytotoxic vs vasogenic oedema. Since the pathology often incorporates vasogenic oedema, it explains why the prognosis of venous infarction is often better than its arterial counterpart.<sup>13,14</sup>

Angiography with a venous phase study is often not used as a first line, but may be useful in demonstrating retrograde flow seen on real-time suggesting underlying venous thrombosis through abnormal collateral channels. It should also be considered when the administration of local fibrinolytic therapy or mechanical clot maceration is planned.<sup>15</sup>

The standard of care is dose adjusted unfractionated heparin, this has been shown to be safe in spite of CNS haemorrhage.<sup>16</sup> Patients who deteriorate and progress despite anticoagulation may be candidates for intraclot interventional therapy and the recent experience, including a report here about pediatric CVT is encouraging in terms of eventual outcome.<sup>17,18</sup>

Those suffering from malignant cerebral hypertension may respond to decompressive hemicraniectomy despite fixed pupils in 3 reported cases.<sup>19</sup> The decompressive procedure usually consists of removal of a large bone flap along with a dural patch either from artificial dura or autologous tissue such as pericranium, temporalis fascia, or fascia lata. In addition to the removal of bone flap, the neurosurgeon may also consider resecting infarcted brain tissue and/or evacuation of haematoma. The recommended size of dural patch is 15 to 20 cm in length and 2.5 to 3 cm in width. The bone flap may be replaced after 4 to 12 weeks depending upon complete resolution of swelling and medical fitness of the patient. If thrombosis is in the cerebellar veins with consequent oedematous cerebellar infarcts suboccipital craniotomy is the appropriate procedure. These extreme measures must be considered especially if widespread irreversible infarction has not set in.

The long term prognosis of survivors is good, both in obstetric and other CVT, with negligible rates of recurrence. Outpatient management consists of using warfarin for upto 6 months (following the venous thrombosis paradigm) and monitoring for recanalization via MRV(magnetic resonance venogram). Data show that CVST patients display a high spontaneous and intrinsic thrombolytic potential, with recanalization rates of 60% during the first 20 days.<sup>20</sup> Thereafter, recanalization rates increase insignificantly. Recanalization may not be the only effective marker of prognosis, the presence of venous collaterals may also be important.

There are also many unanswered questions, what is the distribution of prothrombotic disease in Asia? Would patients benefit from early thrombolysis if they are identified as having poor prognostic factors? Would additional platelet blockade help? The idea of this supplement is to raise as many questions as there are answers. The time is

ripe for a pragmatic Asian cerebral venous thrombosis trial and a collaborative database.

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