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A study of clinico-radiological and management profile of cerebral venous sinus thrombosis

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Abstract
Cerebral Venous Sinus Thrombosis (CVST) and Cortical Venous Thrombosis (CVT) is an uncommon form of stroke, usually affecting young individuals. CVT accounts for about 1% of all cerebrovascular accidents. Despite advances in the recognition of CVT in recent years, diagnosis and management can be difficult because of the diversity of underlying risk factors, protean manifestations and the absence of a uniform treatment approach. We present a series of six cases of cortical venous sinus thrombosis studies in a tertiary care teaching hospital over a period of eighteen months. Out of the six patients studied, four patients (66.7%) were men and two (33.3%) were women. Average and median of age were respectively 39.6 and 50.5 years. The most prevalent symptom was headache, found in five of them (83.3%). The most commonly affected sinus was superior sagittal sinus (66.7%) followed by transverse sinus (50%). All patients except one were managed with anticoagulation. Five patients (83.3%) had good response to treatment with total recovery of signs and symptoms in the early phase of the treatment. Only one patient had residual cranial nerve palsy. CVST can be deceptive as it can present in various forms and confuse the clinicians. Early diagnosis and aggressive management can help in reducing the mortality and morbidity associated with it.

Keywords: Cerebral Venous Sinus Thrombosis, Cortical Venous Thrombosis, MR Venography

1. Introduction
Cerebral Venous Sinus Thrombosis (CVST) and Cortical Venous Thrombosis (CVT) which leads to ischemia and infarction of the brain are now being increasingly diagnosed with the advent of greater awareness amongst the clinicians and availability of newer radio-diagnostic modalities like Magnetic Resonance Imaging (MRI) and MR Venography. Spontaneous thrombosis has an estimated incidence of 1 per 50,000 though the true incidence of the disorder is probably underestimated.[1] The clinical presentation of the patient may be with features suggestive of Transient Ischemic Attack or sometimes an Intracranial Space Occupying Lesion (ICSOL). There may be a wide range of signs and symptoms at presentation, however certain clinical features provide clue to the presence of CVST. The severity of symptoms depends on chronicity of development and on the vessels involved. The commonest aetiology are puerperium and pregnancy, dehydration, use of oral contraceptives, infection, trauma, blood dyscrasias, malignancy and haematological disorders like polycythaemia, essential thrombocytosis, paroxysmal nocturnal haemoglobinuria and collagen vascular disease. High index of suspicion is required in appropriate clinical settings to detect this disease at the earliest and ensure prompt treatment with anticoagulants, which can result in almost complete neurological recovery of the patient. The authors report here six such cases which presented with varying manifestations.

2. Aim
To analyse a series of six patients with cortical venous sinus thrombosis (CVST) presenting with varying manifestations.

3. Materials and Methods
In this study, epidemiological features, clinical presentation, risk factors, and outcome were assessed in six patients with cortical venous sinus thrombosis who presented to the emergency or outpatient department of a tertiary care teaching hospital during the study period of January 2015 to June 2016. Cerebrovascular accidents due to arterial thrombosis, haemorrhage and patients with intracranial space occupying lesions were excluded. All patients with clinical suspicion of CVST were subjected to a detailed history taking with emphasis to find out common aetiology for CVST, followed by a thorough clinical examination including a detailed neurological assessment.

Case 1
30-year old female presented to the emergency department with complaints of pain and difficulty in neck movements and swelling over right side of the neck for one month, fever with chills for 20 days and sudden onset drooping of right upper eyelid for eight hours. There was no history of fall or trauma to head. Patient denied any history of headache, visual disturbance or diplopia. There was no history of weakness or sensory system involvement.
On general examination, patient had a hard, non-mobile, non-tender swelling of 3cm x 4cm x 3cm size over the anterolateral aspect of right side of the neck which was adherent to the underlying structures. She also had complete ptosis, proptosis and chemosis of the right eye with a dilated

pupil, which was not reacting to light. A careful neurological (CNS) examination revealed right third, fourth and sixth cranial nerve palsies. Examination of the left eye was unremarkable. Rest neurological and physical examination was unremarkable; there was no papilledema, sensory deficit, ataxia or signs of meningeal irritation.

Laboratory investigations revealed polymorphonuclear leucocytosis (White Blood Cell Count (WBC) 28,700/mm^3 (normal reference range 3.6–11.1/mm^3). Other investigations including haemoglobin and coagulation profile were normal. MRI Brain (Contrast) revealed generalised cerebral oedema, multilobulated acute small infarcts in right middle cerebral artery, posterior cerebral artery and left anterior cerebral artery territories with discrete spontaneous heterogeneity of the right cavernous sinus suggesting a filling defect after contrast administration. A diagnosis of cavernous sinus thrombosis with septic emboli was made (Figure 1). The patient was treated with intravenous vancomycin, clindamycin and piperacillin / tazobactam based on the culture and sensitivity reports for septic cavernous thrombosis together with subcutaneous Low Molecular Weight Heparin (LMWH) for a duration of five days bridging the oral anticoagulant (Warfarin 5mg once daily). The patient's fever and leucocytosis resolved with treatment. Her proptosis and chemosis of the right eye also resolved. However, despite early and aggressive treatment her cranial nerve palsies persisted, necessitating a right eye patch to prevent diplopia. The patient was deemed stable for discharge after 10 days of hospitalisation. She was asymptomatic at the time of discharge and was prescribed oral Warfarin 5mg once daily for six months and advised regular outpatient follow up.

Fig 1: Multilobulated acute small infarcts in Right Middle Cerebral Artery, Posterior Cerebral Artery and Left Anterior Cerebral Artery territories with discrete spontaneous heterogeneity of the Right Cavernous Sinus.

Case 2

32-year old male presented to the out-patient department with episodic, occipital, non- throbbing, headache associated with two episodes of non-projectile vomiting and blurred vision of one-week duration and transient weakness of right half of the body which lasted for about 12 hours, two days prior to hospitalisation. He denied having fever, seizures or altered sensorium, slurring of speech or deviation of angle of mouth, fall, trauma to head or any sensory system involvement. General physical examination revealed a pulse of 88/min, blood pressure of 112/70 mmHg. CNS examination was unremarkable.

Laboratory investigations including chest radiograph and ultrasound of the abdomen were unremarkable. MRI BRAIN with Venography (MRV) revealed hyper-intensity on T1, T2 and FLAIR images involving superior sagittal sinus, right transverse sinus and right sigmoid sinus with thinned out appearance of superior sagittal sinus throughout its course (Figure 2.1 and 2.2). A diagnosis of thrombosis of superior sagittal sinus, right transverse sinus and right sigmoid sinus was made. The patient was managed with subcutaneous LMWH 40mg twice daily for five days. Oral anticoagulation (Tab. Warfarin 5mg OD) was started simultaneously and optimized at International Normalised Ratio (INR) of 2.5 following which heparin was withdrawn. He was discharged on day 7 of illness without residual neurological deficit and was advised to continue anticoagulation for six months with regular follow up.

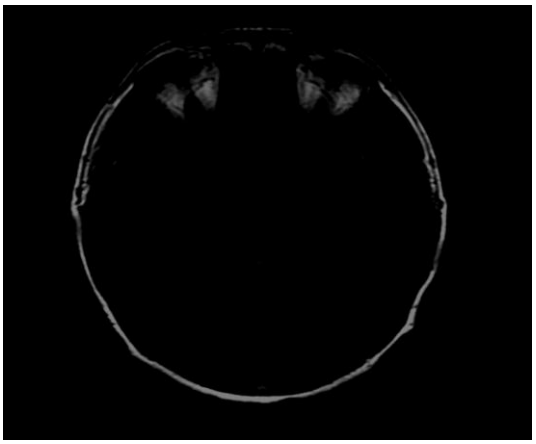

Fig 2.1: Hyperintensity on FLAIR images involving Superior Sagittal, Right Transverse and Right Sigmoid Sinus.

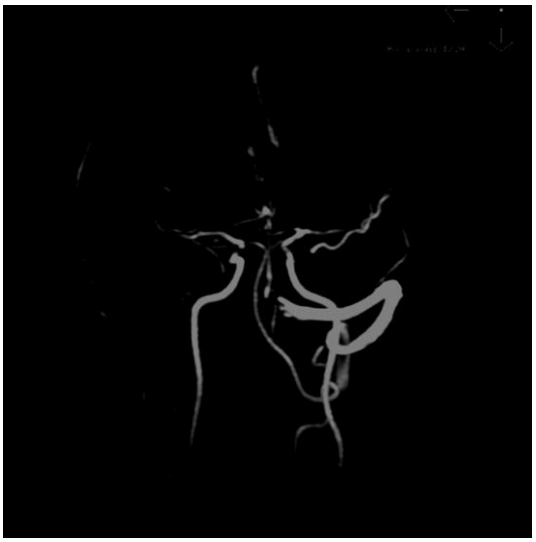

Fig 2.2: MRI BRAIN Venogram showing Thrombosis of Superior Sagittal, Right Transverse and Right Sigmoid Sinus with thinned out appearance of Superior Sagittal Sinus throughout its course.

Case 3

36- year old male presented to the emergency department with severe throbbing occipital headache for two days. The headache was associated with two episodes of projectile vomiting and blurred vision. There was history of one episode of generalised tonic-clonic seizure (GTCS) two days prior to admission. He denied any speech abnormality, weakness of limbs or sensory symptoms. There was no history of fever, ear discharge, fall or head injury. There was no history of similar episode in the past. Physical examination of the patient including CNS examination was unremarkable. All routine laboratory investigations were within normal limits. MRI and MRV brain revealed haemorrhagic venous infarct in cortical and subcortical left temporal region over 6x4 cm size with absence of flow void in superior sagittal sinus, left transverse sinus and sigmoid sinuses and mass effect on adjacent sulci (Figure 3.1 and 3.2). The patient was initiated on anticonvulsant and anti-cerebral oedema measures. Subcutaneous LMWH was withheld in view of haemorrhagic infarct with mass effect. Patient improved symptomatically with no new episodes of seizures during the course of admission. He was then discharged on day 10 of illness and was asked for a regular follow up.

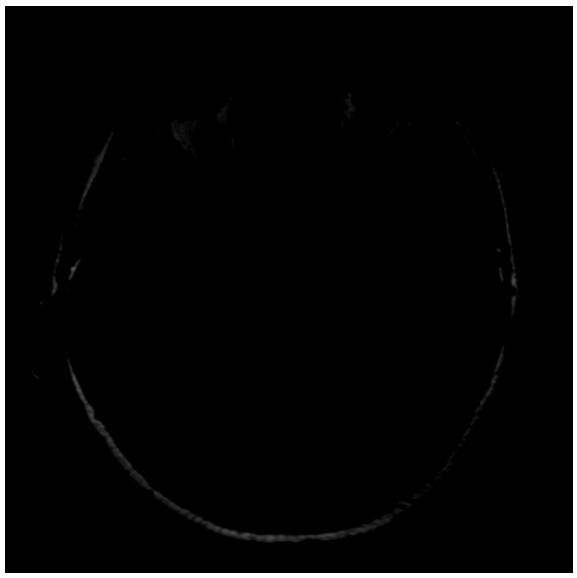

Fig 3.1: MRI BRAIN Flair image showing Haemorrhagic Venous Infarct in cortical and subcortical left temporal region (6*4 cm) with mass effect

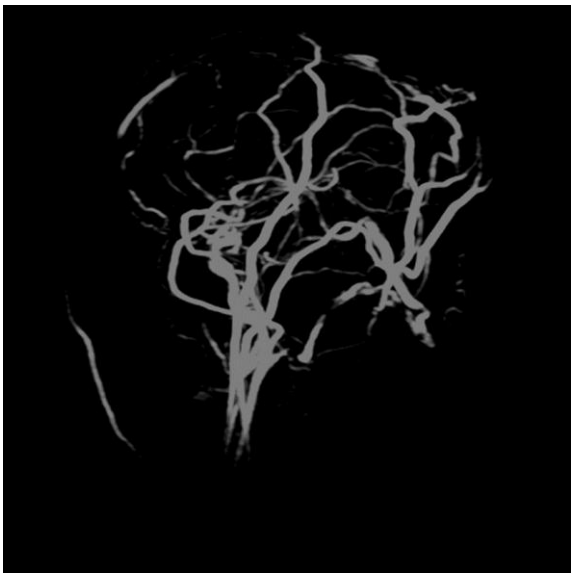

Fig 3.2: MRI BRAIN Venogram showing absence of flow void in Superior Sagittal, Left Transverse and Sigmoid Sinuses and mass effect on adjacent sulci.

Case 4

65-year-old male presented to the emergency department with sudden onset left sided hemiparesis along with altered sensorium. There was history of severe, throbbing and occipital headache of 3-days duration. He denied any associated vomiting or visual disturbance. There was no history of trauma to head, fever, deviation of angle of mouth, any seizure episode or similar complaints in the past. Sensory system was intact. General physical examination was unremarkable. The neurological system examination revealed grade 3/5 power in left upper and lower limbs, brisk deep tendon reflexes and extensor plantar response on the left side. All routine laboratory investigations were within normal limits. MRI Brain revealed circular hyper-intensity on axial T2-weighted images in bilateral thalami and basal ganglia (figure 4.1). MRV Brain showed a hyper-intense signal attributable to the thrombosed vein of Galen on T1-weighted image (figure4.2). The patient was initiated on subcutaneous LMWH for five days, bridged to oral warfarin targeted to maintain INR between 2.5 – 3.0. Patient improved symptomatically with no residual weakness and was discharged after 10 days with an advice to continue oral warfarin for six months.

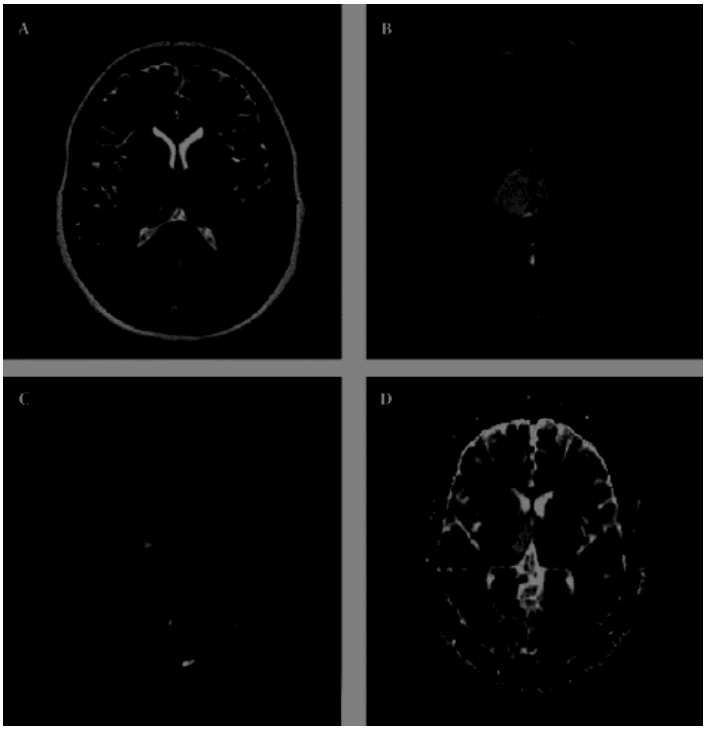

Fig 4.1: Circular Hyperintensity on axial T2-weighted images in Bilateral Thalami and Basal Ganglia

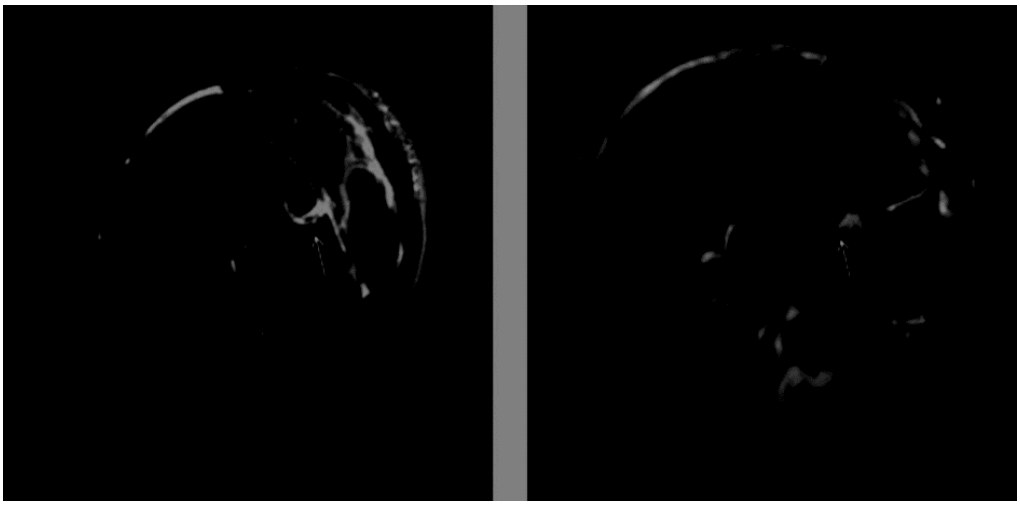

Fig 4.2: Brain Magnetic Resonance Venography Showing Filling Defect in the Vein of Galen

Case 5

33-year-old married woman presented with subacute onset of severe throbbing, frontal headache of one week duration which had worsened over last two days. The headache was unresponsive to conventional analgesics. It was followed by behavioural changes consisting of irritability and agitation with mild confusion and photophobia. She denied having visual disturbance or seizures. Systemic complaints and constitutional symptoms suggestive of chronic infection or malignancies, such as cough, fever, weight loss, chronic diarrhoea, effort intolerance or bleeding per vagina were absent. Patient gave no history of fall or trauma to head or similar complaint in the past. She had started using oral contraceptives for previous two months. General physical examination and systemic examination including central nervous system were unremarkable. Laboratory investigations were within normal limits. CT scan of the brain done in the emergency department showed a low-density filling defect in the posterior part of the sagittal sinus. MRI with MRV brain showed thrombosis of the superior sagittal sinus, straight sinus, transverse sinuses with multifocal acute infarctions in the bilateral fronto-parieto-occipital white matter (Figure 5). Subcutaneous LMWH was started in a dose of 60mg twice daily and subsequently the patient was anti-coagulated with warfarin 5mg for a total period of three months. Patient progressed well in the ward with a full neurological recovery within 48 hours of admission. Patient was ambulating in the ward by day three and had no further behavioural issues, seizures or headaches. She was advised to stop her oral contraceptive pills and to consider barrier contraception instead.

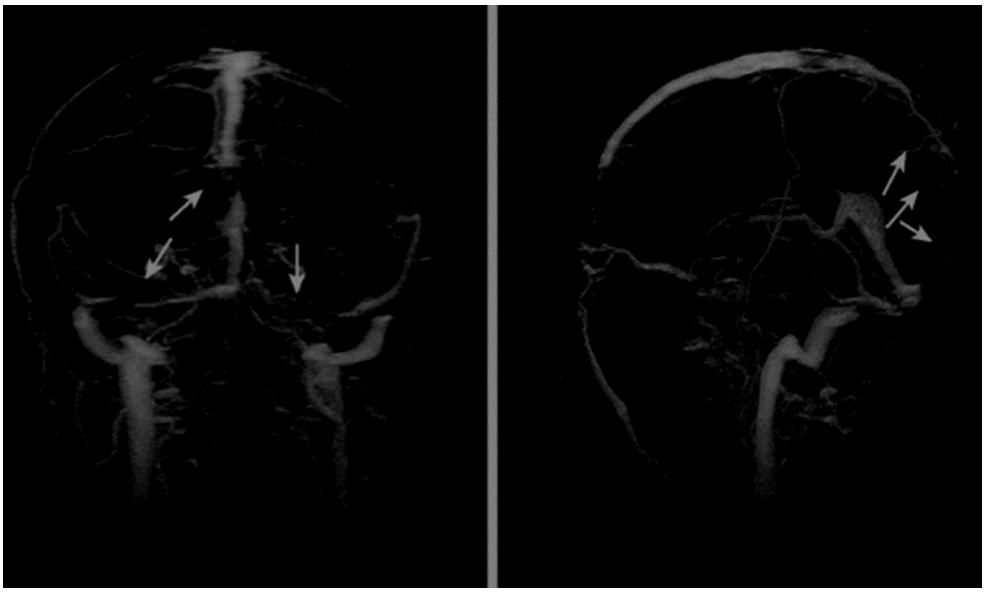

Fig 5: MRI with MRV brain showing Thrombosis of the Superior Sagittal, Straight, and Transverse Sinuses

Case 6

42-year old male presented to the out- patient department with a week-long history of continuous headache that was global, throbbing and not associated with vomiting. He had also noted photophobia, slurring of speech and weakness of his right upper limb on the evening preceding admission. There was no history of trauma, no relevant family, past or drug history. Patient denied history of fever or similar complaints in the past. Clinically, the patient's vital parameters were stable with a GCS of 15/15. His pupils, optic

fundi and speech appeared normal and there was no evidence of any focal neurological deficit or meningeal irritation. Systemic examination was unremarkable. Routine laboratory investigations revealed no abnormalities. Chest radiograph and ultrasound of the abdomen were within normal limits. A computerized tomography (CT) scan appeared normal. Magnetic resonance venography (MRV) confirmed the presence of a superior sagittal sinus thrombosis with a small venous infarct (Figure 6). The patient was subsequently initiated on subcutaneous LMWH and oral warfarin. He improved symptomatically with full neurological recovery. He was deemed stable for discharge after hospitalisation of 7 days and was advised oral anticoagulation for a period of three months.

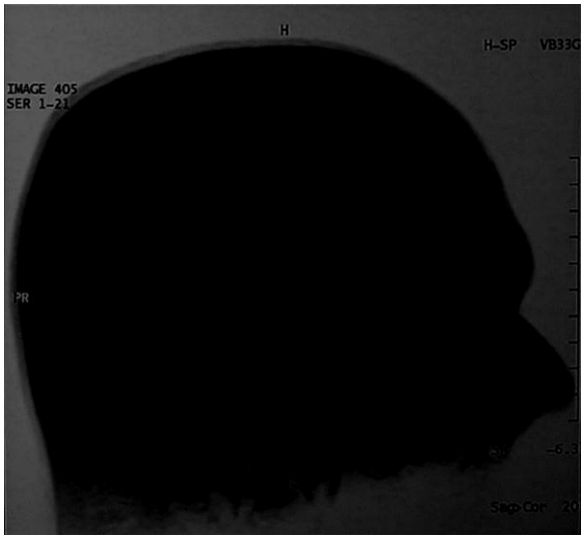

Fig 6: MRV Brain showing Thrombosis of Superior Sagittal Sinus

4. Results

Out of the six patients studied (Table 1), four patients (66.7%) were men and two (33.3%) were women. Average and median of age were respectively 39.6 and 50.5 years. The most prevalent symptom was headache, found in five of them (83.3%). The most commonly affected sinus was superior sagittal sinus (66.7%) followed by transverse sinus (50%). Five patients (83.3%) had good response to treatment with total recovery of signs and symptoms in the early phase of the treatment. Only one patient had residual cranial nerve palsy.

Table 1: Epidemiological and Clinical Features of Patients With Cvst

Case No.	Age/Sex (M/F)	Clinical Picture	Affected Venous Sinus	Risk Factor	Treatment	Outcome
1	30/F	Right eye complete ptosis, swelling over neck	Cavernous	Septicaemia	Antibiotics, LMWH, Oral Warfarin	Residual III, IV & VI cranial nerve palsy
2	32/M	Headache, transient right sided weakness	Superior sagittal, transverse, sigmoid	–	LMWH, Oral Warfarin	Complete recovery
3	36/M	Headache, vomiting, GTCS	Superior sagittal, sigmoid, transverse	–	Anticerebral oedema and anticonvulsant medications	Complete recovery
4	65/M	Headache, Left Hemiparesis	Vein of Galen	–	LMWH, Oral Warfarin	Complete recovery
5	33/F	Headache, behavioural changes	Superior sagittal, transverse, straight	Oral contraceptive pills	LMWH, Oral Warfarin	Complete recovery
6	42/M	Headache	Superior sagittal	–	LMWH, Oral Warfarin	Complete recovery

5. Discussion

Thrombosis of the dural sinus and/or cerebral veins (CVT) is an uncommon form of stroke, usually affecting young individuals [2]. CVT accounts for about 1% of all cerebrovascular accidents. Despite advances in the recognition of CVT in recent years, diagnosis and management can be difficult because of the diversity of underlying risk factors, protean manifestations and the absence of a uniform treatment approach. The risk factors for venous thrombosis in general are linked classically to the Virchow Triad of stasis of the blood, changes in the vessel wall, and changes in the composition of the blood. Of the multiple factors associated with CVT, only some are reversible. Prior medical conditions (thrombophilia, inflammatory bowel disease), transient situations (pregnancy, dehydration, infection), selected medications (oral contraceptives, substance abuse), and unpredictable events (head trauma) are some of the predisposing conditions [3, 4]. Risk factors are usually divided into acquired risks (surgery, trauma, pregnancy, puerperium, anti-phospholipid syndrome, cancer, exogenous hormones) and genetic risks (inherited thrombophilia).

In about 25% of patients, no predisposing risk factor can be discovered despite extensive investigations. CVST most commonly involves Superior sagittal sinus (72%) followed by lateral sinus (70%). In 30-40% cases, more than one sinus is

involved with or without cortical venous thrombosis [5]. The sinuses involved in above cases were superior sagittal sinus, transverse and/or sigmoid in four cases. Only one case had cavernous sinus thrombosis and one had thrombosis of vein of Galen.

The diagnosis of CVT is typically based on clinical suspicion and imaging confirmation. Clinical findings in CVT usually fall into 2 major categories, depending on the mechanism of neurological dysfunction: (1) Those related to increased intracranial pressure attributable to impaired venous drainage and (2) Those related to focal brain injury from venous ischemia/infarction or haemorrhage. Neuroimaging modalities of choice in CVST are computerized tomographic (CT) scan and Magnetic resonant imaging (MRI) with MR Venogram (MRV). CT scan may be normal in 15-30% cases but MRI with MRV is almost 100% diagnostic. CT scan pictures suggestive of CVST are infarcts, which may not conform to an arterial territory, extensive cerebral oedema, haemorrhagic infarcts, falcine and tentorial enhancement and thrombosed cortical vein (Cord sign). MRI with MRV is the investigation of choice, which shows absence of flow void in the thrombosed sinuses [6]. In all our cases, there was conclusive evidence of CVST MRI Brain with MRV. The work-up for underlying primary thrombophilic state is ideally postponed to 8-12 weeks after the acute episode as these tests may be falsely negative or positive in the acute state, and the results are also affected by the administration of anticoagulants [7].

Anticoagulation is the cornerstone of the treatment in CVST. Oral anticoagulants should be overlapped with subcutaneous LMWH and the latter discontinued once therapeutic INR of 2-3 is achieved. Oral anticoagulants should be continued for at least 3 to 6 months if no underlying thrombophilic state is found, or life-long if there is an irreversible procoagulant state. Thrombolysis of the clot using local administration or systemic injection of urokinase or recombinant tissue plasminogen activator (rTPA) has been evaluated and has been found to be effective though it is fraught with danger of haemorrhagic transformation of the infarcts and can be used only in centres equipped with facilities for intensive neurological monitoring.[8]

CVST can be deceptive as it can present in various forms and confuse the clinicians. Early diagnosis and aggressive management can help in reducing the mortality and morbidity associated with it.

6. Conclusion

CVST or CVT is an uncommon form of stroke, usually affecting young individuals accounting for less than 1% of all cerebrovascular accidents. Despite advances in the recognition of CVT in recent years, diagnosis and management can be difficult because of the diversity of underlying risk factors, protean manifestations and the absence of a uniform treatment approach. We have presented a series of six cases of CVST to highlight the varied and non-specific presentation, diversity (or lack) of clinical findings and customised management approach.

7. References

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