CASE REPORT

CEREBRAL VEIN THROMBOSIS: A CASE REPORT & LITERATURE REVIEW

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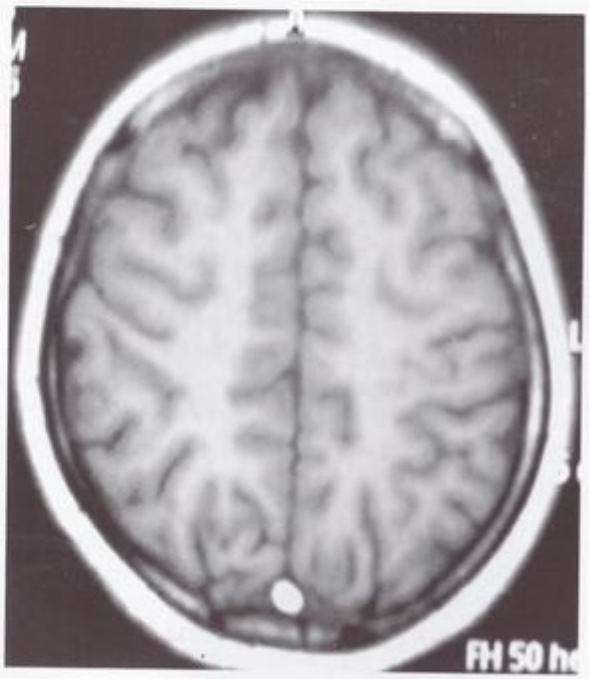
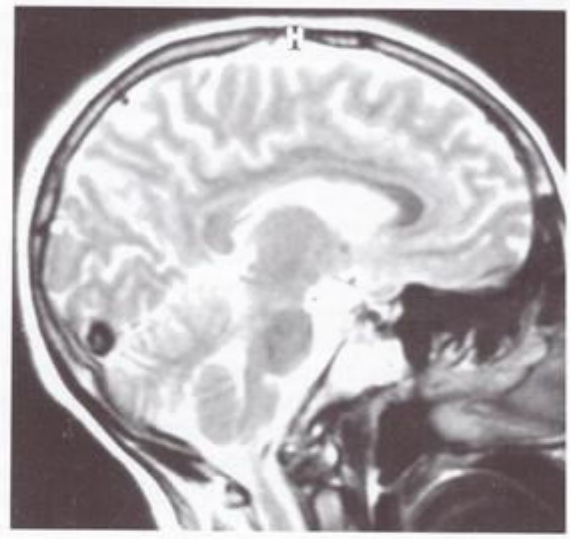
INTRODUCTION

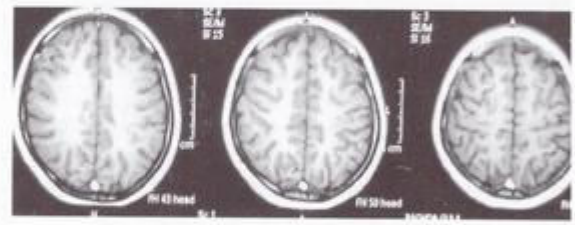
Cerebral vein and dural sinus thrombosis (CVT) is less common than most other types of stroke but can be more challenging to diagnose. Due to the widespread use of magnetic resonance imaging (MRI) and rising clinical awareness, CVT is recognized with increasing frequency. Because of its myriad causes and presentations, CVT is a disease that may be encountered not only by neurologists and neurosurgeons, but also by internists, oncologists, hematologists, obstetricians, pediatricians, and family practitioners.

CASE REPORT

A 20 years old postnatal lady was referred with the complaint of headache, fits, weakness on left side of body and altered consciousness for 20 days. Her past history was insignificant. There was no history of any drug allergy. She received paracetamol and valium. Her father was type II diabetic and mother was hypertensive. She was febrile running 100F temperature, anemic & drowsy. Her blood pressure was 120/70 with regular pulse of 110/min & respiratory rate of 20/min. She was confused, GCS 10/15, left sided weakness & up going planters.







Her full blood count, ESR, renal function test liver function tests, serum electrolytes, uric acid, ca cium corrected for albumin was normal. Her thick an thin blood films for malarial parasites were negativ CSF pressure was normal with lymphocytic pleocyt sis and elevated protein. CT brain with contrast re vealed empty delta sign. She had normal protein C S levels, Factor V Leiden mutation, anti thrombin leve anti-cardiolipin antibodies negative and seru homocystien level was normal. MRI scan was sugge tive of dural sinus thrombosis.

She was started on anticoagulants LMW hepari along with symptomatic treatment. She started impro ing quickly next day of staring treatment she had GC of 15/15. Her power improved gradually. She was pu on warfarin and was sent home. She came for follo up and is now mobile, with no residual symptoms.

DISCUSSION

Cerebral venous thrombosis (CVT) is an uncom mon but serious disorder. Clinical manifestations ca

include headache, papilledema, visual loss, focal or generalized seizures, focal neurologic deficits, confusion, altered consciousness, and coma. Many cases have been linked to inherited and acquired thrombophilias, pregnancy, puerperium, infection, and malignancy. Infarctions due to CVT are often hemorrhagic and associated with vasogenic edema. Treatment, which is started as soon as the diagnosis is confirmed, consists of reversing the underlying cause when known, control of seizures and intracranial hypertension, and antithrombotic therapy. Anticoagulation is the mainstay of acute and sub acute treatment for CVT.

EPIDEMIOLOGY

- < 2% of all strokes
- Predominantly affects young adults and children
- Male: uniform age distribution
- Females: 61% CVT in 20-35 age group
- 75% of adult patients are women (ISCVT study)
- Accounts for up to 50% of strokes during pregnancy and puerperium
- Incidence 3-4 per 1 million population

PATHOGENESIS

The pathogenesis of CVT remains incompletely understood. However, there are at least two different mechanisms that may contribute to the clinical features of CVT.

- Thrombosis of cerebral veins or dural sinus leading to cerebral parenchymal lesions or dysfunction.
- Occlusion of dural sinus resulting in decreased cerebrospinal fluid (CSF) absorption and elevated intracranial pressure.

Obstruction of the venous structures results in increased venous pressure, decreased capillary perfusion pressure, and increased cerebral blood volume. Dilatation of cerebral veins and recruitment of collateral pathways play an important role in the early phases of CVT and may initially compensate for changes in pressure. The increase in venous and capillary pressure leads to blood-brain barrier disruption, causing vasogenic edema, with leakage of blood plasma into the interstitial space. As intravenous pressure continues to increase, mild parenchymal changes, severe cerebral edema, and venous hemorrhage may occur due to venous or capillary rupture. The increased intravenous pressure may lead to an increase in intravascular pressure and a lowering of cerebral perfusion pressure, resulting in decreased cerebral blood flow (CBF) and failure of energy metabolism. In turn, this allows intracellular entry of water from failure of the Na+/K+ ATPase pump, and consequent cytotoxic edema.

RISK FACTORS AND ETIOLOGY

Systemic and local conditions increasing the risk of cerebral venous thrombosis

Infection
Central nervous system
Ear, sinus, mouth, face, and neck
Systemic infectious disease

Inflammatory diseases
Systemic lupus erythematosus
Behçet disease
Wegener's granulomatosis
Tromboangiitis obliterans
Inflammatory bowel disease
Sarcoidosis

Malignancy
Central nervous system
Solid tumour outside central nervous system
Hematologic

Hematologic condition
Polycythemia, thrombocythemia
Anaemia, including paroxysmal nocturnal hemoglobinuria
Pregnancy and puerperium

Central nervous system disorders
Dural fistulae
Other disorders
Dehydration
Congenital heart disease
Thyroid disease

Mechanical precipitants
Head injury
Lumbar puncture
Neurosurgical procedures
Jugular catheter occlusion

Drugs
Oral contraceptives
Hormone replacement therapy
Androgens
Tamoxifen & Steroids

CLINICAL ASPECTS

It has a highly variable clinical presentation [2,3] The onset can be acute, sub acute, or chronic. A case of CVT mimicking a transient ischemic attack has also been reported [4].

Symptoms and signs — Symptoms and signs of CVT can be grouped in three major syndromes:

- Isolated intracranial hypertension syndrome (headache with or without vomiting, papilledema, and visual problems).

- Focal syndrome (focal deficits, seizures, or both).
- Encephalopathy (multifocal signs, mental status changes, stupor or coma). [2]

Headache — Headache is the most frequent symptom of CVT. Headaches associated with CVT are more frequent in women and young patients than in men or older adults. Headache is usually the first symptom of CVT, and can be the only symptom [5], or can precede other symptoms and signs by days or weeks [6].

The features of CVT-related headache are quite variable:

- Head pain is more often localized than diffuse
- Headache onset is usually gradual, increasing over several days. However, some patients with CVT have sudden explosive onset of severe head pain i.e., thunderclap headache) that mimics subarachnoid hemorrhage [7,8].
- Headache caused by intracranial hypertension from CVT is typically characterized by severe, dull, generalized head pain that worsens with Valsalva maneuvers and with recumbency. Visual obscurations may occur, coinciding with bouts of increased headache intensity.
- Headache may resemble migraine with aura

Encephalopathy — Disturbances of consciousness and cognitive dysfunction, such as delirium, apathy, a frontal lobe syndrome, multifocal deficits, or seizures, can be present in severe cases of CVT.

Focal symptoms and signs — Motor weakness with monoparesis or hemiparesis, sometimes bilateral, is the most frequent focal deficit associated with CVT. In the ISCVT cohort, motor weakness was present in 37 percent of patients [1]. Aphasia, in particular of the fluent type, may follow sinus thrombosis, especially when the left lateral sinus is affected. Sensory deficits and visual field defects are less common.

Seizures — Focal or generalized seizures, including status epilepticus, are more frequent in CVT than in other stroke types.

Isolated sinus and vein thrombosis —

Isolated thrombosis of the different sinus and veins produces diverse clinical pictures. In cavernous sinus thrombosis, ocular signs dominate the clinical picture with orbital pain, chemosis, proptosis, and oculomotor palsies. Isolated cortical vein occlusion produces motor/sensory deficits and seizures [9]. With sagittal sinus occlusion, motor deficits, bilateral deficits, and seizures are frequent, while presentation as an isolated intracranial hypertension syndrome is infrequent. Patients with isolated lateral sinus thrombosis frequently present with isolated headache or isolated intracranial hypertension [10]. Less often, they may also present with focal deficits or seizures. Aphasia often follows if the left transverse sinus is occluded. Jugular vein or lateral sinus thrombosis may present as isolated pulsating tinnitus. Multiple cranial nerve palsies may occur in thrombosis of the lateral sinus [11], jugular, or posterior fossa veins thrombosis. When the deep cerebral venous system i.e., the straight sinus and its branches) is occluded, the signs and symptoms of CVT are generally severe, with coma, mental problems, and motor deficits, often bilateral [12]. However, more limited thrombosis of the deep venous system can produce relatively mild symptoms.

DIAGNOSIS

- consider in young and middle-aged patients with
  - recent unusual headache
  - stroke like symptoms in the absence of usual risk factors
  - intracranial hypertension
  - CT evidence of haemorrhagic infarcts, especially if not confined to arterial vascular territories
- Most sensitive examination: MRI + MR venography

Neuroimaging

The characteristics of the MRI signal depend on the age of the thrombus. In the first five days, the thrombosed sinuses appear iso intense on T1-weighted images and hypo intense on T2-weighted images, beyond five days, venous thrombus becomes more apparent because signal is increased on both T1 and T2-weighted images. After the first month, thrombosed sinuses exhibit a variable pattern of signal, which may appear isointense.

Head CT — Head computed tomography (CT) scan is normal in up to 30 percent of CVT cases, and most of the findings are nonspecific. In about one-third of cases, CT demonstrates direct signs of CVT, which are as follows.

- The dense triangle sign, seen on non contrast head CT as a hyper density with a triangular or round shape in the posterior part of the superior sagittal sinus caused by the venous thrombus
- The empty delta sign (also called the empty triangle or negative delta sign), seen on head CT with contrast as a triangular pattern of contrast enhancement surrounding a central

region lacking contrast enhancement in the posterior part of the superior sagittal sinus

- The cord sign, usually seen on head CT with contrast as a curvilinear or linear hyper density over the cerebral cortex caused by a thrombosed cortical vein

Indirect signs of CVT on head CT are more frequent. These can include intense contrast enhancement of falx and tentorium, dilated trans cerebral veins, small ventricles, and parenchyma abnormalities. In serial CT, some lesions may disappear ("vanishing infarcts"), and new lesions may appear

Laboratory tests — Aside from neuroimaging, there is no simple confirmatory laboratory test that can confidently rule out CVT in the acute phase of the disease. An elevated D-dimer level supports the diagnosis of CVT but a normal D-dimer does not exclude the diagnosis in patients with suggestive symptoms and predisposing factors. Lumbar puncture may be useful to exclude meningitis in patients with CVT who present with isolated intracranial hypertension, a syndrome that may account for up to 25 percent of all patients with CVT. In addition, lumbar puncture is valuable in such patients to measure and decrease cerebrospinal fluid pressure when vision is threatened. The cerebrospinal fluid abnormalities in CVT are nonspecific and may include a lymphocytic pleocytosis, elevated red blood cell count, and elevated protein; these abnormalities are present in 30 to 50 percent of patients with CVT[9].

Evaluation for the cause of CVT — searching for a thrombophilic state, either genetic or acquired, should be done in all patients. Screening should include: Antithrombin III, Protein C, Protein S, Factor VIII, and Factor V Leiden, Prothrombin Gene mutation, Serum homocysteine (to exclude homocysteinemia) Lupus anticoagulant and anticardiolipin antibodies. In patients older than 40 years without identified etiology, we suggest searching for an occult malignancy. In patients with sepsis, or with fever and no obvious cause of infection, we recommend performing a lumbar puncture.

PROGNOSIS. Cerebral venous thrombosis (CVT) can result in death or permanent disability, but usually has a favorable prognosis. Approximately 5 percent of patients die in the acute phase of the disorder. The main cause of acute death with CVT is transtentorial herniation secondary to a large hemorrhagic lesion[13]. Other causes of early death include herniation due to multiple lesions or to diffuse brain edema, status epilepticus, medical complications, and pulmonary embolism[14].

Long-term outcome- Mortality after the acute phase of CVT is predominantly related to underlying conditions. In the ISCVT at the end of follow-up (median 16 months), death had occurred in 52 of 824 patients (8.3 percent)[15].

Predictors of poor long-term prognosis in the ISCVT were as follows[15]: Central nervous system infection, any malignancy, thrombosis of the deep venous system, hemorrhage on head computed tomography (CT) or magnetic resonance imaging (MRI), Glasgow coma scale score <9 on admission, mental status abnormality, age >37 years and male gender.

Recurrence — Recurrent CVT appears to be uncommon, with rates ranging from 2 to 7 percent

TREATMENT

While the overall aim of treatment for cerebral venous thrombosis (CVT) is to improve outcome, the immediate goals of antithrombotic treatment are:

- To recanalize the occluded sinus/vein
- To prevent the propagation of the thrombus, namely to the bridging cerebral veins
- To treat the underlying prothrombotic state, in order to prevent venous thrombosis in other parts of the body, particularly pulmonary embolism[14], and to prevent the recurrence of CVT

Anticoagulation–The main treatment option to achieve these goals is anticoagulation, using either heparin or low molecular weight heparin (LMWH). For acute CVT treatment, the choice between IV heparin and subcutaneous LMWH can be made on the basis of availability, patient preference, and cost, as there is no evidence that one is more effective or safe than the other for this indication. The goal of heparin therapy is 2.0 times the control APTT value. The suggested dose of LMWH is 180 anti-factor Xa international units/kg per day, administered by two subcutaneous injections daily. Guidelines from the American Academy of Chest Physicians (ACCP) issued in 2008 recommend unfractionated heparin or LMWH during the acute phase of CVT, even in the presence of hemorrhagic infarction, followed by oral anti-coagulation for up to 12 months (target INR 2.5; range 2.0-3.0)[19]. Chronic oral anticoagulation is reserved for patients with inherited or acquired prothrombotic conditions, including those with the antiphospholipid syndrome.

Endovascular thrombolysis —

For adults and children with CVT who develop progressive neurologic worsening despite adequate anticoagulation with IV heparin or subcutaneous LMWH, endovascular thrombolysis at centers experienced in using this therapy is suggested. The type and doses of thrombolytic drugs used for endovascular treatment of CVT has varied widely[18]. Total doses of local urokinase reported in the literature range be-