cerebral venous sinus thrombosis [created by Paul Young 22/11/07]

investigation

General:
- Although the clinical presentation is highly variable, the diagnosis should be considered in young and middle-aged patients with recent unusual headache or with stroke-like symptoms in the absence of the usual vascular risk factors, in patients with intracranial hypertension, and in patients with CT evidence of hemorrhagic infarcts, especially if theinfarcts are multiple and not confined to the arterial vascular territories. The average delay from the onset of symptoms to the diagnosis is seven days.

MRI:
- The most sensitive examination technique is MRI in combination with magnetic resonance venography. T1-weighted and T2-weighted MRI will show a hyperintense signal from the thrombosed sinuses. The characteristics of the signal depend on the age of the thrombus and are isointense on T1-weighted images during the first five days and after one month.
- The combination of an abnormal signal in a sinus and a corresponding absence of flow on magnetic resonance venography confirms the diagnosis of thrombosis

CT scanning
- CT scanning is a useful technique for the initial examination, to rule out other acute cerebral disorders and to show venous infarcts or hemorrhages, but its results can also be entirely normal. High-resolution CT equipment may show the thrombus as a hyperintense signal in a sinus or even in the cortical veins (the "cord sign"). CT venography is a promising new technique for creating images of the cerebral venous system.

Cerebral angiography
- If the diagnosis is still uncertain after MRI or CT venography has been performed, cerebral angiography may be indicated.
- Angiography provides better details of the cerebral veins and hence is useful in the diagnosis of rare cases of isolated thrombosis of the cortical veins without sinus thrombosis.
- Angiography also shows dilated and tortuous ("corkscrew") veins, which are evidence of thrombosis downstream in the sinuses.

causes, risk factors & locations

Genetic prothrombotic conditions
- Antithrombin deficiency[5]
- Protein C and protein S deficiency[6-8]
- Factor V Leiden mutation[9-11]
- Prothrombin mutation (the substitution of A for G at position 20210)[9,11,12]
- Homocysteinemia caused by gene mutations in methylenetetrahydrofolate reductase[13,14]

Acquired prothrombotic states
- Nephrotic syndrome
- Antiphospholipid antibodies[7,15]
- Homocysteinemia[14]
- Pregnancy[16,17]
- Puerperium[17]

Infections
- Otitis, mastoiditis, sinusitis[6]
- Meningitis
- Systemic infectious disease[6]

Inflammatory disease
- Systemic lupus erythematosus[18]
- Wegener's granulomatosis[8]
- Sarcoidosis
- Inflammatory bowel disease
- Behçet's syndrome[19,20]

Hematologic conditions
- Polycythemia, primary and secondary
- Thrombocythemia
- Leukemia[21]
- Anemia, including paroxysmal nocturnal hemoglobinuria[22]

Drugs
- Oral contraceptives[9,23]
- Asparaginase[6,21]

Mechanical causes, trauma
- Head injury[24]
- Injury to sinuses or jugular vein, jugular catheterization
- Neurosurgical procedures
- Lumbar puncture[25]

Miscellaneous
- Dehydration, especially in children[6]
- Cancer[1,6]

pathogenesis

(i) occlusion of the cerebral veins
- causes localized edema of the brain and venous infarction. Pathological examination shows enlarged, swollen veins, edema, ischemic neuronal damage, and petechial hemorrhages. The latter can merge and become large hematomas, which have a characteristic appearance on computed tomographic scans.

(ii) occlusion of major venous sinuses
- lead to the development of intracranial hypertension. Normally, the cerebrospinal fluid is transported from the cerebral ventricles through the subarachnoid spaces at the base and surface of the brain to the arachnoid villi, where it is absorbed and drained into the superior sagittal sinus. Thrombosis of the sinuses leads to increased venous pressure, impaired absorption of cerebrospinal fluid, and consequently, increased intracranial pressure. The obstruction to the drainage of cerebrospinal fluid is located at the end of its transport pathway, and no pressure gradient develops between the subarachnoid spaces at the surface of the brain and the ventricles. Hence, the ventricles do not dilate, and hydrocephalus does not normally complicate sinus thrombosis.
- About one fifth of patients with sinus thrombosis have intracranial hypertension only, without signs of cortical vein thrombosis

clinical features

- The most frequent but least specific symptom of sinus thrombosis is severe headache, which is present in more than 90 percent of adult patients. It usually increases gradually over a couple of days but can also start in a split second, mimicking a subarachnoid hemorrhage.
- Cerebral lesions and neurologic signs develop in half of patients with sinus thrombosis. Characteristic, but rare, is the occurrence of unilateral hemispheric symptoms such as hemiparesis or aphasia, followed within days by symptoms from the other hemisphere; these are caused by the development of cortical lesions on both sides of the superior sagittal sinus.
- Seizures occur in about 40 percent of patients, a far higher percentage than in patients with arterial stroke. Seizures are limited and focal in 50 percent of these patients but may generalize to a life-threatening status epilepticus.
- Thrombosis of the deep venous system - the straight sinus and its branches - causes centrally located, often bilateral thalamic lesions, with behavioral symptoms such as delirium, amnesia, and mutism, which can be the only manifestation of sinus thrombosis.
- If large unilateral infarcts or hemorrhages compress the diencephalons and brain stem, patients may become comatose or die from cerebral herniation if untreated. Other causes of coma are involvement of the thalamus and generalized seizures.
- Infectious cavernous sinus thrombosis is characterized by headache, fever, and eye symptoms such as periorbital edema, proptosis, chemosis, and paralysis of eye movements due to involvement of the oculomotor, abducent, or trochlear nerves.
- Patients with isolated intracranial hypertension have headache but no other neurologic symptoms, with the exception of diplopia due to involvement of the sixth nerve when the intracranial pressure is quite high.
- Fundoscopic examination will reveal papilledema. Severe papilledema can cause transient visual impairments, and even permanent blindness, if left untreated.

treatment

general measures
- The combination of acutely increased intracranial pressure and large venous infarcts is dangerous, and patients may die within hours from cerebral herniation. Impaired consciousness and cerebral hemorrhage are associated with a poor outcome,but even patients with these manifestations can make a remarkable recovery.
- The priority of treatment in the acute phase is to stabilize the patient's condition and to prevent or reverse cerebral herniation. This may require the administration of intravenous mannitol, surgical removal of the hemorrhagic infarct, or decompressive hemicraniectomy.
- It is not known whether the administration of corticosteroids in the acute phase improves outcome.
- Possible causes of sinus thrombosis, such as infections, should be searched for and treated.

anticoagulation
- The most obvious treatment option is anticoagulation with heparin to arrest the thrombotic process
- However, anticoagulant treatment has raised much controversy because of the tendency of venous infarcts to become hemorrhagic: about 40 percent of all patients with sinus thrombosis have a hemorrhagic infarct even before anticoagulant treatment is started.
- The effect of anticoagulant treatment has been examined in three small, randomized clinical trials.
- The first trial compared the effect of intravenous heparin with that of placebo and was stopped after only 10 patients had been included in each treatment group, because an interim analysis showed a significant benefit with heparin, according to the investigators.
- A repeated analysis, which was based on the usual scales of stroke outcome, did not show a statistically significant difference between the effect of heparin and that of placebo. Also, the average delay of four weeks from the onset of symptoms to the beginning of treatment was exceptionally long.
- The second study compared the effect of fixed high-dose, subcutaneous nadroparin with that of placebo in 60 patients and found no statistically significant difference. This study was criticized for an imbalance at baseline, which may have favored the placebo group.
- The third study compared the effect of intravenous unfractionated heparin with that of placebo in 57 women from India who had puerperal sinus thrombosis but in whom the diagnosis had not been confirmed by MRI or angiography.
- A meta-analysis of these studies showed a nonsignificant reduction in the pooled relative risk of death or dependency of 0.46 (95 percent confidence interval, 0.16 to 1.31).
- A new trial with enough power to demonstrate a similar effect of treatment would require the recruitment of 300 patients. With a rare disease such as sinus thrombosis, this would be challenging but feasible.
- Most neurologists now start treatment with heparin as soon as the diagnosis is confirmed, even in the presence of hemorrhagic infarcts. This treatment was applied to more than 80 percent of the 624 patients in a recent prospective study. In this study, 79 percent of the patients recovered, 8 percent had minor handicaps, 5 percent were severely handicapped, and 8 percent died.
- The optimal duration of oral anticoagulant treatment after the acute phase is unknown. Recurrent sinus thrombosis occurs in 2 percent of patients, and about 4 percent of patients have an extracranial thrombotic event within one year.
- Usually, vitamin K antagonists are given for six months after a first episode of sinus thrombosis, or longer in the presence of predisposing factors, with a target international normalized ratio of 2.5.

thrombolysis
- Endovascular thrombolysis can be attempted with the administration of a thrombolytic enzyme, usually urokinase, into the sinus, sometimes in combination with mechanical thrombo-aspiration. Published reports are limited to case reports and uncontrolled studies, from which it is impossible to conclude that the results associated with endovascular thrombolysis are superior to those with systemic heparin.
- Until better evidence is available, endovascular thrombolysis may be applied at centers where the staff have experience in interventional radiology, and this treatment method should be restricted to patients with a poor prognosis.