Review Article

Cerebral venous thrombosis: Update on clinical manifestations, diagnosis and management

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Abstract

Cerebral venous thrombosis (CVT) has a wide spectrum of clinical manifestations that may mimic many other neurological disorders and lead to misdiagnoses. Headache is the most common symptom and may be associated with other symptoms or remain isolated. The other frequent manifestations are focal neurological deficits and diffuse encephalopathies with seizures. The key to the diagnosis is the imaging of the occluded vessel or of the intravascular thrombus, by a combination of magnetic resonance imaging (MRI) and magnetic resonance venography (MRV). Causes and risk factors include medical, surgical and obstetrical causes of deep vein thrombosis, genetic and acquired prothrombotic disorders, cancer and hematological disorders, inflammatory systemic disorders, pregnancy and puerperium, infections and local causes such as tumors, arteriovenous malformations, trauma, central nervous system infections and local infections. The breakdown of causes differs in different parts of the world. A meta-analysis of the most recent prospectively collected series showed an overall 15% case-fatality or dependency rate. Heparin therapy is the standard therapy at the acute stage, followed by 3-6 months of oral anticoagulation. Patients with isolated intracranial hypertension may require a lumbar puncture to remove cerebrospinal fluid before starting heparin when they develop a papilloedema that may threaten the visual acuity or decompressive hemicraniectomy. Patients who develop seizures should receive antiepileptic drugs. Cerebral venous thrombosis - even pregnancy-related - should not contraindicate future pregnancies. The efficacy and safety of local thrombolysis and decompressive hemicraniectomy should be tested.

Keywords

Cerebral venous thrombosis, intracranial hypertension, stroke

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Introduction

Cerebral venous thrombosis (CVT), i.e., any thrombosis that occurs in intracranial veins or sinuses,[1] is a rare disorder affecting approximately 5 persons per million per year with huge regional variations.[2] It accounts for approximately 0.5% of all the strokes, but are also often revealed by other clinical manifestations without stroke.

Before computed tomography (CT) and magnetic resonance imaging (MRI), CVT was considered as a disorder of infectious origin that usually results in bilateral or alternating focal neurological deficits, which is associated with seizures and coma and usually leading to death. In fact, CVT was usually diagnosed at autopsy or sometimes at angiography, i.e., in patients with severe clinical manifestations. The widespread use of CT- and MRI-scans has completely changed our knowledge on the disease and on its wide clinical spectrum. Nowadays, CVT is regarded in western countries as a noninfective disorder with various clinical presentations and an usually favorable outcome with a case-fatality rate of less than 10%.[1] Clinical trials became possible when CT and MRI became routinely used and showed that heparin reduce mortality and handicap even in cases revealed by an intracerebral hemorrhage.[3]

This review will not address the issue of neonates which is completely different with regard to the clinical presentation, diagnosis, causes, treatments and outcome.

Mechanisms Leading to the Clinical Manifestations

Two different mechanisms have to be identified; however, they are interrelated in many cases.[4]

The occlusion of a cerebral vein leads to localized brain edema and a so-called venous infarction. During pathological examination, swollen veins, edema, ischemic neuronal damage and petechial hemorrhages that can merge and become a large hemorrhage are observed. Cytotoxic edema caused by local ischemia, subsequently damages the energy-dependent cellular membrane pumps and induce intracellular swelling.[4]

Vasogenic edema caused by disruption in the blood-brain barrier and leakage of plasma into the interstitial space is a reversible phenomenon if the venous occlusion is successfully treated.[4]

The occlusion of a major sinus leads to the development of intracranial hypertension because of an impaired absorption of cerebrospinal fluid. The ventricles do not dilate and no hydrocephalus occurs because there is no gradient of pressure.[4]

Clinical Manifestations

Cerebral venous thrombosis has a wide spectrum of clinical manifestations and modes of onset that may mimic many other neurological disorders and lead to frequent misdiagnoses or delay in diagnosis.

Headache

Headache is the most common symptom of CVT. The mechanism of the headache remains unknown in most cases. The two plausible hypotheses are stretching of nerve fibres in the walls of the occluded sinus and local inflammation as suggested by the evidence of contrast enhancement of the sinus wall surrounding the clot.[2] Three types of headache have been reported:

Headache is almost always found in patients who have a reliable medical history.[5] Most patients who are admitted for other neurological symptoms often complain of headache at admission or report a history of headache of unusual type that started a few days or weeks earlier.[5]

Headache may occur in a context of isolated intracranial hypertension: patients with a chronic course or with delayed clinical presentation may have papilloedema but this is not an usual finding in acute cases.[6]

Headache may also be the only symptom and occurs in the absence of intracranial hypertension, subarachnoid hemorrhage or meningitis.[7,8] Isolated headache is sometimes of the thunderclap type, mimicking a subarachnoid hemorrhage.[7] The CT-scan and the analysis of the cerebrospinal fluid may remain apparently normal in these patients and make the diagnosis difficult in the absence of clear clinical hypothesis that may orientate the radiologist towards a diagnosis of CVT. Isolated headache has been reported in 17 of 123 consecutive patients admitted in the same neurological centre either in the stroke unit or in the emergency headache centre. These cases are usually associated with lateral sinus thrombosis.[2] As most patients with isolated headache are treated by heparin,[1] the question of whether in the absence of heparin, CVT would have recovered spontaneously, or would have extended and led to clinical worsening, remains unresolved. Headache being almost always the first symptom of CVT, the rule is to recognize CVT even in case of isolated headache and to start heparin.

Isolated focal neurological deficits

CVT patients may develop the following:

- long-lasting focal neurological deficits due to stroke (either venous ischemia or intra-cerebral hemorrhage) or edema;
- transient focal neurological deficits mimicking transient ischemic attacks.

The diagnosis is sometimes easy because of the pre-existence of unusual headache or a predisposing condition known to be at high risk of CVT, such as puerperium. Sometimes the diagnosis can be picked up during routine MRI or CT done for TIA or stroke.

Diffuse encephalopathies with seizures

In patients with parenchymal lesions, the clinical picture is more severe and may include at various degrees: coma, motor deficits or aphasia and seizures (focal or generalized seizures, including status epilepticus. Seizures are more common in patients with parenchymal lesions, sagittal sinus and cortical vein thrombosis.[9]

Other clinical presentations

Many other clinical presentations have been described in CVT patients;[1,10-12] attacks of migraine with aura, isolated psychiatric disturbances, pulsatile tinnitus, isolated or multiple cranial nerve involvement or subarachnoid hemorrhage

Relationship between clinical manifestations and the site of venous occlusion

Isolated thrombosis of the different sinuses and veins may result in various types of clinical manifestations.

- Occlusions of cortical veins lead to motor or sensory deficits, seizures or both.
- Occlusions of the sagittal leads to sinus motor deficits that are sometimes alternating or bilateral and often seizures and rarely result in isolated intracranial hypertension syndromes.
- Occlusions of the lateral sinus present usually as an isolated intracranial hypertension, associated with aphasia when the left transverse sinus is occluded.
- Occlusions of deep cerebral veins leads to a severe clinical presentation with coma, delirium and bilateral motor deficits, but symptoms may be of milder intensity when the thrombosis is limited.[13]
- In occlusions of the cavernous sinus, the most prominent clinical manifestations are orbital pain, chemosis, proptosis and oculomotor palsies.

Specificities of clinical manifestations in the elderly

In ISCVT, 8.2% of patients were aged 65 years or over.[14] They had less frequently isolated intracranial hypertension and had more frequently impaired consciousness and mental status impairments. Cerebral venous thrombosis is a cause of impairment of consciousness and mental status impairment that should therefore be considered in the elderly. Cancers are more frequently found as the presumed cause than in younger CVT patients.[14]

Diagnosis of CVT

Neuroimaging of the thrombosed vessel

The key to the diagnosis is the imaging of the occluded vessel or of the intravascular thrombus. The gold standard is the combination of MRI, which visualizes the thrombus [Figures 1 and 2], with magnetic resonance venography (MRV), which shows the nonvisualization of the vessel.[15,16]

- At the very early stage of an acute thrombosis, MRI alone is limited by flow artefacts that can lead to false positives and the lack of hyperintense signal on T1- and T2-weighted images.[2]
- During the first 3-5 days, the thrombosed sinus appears as an isointense signal on T1-weighted sequences and a hypointense signal on T2-weighted sequences: it can, therefore be very difficult to differentiate it from normal veins.[2] The diagnostic yield of MRV alone, as that of all other angiographic techniques, is limited because it does not make a clear differentiation between an occluded sinus and hypoplasia, particularly for lateral sinuses.[15,16] Even with the combination of MRI and MRV, the diagnosis can still remain difficult, particularly for isolated cortical vein thrombosis: if the characteristic cord sign is not present on noncontrast-enhanced CT- or MRI-scan,[17,18] a conventional angiography may sometimes still be required.[19] The interobserver agreement for the diagnosis of the location of CVT is not perfect, particularly in the case of cortical vein thrombosis.[20]
- Several studies have shown the value of T2*-weighted sequences: in contrast to T1 and T2, they show the thrombus hypointense with the magnetic susceptibility effect, the signal being similar to that of an intracerebral hemorrhage.[21-23] A hypointense signal on T2*-images is present in 90% of sites of CVT on the first MRI-scan, while a hyperintense signal is detected on T1-images in 84% of sites.[23] This excellent sensitivity of T2*-sequences is of major interest within the first 3 days when the frequency of hyposignal on T2*-sequences is higher than 90% and that of hypersignal on T1*-sequences in only 70%.[2,23] Accordingly, a thrombus located in cortical veins, even in the absence of visible occlusion on MRV, is more easily detected with T2* (97%) than with T1 (78%) or fluid-attenuated inversion recovery (FLAIR) <40%), the proportion of cases detected being 97%, 78% and less than 40% with these 3 sequences, respectively.[2] Therefore, T2*-sequences are of additional value for the diagnosis of CVT, particularly in isolated cortical venous thrombosis and at the very early stage when T1- and T2- sequences are not sensitive enough.[23] The presence of a hyperintense signal of the thrombosed sinus on diffusion-weighted images (DWI) has a low sensitivity as it is detected in less than 40% of patients.[24-26] However, it may be useful to predict nonrecanalization.[26]
- Although none of the MRI sequences (T1, T2, FLAIR and T2*) has a sensitivity and specificity of 100%, the diagnostic yield of their combination together with MRV is so high that conventional angiography is nowadays almost not required in patients who can undergo MRI.[2]

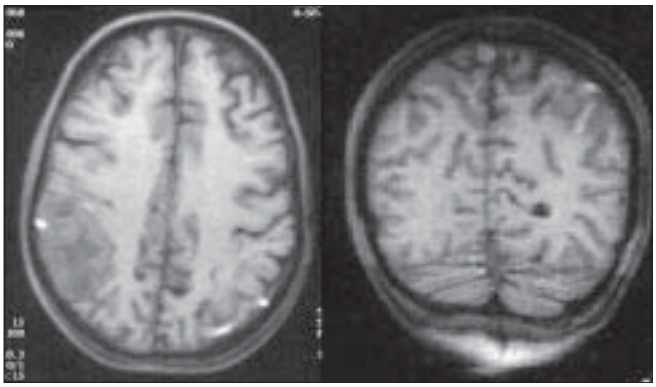

Figure 1: Occlusion of cortical vein associated with a nonhemorrhagic venous infarct

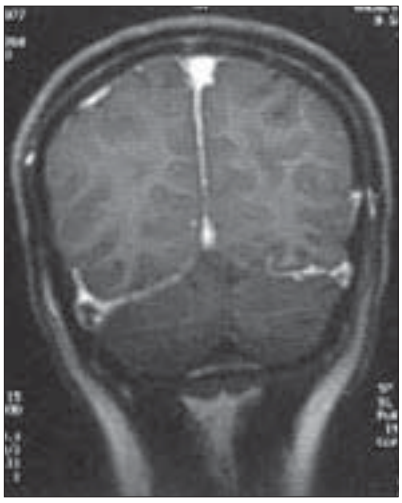

Figure 2: Occlusion of the right lateral sinus

Neuroimaging of parenchymal abnormalities with MRI and DWI

- In contrast to arterial strokes, brain imaging by

itself is of insignificant value for the diagnosis of CVT;[2] it usually shows nonspecific lesions, such as intracerebral hemorrhages or infarcts, edema, isolated or associated with infarcts or hemorrhages [Figure 3], and it can even be normal in up to 30% of patients.[2]

- Changes in DWI were reported in case reports of small series with a wide spectrum range of inclusion criteria.[25,27-33] Various patterns of abnormalities have been reported; however, their frequency and significance remains unknown in the absence of large series of consecutive and nonselected patients.
- The most common pattern is a heterogeneous signal intensity with normal or increased apparent diffusion coefficient (ADC), corresponding to vasogenic edema.[24,25,30,31,33] Only one study showed a decreased ADC in most patients, suggesting a cytotoxic edema.[32] The last but very rare pattern is that of a decreased diffusion with complete resolution and no lesion on follow-up T2-weighted imaging, mostly in patients with seizures.[33] The DWI and ADC patterns differ from that of arterial infarcts and are mostly suggestive of vasogenic edema and less commonly of cytotoxic edema.[2] This difference explains why the lesions that are sometimes described as having venous infarcts have a better recovery than those with arterial infarcts.

D-dimer measurement

Due to the wide range of symptoms that are compatible with a diagnosis of CVT, it would have been useful to have a test that is noninvasive, cheap, easy to perform in emergency and that would confidently rule out CVT in patients with nonspecific symptoms such as isolated headache. Several studies[34-38] have tested the value of D-dimer measurements, because in patients with deep vein thrombosis of the legs, a value below 500 ng/mL has a high negative predictive value. In fact, in most patients with recent CVT, there is an increase in D-dimer concentrations; this implies that a low value of D-dimer makes the diagnosis of CVT unlikely.[35-37] However, the negative predictive value of low D-dimer concentrations is good in patients with encephalic signs, who anyway should undergo MRI, but not in those with isolated headache.[38] Thus, a negative D-dimer assay cannot rule out CVT in patients with recent isolated headache[34,38] and cannot be recommended as a screening test.

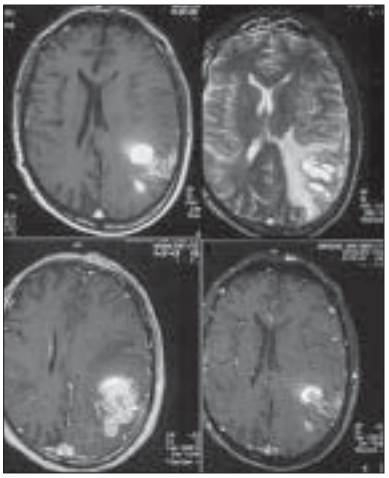

Figure 3: Hemorrhagic venous infarct

Etiologies

Many disorders can either cause or just predispose to CVT. Causes and risk factors are sometimes difficult to differentiate in CVT. They are summarized in Table 1. They include medical, surgical and obstetrical causes of deep vein thrombosis, genetic and acquired

Table 1: Causes and risk factors associated with cerebral venous sinus thrombosis

Genetic prothrombotic conditions
- Antithrombin deficiency
- Protein C and protein S deficiency
- Factor V Leiden mutation
- Prothrombin mutation (the substitution of A for G at position 20210)
- Homocysteinemia caused by gene mutations in methylenetetrahydrofolate reductase.

Acquired prothrombotic states
- Nephrotic syndrome
- Antiphospholipid antibodies
- Hyperomocysteinemia
- Pregnancy
- Puerperium
- Dehydration, especially in children
- Cancer
- Elevation of plasma factor VIII levels
- Elevation of plasma factor von Willebrand levels

Infections
- Otitis, mastoiditis, sinusitis
- Meningitis
- Systemic infectious disease

Inflammatory disease
- Systemic lupus erythematosus
- Wegener's granulomatosis
- Sarcoidosis
- Inflammatory bowel disease
- Behçet's syndrome

Hematologic conditions
- Polycythemia, primary and secondary
- Thrombocythemia
- Leukaemia
- Anemia, including paroxysmal nocturnal hemoglobinuria

Drugs
- Oral contraceptives
- Asparaginase

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

Modified from the study by Stam[4]

prothrombotic disorders, cancer and hematological disorders, inflammatory systemic disorders, pregnancy and puerperium, infections and local causes such as tumors, arteriovenous malformations, trauma, central nervous system infections and infections of the ear, sinus, mouth, face and neck.[1,11] Diagnostic and therapeutic procedures such as surgery, lumbar puncture, jugular catheterisation and drugs such as hormonal contraceptive therapies that are especially of the third generation, hormonal replacement therapy, steroids that are especially combined with a lumbar puncture and treatments of cancer can also cause CVT or predispose to it. The breakdown of these causes varies in different parts of the world.

In ISCVT, 44% of the patients had more than one cause or predisposing factor and congenital or genetic thrombophilia accounted for 22% of patients.[1] Besides the classic deficiencies in antithrombin III, protein C and protein S and having the factor V Leiden or the prothrombin gene mutations,[15,16] more recent studies have emphasized the role of the elevation of plasma factor VIII levels[39] and elevation of von Willebrand factor;[39] both are also associated with an increased risk of CVT. However, the effect of elevation of von Willebrand factor seems to be mediated in part via factor VIII. Among newly identified gene polymorphisms in the coagulation and fibrinolytic systems, no independent association has been found between the protein C promoter CG haplotype and CVT. However, this polymorphism increased the risk in the carriers of the factor II G20210A mutation with an odds ratio rising from 14.7 (95% CI: 2.83-75.3) with the factor II mutation alone to 19.8 (95% CI: 2.1-186.5) with the combination of both the mutations.[40] For classic congenital thrombophilia and hyperhomocysteinaemia,[41] the risk is increased when the protein C promoter CG haplotype is associated with estrogen treatment (odds ratio: 24 [2·26-127·3]).[40] In a small study on 77 patients, there was no significant association between CVT with the polymorphisms of the thrombin-activable fibrinolysis inhibitor or of the protein Z genes;[42] however, this may be the consequence of a lack of statistical power. New genetic risk factors for CVT in the coagulation and fibrinolytic systems will probably be found in the future.[2] The testing for congenital thrombophilia should thus be systematically performed in CVT, even when there is a clear cause, for the following reasons: (i) the presence of congenital thrombophilia potentates the risk of CVT associated with other disorders and (ii) it is important to look for the disorder in family members in order to start preventive measures when needed.[15,16]

Hyperhomocysteinaemia is an independent and strong risk factor for CVT that is present in 27-43% of patients and in 8-10% in the community (odds ratio: 4-7).[41,43,44] The post-methionine load increment of homocysteine has been fund to be strongly associated with CVT in one study;[41] however, this finding has not been confirmed by other studies.[43] No independent association has been found between the C677T mutation in the methylene tetrahydrofalate reductase gene (*MTHFR*) and CVT.[41,43] The question of whether the treatment of hyperhomocysteinaemia with folic acid alone or in combination with cobalamin and pyridoxine reduces the risk of CVT remains unanswered.

Various case reports or small series have recently found other causes that should be added to the list of causes: spontaneous intracranial hypotension,[45] thalidomide,[46] Cushing's syndrome,[47] tamoxifen,[48] erythropoietin,[49] high altitude,[50] phytoestrogens[51] and even Shiatsu massage of the neck.[52]

The cases of unknown causes are still frequent and account for approximately 15% of cases;[1] however, this proportion is decreasing with the discovery of new causes.

Outcome

A meta-analysis of the most recent prospectively collected series, in which the weight of the ISCVT cohort is very important, showed an overall 15% case-fatality or dependency rate.[1,5,53-57]

Predictors of 30-day case fatality are impaired consciousness, mental status disorder, thrombosis of the deep venous system, right hemispheric hemorrhage and posterior fossa lesions.[2] The main cause of acute death is transtentorial herniation, secondary to a large hemorrhagic lesion, multiple lesions or diffuse brain edema.[58] Other causes of acute death include status epilepticus, medical complications and pulmonary embolism.[59]

Deterioration after admission occurs in approximately 23% of patients, with worsening of mental status, headache or focal deficits or with new symptoms such as seizures.[2] Mortality after the acute phase is prominently associated with the underlying cause, especially cancer.[5]

The predictors of poor long-term outcomes are infection of the central nervous system, cancer, deep venous system thrombosis, intracranial hemorrhage,[60] Glasgow Coma Scale score at admission below nine, mental status disorder, being older than age 37 years and being of male gender.[1] This predictive model has been validated in an independent cohort, but the study has not yet been published.[2] The overall outcome is far better than that of arterial stroke as approximately

two-thirds of patients recover without sequelae. In elderly patients, in whom the most frequent cause is a carcinoma, the outcome is worse, 49% of patients being dead or dependent at the end of follow-up. Because of an increased risk of further thrombotic events, anticoagulation for more than 6 months may be necessary in these patients.[14]

In the subgroup of patients with intracerebral hemorrhage, men who were older, had a thrombosis of the deep cerebral venous system or of the right lateral sinus and a motor deficit were at higher risk for death or dependency at the sixth month.[60] These patients could be the target for new therapeutic strategies.

Treatment

Recent guidelines[61] for the treatment of CVT have been published. They are summarized in Table 2.

Acute treatment

- Heparin therapy and other procedures of recanalization

The aims of heparin therapy in CVT are: (i) to prevent the extension of the thrombus; (ii) to treat the underlying prothrombotic state, (iii) to prevent venous thrombosis in other parts of the body or pulmonary embolism; and (iv) to prevent the recurrence of CVT.[11] However, the use of heparin has raised considerable controversy because of the natural tendency of venous infarcts to become hemorrhagic.

Three small randomized clinical trials[3,62,63] have been conducted to test the efficacy and safety of heparin in CVT. The German trial[3] that compared intravenous unfractionated heparin with placebo was stopped after the recruitment of 10 patients in each arm because the interim analysis already showed a significant benefit with heparin. Another analysis, based on more usual scales of stroke outcome, failed to show any statistically significant difference between the two groups but showed just a clear tendency. The delay of 4 weeks from onset of symptoms to treatment was very long and probably influenced the results. The Dutch trial[62] compared fixed high-dose of subcutaneous nadroparin with placebo in 60 patients. It failed to show any statistically significant difference between groups. However, there was an imbalance at baseline that favored the placebo group. The Indian trial[63] compared the effect of intravenous unfractionated heparin with placebo in 57 Indian women with puerperal sinus thrombosis in whom the diagnosis had not been confirmed by MRI or angiography. It also showed an insignificant tendency for a benefit of anticoagulant treatment as compared with placebo. A meta-analysis of these 3 trials showed a insignificant reduction in the relative risk of death or dependency of 0.46 (95% CI, 0.16-1.31).[64] Based on these 3 trials and the meta-analysis, most neurologists now start treatment with heparin as soon as the diagnosis is confirmed, even in the presence of hemorrhagic infarcts.

Systematic reviews of thrombolysis in CVT did not provide any evidence to support the use of systemic or local thrombolysis.[61,65] There is a probable publication bias as often encountered in such cases with the under-reporting of series with poor outcome by authors and over rejection by journal editors. The treatment and assessment were not blinded, leading to bias in assessing outcomes. In ISCVT, out of 13 patients treated with local thrombolysis, 5 were dead or dependent at the sixth month.

Table 2: Main recommendations for the treatment of cerebral venous thrombosis from the European Federation of Neurological Societies[61]

Antithrombotic therapy

Acute phase

No contraindication for anticoagulation:
- Body-weighted subcutaneous low-molecular-weight heparin in full therapeutic dosage or Dose-adjusted intravenous heparin (activated partial thromboplastin time two times above normal values)

Worsening despite best medical therapy and other causes of deterioration excluded:
- Local intravenous thrombolysis*
- or mechanical thrombectomy*

Prevention of recurrent thrombotic events with oral anticoagulants

CVT related to a transient risk factor: 3-6months

Idiopathic CVT or related to mild hereditary thrombophilia: 6-12 months

Recurrent CVT or severe hereditary thrombophilia: indefinite

Symptomatic treatment

Antiepileptic drugs

Acute phase
- Patients with acute seizures
- Patients with focal parenchymal lesions*
- Patients with focal neurological deficits*

Prevention of seizures after the acute phase
- Patients with acute seizures
- Patients with focal hemorrhagic lesions*

Treatment of intracranial hypertension

Threatened vision
- Lumbar puncture (if no parenchymal lesions)
- Acetazolamide
- Surgical procedures (lumboperitoneal shunt, ventriculoperitoneal shunt, optic nerve fenestration)

Impairment of consciousness or herniation
- Osmotic therapy
- Sedation and hyperventilation
- Hemicraniectomy*

*indicates that this option is either debated or optional.

However, when a patient deteriorates despite an adequate anticoagulation, local or systemic thrombolysis or thrombectomy may be considered when other causes of deterioration have been ruled out.[11]

Symptomatic therapies

None of the symptomatic therapies is evidence-based.

Patients with isolated intracranial hypertension may require a lumbar puncture to remove cerebrospinal fluid before starting heparin when they develop a papilloedema that may threaten the visual acuity. This is usually followed by a rapid improvement of headache and vision. When the intracranial pressure is severely increased, other recommendations are raising the head off the bed, glycerol or mannitol therapy and sedation, hyperventilation and intracranial pressure monitoring.[61] There is no indication that steroids are useful even in patients with a parenchymal lesion. In case of herniation secondary to an unilateral hemispheric lesion, decompressive hemicraniectomy can be performed and is sometimes associated with a good functional recovery.[66]

Patients who develop seizures should receive antiepileptic drugs because they have a high risk of new seizures.[9] By contrast, the risk late-onset seizures in patients free of any seizure at the acute stage is very low.[9]

Treatment of the cause

Any cause that can be treated, e.g., infection, should be treated?.

Long-Term Management

Oral anticoagulation

After the acute stage, heparin should be replaced by oral anticoagulation. The aim of oral anticoagulation is to prevent any recurrence of CVT, any other venous thrombosis and pulmonary embolism. Recurrent CVT is rare and difficult to prove, especially when there is no follow-up magnetic resonance angiography available after the first thrombosis. Other thrombotic events such as deep venous thrombosis and pulmonary embolism occur in up to 5% of patients.[1] Following evidence-based data and recommendations in deep venous thrombosis oral anticoagulation is recommended for 6-12 months, aiming at an international normalized ratio between two and three. More prolonged oral anticoagulation may be necessary in patients with inherited or acquired prothrombotic disorders, including antiphospholipid antibodies.

Antiepileptic therapy

Seizures occur in 11% of the patients and are more likely to occur in patients who had seizures at the acute phase or had a hemorrhagic parenchymal lesion.[9,67] Such patients can be given antiepileptic drugs to prevent the recurrence of seizures. The optimal duration of treatment is unknown.

Visual loss

Severe visual loss is nowadays very rare.[1,5,53,56,68] The fenestration of the optic nerve sheet has been used to relieve pressure and to prevent optic nerve atrophy.

Anxiety and depression

Although the overall outcome is good in CVT patients, almost 50% of survivors are depressed or anxious.[1,5,53,56,68] Minor cognitive deficits may prevent them from returning to their previous level of activity.[69]

Future pregnancies

Pregnancy and puerperium being important risk factors for CVT, the risk of future pregnancies in women who have had a CVT has been evaluated in five studies[1,54,70-72] In this cohort of 855 women who had had CVT, 101 pregnancies occurred in 83 women. 88% of these pregnancies enter in normal birth, others had induced or spontaneous abortions. There was no recurrent CVT and only two cases of deep venous thrombosis. Therefore, CVT - even pregnancy-related - should not contraindicate future pregnancies. Antithrombotic prophylaxis after delivery is often recommended, but there is no evidence-based data for its use.

Conclusion

CVT is nowadays a disease that is easy to diagnose with MRI provided the clinician raised this hypothesis even in patients with only mild and nonspecific symptoms. The outcome is usually good under heparin therapy, provided the diagnosis has been made in patients with mild symptoms. Infectious causes are less frequent, especially in western countries.

Many issues remain however unsolved, concerning its pathophysiology and management. Because of the rarity of the disease research needs an international network, as it was the case in ISCVT. The identification of new gene polymorphisms in the coagulation and fibrinolytic system and their role in CVT will continue. Local thrombolysis and decompressive hemicraniectomy should be properly tested in patients who deteriorate despite an appropriate heparin therapy.

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