Young Females and Cerebral Venous Thrombosis

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Abstract

Cerebral venous thrombosis (CVT), is an under diagnosed condition for acute or slowly progressive neurological deficit. CVT has a wide spectrum of signs and symptoms, which may evolve suddenly or over the weeks. It is clinically challenging and mimics neurological conditions, such as: meningitis, encephalopathy, benign intracranial hypertension, and stroke. We have seen 12 female patients of CVT, during 2011-2012. The mean age was 29.75 years (25-40 years old). Of the 12 females, 8 were postpartum, 2 were pregnant, one was on oral contraceptives and in one Antiphospholipid antibodies were positive.

CVT cases are now being diagnosed more frequently. Newer imaging procedures have led to easier recognition of CVT, offering the opportunity for early therapeutic measures. Headache is the most frequent symptom in patients with CVT, present in about 80% of cases. Sixth cranial nerve palsy usually manifests as false localizing sign. Patients may have seizures that can be recurrent. CVT, an important cause of stroke in puerperium is frequently observed in Albania.

Introduction

Cerebral venous thrombosis (CVT), which mean thrombosis of major dural sinuses and cerebral veins, constitutes a small part of cerebrovascular disorders. Although it is rare, we found it more often among young people. Annual incidence is found 3-4 cases / 1 000 000 (1).

In 1825, it was described the first case of CVT in a 45 years old man, by Ribes (2).

The CVT encountered more frequently in young adults, in which is much more common in women than in men with the ratio female: male = 3:1 (3).

Nowadays that we are going to have more and more either diagnostic tools and techniques available, or medical knowledges and awareness, the CVT is diagnosed more frequently, nevertheless some cases remain undetected. Even there are some main clinical signs, thanks to the use of neuroimaging, we can diagnose and treat adequately and earlier patients with CVT.

CVT is now defined as a non-septic disorder with various clinical presentations, because of different localizations of thrombosed cerebral veins / sinuses and a usually favorable outcome, with mortality below 10% 4, in which neuroimaging constitutes the diagnostic golden standard and heparin constitutes the first line treatment (4, 5).

Recently, we have available information as by individual studies focused in different aspects of CVT, also by ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis), a multicenter prospective cohort of 642 patients (4, 6).

Theoretical review

AETIOLOGY

CVT is much more common in women than in men, and it is usually more related with gender specific risk factors, as oral contraceptives, hormonal replacement therapy, pregnancy and puerperium (7, 8). This is supported by epidemiological studies realized before the widespread of oral contraceptives use too, where it is not shown differences in gender distribution8. In women who used oral contraceptives, obesity was strongly associated with the risk of CVT (9, 10).

---Hypercoagulable state of the blood is the second main risk factors for CVT. Key responsible factors of above conditions are inherited and acquired. There are: deficiencies of antithrombin III, protein C, protein S; mutation on factor V Leiden and prothrombin gene; antiphospholipid antibodies and hyperhomocysteinemia (9).

---Infections, which may be local or systemic

---Traumatic factors and neurosurgical procedures

---Oncologic factors

Main risk factors of CVT

I. Gender (women)

Pregnancy

Puerperium

Oral contraceptive

Hormonal replacement therapy

II. Prothrombotic state (hypercoagulable state)

Deficiencies of antithrombin III

Deficiencies of Protein S & C

Hyperhomocysteinemia
Mutations 20210 of prothrombin gene
Antiphospholipid antibodies syndrome

III. Infectious disorders
a) Local infection
Meningitis
Otitis
Sinusitis
b) Systemic infection
Vasculitis
Inflammatory bowel disease

IV. Traumatic & neurovascular factors
Head trauma
Cerebral veins / sinuses injury
Jugular venous cannulation
Lumbar puncture

V. Oncological diseases

PATHOPHYSIOLOGY
There are defined two important mechanisms responsible for clinical patterns of CVT:
It is thought that venular and capillary pressure are going to increase because of thrombosis of cerebral sinuses / veins. As a consequence of the constant increase of local venous pressure, there is cerebral perfusion decreased having as consequent results: ischemic injury of the brain and cytotoxic edema, and on the other hand disruption of blood brain barrier followed by vasogenic edema and the rupture of venous and capillary followed by parenchymal hemorrhage (9).

Cerebrospinal fluid (CSF) is normally absorbed through arachnoid granulations into the superior sagittal sinus (SSS). This absorption of CSF, is decreased because of thrombosis of cerebral sinuses / veins. In the same time the venous pressure is increased because of thrombosis of cerebral sinuses, causing alterations / reduction of CSF absorption. All of above, consequently is followed by increased intracranial pressure, attenuated venular and capillary hypertension with cerebral hemorrhage and vasogenic and cytotoxic edema (9).

Clinical presentation and diagnosis

CLINICAL PRESENTATION (4, 9)
While there are identified strong differences in clinical presentation and outcome between men and women for arterial stroke, there aren’t so much differences for CVT (7). Furthermore, it is clear that CVT appears by a wide range of symptoms and clinical signs, making it difficult to diagnose quickly and accurately, due to similarities with other disorders, particularly vascular disorders.
The first signs and symptoms may appear in an acute, subacute or chronic way. They are summarized and described as four major clinical syndromes:
Isolated intracranial hypertension;
Focal neurological deficits;
Seizures;
Encephalopathy (9)
The CVT’s clinical presentation depends on location of CVT, age of patient, time of admission to hospital, and the presence of damage on cerebral parenchyma (4, 7, 11). Headache is the first complaint in about 90% of patients, and it appears in most cases as subacute one (9). Its localization may be clear and focused, or it may be a generalized headache which worsen with change of body position or Valsalva maneuvers (12). Other signs and symptoms of isolated intracranial hypertension, especially for patients with chronic course or delayed clinical presentation are papilloedema and visual complaint (4).

Sometimes, the isolated headache remains the single symptom of CVT, becoming the diagnosis of CVT a great challenge in these patients. Nevertheless, it is so important to differentiate the CVT in patients with isolated headache as initial symptom, because of the importance of prompt treatment (4).
Focal neurological signs depend on localization of CVT: CVT of cavernous sinus, appears with chemosis, pain of orbital region, proptosis and oculomotor palsy (4). the occlusion of cortical vein may appear with sensitivity disorders and seizures; superior sagittal sinus thrombosis appears mostly with motor deficits and the thrombosis of the lateral sinus is the main cause of an isolated syndrome of intracranial hypertension (4, 13).
Seizures, either focal or generalized occur more often in CVT than in other cerebrovascular disorders. They become evident more often in patients with parenchymal lesions, and in them with thrombosis of cortical veins or sagittal sinus (4, 14).

DIAGNOSIS
The neuroimaging is the golden standard tool for the diagnose of CVT.
Although brain CT is the most frequent neuroimaging screening for patients with CVT clinical pattern, it is found to have poor sensitivity for the diagnose of CVT in these patients (9, 17). The crucial point for an adequate diagnose is the combination of MRI
visualization of thrombosed vein / sinuses) with magnetic resonance venography, which helps to make clear the non-visualization of the same vessels (4, 5, 15, 16). In the beginning of CVT, for 3 -5 first days, it is difficult to differentiate the normal vein from the thrombosed one, even with the combination of neuroimaging mentioned above.

The invasive neuroimaging techniques, like cerebral arteriography with cerebral phase, and cerebral venography, are recommended to use in patients with high clinical suspicious of CVT, in which the other neuroimaging techniques used (CT/ MRI) remain inconclusive (9, 17).

Laboratory testing, D-Dimer measurement, was first taken in consideration, because of high predictive value of it, in deep venous thrombosis of the lower extremities (4). But, based on a series of studies, we can confirm that a negative D-dimer level, does not exclude a CVT, especially in patients with a recent isolated headache (4, 18, 19).

All patients with CVT suspicion, should perform a screening for prothrombotic states, including evaluation of antithrombin III levels, Protein S & C levels, homocysteinemia, mutations 20210 of prothrombin gene and Antiphospholipid antibodies levels (9, 17).

Treatment

There are recommended three main pillars of management and treatment of CVT (4, 17, 21):

Antithrombotic treatment; Etiological treatment, and Symptomatic treatment

Most patients need the combination of these drugs groups.

The antithrombotic treatment which consists in the use of low molecular weight heparin or intravenous heparin, is intended to be the first line treatment with focus either on recanalization of occluded vein / sinus, or on prevention of thrombus propagation and treatment of the prothrombotic state (1, 4, 9, 16, 20, 21).

The etiological treatment is so necessary to manage and treat risk factors as soon as they are identified, even though there are no so few cases with unrecognizable risk factors.

Symptomatic treatment depends on signs and symptoms and their severity, as well. For example: if patients with isolated intracranial hypertension as papilloedema is followed by vision disorders, it is necessary the lumbar puncture to remove cerebrospinal fluid, before starting heparin; patients who have seizure as debut sign, should begin antiepileptic drugs as soon as possible, because of the risk of recurrence is high in these patients (4, 14).

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