Abstract

Objective: The cerebral venous and sinus thrombosis (CVST), severe neurological emergencies is an important pathology of the venous brain system. This paper is an on-going study about CVST, the first report was done in 2008. Material and methods: We received 32 patients hospitalized on emergency between February 2006 – February 2013 (only self-casuistry). Demographic (sex, age), clinical, imagistic (cerebral MRI – venous angiography, cerebral CT), paraclinic (CSF, factor V Leiden mutation) data, as well as risk factors, treatment, evolution and neurologic recovery were all considered. Results: We studied 20 females and 12 males (62% versus 38%). Etiology: oral contraceptives (8 cases), otomastoiditis (7cases), dental abscess of the upper jaw (3 cases), maxilar sinusitis (2 cases), penetrating skull trauma (3 cases), ethmoidal puncture for frontal sinusitis (1 case), provoked abortion (2 cases), pregnancy (1 case), puerperium (1 case), hereditary thrombophilia- factor V Leiden mutation (heterozigot phenotype - 3 cases), encephalitis with HSV (1 case). The symptomatology varied according to the disease etiology and the location of CVST. Initial clinical symptoms include: coma (3 cases), headache (26 cases), seizures (20 cases), motor and mental disturbances (18 cases), cranial nerves palsy (18 cases), intracranial hypertension (8 cases), papilledema (4 cases), nausea and vomiting (20 cases). Cerebral MRI- venous angiography is the optimum diagnosis method we applied to all patients. Conclusions: CVST even with a reduced occurrence, represents a severe neurovascular emergency. CVST is more common in women, frequently associated with oral contraceptives, abortion, pregnancy or puerperium (37 %). Young patients with CVST should be screened for thrombophilia. If diagnosed at an early stage, especially by cerebral MRI-venous angiography and correctly treated, the patients have a favorable evolution, the lethal cases decreasing until 3 %. Patients with septic CVST and coma from the beginning have bad prognosis. The efficacy of heparin with APTT controlled has been shown.

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1. Introduction

Cerebral venous and sinus thrombosis (CVST) is a rare disease responsible for less than 1% from the total of AVC causes (Bajenaru, 2010). CVST, major neurological emergencies represent an important feature of the cerebral venous pathology. The venous circulation of the brain is done through the cerebral veins and the dural sinuses (Netter, 1983). The superficial cerebral veins show a big anatomic variability, draining the blood from the biggest part of the cortex (excepting the internal surface of the temporal and occipital lobe). As a consequence of the several anastomoses, of the anatomical structure particularly venous (thin wall, without muscular tunica, without valves) there are emphasized two features: the absence of some venous territories well determined and the possibility of supplementation that may contribute to limitation of the lesions severity. The deep venous system drains the serum at the level of the profound nuclei of diencephalon and profound white matter (Ticmeanu, 2006). The thrombosis extension is variable, involving the sinuses and/or dependent veins. The cortical veins appear to be thick, inelastic and full of blood and they do not drain at the digital pressure. The dural sinuses have the lumen closed by a grey thrombi in the middle, color due to the fibrin deposit (Ticmeanu, 2006). CVST etiology is various, including three large types: septic, aseptic and idiopathic (de Veber at al, 1998; de Veber at al, 2001; Bradley at al, 2008). 75% of the cases generating cerebral thrombosis are non-infectious and 8-10% of the cases have an unclear etiology (Ameri at al, 1992; Bousser at al, 1998). Septic intracranial venous thrombosis was determined by:

- local infectious causes: sinusitis, otitis, mastoiditis, dental abscesses, suppurative tonsillitis, erysipelas of the face, furuncles of the face and nose, infections of midface, calvaria osteomyelitis after infected skull traumatisms.
- infectious cases far from the endocranial venous system: abdominal-pelvic suppurative processes, surgical interventions at the level of pelvis.
- general infectious causes: sepsis, endocarditis, encephalitis, meningitis (pneumococcal), trichinosis, syphilis, VZV infections, HIV infections, mucormycosis, aspergillosis.

Aseptic intracranial venous thrombosis is divided into dural venous sinus thrombosis, deep venous thrombosis and cortical vein thrombosis. The superior saggital sinus is most frequently involved. Alteration in hemostasis is associated with an increased risk of stroke, particularly venous and less commonly arterial (Hart & Kanter, 1990). These disorders have been implicated in 2% to 10% of all strokes, with a higher proportion in young patients, and the discovery of new coagulation disorders has increased the rate of stroke attributable to hypercoagulable states to 19% (Ferro at al, 2004; Biller, 2009). Idiopathic intracranial venous thrombosis has unclear etiology 8-10% (Bradley at al, 2008; Ameri at al, 1992)

2. Aim of the study

The cerebral venous and sinus thrombosis (CVST), severe neurological emergencies is an important pathology of the venous brain system. CVST is an infrequent condition that is extremely variable in its clinical presentation, mode of onset, imaging appearance and outcome. This paper is an ongoing study about CVST, the first reports being done in 2008 (Gogu, Vlad & Birsasteanu, 2008)

3. Material and methods

3.1 Patients

We received 32 patients hospitalized on emergency with diagnosis CVST between February 2006 – February 2013 (only self-casuistry). Demographic (sex, age), clinical, imagistic (cerebral MRI – venous angiography, cerebral CT), paraclinic (CSF, factor V Leiden mutation) data, as well as risk factors, treatment, evolution and neurologic recovery were all considered. We considered 20 females and 12 males; 14 cases between 20-30 years old, 10 cases between 30-40 years old; 8 cases 60-70 years old. The number of hospitalization days ranged between 5-34, with an average of 16 days (5 hospitalization days have been reported in the case of one single death).
3.2 Investigations

- Cerebral MRI – venous angiography
  The optimal method for the cerebral thrombophlebitis is MRI-venous angiography (2D-TOF-MRA), which is accurate in giving the slow flow using a volume of arterial presaturation caudally placed from the investigated. A venogram in minimum two plans is useful (axial, coronal and / or sagittal). The difference of a venous and sinus thrombosis from anatomical versions and signal loss by flow artifacts flux is difficult and may give positive results. The false negative in the case of the dural sinuses thrombosis may be given by the subacute thrombi with strong T1 hypersignal. At the MRI venogram the superior longitudinal sinus and the right sinus are given with an accuracy of 100%; the transverse sinus with an accuracy of 95% and the inferior longitudinal sinus with an accuracy of 45% (Opris, 2004). The parenchymatous lesions occur with hypersignal in T2 for localized or ischemic edema. In the hemorrhagic lesions T1 and T2 hypersignals occur often surrounded by a hypersignal black ring. Cerebral MRI, with angiographic sequence and venous time was performed in all patients using Signa Horizont Lx 1 OT RMN. The examined casuistry includes within the MRI patterns from the field literature.
- Native computer tomography (CT) shows unspecific images of diffuse cerebral edema or localized in the cerebral ventricles.
- Computer tomography with contrast substance (SDC) reveals venous softening of the brain with gyriform contrast medium uptake, spontaneous hyperdensity localized cortically and subcortically, with multifocal character. (Fig. 7b)
- Other tests: - lumbar puncture with CSF analyses did not bring specific diagnosis data (CSF blood stained in one case).
  - fundus eye (FO) showed a papillary edema in one case of cavernous sinus thrombophlebitis and in the other three cases of transverse sinus thrombophlebitis.
- In all young patients with unclear etiology we verified the primary hypercoagulable states:
  - Antithrombin deficiency
  - Protein C deficiency
  - Protein S deficiency
  - Activated protein C resistance
  - Factor V Leiden mutation
  - MTHFR gene mutation
  - Prothrombin G 20210A mutation
  - Disorders of fibrinogen (afibrinogenemia, hypofibrinogenemia )
  - Disorders of the fibrinolytic system (hypoplasminogenemia )

4. Results

The current study included 32 patients (mean age: 31 years), 20 females and 12 males (62% versus 38%).

4.1 Etiology

Etiology involved in the onset of the CVST studied cases:
- oral contraceptives (8 cases).
- otomastoiditis (7 cases).
- superior maxillary dental abscesses (3 cases).
- maxillary sinusitis (2 cases).
- penetrating skull trauma (3 cases) with an infected wound of scalp (3 cases).
- factor V Leiden mutation (3 cases).
- provoked abortions (2 cases).
- pregnancy (1 case).
• puerperium (1 case).
• encephalitis with HVZ (1 case).
• ethmoidal puncture for frontal sinusitis (1 case).

4.2 Topography:

• superior longitudinal sinus (SLS) thrombophlebitis - 4 cases (1 case skull trauma, 1 case encephalitis with HVZ, 2 cases with oral contraceptives)
• transverse sinus (TS) thrombophlebitis - 14 cases (7 cases otomastoiditis, 2 cases oral contraceptives, 2 cases factor V Leiden mutation, 1 case provoked abortion, 1 case pregnancy, 1 case puerperium)
• superior longitudinal sinus thrombophlebitis and one transverse sinus - 2 cases (1 case otomastoiditis, 1 case skull trauma)
• superior longitudinal sinus thrombophlebitis and petrosal sinus - 1 case (ethmoidal puncture)
• sigmoid sinus thrombophlebitis - 1 case (postabortion)
• cavernous sinus thrombophlebitis - 10 cases (4 cases - oral contraceptives, 3 cases superior dental maxillary abscesses, 2 cases maxillary sinusitis, 1 case factor V Leiden mutation).

4.3 Clinical findings:

• Onset: - acute (24 hours) - 1 case.
  - subacute (7 days) - 26 cases.
  - chronic (30 days) - 5 cases.
• The symptomatology was various, related both to the disease etiology as well as to the topography of the venous cerebral thrombosis: coma at the onset (3 cases), headache (26 cases), focal or generalized seizures (20 cases), motor deficiencies like hemiparesis, ataxic tetraparesis, slight hemiparesis (18 cases), mental deficiencies (16 cases), cranial nerves palsies (18 cases), HIC (8 cases), papillary edema (4 cases), nausea and vomiting (20 cases).
• We show the most special cases, having a various clinical symptomatology.
• Superior longitudinal sinus and transverse sinus thrombophlebitis have been met in two cases:
  • first case, C.C., male, 27 years old, with penetrating skull trauma is hospitalized with superficial coma, severe psychomotor agitation, stiff neck, vomiting, generalized seizures, slight hemiparesis. During the evolution, as a consequence of the cerebral post thrombotic syndrome as well as edematous encephalopathy, the patient shows major seizures with a frequency of 2-3 episodes per month under anticonvulsant treatment and psychical disturbances (aggressiveness, irritability) The patient was clinically assessed, paraclinically - RMN venography at 18 months and 6 years from the onset of the disease (fig. 1, 2, 3a, 3b, 3c).
Figure 3a, 3b, 3c. C.C., 28 years old. Permeabilization of the SLS and right TS after 18 months from the onset.

-A second case, B.F., male, 28 years old, with bilateral otomastoiditis, hospitalized in profound coma (Glasgow=3), massive cerebral edema and death after 5 days, probably by the extension of venous thrombosis in the right sinus or/and in the other transverse sinus. (fig. 4a, 4b).
Transverse sinus thrombophlebitis was diagnosed in 14 patients; as involved etiology we mention: otomastoiditis (7 cases), oral contraceptives (2 cases), provoked abortion (1 case), pregnancy (1 case), puerperium (1 case), thrombophilia – heterozygote phenotype for factor Leiden V mutation (2 cases).

First case, K.I., female, 25 years old, with an etiology of suppurative otitis, complicated with otomastoiditis, hospitalized in superficial coma, with meningeal symptoms and HIC, considerable psychomotor agitation and 3 generalized seizures. The local examination of mastoiditis area shows a painful edema at compression (Grisinger sign is present). FO examination indicates the lack of the papillary edema and Beck-Crowe sign – positive. During evolution, the patient does not show any residual symptomatology related to thrombophlebitis (fig. 5a, 5b).

Second case, C.E., female 31 years old, with an etiology of thrombophlebitis emphasized by the presence of the factor V Leiden mutation – heterozygote phenotype. During evolution, she presented Gradnigo syndrome with pains in the right hemiface, internal strabismus, diplopia by the involvement of trigeminal nerves and abducens. This was possible by the extension of the venous thrombosis towards the petrosal sinuses (superior and inferior), that are in anatomical relationships with the trigeminal nerve and abducens. (Algo-strabic syndrome) – fig. 6.
third case, C.I., female, 40 years old, postabortal etiology, is hospitalized with cephalalgia, nausea, vomiting, five generalized seizures. The patient was clinically assessed and imagistically (cerebral MRI- venous angiography) after 6 months from the onset of the disease, period when she also had two major seizures, although she was under anticonvulsant treatment (fig. 7a, 7b).

- SLS and left superior petrosal thrombophlebitis was met in just one of the patients, D.O., male, 35 years old, who presented after 3 months from a ethmoidal puncture for ethmoid-sphenoid pansinusitis, ataxic tetraparesis and left trigeminal neuralgia (fig. 8a, 8b).
Figure 8a. D.O., 35 years old. Ethmoid-sphenoid pansinusitis. Figure 8b. D.O., 35 years old. SLS thrombophlebitis and left superior petrosal sinus (onset after 3 months from the ethmoidal puncture).

- Cavernous sinus thrombophlebitis was met in 10 patients, having as an etiology superior maxillary dental abscess (3 cases), maxillary sinusitis (2 cases), oral contraceptives (4 cases), factor V Leiden mutation (1 case).
  - one of the cases, male, 32 years old, etiology – superior maxillary dental abscess; the symptomatology was severe: fever, right cranio-orbital-ocular pains, palpebral and conjunctival edema, incomplete paresis of common oculomotor nerve, homolateral trigeminal neuralgia (ophthalmic branch), with removal of the photomotor reflex and depreciation of the corneal reflex on the affected side. The examination of the eye fundus discovers papillary edema which indicates the extension of the thrombosis in the homolateral ophthalmic vein.

4.4 Evolution.

- Generally it was a favourable one. There was a case of death in one young patient of 28 year: coma IV degree; superior longitudinal sinus thrombophlebitis; massive cerebral edema; bilateral otomastoiditis.
- As residual symptoms, two cases show generalized seizures, due to the cerebral postthrombotic syndrome, accompanied by psychic disorders. Both cases showed superior longitudinal sinus thrombophlebitis, a possible explanation could be the involvement of the frontal lobe.

4.5 Treatment

- Etiological treatment – performed for septic cerebral thrombophlebitis: wide range cephalosporins;
- Symptomatic treatment: - all patients have performed the anticonvulsant therapy since hospitalization, and it has been continued for those with seizures episodes even in the present. (Phenobarbital, Valproic Acid, Levetiracetam, Diazepam, Propofol);
- Therapy of depletion with Mannitol was performed for the patients with intracranial hypertension;
- Antithrombotic treatment - Heparin proved its efficiency and it was administrated since hospitalization to all patients, on an average of 14 days, followed by an antiagregant treatment with Clopidogrel 75mg/day, for 3 more months.;
- Oral anticoagulation on an unspecified term was used in the patients with a serious coagulation deficiency as the antithrombin III and heterozygote phenotype for factor V Leiden mutation. The oral anticoagulation decision and the duration of this treatment was individualized; the INR interval was between 2-3.
5 Discussions

Intracranial venous thrombosis may occur at any time from infancy to old age, but most reported modern cases have been at young patients. The intracranial venous anatomy is complex, and anatomic variations of important intracranial venous structures are common. Knowledge of the anatomy of the sinovenous system is particularly important today with the many imaging modalities available. Cerebral lesions and clinical syndromes resulting from CVST occur in patterns directly related to the venous anatomy and infarctions usually cross a particular arterial distribution, often with hemorrhagic transformation (Biller, 2009). The parenchymatous lesions are represented by venous infarctions, most often hemorrhagic, involving the cortex and the white matter close to the thrombosed vein or sinus. Intracranial venous thrombosis can be septic or aseptic. Septic intracranial venous thrombosis has been rare lately, frequently involving the cavernous sinus. Cavernous sinus thrombophlebitis is a typical complication of an infection at the facial, orbital level, clinically presenting palpebral ptosis, chemosis, painful ophthalmoplegia. Lateral sinus thrombophlebitis is a rare complication of medium otitis and mastoiditis, clinically showing headache, fever, dizziness, pulsatile tinnitus, papillary edema and horizontal binocular diplopia owing to sixth cranial nerve (abducens) palsy (Bradley, Daroff, Fenichel & Jankovic, 2008). Aseptic intracranial venous thrombosis involved most frequently the superior sagittal sinus. Causal factors are protean and the onset often insidious (Bradley, Daroff, Fenichel & Jankovic, 2008). Despite the variable clinical presentation, CVST should be suspected on clinical grounds at young adults presenting with new-onset headaches and focal neurologic deficits even in the absence of risk factors for stroke (Biller, 2009). MRI-venous angiography was preferred imaging modality to detection of CVST but these visual images should be interpreted with caution, especially findings of the transverse sinus, because hypoplasia of one of sinuses is a common anatomic variation. We have two patients in this situation but the missed diagnosis was corrected with cerebral angiography which offers better details of cavernous sinus. The number of patients in this study was relatively small but CVST is an uncommon disease, accounting for less then 1% of stroke cases. The examined casuistry described the pattern-disease from the field literature.

6 Conclusions

CVST even with a reduced occurrence represents a severe neurovascular emergency. CVST is more common in women, frequently associated with oral contraceptives, abortion, pregnancy or puerperium (37%). Young patients with CVST should be screened for thrombophilia. Thrombophilias (prothrombotic state) is the term used to describe a tendency toward thrombosis. Symptomatology varied according to the disease etiology and location of CVST. An extensive laboratory workup is required to determine the underlying cause of the thrombosis. The diagnosis of this pathology has been rehabilitated by the imaging development, especially a cerebral MRI - venous angiography. It shouldn’t be forgot that the right diagnosis has been missed due to the wide spectrum of clinical manifestations as well as the subacute onset with a slow evolution. If diagnosed at an early stage, especially by cerebral MRI-venous angiography and correctly treated, patients have a favorable evolution, the lethal cases decreasing to 3% (1 case). Patients with septic CVST and coma from the beginning have bad prognosis. The efficacy of heparin with APTT controlled has been shown, even in patients who have evidence of some intracranial hemorrhage by neuroimaging studies.

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