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Cerebral venous thrombosis study of a series of 20 cases

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Summary:

Objective: The aim of our work is to study the clinical, risk factor and evolutionary characteristics of cerebral venous thrombosis (CVT) in our series and compare it with data from the literature.

Methods: This is a retrospective study including 20 patients hospitalized and followed up in the neurology department of the Moulay Ismail military hospital in Meknes.The diagnosis of CVT was confirmed in all patients by magnetic resonance imaging (MRI) with magnetic resonance venography (MRV), and/or cerebral CT scan with computed tomography venography (CTV). Clinical and biological risk factors for CVT were analysed.The average follow-up was 12 months (6 to 18 months) and evolution was evaluated clinically and radiologically.

Results: In our series, the mean age was 32.6 years with a predominance of females (sex ratio of 4Women/1Men). The clinical was subacute in 70% of cases.The inaugural signs were essentially represented by headaches. Topographically, superior longitudinal sinus thrombosis was the most common, estimated at (70%). Parenchymatous lesions were observed (45%), mainly of haemorrhagic infarction type (30%).Etiologically, thrombophilia and gynaeco-obstetrical causes were predominant with a respective prevalence of 50% and 40 % .In 80% cases, the evolution was good, with heparin therapy relayed by anti-vitamin K coupled with etiological treatment as needed.

Conclusion: The characteristics of CVT in our study stands out from the data in the Western literature by a high frequency of thrombophilia and gynaeco-obstetrical causes.

Keywords: Cerebral venous sinus thrombosis clinic Risk factors Outcomes

Introduction:

Rare vascular pathology, Cerebral venous thrombosis are relatedas an occlusion of a venous sinus and/or a cerebral vein by a thrombus. Its accounts for 0.5% of all strokes and mainly affects young adults and children [1]. Cerebral venous thrombosis are characterized by the great diversity of their clinical presentations, risk factors and causes, which represents a real challenge for neurologists. Diagnosis is made by MRI and treatment is based on anticoagulants. The prognosis is generally much more favourable than for other strokes. We considered it useful to study this condition in our context,

analyzing its various clinical, risk factor and evolutionary aspects and comparing them to the data in the literature (why??).

Patients and Methods:

This is a retrospective study carried at the neurology department of the Moulay Ismail military hospital in Meknes between January 1, 2011 and January 1, 2021 concerning 20 patients monitored for cerebral venous thrombosis (CVT). The diagnosis of CVT was confirmed by magnetic resonance imaging (MRI), magnetic resonance venography (MRV), and/or cerebral CT scan with computed tomography venography (CTV). For each patient, we collected from the medical record age, gender, past medical history, current treatment ,risk factor, Time since the onset of symptoms (acute [48 h], subacute [48 h to 30 days], and chronic [superior than 30 days]), detailed clinical presentation, results of medical imagery (thrombus site, associated parenchymal abnormalities), biological results, results of the etiological research, various treatments given: symptomatic and anticoagulants and the clinical evolution: mortality, sequelae. a basic biological assessment is carried out in all our patients upon admission, including complete blood count, serum chemistries , prothrombin level (PT), activated partial thromboplastin time (aPTT), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine serologies (HIV,syphilis), and tumor markers. Lumbar punctures were performedin allpatients andCSF analysis (presence of cells, protein and glucose levels, Gram stain, fungal and bacterial smear, virus antibodies.) was examined.

Thrombophilia screening including: anti thrombin III; proteins C and S; resistance to activated protein C. Factor V leiden mutation, anti-phospholipid, anti-cardiolipin, and anti-ds DNA antibodies; homocysteine; lupus anticoagulant; and thyroid hormones were performed.

All patients were treated by adjusted dose of intravenous unfractionated heparin, with the target activated partial thromboplastin time 2-2.5 times of the control. Pregnant woman were treated with a curative dose of subcutaneous low–molecular weight heparin. All patients were treated with oral anticoagulation therapy (anti-vitamin K therapy)with a target international normalized ratio of 2-3 for a period of 6 to 12 months or longer months in patients with persistent hypercoagulable states. A symptomatic treatment with analgesics, anti-edemas, anti-epileptics were givenif needed. The clinical course was assessed over an average of 12 months with extremes of 6 to 24 months. Patients benefited a neurological examination and follow-up brain imaging (MRI or CT scan). We scored according to modified Rankin scale (mRS) as no dependency (modified Rankin Scale [mRs]: 0-2) and dependency or death (mRs :3-6). This data was compiled using Microsoft Office Excel and analysed with Epi Info TM 3.5.4 software.

Results:

The mean age of our patients was 32, 6 years old (range 19–54), the sex ratio was 4 (16

women, and 4 men), Clinical and topographical characteristics of patients are listed below in table 1. The onset of symptoms was sub-acute (48 hours to 30 days) in the majority of patients (70%),it was acute in 25% of patients and chronic in 5%.The main inaugural signs were headaches in 16 cases (80%). focal neurological deficit were present in 5 cases (25%) and seizures in 4 cases (20%) and aphasia of broca in 1 case (5%). Papillary edema was found in 5cases (25%). In addition, rarer signs (diplopia, strabismus) were also observed in 1 case (5%). The diagnosis of CVT was established in all patients by multiple imaging methods, Brain CT scan was normal in 8 patients (40%), MRI/MR venography was performed in 18 patients (90%). Concerning the topographical imaging results, involvement of the superior sagittal sinus (SSS) was found in (70%) of patients, lateral sinus (LS) in (55%), and cavernous sinus thrombosis in (5%). Multiple sinuses were involved in 30 % of cases. Parenchymal involvement was noted in 45 % (9of 20 patients): haemorrhagic infarcts in 30%, Non haemorrhagic infarcts, cerebral edema and subarachnoid haemorrhages were rarer and evenly distributed (5%). Lumbar puncture was performed in all patients: cerebrospinal fluid (CSF) was clear and it pressure was greater than 25 cm H2O in all patients, 2 patients (10%) had >5 cells and protein >45 mg/dL.

In our series, cerebral venous thrombosis was associated with 2 or more underlying risk factor in 8 (40%) patients. The most common risk factor was thrombophilia found in 10 patients (50%). Deficit in protein S was the most frequently found anomaly in the thrombophilia research, it was present in 5 of the 10 patients followed by deficit anti thrombin in 3 cases and deficit in protein C in 2 cases. After thrombophilia, gynaeco-obstetrical causes (postpartum and pregnancy) were the second most frequent risk factor, It were found in 8 patients (40%). oral contraceptives use were noted in only 5%.myeloproliferative syndrome in 10% and behcet disease in 10%. Despite an exhaustive etiological assessment, in 3 cases no cause was found (15%). Risk factors and causes are summarized in Table 2. As soon as diagnostic is acquired, all the patients were given an anticoagulant (therapeutic dosages) consisted of unfractionated heparin even in the presence of parenchymal lesion and in particular hemorrhagic. Aside from the deceased patient, all patients received AVK therapy after the acute phase (acenocoumarol) for a period of 6 to 12 months or longer in patients with persistent hypercoagulable state. For the pregnant patient, she was treated by curative dose of subcutaneous low–molecular weight heparin until childbirth. Most patients were given symptomatic treatment with analgesics for headaches but anti-edemas and anti-epileptics were given on a case by case regimen, Anti-epileptic drugs were given in 4 of the 20. For the large majority of the patients (80%), the outcome was favourable, with complete recuperation from any neurological symptoms that were present at the time of onset of thrombosis andWe noted:

- 1 death on the 8 th day, (no 17) despite reanimation following a complication inherent to his pathology.
- 3 patients presented sequelae at 18 months follow-up with a mRSs of 1 to 2: motor deficits in 2 patients, moderate epilepsy in 1 case. Ten patients underwent follow-up imaging (IRM and MRV) after six months with complete repermeabilization.

Table 1 : characteristics of patients and inaugural signs of CVT./.

patient	**Age /gender**	**installation Mode**	**Symptoms and clinicalsigns**	**Circumstance of occurrence or associated disease**	**Parenchymallesions**	**Topography**
1	52/W	Subacute	Cranial nerve domage V ; VI ; III.	**None**		Cavernous sinus
2	19/W	Subacute	headache+epilepticcrisis	Pregnacy	**CO**	SSS+ RLS
3	49/W	Subacute	headache + PO+ motordeficit	Thrombocythemia	**CHI**	SSS
4	45/W	Acute	headache + motordeficit.	Diabetes	**SH**	RLS
5	23/W	Subacute	epileptic crisis + headache + motor deficit.	Postpartum	**CHI**	SSS
6	47/W	Subacute	headache +PO+ motordeficit	**None**	**CHI**	SSS
7	19/W	Acute	Headache	**None**		LLS
8	20/W	Chronic	headache + motordeficit.	Oral contraception	**CHI**	SSS
9	22/W	Subacute	aphasia of broca +headache +PO	**None**	**CHI**	SSS
10	19/W	Subacute	Headache	Postpartum+obesity		SSS et LLS
11	35/M	Acute	headache + epilepticcrisis	**None**	**CHI**	SSS et LLS
12	32/W	Subacute	headache	Postpartum		SSS
13	40/W	Subacute	Headache	Postpartum		SSS et LLS
14	29/W	Subacute	Headache	**None**		LLS
15	25/M	Subacute	headache +PO	Behcetdisease		SSS et SLD
16	29/W	Subacute	epilepticcrisis+ headache	Postpartum	**CNHI**	LLS
17	54/M	Acute	headache +PO	Vaquez disease		SSS et LLS
18	30/W	Subacute	Headache	Postpartum		SSS
19	30/M	Subacute	Headache	Behcetdisease		SSS
20	33/W	Acute	headache	Postpartum		LLS

CHI :cerebral hemorrhagicinfarcts ; **CNHI** : cerebral non hémorragique infracts : ; **OC** : cerebraledema ; ; **CS** : cavernous sinus ; **RLS** :right laterl sinus; **LLS** : Leftlateral sinus ; **SSS** : superiorsagital sinus ; **SH** :subarachnoidhaemorrhagie. **OP**: papillaryedema.

Table 2:Distribution of patient according factor risk and causes.

Circumstance of occurrence	Nomber of patients	
Septicthrombosis	0	
Aseptictthrombosis		
pregnacy	1	(5%)
Postpartum	7	(35%)
Prothrombotics factor	**10**	**(50%)**
proteine C deficiency	2	(10%)
proteine S deficiency	5	(25%)
anti thrombin deficiency	3	(15%)
Hyperhomocysteinemia	0	
Resistance to activated protein C	0	
Factor V mutation	0	
Haematological diseases	**2**	**(10%)**
Vaquez disease	1	(5%)
Thrombocythemia	1	(5%)
Inflammatory disease	**2**	**(10%)**
Behcet disease	2	(10%)
Diabetes	1	(5%)
Obesity	1	(5%)
oral contraceptive	1	(5%)
None identified	3	(15%)

Discussion:

Over a period of 10 years, we collected 20 cases of CTV. This remains a relatively small number because we only recruit military patients and their families who reside in the drainage area of our military hospital. The estimated annual incidence of CVT in general population is 3-4 cases per 1 million. [1] The real incidence of CVT is still unknown in our country. Hence the need for a multi-centre study across Morrocco. In our series, CVT was predominant in women (80%), occurring more frequently during childbearing age[2;3;4;5].The mean age in our study was 32,16 years, similar to South American and Asiatic publications[6;7]; but lower than North American and European studies[8], this could be a possible explanation for the hight rate of CVT in pregnancy and postpartum (40%) in our study.

Clinical presentation of CVT is extremely variable [9]. Most common presenting features in the present study were headache (80%), seizures (30%), focal motor deficits (25%), and papillaryedema (25%). Subacute mode of onset is the most frequent (70%). These results are similar to that reported in most western studies [10; 3]. Head CT is normal in up to 30% of CVT cases [**3**]. In our cohort, 40% of

CT scans were normal . CT is often the first investigation performed in our country, It is useful to rule out other acute or subacute cerebral disorders. However, MRI/MRV is the best method for the diagnosis and follow-up of CVT [**3**].

Regarding the location of the thrombus, several publications [3; 11; 12; 13; 1] show that superior sagittal sinus and lateral sinuses are the most affected, which was concordant with our findings. Cavernous sinus thrombosis is rare (5% in our series), as shown by the low proportion in the large published series [3; 12]. The association of direct CVT signs with parenchymal lesions (haemorrhage, infarction, edema) was not uncommon as it was present in 45% of cases as in the study by Gaye et al. (2020) who identified a 42,85% prevalence [15] .Parenchymal lesions were largely dominated by hemorrhagic infarction 30% of patients which is close to that reported in most studies. [16; 17] The pathogenesis of CVT is often multifactorial as illustrated in our study where up to 40% of the patients had more than 1 risk factor. This figure is close to that reported by the study by benssasi et al, which was 39%.[18] Aseptic risk factors, mainly thrombophilia (50%) and gyneco-obstetricalcauses (40%), were the most frequent predisposing factors in our study. According to the ISCVT study [3], thrombophilia represents the most common risk factor (38.1%). Daif et al, [19] from Saudi Arabia, reported genetic thrombophilia in 5 of 40 (12.5%) patients. This high frequency of thrombophilia in our study is most likely the result of an exhaustive screening performed in all patients even when other risk factors were identified. [20]

Pregnancy and the postpartum are known risk factors for CVST. They represented 40% of the predisposing factors to CVT in our study, which is higher than those described in ICVST (20.1%) [3]. Possible explanations for this difference include home delivery and some rituals that are widely practiced in Arab countries, such as eating high-fat foods and prolonged bed rest during the peripartum period. In addition to these factors related to the conditions of delivery or the postnatal rituals, we found that the majority of our postpartum women in our series had at least one other prothrombotic cause or risk factor, most often thrombophilia.

Oral contraceptives use have also long been knowen as risk factor in the occurrence of CVT in women: it was present in 47% in ISCVT, and 96% in an Italian study [21]. In our study, oral contraceptives were not a major risk factor for CVT in our patients. They were used in only 5% of cases. It may be explained by the more frequent use of other contraceptive methods such as intrauterine devices instead of oral contraceptives in our region.

Behcet's disease is a classic etiology of venous thrombosis, particularly cerebral thrombosis. Its prevalence is high in Arab countries, but it has been diagnosed in only 10% of our patients, which is lower than what has been reported in Middle Eastern studies [22;19] but much higher than in Western studies.[3;23]. This could be explained by a better management of this disease in our country compared to Middle Eastern countries even

before the appearance of neurological complications.

Myeloproliferative syndrome is a significant risk factor in the development of cerebral venous thrombosis. In a retrospective study of 20 patients with venous thrombosis, Bertolino et al. found that 15% of the patients had a cerebral venous thrombosis initiating myeloproliferative syndrome [24]. In our series it was estimated at 10%.

Contrary to what is reported in most western series and developing countries [3; 15; 18; 26]. The infection risk is not found in our study. This can be explained by easy access in our hospital structure and adequate management of infection before it is complicated by CVT.

In most series, no underlying etiology or risk factors for CVT are found in approximately 20%-35% of cases [25; 16; 17].While in our study it was estimated to be 15% despite a comprehensive review including a systematic review of thrombophilia. Hence the interest in continuing this etiological research beyond the acute phase, as certain pathological conditions may only appear during follow-up (blood cramps, cancer, etc.). From the follow-up point of view, we had 1 death (5%, versus 4% in the ISCVT group and 2% at Lariboisière Hospital) [26; 3], sequelae in only 15% of our patients, versus 30% in the ISCVT study and 27% at Lariboisière [26; 3]. A total of 80% of our patients were free of symptoms. The frequency of recurrence of CVT is known to be low, 2.2% in the ISCVT [3]. In our series, no cases of recurrence were noted. This is thanks to a well-conducted anticoagulant treatment.

The limitations of our study were its retrospective nature as well as potential selection bias with the recruitment of all patients from a single department. In addition, D dimere and some prothrombotic conditions such as MTHFR C677 T mutation and prothrombin G20210A mutation have not been investigated in our patients.

Conclusion:

This study showed differences in CVT risk factor profile in our patients from that reported in western studies with a high incidence of thrombophilia and gynaeco-obstetrical causes. Infection and Oral contraceptive use are not a major risk factor in our series. We suggest suspecting this disease in every postpartum woman with neurological symptoms and we recommend in the setting of CVT an exhaustive screening for thrombophilia even in the presence of other risk factor. To better characterize the epidemiologic and clinical aspects of CVT in our country, multicentercohort study is necessary.

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