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ORIGINAL ARTICLE

Post-traumatic cerebral venous sinus thrombosis in an intensive care unit: A case series of ten patients

Kamilia Chtara[a,*], Sabrine Bradai[a], Najeh Baccouche[a], Nozha Toumi[b], Wiem Ben Amar[c], Hedi Chelly[a], Mabrouk Bahloul[a], Mounir Bouaziz[a]

[a] *Department of Intensive Care, Habib-Bourguiba University Hospital, University of Sfax, 3029 Sfax, Tunisia*
[b] *Department of Radiology, Habib-Bourguiba Hospital, University of Sfax, Sfax, Tunisia*
[c] *Department of Forensic Medicine, Habib-Bourguiba Hospital, University of Sfax, Sfax, Tunisia*

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Summary Post-traumatic cerebral venous sinus thrombosis is one of the several causes of cerebral venous thrombosis, but its early diagnosis and management are still difficult in this traumatic context. Our objective is to describe clinical and radiological presentations and to report specific management and outcomes of this rare post-traumatic complication. We reported in this manuscript a case series of 10 patients hospitalized in the intensive care department with post-traumatic cerebral venous thrombosis. Demographic, clinical, and radiological data and their medical management are reported. The incidence of post-traumatic cerebral venous sinus thrombosis in our institution was 4.2%. Cerebral thrombophlebitis was diagnosed incidentally on the initial body scan, on ICU admission in five patients. The left or right lateral sinus was affected in four patients; the sigmoid sinus was affected in 6 patients. Five patients had a thrombosis in the jugular vein. Seven patients had 2 or 3 sites of occlusion. All patients had medical treatment. No hemorrhagic complications were reported. The total duration of anticoagulation was available in 5 cases. A follow-up of MRI or CT scan at 3 months revealed complete sinus recanalization in three patients. Post-traumatic cerebral venous sinus thrombosis in the intensive care department remains underdiagnosed because of the common clinical presentation of traumatic brain injury. Its incidence is increasing because of the increase in high-velocity accidents. And, it seems necessary to conduct prospective studies with a large cohort of patients in the intensive care department.

* Corresponding author.
E-mail address: kamilia.chtaraelaoud@gmail.com (K. Chtara).

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Introduction

Post-traumatic cerebral venous sinus thrombosis (PTCVST) is a potentially life-threatening condition. The pathogenesis of PTCVST implicates several factors, such as extravascular compression by edema or endothelial damage to the venous sinus caused by skull fractures.

Early diagnosis is not always possible, and its management remains a challenge [1,2]. On the one hand, its clinical presentations are non-specific, and when the diagnosis is delayed, there is an increased risk of morbidity. Moreover, the initiation of anticoagulation is still a matter of debate because of the risk of worsening traumatic hemorrhage. To date, there are no specific guidelines for anticoagulation (ACT) in this traumatic context [2]. Also, few data reported on the management and impact of this complication are available in the literature [2]. In addition, to our best knowledge, this complication has not been previously reported in patients hospitalized in an intensive care unit.

For all these reasons, we conducted this present study and included a case series of patients with PTCVST who were admitted to the intensive care department. The current study aims to describe clinical and radiological presentations and report specific management and outcomes of this rare post-traumatic complication.

Materials and methods

This study was approved by an internal review board. The need for informed consent was waived because of the study design.

This study was a retrospective analysis of a case series of ten patients with consecutive post-traumatic cerebral venous thrombosis who presented to the intensive care department from January 2016 through December 2016.

Our institution had, and still has, the same initial standardized treatment protocol for all post-traumatic patients. They received appropriate resuscitation and stabilization according to SFAR guidelines [3]. Patients were examined by unenhanced CT as soon after stabilization as possible. A CT scan was repeated at 6 hours and 24 hours after injury. If patients were operated on, another CT scan was indicated.

The diagnosis of PTCVST was either incidentally done or suspected if there was a fever, or neurological manifestations (such as seizures, wake-up delay, and/or signs of localization). It was confirmed by Contrast-enhanced computer tomography (CECT), and/or MRI.

Anticoagulation using intravenous (IV) unfractionated heparin (UFH) was administered for patients with PTCVST after a collaborative decision by the medical staff. The initial dose was 100 to 200 IU/kg/day, and it was gradually increased with clinical and radiological follow-up.

Demographic characteristics, clinical manifestations, radiological data, thrombosis topography, management, and outcomes were recorded retrospectively from medical files. The follow-up of patients was performed 6 months after ICU admission.

Results

During the study period, 237 patients were admitted to the intensive care department with brain trauma. Ten patients presented with post-traumatic cerebral venous sinus thrombosis (PTCVST) (4.2%). All patients were males. Four patients were under 18 years. The Glasgow Coma Scale was less than or equal to 8/15 in 5 patients. Nine out of 10 patients were victims of a traffic accident. All mechanisms of trauma were reported in Table 1. All patients were intubated and placed under sedation (midazolam + fentanyl) for at least 48 hours. The median Simplified Acute Physiology Score (SAPS II) was 26 points [ranging from 7 to 54]. Seven patients had Subarachnoid hemorrhage. Six patients had a hemorrhagic contusion. The acute subdural hematoma (ASDH) and extradural hematoma (EDH) were observed in 3 patients. Fig. 1A shows a preoperative axial section of the brain CT scan of patient # 6, showing a right frontoparietal EDH with a hard mass effect on the lateral ventricle. All patients had a direct impact and skull fractures. Tables 2 and 3 summarizes all radiological data for all included patients.

Cerebral thrombophlebitis was diagnosed incidentally on the initial body scan, on ICU admission in 5 patients (Fig. 2). However, the diagnosis was delayed in the 5 other patients. Clinical manifestations in the latter group were variables. Agitation and seizures were observed, respectively, in 5 and 3 patients (Table 4). Fever and neurological impairment were observed in 1 and 2 patients, respectively. The left or the right lateral sinus was affected in 4 patients; the sigmoid sinus was affected in 6 patients. Fig. 1B shows a right sigmoid sinus thrombosis of Case 6; it was diagnosed after EDH evacuation. The transverse and upper sagittal sinuses were affected in one patient (Tables 2 and 3). In addition, 5 patients had a thrombosis in the jugular vein. Fig. 1D shows an axial section of the cerebral angio-CT scan of case 9 with a left internal jugular vein. Seven patients had 2 or 3 sites of occlusion (Table 4).

Anticoagulation using intravenous (IV) unfractionated heparin (UFH) was administered for all patients. This was delayed 2 to 5 days in patients with early diagnosis, and it was immediately administered after radiological confirmation in others. Low doses ($\leq$ 3 mg/kg/day) were initiated and were increased after stabilization of the hemorrhagic lesions on the control brain scan. There were no reported hemorrhagic complications related to anticoagulation therapy.

The total duration of anticoagulation was available in only 5 cases. This duration was 6 months in these patients. The wake-up delay was observed in 3 patients and one focal sign was reported. The median length of stay was 8.5 days [ranging from 4 to 29]. One patient (Patient #1) developed right hemiparesis and presented a scholar failure. Another patient (Patient #3) developed hearing loss and post-traumatic epilepsy. In 3 patients (patients #2, #9, #10), no complications were reported. Finally, in 3 patients (patients #2, #3, and #10), a follow-up MRI or CT scan at 3 months revealed complete sinus recanalization.

Table 1 Patient characteristics, mechanism, length of stay, and outcomes.

Patient No.	Sex	Age (years)	GCS	Mechanism	Length of ICU stay (days)	Outcomes
1	M	10	15/15	Fall off a bicycle	6	Right hemiparesis/Scholar failure
2	M	12	8/15	Fall from a height of 6 meters	4	No after effects
3	M	32	9/15	Pedestrian hit by a car	9	Right hearing loss/PTE
4	M	45	8/15	Motorcycle-car collision	12	—
5	M	43	14/15	Motorcycle skidding	29	—
6	M	53	4/15	Falling down a staircase	16	—
7	M	22	10/15	Motorcycle-car collision	8	—
8	M	17	5/15	Motorcycle-car collision	20	—
9	M	23	6/15	Motorcycle-car collision	7	No after effects
10	M	12	13/15	Hit by a bus	4	No after effects

M: male; F: female; GCS: Glasgow coma scale; PTE: post-traumatic epilepsy; ICU: intensive care unit.

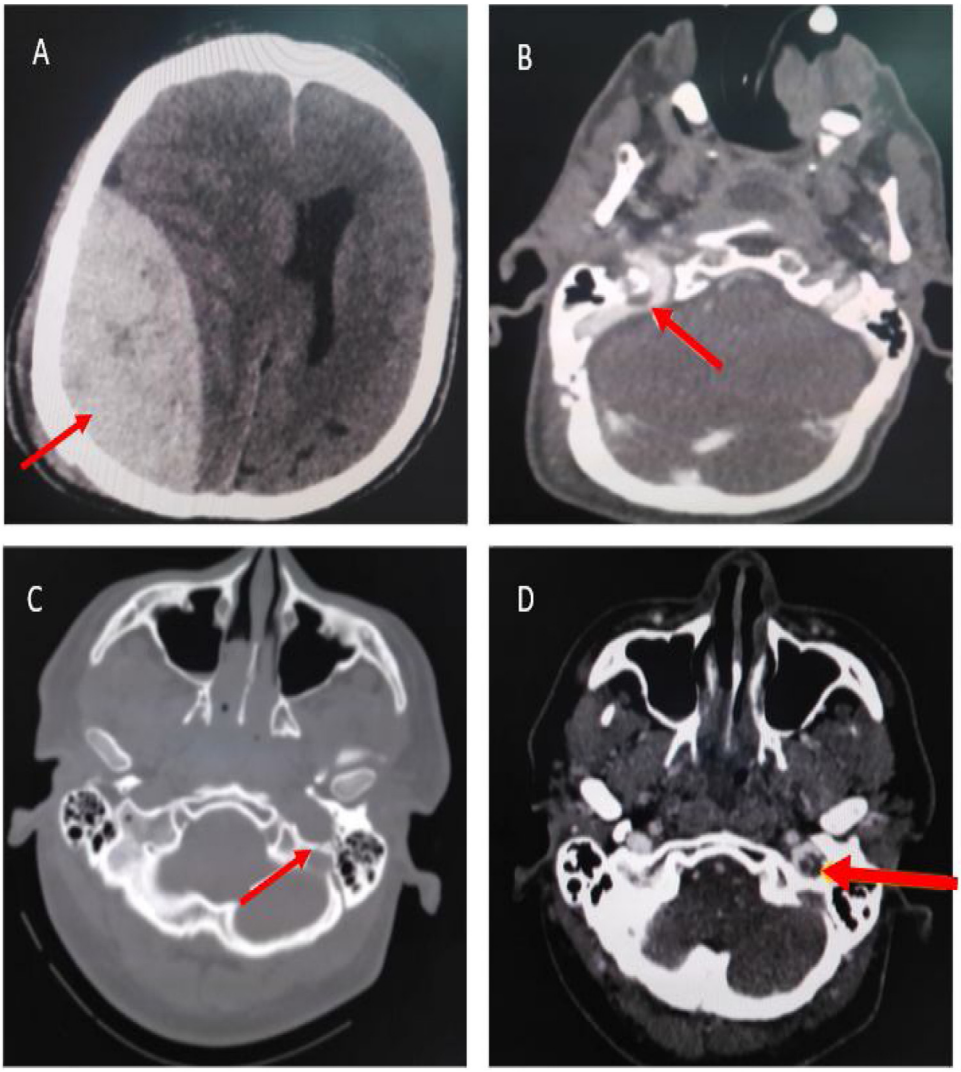

Figure 1 A. Preoperative axial section of brain CT-scan of Case 6 showing a right frontoparietal EDH with a hard mass effect on the VL. B. Postoperative axial section of angio-CT-scan of the brain of Case 6 showing a right sigmoid sinus thrombosis. C. Axial section of brain CT-scan of Case 9 showing a fracture of the left occipital condyle with refound line passing through the jugular gulf. D. Axial section of angio-CT-scan of the brain of Case 9 showing left internal jugular vein.

Table 2 Radiological data (a).

Patient No.	Cerebral lesions	Skull fractures	Locations	CT scan/MRI	Radiological control
1	LT parieto-occipital ASDH	Fracture of the LT parietal bone	Upper sagittal sinus LT transverse sinus	MRI	—
2	Subarachnoid hemorrhage LT parietal EDH LT temporal edematous hemorrhagic contusion	Fracture of the LT temporal bone	LT lateral sinus LT sigmoid sinus	CT scan	MRI normal at 3 months
3	Subarachnoid hemorrhage LT frontal ASDH Bilateral frontal petechial hemorrhagic contusion	Fracture of the LT occipital condyle Fracture of the RT occipital bone passing through the RT jugular gulf Fracture of the body of RT sphenoidal bone	RT sigmoid sinus RT internal jugular vein	CT scan	CT scan normal at 3 months
4	Subarachnoid hemorrhage LT frontal edematous hemorrhagic contusion Diffuse cerebral edema	Fracture of the RT temporal bone extended to the rock and walls of the sphenoidal sinus	RT sigmoid sinus	MRI	—
5	Right parietal ASDH Bilateral frontal petechial hemorrhagic contusion Diffuse cerebral edema	LT sphenoidal sinus wall fracture	LT lateral sinus	MRI	—

LT: left; RT: right; ASDH: acute subdural hematoma; EDH: extradural hematoma.

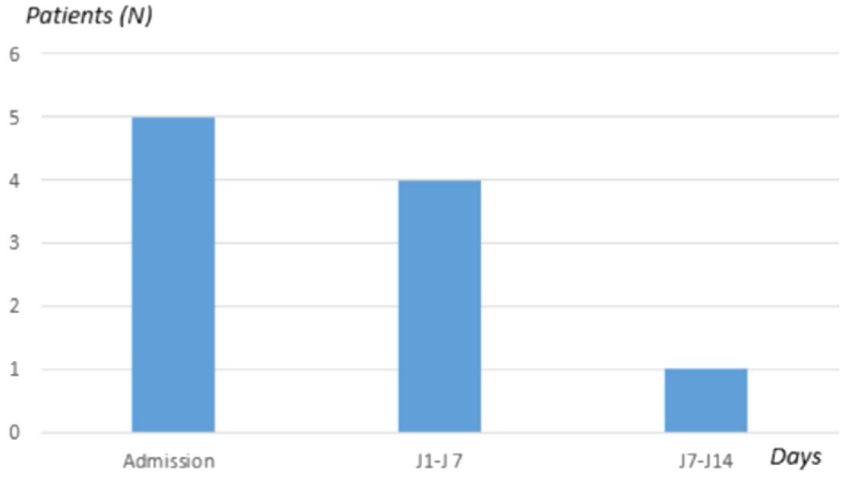

Figure 2 Diagnostic delay of post-traumatic cerebral venous sinus thrombosis (PTCVST).

Discussion

This report describes a case series of ten patients with PTCVST in the context of traumatic brain injury who required admission to an intensive care unit. It is one of the rare studies performed in the ICU on this subject. It reports the outcomes and management of both adults and children.

We reported an incidence of PTCVST at 4.2%. All patients had at least one skull or base fracture near the thrombosed sinus. The specific treatment was introduced in all of them,

Table 3 Radiological data (b).

Patient No.	Cerebral lesions	Skull fractures	Locations	CT Scan/MRI	Radiological control
6	RT frontoparietal EDH Bilateral frontal hemorrhagic contusion	Fracture of the RT parietal and temporal bone	RT sigmoid sinus RT internal jugular vein	CT scan	—
7	Subarachnoid hemorrhage LT parietal EDH LT temporal edematous hemorrhagic contusion	Fracture of the LT temporal bone extended to the jugular foramen fracture of the posterior wall of the sphenoidal sinus bilateral fracture of the occipital bone	LT sigmoid sinus LT internal jugular vein	CT scan	
8	Subarachnoid hemorrhage LT hemispheric ASDH RT parietal ASDH Frontal and temporal hemorrhagic contusion	Frontoparietal longitudinal fracture passing through the RT frontal sinus	RT lateral sinus	CT scan	
9	Subarachnoid hemorrhage Basal frontal hemorrhagic petechial lesions	Fracture of the LT occipital condyle with refund line passing through the jugular gulf	LT lateral sinus LT internal jugular vein	CT scan	
10	Subarachnoid hemorrhage Bilateral temporal edematous hemorrhagic contusion	LT parietal occipital embarrassment extended to the LT lateral sinus LT temporal communal fracture	LT lateral sinus LT sigmoid sinus LT internal jugular vein	CT scan	Normal at 3 months

Table 4 Clinical manifestations, delay of diagnosis, and management of sinus thrombosis.

Patient No.	Clinical manifestations	Delay of diagnosis (days)	Delay of heparin (days)	Initial heparin dose	Duration of treatment (months)
1	Agitation/Left facial paralysis/fever	3	0	2 mg/kg/day	6
2	Neurological impairment	0	2	2 mg/kg/day	6
3	Agitation/Wake-up delay Infra-clinical seizures	4	0	2 mg/kg/day	6
4	Wake-up delay Clinical seizures	4	0	2 mg/kg/day	—
5	Neurological impairment	7	0	3 mg/kg/day	—
6	Deep coma/Epileptic seizure disorder	0	5	2 mg/kg/day	—
7	Agitation	0	2	1.5 mg/kg/day	—
8	Agitation/Wake-up delay	12	0	3 mg/kg/day	—
9	Coma	0	2	2 mg/kg/day	6
10	Agitation	0	2	3 mg/kg/day	6

with low doses initially, and no hemorrhagic complication was reported.

In the literature, the prevalence of this pathology is unknown. In fact, with full-body scanning procedures, arterial injury is commonly recognized, whereas the venous condition is probably underdiagnosed. Moreover, its clinical signs are non-specific and neurological troubles are usually explained by the traumatic injury. In Grangeon et al.'s

data [2], the incidence of PTCVST was 2.9% of patients with severe traumatic brain injury. However, Delgado Almandoz et al. reported an incidence of 40.7% because one of the inclusion criteria was the presence of skull fractures extending to a dural sinus or jugular bulb [4].

Sinus thrombosis depends on local factors such as the location and type of skull fracture [5]. Indeed, Wang et al., in a retrospective study, reported that cerebral venous flow obstruction was found in 38.5% of cases with trans-sinus linear fracture alone, 78.5% of cases with trans-sinus depressed fracture, and 79.4% of cases with trans-sinus fracture and epidural hematoma [5].

Diagnosis delay is variable in literature [2]. It can be immediate with the presence of a hyper-dense sinus on the initial CT scan [2]. However, a mean delay of 7 days after admission was reported [5]. In our report, the diagnosis of PTCVST was immediate in five patients among ten and was delayed until 12 days.

If the superior sagittal sinus is most often involved in cerebral venous thrombosis whatever the etiology [6], in a traumatic context, sinus thrombosis depends on local factors, such as the location of skull fracture [2]. According to Moscote-Salazar et al. [7], the most affected areas are in order: transverse sinus, sagittal sinus, sigmoid sinus, and straight sinus. Delgado Almandoz et al.'s study [4] reported a greater risk of PTCVST of the transverse sinus, sigmoid sinus, or jugular bulb in cases of petrous temporal bone involvement rather than occipital fracture. In our report, the sigmoid sinus, lateral sinus, and internal jugular bulb were the common locations of thrombosis. This can be explained by the severity and direct impact on the patients' skulls.

Pathophysiological determinants of PTCVST were those of Virchow's triad (Endothelial injury, hypercoagulability, and reduced blood flow and stasis) and acute inflammation due to the severity of trauma [8]. So, after traumatic brain injury, the trans-sinus fracture might explain the early genesis of thrombosis by damaging the endothelial lining of the sinus wall. According to Delgado Almandoz et al.'s case series [4], more than 80% of the cases reported in the literature on PTCVST presented a skull fracture. In our present series, all patients presented skull fractures in front of the affected sinus. In addition, extrinsic compression on the dural sinus caused by extra-axial hemorrhages is responsible for hemodynamic changes inside the sinus, contributing to intra-luminal clot formation [9]. This was the main mechanism for patient #6. Moreover, hypercoagulability observed after traumatic brain injury, with increased thrombin generation and reduced production of natural anticoagulants — such as anti-thrombin — contributes to thrombosis genesis [2]. Finally, the hypothesis that inflammation of the vessel wall could cause thrombosis in undamaged veins exists [8]. Severe injuries strongly stimulate the production of cytokines, leading to excessive systemic inflammation. This phenomenon may trigger coagulation pathways [8]. Moreover, PTCVST leads to complications involving the specific drainage area of the affected dural venous sinus [10]. Thrombosis of dural venous sinuses increases hydrostatic pressure in upstream veins and capillaries. The consequences of this are parenchymal edema, decreased arterial perfusion, and rupture of vessels causing venous ischemia and parenchymal hemorrhage, respectively. A recent retrospective study [10], including 73 patients with cerebral venous thrombosis after traumatic brain injury, reported venous infarction in 18% of cases, intracerebral hemorrhage in 11%, and edema in 19% [10].

Dural venous sinus patency is the objective of this pathology. However, in this traumatic context, determining when to initiate anticoagulation remains a challenge because of the high risk of intracranial hemorrhage. To the best of our knowledge, there are no recommendations concerning the optimal delay of anticoagulant treatment. In Grangeon et al.'s case series, heparin was initiated within 72 h after the traumatic brain injury [2]. In Fujii et al.'s study [11], anticoagulation initiation was delayed by a median of 7 days because of unstable hemorrhage. In our patients, the specific treatment was introduced between 2 and 12 days after brain injury after a collaborative decision of our medical staff.

The prognosis of PTCVST and its effect on the outcome of TBI patients remains undetermined [10], and available data are diverging [5,10,12]. According to Netland et al., cerebral venous thrombosis is associated with four-times-higher 30-day mortality (16% versus 4%) [10]. Wang et al. reported that delayed diagnosis of PTCVST results in higher mortality rates [5]. Moreover, and to the best of our knowledge, no study has compared adults and children in terms of prognosis [12]. According to Rivkin et al., thrombosis in children seems to have a better prognosis [12]. In these data, pediatric patients had significantly shorter length of stay (4 vs. 11 days, $P < 0.01$) compared to adults [12].

Despite the retrospective type of our study and the limited number of patients, this data reports a case series of PTCVST in patients admitted immediately to the intensive care unit.

Conclusion

PTCVST in the intensive care department remains underdiagnosed because of the common clinical presentation of traumatic brain injury. We believe that its incidence is increasing because of the increase in high-velocity accidents. Moreover, the prognosis of this complication remains unclear. It seems necessary to conduct prospective studies with a large cohort of patients in the intensive care department.

Disclosure of interest

The authors declare that they have no competing interest.

Human and animal rights

The authors declare that the work described has not involved experimentation on humans or animals.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient.

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Authors' contributions

All authors attest that they meet the current International Committee of Medical Journal Editors (ICMJE) criteria for Authorship.

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