RATE, Clinical Presentations and Maternal Outcome of Cerebral Venous Sinus Thrombosis in Pregnancy at Omdurman Maternity Hospital Khartoum, Sudan

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Abstract

Introduction: Cerebral venous sinus thrombosis (CVST) is a relatively rare cerebrovascular disease. The clinical presentation is highly variable and diagnosis of CVST relies presence of thrombus by neuroimaging modality. CVST results in maternal mortality.

Objective: The aim of this study is to identify rate, clinical presentations and maternal outcomes of cerebral venous sinus thrombosis at Omdurman Maternity Hospital, Khartoum, Sudan.

Methodology: Its hospital based study for 42 cases diagnosed with CVST; the data are managed and analyzed using Statistical Package of Social Sciences (SPSS) version 17.

Results: CVST rate 0.25=2.5/1000. Half of the patients are primiparous. Headache is the main presenting symptom 90.5%, papilledema (66.7%), convulsions (21.4 %), coma (9.5%), neurological deficits (9.5%) and abnormal behavior (7.1%). Overlapping of the symptoms is reported. CVST risk factors are oral contraceptive pills history (26.2%), Diabetes Mellitus (11.9%), Pregnancy Induced Hypertension (9.5%) and deep venous thrombosis (9.5%). 18 patients (42.9%) reported no relevant history or apparent risk factor. (71.4%) recovered with no disability, symptom 90.5%, papilledema (66.7%), convulsions (21.4 %), coma (9.5%), neurological deficits (9.5%) and abnormal behavior (7.1%). Overlapping of the symptoms is reported. CVST risk factors are oral contraceptive pills history (26.2%), Diabetes Mellitus (11.9%), Pregnancy Induced Hypertension (9.5%) and deep venous thrombosis (9.5%). 18 patients (42.9%) reported no relevant history or apparent risk factor. (71.4%) recovered with no disability, and those between 26 and 30 years (P=0.043). It was also higher with PH (P=0.013), OCP (P=0.004) and cerebral hemorrhages (P=0.043).

Conclusion: CVST reported high at OMH and most of them are primiparous. CVST can happen independently, CVST contributes in maternal mortality. Neuroimaging modalities improve CVST diagnosis.

Keywords: Cerebral venous sinus thrombosis; Case fatality rate

Introduction

Cerebral venous sinus thrombosis (CVST) is a relatively rare cerebrovascular disease that particularly affects young and middle aged women in child bearing years [1]. Patients usually present with one or more of clinical conditions related to increased intracranial pressure. Considering this diagnosis in the right clinical context might prove life-saving while magnetic resonance imaging (MRI) with venography (MRV) confirms the diagnosis [2,3].

Subjects are at increased risk of developing CVST if they have genetic or acquired thrombophilic disorders [4,5]. Despite extensive search, in about 13% of adult patients with CVST, no underlying risk factor could be found [3]. In the etiological investigations of a patient with CVST, a systematic search for prothrombotic conditions is warranted even in the presence of a clear precipitant such as the use of contraception, puerperium or infection. If uncovered, a prothrombotic condition increases the risk of recurrence of thrombotic events and would modify the duration of anticoagulation therapy following the acute phase.

Clinical presentation of CVST is highly variable and onset could be acute, sub-acute or even chronic but the latter is less frequent. Symptoms and signs of CVST could be grouped into three possible clinical scenarios: 1) A syndrome of Isolated intracranial hypertension constituting headache with or without vomiting, visual symptoms and possible papilledema on clinical examination. 2) A syndrome depicting focal deficits such as face or limb weakness, speech deficit, symptomatic seizures or a combination of these. 3) A syndrome simulating encephalopathy with delirium, disturbances of consciousness and possible bilateral or multifocal symptoms and/or signs [1,6]. However, less frequent presentations are related to the cavernous sinus, multiple lower cranial nerve palsies and generalized or localized subarachnoid hemorrhage caused by single or few cortical hemorrhages.
sulci found on hemispheric convexity [7]. It is worth emphasizing that
headache is the most frequently presented symptom of CVST, usually
the initial presentation and might be the sole manifestation of CVST
[7]. Typically CVST produces motor and/or sensory deficits and
seizures in the context of headache in women around childbearing
aged [2,5]. Motor deficits caused by thrombosis of the sagittal sinus
could be unilateral or bilateral and seizures could be symptomatic focal
or generalized. Patients with isolated thrombosis of the lateral sinuses
often present clinical syndromes of isolated intracranial hypertension,
while thrombotic occlusion of the left transverse sinus frequently
present with aphasia. Thrombosis of deep cerebral venous system often
causes coma, cognitive deficits and paresis.

Confirming the diagnosis of CVST relies on the demonstration of
thrombus in the cerebral veins and/or sinuses by a suitable
neuromaging modality. Clear-cut radiological signs of CVST could be
found in approximately one-third of patients diagnosed with CVST.
These include the cord sign (thrombosed cortical or deep cerebral
vein), dense triangle sign (visualization of a clot inside cerebral sinus),
and empty delta sign (visible in the cavity of cerebral vein after
injection of a contrast material). Parenchymal lesions might be seen in
60-80% of patients diagnosed with CVST; and some of these
topographic radiological lesions are suggestive of specific patterns of
cerebral venous sinus occlusion.

For instance, bilateral para-sagittal hemispheric, temporo-occipital
and bilateral thalamic lesions are highly suspicious of thrombosis of
superior sagittal sinus, lateral sinus and deep cerebral venous system,
respectively. Rarely, a small subdural hematoma or subarachnoid
hemorrhage might be demonstrated. The combination of magnetic
resonance imaging (MRI) with magnetic resonance venography
(MRV) using contrast material largely accepted as the best
investigational method used to confirm the diagnosis of CVST. For
instance, an abnormal MRI signal from a cerebral sinus with
corresponding signal flow void on MRV supports the diagnosis [8].

A cohort International Study on Cerebral Vein and Dural Sinus
Thrombosis (ISCVT) showed that 79% of patients with CVST
recovered completely [3]. In a meta-analysis of retrospective studies,
overall rate of acute death was 5.6%, death at the end of follow up was
9.4% and complete recovery was 88% [9]. Poor outcome is linked to
age over 37 years, male gender, Glasgow Coma Scale score of less than
9 on admission, disorder of cognitive status, thrombosis of the deep
cerebral venous system, intracranial hemorrhage on admission CT or
MRI, malignancy and central nervous system infection [3]. For
the majority of patients dying in the acute phase, the cause of death was
trans-tentorial herniation secondary to large hemorrhagic lesions [6].
Other patients die due to complications such as herniation secondary
to diffuse cerebral edema, status epilepticus and other related medical
complications including pulmonary embolism [10].

Complications taking place following the initial acute phase include
venous thrombotic events, seizures and follow on headaches. In spite of
the apparent good general recovery, several studies pointed out that
subsequent psychological and cognitive complaints are not uncommon
among CVST survivors. It transpires that half of the survivors
following diagnosis of CVST feel depressed or anxious. They might
demonstrate minor cognitive or language deficits that might preclude
resumption of pre-illness level of professional activity [11].
Recanalization of the thrombosed cerebral veins and/or sinuses takes
place in 40–90 percent of patients following CVST and is mostly seen
within the first four months from onset [11].

Treatment of acute CVST might include emergency stabilization of
an ill patient in pain with neurological deficits and seizures. The
mainstay of treatment might include: 1) Antithrombotic treatment; 2)
Symptomatic treatment of headache, seizures, visual impairment and
symptoms of raised intracranial pressure; and 3) Treatment of
underlying conditions or associated risk factors related to the aetiology
of CVST [8]. The aim of antithrombotic treatment in CVST includes:
1) attempting to re-canализ occluded sinuses or veins; 2) hinder
the propagation of thrombus or thrombi; and 3) prevent any possible
pulmonary embolism or any other venous thrombosis; 4) treat
the underlying prothrombotic condition or state. For current treatment
options, there is a consensus for the use of unfractionated heparin or
Low molecular weight heparin (LMWH) for acute CVST.

Treatment guidelines recommend that patients diagnosed with
CVST and have no contraindications to anticoagulation should be
treated with heparin, either with Activated Partial Thromboplastin
Time (APTT) adjusted heparin or body-weight-adjusted LMWH [12].
Case control study and randomized clinical trial both support
preference for the use of low molecular weight heparin over
unfractionated heparin [13]. Direct thrombolysis and re-canализation
through endovascular procedures using venous access has been used in
some centers as an alternative to anticoagulation. This is particularly
used in patients with CVST with severe co-morbidities or patients who
are either not improving or worsening despite anticoagulation.

Recurrence of cerebral venous thrombosis occurs in 2 to 7% of
patients, with extra cerebral venous thrombosis in about 5% of
patients. To prevent recurrent thrombotic events among other
therapeutic benefits, anticoagulation is recommended, usually for 3 to
12 months following an acute CVST. In patients with idiopathic CVST,
with no obvious underlying thrombotic condition is identified, or
CVST associated with “mild” thrombophilia, the duration of
anticoagulation might be slightly longer (6 to 12 months). In patients
with “severe” Thrombophilia, “combined” thrombotic condition or
recurrent venous thrombosis, anticoagulation might be given for life.
In patients with acute CVST, severe headache with or without
papilledema, intracranial hypertension should not be reduced or
headache relieved through therapeutic lumbar puncture due to
concurrent cerebral edema. This might be much more obvious in
patients with parenchymal lesions, with severe acute disease, one or
multiple hemorrhagic lesions, infarcts or massive brain edema, where
serious and possibly fatal brain herniation might be precipitated. Some
of these patients might symptomatically improve or transiently
stabilize by osmotic diuresis using mannitol as well as elective
intubation sedation and hyperventilation. Corticosteroids could
decrease vasogenic edema but might also promote further thrombosis
and a case-control study failed to demonstrate any benefit for steroids
even when used for patients with parenchymal lesions [11].

In CVST patients with impending herniation due to large unilateral
hemispheric lesions, decompressive surgery might be life-saving. This
is achieved through either hemi-craniotomy or hematoma evacuation,
and often results in good functional outcome even in patients with
severe disease [5,6,8,10]. Acute obstructive hydrocephalus is rare in the
context of acute CVST. Shunting procedure alone is not effective in
preventing death from brain herniation in acute CVST [5], as despite
shunting half of these patients displayed bad outcomes [5].

In patients left with long-term (chronic) increase of intracranial
pressure, treatment might be necessary to improve headache and
prevent visual impairment. Diuretics such as acetazolamide might be
used for this purpose. In the acute phase, CVST patients who present

with seizures should be treated with antiepileptic medications, however prophylactic use of these medications is not recommended. To prevent recurrent (cluster) seizures and any possible status epilepticus, antiepileptic medications are recommended for use in patients with seizures in the acute phase or, especially in the presence of other risk factors for provoking seizures such as supratentorial hemorrhagic lesions or motor deficits [11]. The long-term risk of seizures is approximately 11% [3]. In follow up, the CVST is not an absolute contraindication for future pregnancy.

However, women who suffered CVST must not become pregnant while taking oral anticoagulants, and they should use contraception other than hormonal methods. The risk of further venous thrombotic events in subsequent pregnancies of women with history of CVST is low; however a high number of miscarriages were observed [5]. The aim of this study is to identify at Omdurman maternity hospital.

**Methods**

This is a hospital based cross-sectional study. All patients seen at Omdurman Maternity Hospital (OMH), Khartoum, Sudan between January 2015 and June 2015 were included in the study. OMH is the leading maternity hospital in Sudan being the largest and most specialized in this vast Sub-Saharan African country. OMH was established in 1957, continued to provide obstetrics and gynecology services and training medical, nursing and other allied health specialties in this and related field. OMH registered around 36,453 deliveries in the year 2014.

Ethical approval was obtained from the Ethical Committee of the Sudan Medical Specialization Board (SMSB) and the approval was countersigned by the medical director of OMH as a standard procedure. Informed consent was obtained from all patients and/or their guardians where appropriate. Confidentiality of these patients was maintained throughout and after the study, with only anonymous data sets being used with no patients’ identifying details. All patients participating in this study were treated as they would normally be according to clinical practice standards used at OMH. When clinically suspected as having CVST and diagnosis subsequently confirmed, management of the patients is commenced with unfractionated Heparin as treatment of choice, followed by oral anticoagulants and serial investigations to establish any possible underlying or related conditions. The in hospital care is initially carried in the hospital ICU followed by transfer to the hospital wards once patients are clinically very stable.

Data was collected using purpose-designed structured data collection sheets. The sheet included demographic details, gestational age, the mode of delivery, medical history, clinical findings, laboratory findings, ICU admission and overall hospital stay, persistent morbidity and any incidences of mortality. All the data obtained was entered in a master flow chart and was analyzed using statistical package program for social science (SPSS) version 17.

**Results**

**Participants’ characteristics**

The total number of hospital registered deliveries during the study period is 16602 deliveries and CVST are 42 cases this makes CVST rate 0.25%=2.5/1000. The commonest age group affected by CVST is 21-25 years (40.5%). The majority of them (73.8%) have normal BMI. Half of the patients are primiparous, 42.9% are multiparous and 7.1% are grand-multiparous women. With regard to mode of delivery, 54.8% delivered through spontaneous vaginal delivery, 38.1% via cesarean section, and 7.1% with instrumental delivery.

Among 16 patients who underwent caesarean section, (75%) used spinal anesthesia and (25%) used general anesthesia. All patients are seen during puerperium except three who developed CVST in the antenatal period (Table 1).

<table>
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<td></td>
<td>&gt;35</td>
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<td>Normal</td>
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<td>73.80%</td>
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<td>Over weight</td>
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<td>Parity</td>
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<td>54.80%</td>
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<td>General</td>
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<td>25%</td>
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</table>

Table 1: CVST participants’ characteristics.

**The clinical presentations**

The clinical presentations of patients with CVST varied greatly on arrival to hospital, with overlapped and combined features of CVST. The commonest clinical presentations were headache (90.5%), papilledema (66.7%), convulsions (21.4%), coma (9.5%), neurological deficits (9.5%) and abnormal behavior (7.1%).

Risk factors for the development of CVST included usage of oral contraceptive pills (26.2%), Diabetes Mellitus (11.9%), Pregnancy Induced Hypertension (PIH) (9.5%) and DVT (9.5%). 18 patients (42.9%) reported no relevant history or apparent risk factors suggesting independent CVST. MRI and MRV studies were performed for all 42 patients to confirm the diagnosis. 88.1% of patients showed only the radiological signs of CVST and 11.9% also had additional cerebral hemorrhages (Table 2).
Table 2: Clinical presentations of the CVST cases.

Maternal Outcomes

Five out of the 42 patients died resulting in case fatality rate of 11.9%. 7 patients developed disability resulting in case disability rate of 16.7%. Disability included hemiplegia (4 patients) and maternal blues and abnormal behavior (3 patients). The majority of patients (71.4%) were treated, recovered and discharged with no disability. Case fatality rate was found to be statistically significant higher among those less than 20 years and those between 26 and 30 years (P=0.023). It was also higher with PIH (P=0.013), OCP (P=0.004) and cerebral hemorrhages (P=0.043) (Table 3).

Table 3: Cases' variables correlation with maternal death.

Discussion

CVST should be considered in the differential diagnosis of patients presenting with unusual headache, convulsions, abnormal behavior and other neurological manifestations. The rate of CVST in this study was found to be 2.5% which is relatively high in comparison with other studies especially with the relatively short (6 months) duration of this study. Generally, robustness of the diagnosis of CVST patterns has improved most likely due to increased clinical suspicion of CVST and availability of MRI/MRV modalities to confirm the diagnosis. The majority of patients participating in this study are younger age groups of 21-25 years, who are much younger than the most affected age groups of 31-35 years, when compared with other studies performed, as in Fink et al. [14].

Headache is the most common presenting symptom in this study similar to most previously published studies, and this has been clearly stated by Shelley et al. that “Headache is often the first and most frequent symptom occurring in 74–90% of all patients with CVST” [15]. In this study, similar to previously published data, it is established that individuals with precipitating factors carry similar risks for CVST. Thrombophilia screening and investigations in search for any CVST predisposing factors is necessary, however thrombophilia screening could not be done while these patients already started taking anti-coagulants. It has been described that patients should be free of the effects of anti-coagulation treatment for a minimum of six weeks prior to thrombophilia screening. This has been outlined as one limitation of this study due to the short follow up period (6 months) and design being cross-sectional study. All patients seen and diagnosed with CVST, except three being antenatal, were during the puerperium, which is a valid result and in line with others studies such the findings by Fink et al [14].

Outcome of this study indicates that 71.4% were treated, recovered and discharged with no disability, 16.7% developed morbidity in the form of hemiplegia (4 patients), maternal blues and abnormal behavior (3 patients) and unfortunately 11.9% (5 patients) died.
Conclusion

Cerebral venous sinus thrombosis risks the mothers’ lives as it might occur independently when the Thrombophilia is excluded.

The rate of CVST is high in this study which reflects the clinical importance and implication of such diagnosis in the reported maternal mortality among cerebral venous sinus thrombosis cases may be unavoidable deaths with the combination pathology of thrombosis and hemorrhage.

More research and data are highly needed to elaborate more about the cerebral venous sinus thrombosis as it not that common condition but it carries a significant clinical weight and contributes in maternal mortality.

Encouragement of multi-disciplinary team work in cerebral venous sinus thrombosis management will improve the outcome in timely diagnosis, investigations availability and informative interpretation results.

References