ORIGINAL ARTICLE

Cerebral venous sinus thrombosis: review of cases in a single centre in Malaysia

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ABSTRACT

Introduction: Cerebral venous sinus thrombosis (CVST) is a potentially fatal neurological condition. However, due to the non-specific clinical and radiological features of CVST, it can sometimes result in a delay in the diagnosis and subsequent management. The aim of this study was to evaluate the demography, risk factors and one-year outcome of CVST patients treated in Hospital Universiti Sains Malaysia.

Methods: In this retrospective study, we reviewed the cases diagnosed with CVST admitted to our centre from January 2011 until November 2015.

Results: A total of 15 patients were included in this review. The patterns of imaging findings as well as risk factors for CVST is discussed with a review of the literature and current management practices. One year followed-up showed full recovery (Glasgow Outcome Scale (GOS) of 5) in 10 cases (66.7%), whereas 4 cases (26.7%) with GOS of 4 (three cases with neurological deficits, and 1 case with mild symptom. There was one case of mortality in this study secondary to sepsis during hospitalisation. The presenting symptoms were mainly headache, focal neurology deficits, seizure and altered sensorium. Risk factors identified were oral contraceptive pills usage, chronic sinuses or ear infections, and obesity. Initial computed tomography (CT) scan showed various findings and haemorrhagic infarct was one of the common findings. Magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) revealed majority of the patients had occlusion at two or more venous sinus sites. No patients had new or recurrent intracranial haemorrhage following initiation of anticoagulation therapy.

Conclusion: Thus it is considerable safe to start anticoagulation therapy in CVST patients including those with intracranial haemorrhage. We propose further neuroimaging to avoid missed diagnosis of CVST in patient presented with recent onset headache and CT evidence of unusual cerebral infarction.

KEY WORDS:
Sinus thrombosis, stroke, anticoagulation, intracerebral haemorrhage

INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is a neurological condition involving thrombosis of one or more of the cerebral veins (both cortical and deep venous systems) as well as the dural sinuses. It accounts for 0.5 to 1% of all strokes.[1,2] Due to the non-specific clinical presentations, the diagnosis of CVST can sometimes be difficult. The initial computed tomography (CT) scan may not show any conclusive finding, thus in any suspicion situation, a further neuroimaging must be carried out immediately to confirm the diagnosis and to prevent the delay in the initiation of anticoagulant therapy.[2] Besides, CVST might often be referred to the neurosurgical team for intervention due to the occurrence of intracranial haemorrhage or mass effect, or for the opinion on the safety to start anticoagulant therapy. In view of this, neurosurgeons need to be aware of the varied manifestations and radiological features of CVST as well as its complications. The aim of this study was to evaluate the demography, risk factors and one-year outcome of CVST patients treated in our centre.

MATERIALS AND METHODS

This was a retrospective study conducted in Hospital Universiti Sains Malaysia (HUSM) and data collection was in accordance with the Declaration of Helsinki for human research. Medical records of all consecutive patients aged above 12-year-old who was admitted to the Department of Neurosciences, HUSM from January 2011 to November 2015 were reviewed. All patients included in the study must have had neuroimaging done to confirm the diagnosis of Cerebral Venous Sinus Thrombosis (CVST) and been admitted into HUSM for further management.

The inclusion criteria were: a) age above 12 years old, b) diagnosis confirmed with neuroimaging (either CT venography or magnetic \resonance venography), c) admitted and received treatment in HUSM. \Whereas the exclusion criteria were: radiologically demonstrated infarction in arterial territory, b) hypertensive intracranial haemorrhage and c) on antiplatelet or anticoagulant therapy for other medical conditions.

Patient interventions: The routine practice in managing CVST patients in HUSM was, after receiving the referral from the Emergency Unit, the patients would be reviewed by the medical officers from the Department of Neurosciences, consisting of Neurology and Neurosurgery Units. Once the diagnosis was confirmed with neuroimaging, the patients are admitted to Neuro High Dependency Unit. The consultant neurologist would review the patients before the

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Table I: Characteristics of patients with CVST and their clinical presentation, treatment and outcome

Case	Age	Sex	Clinical Picture	Site	Radiological Findings	Associated Risk Factors	Treatment	Outcome
1	31	F	Headache, left hemiparesis, generalized seizure	Cortical venous channel	Right frontoparietal lobar haemorrhage	Post-partum	Anticoagulant, anti-epileptic	Residual left hemiparesis
2	30	M	Right focal seizure, headache, cerebral salt wasting syndrome	SSS, left TS	Left temporal SAH	Obesity, uncontrolled diabetes with dehydration	Anticoagulant, anti-epileptic, hydration	Recovered
3	16	M	Headache, bilateral 6th nerve palsy with papilloedema	Left TS, SS, IJV	Right parietal haemorrhagic infarct	Otitis media	Anticoagulant, Antibiotics	Recovered
4	27	F	Left focal seizure, headache, bilateral 6th nerve palsy	SSS, right TS, IJV	Left frontal lobar haemorrhage	Oral contraceptive, obesity, essential hypertension	Anticoagulant	Recovered
5	25	M	Headache, generalized seizure, altered sensorium, papilloedema	Right TS, SS	Right parietooccipital haemorrhagic infarct	Systemic infection	Surgical decompression, anticoagulant, antibiotics	Deceased: due to sepsis
6	30	M	Headache, right temporal hemianopia	Anterior 1/3 SSS, ISS	Right temporal infarct	Chronic sinusitis	Anticoagulant, antibiotics	Intermittent headache
7	24	F	Headache, generalized seizure	Left TS	Bifrontal haemorrhagic infarct	Oral contraceptive, obesity	Anticoagulant	Recovered
8	39	F	Headache, left gaze palsy, right focal seizure	SSS, ISS, bilateral TS	SAH, left parietooccipital lobar haemorrhage	Oral contraceptive	Anticoagulant, anti-epileptic	Recovered
9	31	F	Headache, left hemiparesis, generalized seizure	SSS	Right parietal infarct	Oral contraceptive	Anticoagulant, anti-epileptic	Residual left hemiparesis
10	22	F	Headache, right hemiparesis, generalized seizure, bilateral 6th nerve palsy	SSS, left TS	SAH, IVH, deep nuclei haemorrhagic infarct	Familial hypercoagulability disorder	Anticoagulant, anti-epileptic	Frontal and left parietal lobe syndromes, residual right hemiparesis
11	27	M	Headache, altered sensorium, generalized seizure	SSS	Bifrontal haemorrhagic infarct	Systemic infection with dehydration	Anticoagulant, anti-epileptic	Recovered
12	45	F	Headache, altered sensorium	right TS, SS	Right parietooccipital haemorrhagic infarct	Otitis media with mastoiditis	Anticoagulant	Recovered
13	36	F	Headache, generalized seizure, left hemiparesis	Right TS, SS	Right temporal infarct	Oral contraceptive	Anticoagulant, anti-epileptic	Recovered
14	54	F	Headache, left hemiparesis	Posterior 1/3 SSS	Left parietal haemorrhagic infarct	Systemic lupus erythematosus	Anticoagulant, anti-epileptic, steroid therapy	Recovered
15	50	M	Headache, aphasia, papilloedema	SSS, left TS, left IJV	Left temporal haemorrhagic infarct	idiopathic	Anticoagulant	Recovered

SSS = superior sagittal sinus; ISS = inferior sagittal sinus; TS = transverse sinus; SS = sigmoid sinus; IJV = internal jugular vein; SAH = subarachnoid haemorrhage; IVH = intraventricular haemorrhage; Recovered = Glasgow Outcome Score (GOS 5)

Table II: Risk factors identified in the 15 cases of CVST

Risk Factors	Number of Patients (%)
Oral contraceptive pills usage	5 (33.3)
Infection (chronic sinusitis, middle ear infection)	5 (33.3)
Obesity	3 (20)
Post-partum	1 (6.7)
Familial hypercoagulability disorder	1 (6.7)
Systemic lupus erythematosus	1 (6.7)
Essential hypertension	1 (6.7)
Idiopathic	1 (6.7)

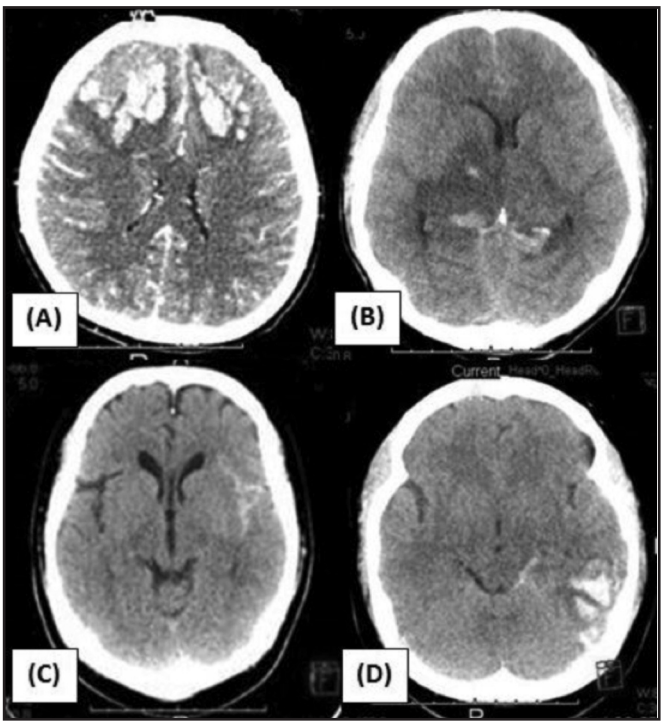

Fig. 1: The various radiological findings seen on the initial CT scan done during admission. (A) bifrontal haemorrhagic infarct; (B) deep nuclei infarct with haemorrhagic transformation; (C) left sylvian fissure subarachnoid haemorrhage; (D) left parieto-occipital haemorrhage.

anticoagulant therapy was initiated. The neurosurgical team would be referred if radiologically demonstrated intracranial haemorrhage or related mass effect is observed. If surgery was not indicated, anticoagulant therapy is started by the neurology team. The anticoagulant therapy given was subcutaneous injection of low molecular heparin (1mg/kg, 12 hourly) for six months. A repeat neuroimaging is conducted at six months to look for the patency of the involved venous sinus system and to further decide the continuation or discontinuation of the anticoagulant therapy. Upon discharge, patient are followed up with clinical assessment in the clinic every 3-monthly, and one year Glasgow Outcome Scale (GOS) then documented.

Data collection: Patient demographics (age, gender, and race), clinical presentations and risk factors, investigations (neuroimaging findings including site of occlusion; biochemistry tests), treatment given and outcome (GOS at one-year follow-up) were recorded. Baseline biochemistry tests including full blood count, serum electrolytes, renal and liver function tests, coagulation studies, blood sugar levels were done for all patients. Protein C, Protein S and Homocysteine levels were not routinely done but in selected patients only.

Data analysis: Descriptive data was analysed with statistic software SPSS as frequency, mean and standard deviation or percentages. Difference in continuous variables was evaluated by using independent t-test while chi-square test was performed in categorical variables. Statistical $p<0.05$ was considered statistically significant.

RESULTS

Of the evaluated records, a total of 15 patients were diagnosed with CVST. Majority of patients in this cohort were females (60%). The ages of patients ranged from 16 to 54 years old, and the mean age of presentation was 32.5 years. The most prevalent symptom was headache, which was found in all the patients. Other common clinical features included i) seizures (66.7%), ii) eye signs (46.7%), iii) hemiparesis (33.3%), iv) altered sensorium (20%), v) aphasia (6.7%) and vi) cerebral salt wasting syndrome (6.7%). The duration of symptoms prior to admission ranged from 5 to 96 hours (average 32±4.8 hours). The admission GCS score for all patients were 15, except one patient (case no. 5 in Table I) who came in with a GCS score of 11/15. All the patients had initial computed tomography (CT) scan done during admission at the Emergency Department. Cerebral infarction was a common finding among them (11 patients, 73.3%), in which eight of them being associated with haemorrhagic transformation (58.3%), whereas three patients presented with venous infarct alone (20.0%). Other associated radiological findings included lobar haemorrhage (20%), subarachnoid haemorrhage (20%) and intraventricular haemorrhage (6.7%). Figure 1 shows the various radiological findings seen on the initial CT scan done during admission. Table I summarises the characteristics of the CVST patients in this cohort, including their clinical presentations, treatment and outcome. The use of oral contraceptive pills and infections (three cases of sinusitis, and two cases of middle ear infection) appeared to be the most common risk factors in this study (Table II).

The diagnosis of CVST was confirmed with magnetic resonance imaging (MRI) and magnetic resonance venography (MRV) in all 15 cases by means of a demonstration of the intravenous clot based on alteration of the signal in sequences T1 and T2 as well as the absence of flow in MRV. In all 10 cases (66.7%) had multiple venous

systems (at least two) involvement. The most common affected sites were the transverse sinus (66.7%) and superior sagittal sinus (60%).

We did not find any abnormality in the laboratory findings that suggested that any of the patients studied had the risks of thrombosis. Following radiological confirmation, anticoagulation therapy was initiated in all cases except one patient (due to rapid deterioration of that patient requiring surgical decompression). The anticoagulant therapy was prescribed by consultant neurologist for a total of six months (subcutaneous injection of low molecular weight heparin). In this patient who underwent surgical decompression, anticoagulant therapy was started at post-operative day-14 when a repeat CT scan showed no new evidence of bleeding. None of the patients started on anticoagulation had subsequent clinical deterioration or demonstrated any radiological evidence of increase in the haematoma size. The mortality rate in this series was 6%. The deceased patient (undergone surgical decompression) was complicated with sepsis and multi-organs failure following hospital acquired infection. All the patients in this study were followed up for a period of one year after being discharged. None of the cases presented with a new thrombotic event after the initial presentation (repeated MRV at six months and clinical assessment every subsequent three months for up to one year). Eleven patients (73.3%) exhibited good clinical recovery (GOS 5) with resolution of symptoms and clinical signs. Three patients had residual hemiparesis (GOS 4), of whom one additionally suffered from left frontal and parietal lobe dysfunctions (GOS 4). One patient complained of intermittent headache, which occasionally affected his daily activities (GOS 4).

In this study, there were no associations found by statistic between the age of patients, duration of symptoms, and radiological findings (venous infarct alone/haemorrhagic transformation) with the one-year outcome. The small sample size has limited the data analysis in this study.

DISCUSSION

Cerebral venous sinus thrombosis (CVST) represents approximately 0.5-1% of all stroke conditions.[1,2] It can be a life-threatening disease, especially when there are delays in diagnosis or initiation of therapy due to the variable presentations. The onset of the symptoms in CVST cases can be acute, subacute, or chronic.[3] Approximately 30% of cases present acutely, and the symptoms appear within 48 hours. In the subacute type, which is the most common (50%), the symptoms appear between 48 hours and 30 days. In the chronic type (20%), the symptoms develop between 1 and 6 months. The gradual onset of symptoms over weeks and months is probably related to the intact collateralisation of the cerebral venous vessels in the event of an occlusion. All the cases in our series were presented in between acute and subacute phases.

In our study, the characteristics of patients with CVST were consistent with previous studies.[1–4] Women prone to CVST were of reproductive age, which is probably related to pregnancy and oral contraceptive use. Majority of our patients had multiple sinus venous systems involvement, in which the two main venous sinuses systems affected were the transverse sinus (66.7%) and superior sagittal sinus (60%).

Ferro et al., reported that approximately 4% of CVST patients died in the acute phase, whereas the majority of CVST patients (75%) had a favourable outcome.[5] Large oedematous venous infarctions or parenchymal haemorrhages were the major causes of acute death in CSVT.[3,5] In our cohort of patients 73.3% had good recovery (GOS 5) with one mortality (6.7%).

Infective causes were responsible for 33.3% of CVST cases in our series. The causes of infection identified were sinusitis and middle ear infection. All of these patients were referred and reviewed by Ear, Neck and Throat (ENT) team. Elimination of the infective source was part of the treatment with initial empirical antibiotic therapy and subsequent selected antibiotics based on the culture and sensitivity results. Anti-epileptic medication was initiated in all our CVST patients who presented with seizure episodes, and there was no recurrence of seizure episodes in those patients. The anti-epileptic medication was discontinued about one-year after the initial presentation in these patients. We also gave prophylactic anti-epileptics for a duration of one week to patients with haemorrhagic infarction in recognition of the risk of anoxic damage if seizure occurred.

Anticoagulation therapy is the main treatment in CVST cases. The rationale for initiating anticoagulant in CVST patients is to promote recanalization and to prevent propagation of the venous thrombosis.[7] Patients in our centre were reviewed closely with frequent neurological, biochemical, and radiographic monitoring in Neuro High Dependency Unit when anticoagulation was initiated.

In the management of patients with haemorrhagic venous infarct, studies have shown that the use of either intravenous unfractionated heparin infusion or high-dose subcutaneous low-molecular-weight heparin (LMWH) is safe, with no new symptomatic intracerebral haemorrhages reported.[7,8] In addition, there was a 13% absolute reduction in the risk of death in the patients receiving anticoagulant therapy.[7,8] The "European Federation of Neurological Societies" (EFNS) guideline recommends the use of LMWH because it is easy to antagonize in situations such as the need for surgical intervention.[8] Besides, LMWH in therapeutic doses provides more steady anticoagulation and does not require dosage adjustment based on coagulation times. In our series, 73.3% of patients presented with intracranial haemorrhage. All except one was initiated with LMWH subcutaneous injection and continuous for six months. None of the patients developed any complication from the anticoagulation therapy or suffered from recurrence of CVST at the one-year follow-up. The only one patient who underwent surgical decompression due to rapid neurological deterioration, although anticoagulation therapy was initiated for him at post-operative day 14, the treatment was stopped at the 8th week following coagulopathy secondary to sepsis.

In view of a lack of expertise in endovascular intervention in our centre, surgical decompression will be the last modality

pursued here in the treatment of CVST patients. Surgical decompression is a life-saving procedure to reduce intracranial pressure in severe CVST cases, as in the condition of haemorrhagic infarction with significant mass effect.[5] It is believed that through surgical decompression, both cortical veins and collapsed veins may recirculate, reducing venous congestion and improving venous blood flow in collaterals.[5,6] This also creates favourable conditions for anticoagulant to reach the thrombosed venous side.[5,6] Ferro et al., reported that at least one third of their patients with severe neurological conditions such as coma, bilateral fixed pupils and bilateral lesions achieved good recovery following surgical decompression.[5] However, Sober et al., reported that craniectomy did not improve outcomes in comparison with the absence of craniectomy for patients with similar severity.[9] There was only one patient in our series who underwent decompressive craniectomy. The indication of surgery for this patient was cerebral oedema secondary to venous infarct with depressed conscious level. However, the patient died following sepsis with multi-organs failure.

Our study was limited as it was retrospective in nature and the mall sample size was small. However, study on this series of patients have given few points to be borne in mind when facing suspicious cases of CVST and thus further neuroimaging is required to confirm the diagnosis: young-middle age patients present with recent unusual headache (especially with neurological symptoms and raised intracranial pressure), with atypical CT evidence of cerebral infarct not within the common arterial territory (with or without haemorrhagic transformation)

CONCLUSION

The study on this series of patients demonstrated favourable outcome (GOS 4 and 5) in 93.3% of CVST patients. There was one mortality secondary to sepsis during hospitalisation. The presenting symptoms were mainly headache, focal neurology deficits, seizure and altered sensorium. Risk factors identified were oral contraceptive pills usage, chronic sinuses or ear infections, and obesity. Initial CT scan showed various findings and haemorrhagic infarct was one of the common findings. MRI and MRV revealed that majority of our patients had occlusion at two or more venous sinus sites. No patient had new or recurrent intracranial haemorrhage following initiation of anticoagulation therapy. Thus it is considerably safe to start CVST patients on anticoagulation including those cases with intracranial haemorrhage.

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CONFLICT OF INTEREST

All authors declare no competing conflict of interest.

REFERENCES

1. Filippidis A, Kapsalak E, Patramani G, Fountas KN. Cerebral venous sinus thrombosis: review of the demographics, pathophysiology, current diagnosis, and treatment. Neurosurg Focus 2009; 27(5): E3.
2. Cohen JE, Boitsova S and Itshayek E. Cerebral Venous Sinus Thrombosis. IMAJ 2009; 11: 685-8.
3. Alvis-Miranda HR, Castellar-Leones SM, Alcala-Cerra G, Moscote-Salazar LR. Cerebral sinus venous thrombosis. J Neurosci Rural Pract 2013; 4: 427-38.
4. Saposnik G, Barinagarrementeria F, Brown RD, Bushnell CD, Cucchiara B, Cushman M, et al. Diagnosis and management of cerebral venous thrombosis. Stroke 2011; 42: 1158-92.
5. Ferro JM, Crassard I, Coutinho JM, Canhao P, Barinagarrementeria F, Cucchiara B, et al. Decompressive surgery in cerebrovenous thrombosis: a multicenter registry and a systematic review of individual patient data. Stroke 2011; 42: 2825-31.
6. Vivakaran TTR, Srinivas D, Kulkarni GB, Somanna S. The role of decompressive craniectomy in cerebral venous sinus thrombosis. J Neurosurg 2012; 117: 738-44.
7. Coutinho JM, Bruijn SFTM, Veber G, Stam J. Anticoagulation for Cerebral Venous Sinus Thrombosis. Stroke 2012; 43: e41-2.
8. Einhaupl K, Stam J, Bousser MG, Bruijn SFTM, Ferro JM, Martinelli I and Masuhr F. EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients. Euro J Neurology 2010; 17: 1229-35.
9. Soyer B, Rusca M, Lukaszewicz AC, Crassard I, Guichard JP, Bresson D, Mateo J and Payen D. Outcome of a cohort of severe cerebral venous thrombosis in intensive care. AnnIntensive Care 2016; 6: 29-36.