Brief Communication

Clinical characteristics of cerebral venous sinus thrombosis

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ABSTRACT

Objectives: To investigate the risk factors, clinical presentation, neuroimaging features, treatment, and prognosis of patients with cerebral venous sinus thrombosis (CVST).

Methods: We retrospectively analyzed the data of 19 patients with a diagnosis of CVST admitted to Beijing Chao-Yang Hospital affiliated to Capital Medical University, Beijing, China between January 2010 and December 2013.

Results: There were 9 men and 10 women (age range: 27-75 years). Headache (84.2%) and focal signs (57.9%) were the 2 most common symptoms. Direct evidence of thrombosis was found on CT in 42.1%, and on MRI in 52.6%. Two or more sinuses were involved in 78.9% of cases, in which the transverse sinus plus sigmoid sinus were the most commonly involved combination. All patients received anticoagulant therapy. Most patients (84.2%) had no neurological sequelae at discharge, and only 3 patients (15.8%) recovered with sequelae.

Conclusion: Our study provides detailed information on the clinical manifestations, neuroimages, management, outcome, and risk factors of the patients with CVST.

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As an uncommon and frequently unrecognized type of stroke, cerebral venous sinus thrombosis (CVST) affects around 5 people per million annually, and accounts for less than 1% of all strokes.[1,2] Cerebral venous sinus thrombosis usually presents with a wide spectrum of clinical manifestations and various models of onset, which is predisposed to overlook or delay its diagnosis. Previous studies have also indicated that the outcome of patients with CVST may vary from complete recovery to permanent neurological deficits in the natural course of the disease.[3] Although CVST is a known entity, there remain difficulties in the diagnosis and management because the underlying risk factors are diverse and the standard treatment strategy is relatively lacking. The aim of the present study was to retrospectively analyze 19 cases with CVST and to provide clinical clues for its diagnosis and management.

Methods. The present study was based on a retrospective analysis of all the patients with the diagnosis of CVST admitted to Beijing Chao-Yang Hospital affiliated to Capital Medical University, Beijing, China between January 2010 and December 2013. The study protocol conformed to the institutional ethical committee requirements and the principles of the Helsinki Declaration. In our hospital, all paper versions of medical records are scanned into electronic versions after patient discharge and then stored. In addition, the names of disease categories for every patient are filed on computer. Thus, in the present study, we searched the lists of names for patients with CVST, and then studied the medical records. The diagnosis of CVST and associated parenchymal lesions had to be confirmed by CT, MRI combined with magnetic resonance venography (MRV), and/or cerebral angiography with digital subtraction angiography (DSA) following the established diagnostic criteria.[1,2] The following information in the medical records was extracted by the data extraction forms: demographic data, models of onset, potential risk factors, history of illnesses, clinical symptoms and signs, neuroimaging methods used, laboratory examinations, location and number of the thrombus, any parenchymal lesions, individual treatment strategy, and neurological function at discharge.

The statistical analysis was performed using the Statistical Package for Social Sciences version 12.0 (SPSS Inc., Chicago, IL, USA). Values were expressed as means ± standard deviation (SD) or as percentages. Means were compared by the Student's t-test, or one-way ANOVA test. The percentage was calculated in the presence and absence group by Pearson's Chi-square test. The limit of statistical significance was set at $p<0.05$.

Results. There were 9 men and 10 women with a mean age of 46.7 years (SD: 13.1, range: 27-75 years). As shown in the **Table 1**, 16 patients (84.2%) presented with headache, which was the isolated manifestation in 8 patients and associated with other focal deficits in the

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Table 1 - Presenting symptoms/signs and parenchymal lesions on CT/MRI scan in 19 patients with CVST.

Variable	n	(%)
Symptoms/signs		
Headache	16	(84.2)
Seizures	6	(31.6)
Generalized	2	(10.5)
Focal	4	(21.1)
Focal deficits	11	(57.9)
Motor	10	(52.6)
Sensitive	1	(5.3)
Altered consciousness	1	(5.3)
Parenchymal lesions on CT/MRI scan		
Normal	6	(31.6)
Non-hemorrhagic venous infarct	6	(31.6)
Hemorrhagic venous infarct	5	(26.3)
Intracerebral hemorrhage	2	(10.5)

CVST - cerebral venous sinus thrombosis

Table 2 - Sites of involvement in 19 patients with CVST.

Variable	n
One site	4
Superior sagittal sinus	2
Transverse	1
Sigmoid	1
Two sites	8
Superior sagittal + transverse	1
Transverse + sigmoid	7
Three or more sites	7
Superior sagittal + transverse + straight + sigmoid	1
Superior sagittal + transverse + deep veins	1
Superior sagittal + transverse + sigmoid	5
Total	**19**

CVST - cerebral venous sinus thrombosis

other 8 cases. There were focal motor or sensitive deficits in the remaining 3 patients without headache. In the clinical course, 3 patients demonstrated worsening of the presenting symptoms, and one patient developed additional symptoms. The models of onset of symptoms were also highly variable. It was acute (<48 hours) in 8 patients (42.1%), sub-acute (≥48 hours, <1 month) in 9 patients (47.4%), and chronic (≥1 month) in the remaining 2 patients (10.5%).

Table 3 - Risk factors in 19 patients with CVST.

Risk factors	n
Unknown	2
Thrombophilia	8
Hyperhomocysteinemia	4
Protein C deficiency	1
Protein S deficiency	3
Systemic disorders	4
Systemic lupus erythematosus	1
Thyroid disease	1
Kidney transplantation	1
Hepatic dysfunction	1
Tumor*	2
Infection	9
Central nervous system	1
Ear, sinus, mouth, face, and neck	8
Puerperium	2
Drugs	3
Oral contraceptives	1
Immunosuppressor	2

*Includes 2 gastrointestinal carcinomas
CVST - cerebral venous sinus thrombosis

Cranial CT and MRI scans were performed in all the 19 patients. The CT scan in 8 patents (42.1%) revealed signs suggestive of CVST (empty delta sign, dense sinus sign, or cord sign) while the MRI scan in 10 patients (52.6%) showed signs of CVST (the combination of absence of a flow void with alteration of signal intensity in the dural sinus). **Table 1** summarizes the neuroimaging characteristics of the parenchymal lesions on CT/MRI scan in 19 patients with CVST. An MRV scan was performed in 11 cases, and a DSA scan was performed in 8 cases. The results of the MRV and DSA scans demonstrated the involvement of different sinuses and veins in the patients with CVST (**Table 2**). The superior sagittal sinus was involved in 10 patients (52.6%), while the transverse sinus was involved in 16 (84.2%) patients, and the sigmoid sinus in 14 (73.7%) patients.

As far as treatment was concerned, most patients (12 cases, 63.2%) were anti-coagulated with subcutaneous low-molecular-weight heparin (LMWH) in therapeutic dosages followed by oral anticoagulants. A few patients received only subcutaneous LMWH in prophylactic dosage (6 cases, 31.6%) or oral anticoagulants (one case, 5.2%). During the treatment, subcutaneous LMWH treatment in prophylactic dosage was stopped in 2 patients developing significant expansion of the initial hematoma. One patient who demonstrated significant worsening of neurological function following treatment with subcutaneous LMWH in therapeutic dosages was treated with endovascular mechanical thrombectomy after repeated MRI indicated the fresh venous infarction. Additional treatments included antiepileptic drugs (6 cases, 31.6%) and osmotherapy (7 cases, 36.8%). Risk factors are listed in **Table 3**. Most patients (16 cases, 84.2%) had no neurological sequelae and were symptom-free at the time of discharge. Three of the patients (15.8%) recovered with sequelae.

Discussion. As shown in our study, headache was the most common symptom, and present in 84.2% of patients with CVST, which is consistent with the data from the International Study on Cerebral Venous and Dural Sinuses Thrombosis.[1] Generally, headache is indicative of intracranial hypertension resulting from impaired venous drainage in the patients with CVST. In addition to increased intracranial pressure, another important pathological mechanism in CVST is focal brain injury attributable to venous infarction or hemorrhage, which can lead to focal neurological deficits or seizure. Neurological signs and symptoms in patients with CVST are commonly related to the affected brain regions. Previous research has indicated headache may occur either alone or in combination with focal deficits.[4] Isolated headache without focal neurological deficits occurred in 8 patients (42.1%) in our study, which often presents a significant diagnostic challenge and delay in treatment in the clinical practice. In addition, one patient in our series showed altered level of consciousness due to involvement with the deep venous drainage system, and bilateral involvement of deep venous system has been indicated as a diagnostic clue for CVST.

Apart from the clinical presentation, the current diagnosis of CVST is mainly based on the neuroradiological findings. Empty delta sign, dense sinus sign, or cord signs on CT image and the combination of absence of a flow void with alteration of signal intensity in the dural sinus on MRI image are the suggestive signs of CVST.[5] The 2 most frequent sites of thrombosis in our study were the transverse (84.2%) and the sigmoid sinus (73.7%), which is compatible with previous reports.[6] Another remarkable feature of CVST is that thrombosis often affects several sinuses, and 78.9% of cases (15 out of 19 patients) in our study showed involvement of 2 or more sinuses. According to previous research, thrombosis in the transverse and sigmoid sinus has been strongly associated with the incidence of local infection such as otitis media,[6] which was present in 8 (42.1%) patients in the present study.

Evidence is emerging that initial anticoagulant therapy in CVST is beneficial in preventing thrombus growth and venous thromboembolism, facilitating recanalization, and improving outcome in patients with CVST.[1,7] However, there are controversies regarding the administration route and dosage of the anticoagulants because venous infarction with hemorrhagic transformation or intracranial hemorrhage (ICH) is commonly present in the course of CVST.[8] All patients with CVST in our study received anticoagulant therapy. Previous randomized controlled trials[3] demonstrated that anticoagulation with LMWH did not increase the risk of cerebral bleeding, even in patients with cerebral hemorrhage. Data from observational studies indicated a range of risks for ICH after anticoagulation for CVST from 0 to 5.4%.[2,4,8,9] There is a lack of evidence supporting hemorrhage enlargement or that fresh hemorrhage is associated with treatment with anticoagulant therapy, which is compatible with our results indicating that hemorrhage enlargement occurred in patients with LMWH treatment in a prophylactic dosage instead of in a therapeutic dosages.

In the present study, one patient (5.3%) developed significantly poorer neurological function. The reasons leading to a poorer clinical condition during LMWH treatment in therapeutic dosages may be persistent thrombosis,[10] which is supported by the repeated MRI scan showing fresh venous infarction. In recent years, there are increasing case reports and small case series showing that endovascular mechanical thrombectomy is beneficial for the patients with clinical deterioration despite use of anticoagulation or uncontrolled intracranial hypertension resistant to standard therapy.[11,12] Continued research is essential to better understand the role of aggressive intervention such as mechanical thrombectomy in the treatment of CVST.

Our data indicated there were 2 or more risk factors in 47.3% of patients with CVST, which is consistent with previous reports.[9] Therefore, the identification of

one risk factor should not stop the search for additional risk factors, in particular inherited or acquired thrombophilia. It is notable that the laboratory examination for inherited thrombophilia such as factor V Leiden positivity and prothrombin G20210A mutation is not carried out in our hospital, which is a limitation of the present study. Previous study has demonstrated that coma, cerebral hemorrhage, and malignancy are the important prognostic factors for death or dependence,[13] which agrees with our findings of cerebral hemorrhage in the 3 patients with neurological sequelae at discharge in our series. These findings remind us that we should pay close attention to the patients with poor prognostic factors.

In conclusion, our study provided details on the clinical manifestations, neuroradiological findings, management, outcome, and risk factors of the patients with CVST in our hospital.

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