A retrospective analysis of cerebral venous sinus thrombosis—a series of 25 cases

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Received: June 10, 2015
Published online: August 20, 2015

Objectives: To explore the character of Cerebral Venous Sinus Thrombosis (CVST), and to improve the early diagnosis and treatment of such a disease. Methods: Retrospective analysis of the patient ages, risk factors, clinical presentations, imaging characters and treatment of 25 CVST cases. Results: The most common age coverage of CVST attacks is from 18 to 45, the most common risk factors include female oral contraceptive (32%) and post-delivery or post-abortion (20%). The most common symptoms are headache (80%), followed by paralysis (44%) and seizure (40%). Neuroimaging shows that transverse sinus is the most commonly affected sinus, followed by superior sagittal sinus. Low molecular heparin is effective to CVST and the prognosis of most patients is good. Conclusion: The diagnosis of CVST should be considered in young patients with recent unusual headaches or with stroke-like symptoms, in patients with intracranial hypertension, and in patients with hemorrhagic infarcts. To make a correct diagnosis and to treat the patients in time, Enhanced MRI+MRV or Enhanced CT+CTV should be performed immediately, and if necessary, digital subtraction angiography (DSA) should be performed.

Keywords: cerebral venous sinus thrombosis; magnetic resonance imaging; Computed Tomography; DSA; low molecular heparin


Introduction

Cerebral venous sinus thrombosis (CVST) is an unusual ischemic cerebrovascular disease, being able to appear on any age of people including new-born babies, and accounting for approximately 0.5% of all strokes [1]. However, the clinical presentation of CVST is nonspecific, and thus is easy to misdiagnose. The death rate could reach to 30% if the patient were not diagnosed and treated in time [2]. In this study, we analyzed 25 cases from clinical presentations, diagnose and treatment of CVST.

1. Clinical Documents

1.1 Introduction

25 in-patients at the First Affiliated Hospital of Chongqing Medical University and the First People’s Hospital of Jiangbei District of Chongqing from March 2009 to December 2014, with 16 females and 9 males. Their ages are from 11 to 53, with an average of 33.8. 20 Patients age from 18 to 45, accounting for 80% of the cases. 12 cases are acute onset (within 1 week), 10 are sub-acute onset (1 week-1 month), and 2 are chronic onset (over 1 month).

1.2 Risk factors
Among the 25 patients, 8 females had oral contraceptive, accounting for 32%; 2 patients had delivery and 3 patients had abortion, accounting for 20%; 1 patient had systemic lupus erythematosus and 1 patient had Behcet’s disease, accounting for 8%; 2 patients had brain trauma, accounting for 8%; 1 patient had otitis media, accounting for 4%; 1 patient had lung cancer, accounting for 4%; there were no obvious risk factors in the rest 6 cases, accounting for 24%.

1.3 Clinical presentations and signs

Among the 25 patients, 20 patients had headache (80%); 14 patients had paralysis (56%) among which 1 had one side lower limb paralysis and appeared the other side lower limb paralysis with numbness 2 days later; 10 patients had seizure (40%) among which 4 were generalized tonic clonic seizure, 5 patients were simple exercise and 1 was epileptic state; 5 patients had hypopnia; 2 patients had aphasia and 2 coma; 1 patient had lethargy; 1 patient had delirium and mental symptom; 1 patient had tinnitus. Physical examination demonstrated that 10 had papilloedema (40%), 7 had abducens Nerve Palsy (28%), 6 patients had signs of meningeal irritation (24%), 2 patients had ataxia, 2 patients had Horner sign, and 1 patient had Romberg’s sign.

1.4 Imaging examination

All the patients had MRI+MRV or/and CT+CTV scan, with 1 patient having digital subtraction angiography (DSA). 16 patients had enhanced MRI+MRV. MRI showed 6 cases of all the patients had point or slice hemorrhagic infarction and extensive cerebral edema. MRI found thrombus in cerebral venous sinus in 7 cases (Figure 1A). Enhanced MRI uncovered 12 cases of corresponding venous or venous sinus filling defects (figure 1B). MRV discovered 16 cases of poor or no visualization of venous sinus at affected venous sinus (figure 1C).

Among the 12 cases with enhanced CT+CTV, 6 were discovered indirect signs including venous cerebral infarction (with 2 having hemorrhagic infarct, see figure 2A), thrombosis venous sinus peripheral venous dilatation (see figure 2B), smaller ventricle, and extensive cerebral edema. 4 were discovered direct signs including cord sign (see figure 2C), high density triangle sign, Delta sign, and empty triangle sign. All the 12 cases with CTV were discovered cerebral venous sinus thrombosis (figures 2D, 2E, 2F), demonstrated as no visualization and filling defects of corresponding venous or venous sinus.

Three patients had MRV followed by CTV and results are generally the same. 1 had no focal neurologic signs due to headache. This patient had had DSA when earlier diagnosis was uncertain before coming to the current hospital and results had not shown obvious abnormality in intracranial arterial phase. Since CVST had probably not been considered, there were no documents of DSA venous phase for this patient.

Among the 25 patients, 16 patients involved more than 2 venous sinuses simultaneously, 20 patients involved transverse sinus, 14 patients involved superior sagittal sinus, 5 patients involved sinuses sigoideus, 3 patients involved straight sinus, and 2 patients involved vena jugularis interna, demonstrating that the most easily involved by thrombosis is transverse sinus.

1.5 Laboratory Examination

1.5.1 Lumbar puncture (LP) and cerebrospinal fluid (CSF) examinations
All the 25 patients had more than one time LP examinations, 22 had intracranial hypertension (88%), with 7 initial pressure of 200-300 mmH2O, 15 of 300 mmH2O. 3 had normal intracranial pressure. 22 had normal number of white blood cell (WBC) in CSF (88%), 3 had increased number of WBC in CSF (12%), all less than 100×10\(^6\)/L. 20 had normal protein content in CSF(80%), 5 had increased CSF protein (20 %), all less than 1.0 g / L.

1.5.2 D2 Dimer

All the 25 patients had D2 Dimer detection, 15 had increased D2 Dimer (60%), 10 had normal results (40%).

1.6 Treatment and Outcome

All the 25 patients were treated with low molecular weight heparin. Patients with intracranial hypertension were treated with mannitol and/or furosemide in order to decrease intracranial pressure. 1 patient with severe cerebral edema was treated with decompressive craniectomy. Patients with epileptic seizures got antiepileptic treatment. After the treatment, 2 patients died and 23 patients were improved, 20 of which could take care of themselves (86.96%). Among the 23 improved patients, 22 patients insisted on oral warfarin after discharged from hospital for over 3 months, and 1 patient with Behcet's disease has insisted on oral warfarin till present. The death of 2 patients was both due to hemorrhagic infarction and severe cerebral edema resulting in conscious disturbance and foramen magnum herniation.

2. Discussion

CVST may have bad outcomes without timely diagnosis and correct treatment. Early diagnosis and early treatment can improve the outcome obviously. Consequently, it is necessary to know well about the diagnosis and treatment of CVST.

2.1 Causes and Risk Factors

According to literatures, causes can be found out in 80% of CVST patients, the rest with unknown causes may be related to genetic factors. The known causes can be divided
2.2 Clinical Characters

Headache is the most common clinical presentation. Literatures reported that around 75% of CVST patients have headaches [3]. This is similar to our study (80%). However, headache is nonspecific, and some patients present severe thunderclap headache similar to that of subarachnoid hemorrhage [6]. Some patients have presentations of intracranial hypertension: dizziness, nausea, vomiting, and papilloedema. Such presentations make it easy to confuse CVST with idiopathic intracranial hypertension. Lin et al. [7] analyzed 106 cases which had been diagnosed as idiopathic intracranial hypertension. About 20% of patients may not be found out clear causes of this disease, although lots of examinations have been performed.

### Table 1. Clinical Presentations of 25 CVST Patients

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>n</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>headache</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>paralysis</td>
<td>14</td>
<td>56</td>
</tr>
<tr>
<td>seizure</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>hypoplasia</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>aphasia</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>coma</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>lethargy</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>delirium</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>tinnitus</td>
<td>1</td>
<td>4</td>
</tr>
</tbody>
</table>

It has been reported that over 50% of CVST patients have seizures [8]. The percentage in our cases is 40%, relatively low. 64% of our cases presented focal neurological dysfunctions such as paralysis, sensory disturbance, aphasia and visual-field defect. Some patients presented papilloedema, ataxia, and thus a thorough examination of the neurological system is very important. The death rate of patients with conscious disturbance (lethargy or coma) is high. Conscious disturbance is indicator for poor prognosis [9].

2.3 Laboratory examination

All the patients in our cases had lumbar puncture, and about 88% (22/25) had intracranial hypertension. Increasing of WBC and protein in CSF was uncommon.

Since literatures reported the application of D2 dimer to evaluate the risk of CVST [10-12], all of our cases had D2 dimer examination. Results revealed that 60% of the cases had increased D2 dimer while 40% were normal. Consequently, we believe that D2 dimer may not be significant for CVST diagnosis. Nevertheless, the number of our cases is small, and thus further studies with more cases need be performed to confirm the conclusion.

2.4 Neuroimaging

Generally, CT scan is the first neuroimaging for CVST because it is simple and quick. CT scan can provide direct and indirect signs of CVST. Direct signs include belt sign, high density triangle sign, Delta sign and empty triangle sign, with high specificity but low positive rate. Indirect signs include venous cerebral infarction, cerebral perforating vein dilation, ventricle becoming small, abnormal enhancement of falx cerebri and tentorium cerebelli, and non-enforced alba low density etc. [13]. CT scan in 83.3% of our cases demonstrated direct and/or indirect signs of CVST, while literatures reported that CT scan results may be normal for 25% of CVST patients [14].

Presently, MRI+MRV are recommended as the optimal way to diagnose CVST. The manifestations of MRI vary during various periods of CVST. During the acute phase (within 1 week after onset), the flowing void in venous sinus disappears. Equisignal is showed primarily on T1W1 and high signal is also showed. Low signal is showed primarily on T2W1 and sometimes equisignal is manifested. In some cases, the blood flowing void signal in venous sinus can be difficult discerned from the normal status. Under this circumstance, blood flow deficiency in venous sinus can be showed by MRV results, and thus false negative results of MRI can be eliminated. During the subacute phase (1 week to 2 weeks after onset), high signal is showed on both T1W1 and T2W1. During the chronic phase (over 3 weeks after onset), thrombosis signal is generally weaker than that of subacute phase, and becomes uneven, but high signal is still manifested primarily on T1W1 and T2W1 [15].

Enhanced CT and CTV: Khandelwal et al. [14, 16] compared CTV with MRV, taking MRV as standard, and uncovered that the sensitivity and specificity of CVST diagnosis by CTV can also achieve 75%-100%. Accordingly, some of our cases were detected by CTV for cerebral vein and also got
correct diagnosis. Thus, CTV provides important way of diagnosis for patients who cannot have MRI (e.g. after intravascular stent implantation).

2.5 Treatment

2.5.1 Anticoagulant therapy

CVST patients without contraindications should be treated with low molecular weight heparin or heparin. Compared with intravenous heparin to treat CVST, subcutaneous injection of low molecular weight heparin has less hemorrhagic complications. For those with intracranial hemorrhagic lesions showed by CT scan results and such intracranial hemorrhage is not contraindication of using heparin, it is only needed to adjust the dose of low molecular weight heparin according to body weight and hematology monitoring is not needed [17, 18]. As a result, we used low molecular weight heparin to treat all the 25 patients, 2 severe patients died and the rest had good prognosis, proving the effectiveness of low molecular weight heparin therapy. Oral anticoagulant should continue after the termination of heparin anticoagulant therapy. It is believed so far that such treatment should last for 3-6 months. If the patient is subject to high risk of recurrence, such treatment should continue until the risk of recurrence disappears. Long-term anticoagulation should be considered for those with thrombophilias.

2.5.2 Thrombolytic therapy

With the development of neural interventional technique, some neurologists advocate local drug thrombolysis adopting catheter intervention venous sinus thrombosis. Stent implantation in venous sinus particularly superior sagittal sinus can be applied to patients with severe side effects of thrombolysis. Neurologists should attempt such therapy when technique conditions exist in the future.

2.5.3 Symptomatic treatment

Symptomatic treatment includes antiepileptic, dehydration, intracranial decompression, anti-infection, dilatation and supportive symptomatic treatment.

Conclusion

CVST is a rare clinical disease, its possibility of occurrence should be considered under 1 of the following 3 circumstances: (1) Young and middle aged patients without common risk factors of cerebrovascular disease recently have unusual headaches or stroke-like symptoms; (2) Patients with intracranial hypertension; (3) Patients with CT scan showing cerebral hemorrhagic infarction particularly multiple cerebral infarction and lesions not limited to arterial region. Under these circumstances, corresponding neuroimaging examinations (MRI+MRV ; CT+CTV ; DSA) should be performed timely to ensure diagnosis. Low molecular weight heparin anticoagulation is effective treatment of CVST. Patients diagnosed as CVST should be treated with low molecular weight heparin as early as possible, in order to improve prognosis.

References

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