

## Cerebral venous sinus thrombosis presentation in emergency department in Van, Turkey

Sevdegül Karadas,<sup>1</sup> Aysel Milanlioglu,<sup>2</sup> Hayriye Gönüllü,<sup>3</sup> Refah Sayin,<sup>4</sup> Mehmet Nuri Aydın<sup>5</sup>

### Abstract

**Objective:** To examine the distribution of age, gender, time between onset and presentation, clinical findings, predisposing factors, platelet distribution width, mean platelet volume values and neuroimaging findings, together with the treatment regime and the outcome for patients of cerebral venous sinus thrombosis.

**Methods:** The retrospective, descriptive cross-sectional study was conducted at Yuzuncu Yil University, Medical Faculty Hospital in Van, Turkey, comprising 51 cases diagnosed with cerebral venous sinus thrombosis between January 2008 and September 2011. The diagnosis was based on the results of clinical evaluation, cranial magnetic resonance imaging and venography. SPSS 16 was used for statistical analysis.

**Results:** Overall, 43 (84.3%) of the cases were female, and 8 (15.7%) were male. The average age was 32±11.13 years. The most frequent symptom was headache in 41 (80.4%) cases. The postpartum period was one of the most observed predisposing factors in 17 (33.3%) patients. The magnetic resonance imaging was normal in 35 (68.6%) cases, but in all of the cases, magnetic resonance venography was abnormal. Topographically, the most frequent involvement was transverse sinus in 40 (78.4%) cases. Besides, 50 (98%) patients were discharged following full recovery or mild sequela and only 1 (2%) case had severe sequela.

**Conclusion:** Patients presenting with headache should be examined carefully in the emergency department. Early diagnosis and treatment with clinical and neuroimaging techniques for such patients is recommended.

**Keywords:** Cerebral venous sinus thrombosis, Transverse sinus, Headache, Prognosis. (JPMA 64: 370; 2014)

### Introduction

In comparison with arterial stroke, cerebral venous sinus thrombosis (CVST) is rarely seen and is usually observed in those of younger age.<sup>1</sup> It accounts for approximately 1-2% of all strokes though its actual incidence is unknown.<sup>2,3</sup> Daif and et al., noticed the frequency of CVST as 9 in 100,000 patients who were treated in hospital.<sup>4</sup> A number of cases have been reported from European and Asian countries.<sup>1,4-6</sup>

Predisposing factors include pregnancy, puerperium, use of oral contraception (OCC), coagulopathies, intracranial infections, cranial tumours, penetrant head traumas, lumbar puncture, malignancy, dehydration, inflammatory bowel disease, connective tissue diseases, Behcet's disease, sarcoidosis, nephrotic syndrome, parenteral infusions and various medicines.<sup>7</sup> Kamisli et al., found a relationship between the mean platelet volume (MPV) and platelet distribution width (PDW), and the severity of the disease.<sup>8</sup>

Ferro et al., stated that their multicentre prospective series

study on cerebral vein and dural sinus thrombosis was the start of gaining reliable evidence on demographical features and prognostic factors of patients with CVST.<sup>1</sup> In the current study records of patients with various neurological problems who had presented to the emergency department (ED) and were diagnosed with CVST and were evaluated by using different parameters such as distribution of age and gender, time between onset and presentation, clinical findings, predisposing factors, MPV and PDW values, neuroimaging findings and their treatment regime were reviewed.

### Patients and Methods

The retrospective study was conducted at Yuzuncu Yil University, Medical Faculty Hospital in Van, Turkey, and comprised patient data from January 2008 to September 2011. The approval of the institutional Ethics Committee was obtained. The data related to patients diagnosed with CVST and admitted to ED. CVST was diagnosed after magnetic resonance imaging (MRI) and magnetic resonance venography (MRV).

The demographic, etiologic, radiological and prognostic characteristics of the patients were evaluated. The demographic features, clinical symptoms during the application, the time elapsed before diagnosis, predisposing factors, MPV and PDW values, neuroimaging

<sup>1,3</sup>Department of Emergency Medicine, <sup>2,4,5</sup>Department of Neurology, Yuzuncu Yil University, Faculty of Medicine, Van, Turkey.

**Correspondence:** Refah Sayin. Email: refahsayin@yahoo.com.tr

findings, treatment regime and the outcome after treatment were evaluated.

The diagnosis of CVST was based on the clinical evaluation, cranial MRI and venography. The patient's medical history and medication usage were determined and all the patients had undergone physical and neurological examinations.

Routine haematological and biochemical tests were administered to all the patients. The values of the platelet (PLT) and MPV counts were obtained within the first 24 hours after presenting to ED. From the hospital laboratory, the normal values were as follows: MPV: 6.0 to 10.0 fL; PLT:150,000 to 400,000 m/L. We compared the values of PLT\MPV and the time elapsed from the onset of symptoms to diagnosis. The CVST diagnosis was labelled as sub-acute, acute and chronic. This diagnosis was combined with the time elapsed between onset of symptoms and diagnosis.

Statistical analysis was performed using SPSS 16.0.

Descriptive statistics were presented as mean  $\pm$  standard deviation for the continuous variables, and minimum and maximum values, while categorical variables were given as a frequencies and percentages. Chi-square test was used in order to determine the relation between the groups and categorical variables, and  $p \leq 0.05$  was taken to be significant.

## Results

Of the total 51 patients in the study, 43 (84.3%) were women, while 8 (15.7%) were men. The overall mean age was  $32 \pm 11.13$  years (range: 17-70 years). In terms of sub-grouping, 41 (80.4%) patients were in the sub-acute phase (48 hours-30 days); 6 (11.8%) were in the acute phase (<48 hours) and 4 (7.8%) were in the chronic phase (>30days). Headache was observed in 41 (80.4%), epileptic seizure in 10 (19.6%), impaired consciousness in 3 (5.9%), weakness and/or numbness in 7 (13.7%) cases.

The ratios were determined according to the neurological examination findings (Table-1). Taking the admission time into consideration, the most frequent presentation was

**Table-1:** Distribution of patients according to neurological symptoms.

Symptoms	n	%
Papilloedema	12	23.5
Hemiparesis-hemihypoesthesia	12	23.5
Others (aphasia, dysmetria, disdiadokokinesia, ataxia, etc.)	10	19.6
Cranial nerve palsy	2	3.9
Normal	15	29.5

**Table-2:** Distribution of patients according to the predisposing factors.

Predisposing factors	n	%	p value
Idiopathic	20	39.2	$p < 0.05$
Postpartum period	17	33.3	$p < 0.05$
Pregnancy	8	15.7	$p < 0.05$
Use of oral contraceptives	3	5.9	$p < 0.05$
Protein C-S deficiency	2	3.9	$p < 0.05$
Homocysteinaemia	1	2	$p < 0.05$
Total	51	100	

**Table-3:** Distribution of patients according to the number of affected dural sinus.

Number of the affected dural sinus	n	%	p value
A single dural sinus	25	49	$p > 0.05$
Two dural sinuses	19	37.3	$p > 0.05$
Three or more dural sinuses	7	13.7	$p > 0.05$

seen in spring 29 (56.8%) was followed by winter 13 (25.5%), summer 6 (11.8%) and fall 2 (5.9%).

Predisposing factors causing CVST were noted separately (Table-2). When these factors were compared, the difference between them was statistically significant ( $p < 0.05$ ).

In the examination of the cranial MRI, brain parenchyma of 35 (68.6%) cases was normal, while a venous infarct was detected in 11 (21.5%), haematoma in 3 (5.9%), cerebral oedema in 1 (2%), and a subdural haemorrhage in 1 (2%) case.

The dispersion of the number of dural sinus thrombosis was also noted (Table-3). In MRV, superior sagittal sinus was observed in 31 (60.8%) patients, transverse sinus in 40 (78.4%), sigmoid sinus in 16 (31.4%) patients, and cavernous sinus involvement in 1 (2%). Statistically, there was no difference in the location of thrombosis ( $p > 0.05$ ).

The mean values of PLT and MPV were found to be  $261.261 \pm 84.243$  mL and  $7.96 \pm 0.894$  fL, respectively. There were no significant differences between PLT\MPV values and among the 3 subgroups based on the time elapsed between the onset of symptoms and the time of diagnosis ( $p = 0.45$  and  $p = 0.14$ , respectively).

Low molecular weight heparin treatment was started in all the cases in the acute state. Besides, 36 (70.6%) cases were discharged having been prescribed an oral anticoagulant, 13 (25.5%) with low molecular weight heparin, and 2 (3.9%) were discharged with low molecular weight heparin and acetyl salicylic acid.

After treatment, 1 (2%) case was discharged with severe sequela, and others were discharged with mild sequela or without sequela. None of the patients in our study died.

## Discussion

CVST is a rare but serious neurological disease and usually affects younger adults, especially women of childbearing age. However, individuals from different age groups can be affected.<sup>7,9,10</sup>

The ISCVT (International Study on Cerebral Vein and Dural Sinus Thrombosis) was a multinational, multicentre, prospective study with 624 patients with a mean age of 37.<sup>1</sup> Similarly, in another prospective trial, the average age was 37 years.<sup>5</sup> In our study, it was found that the disease mostly affected the younger age group and the average age was 32 years.

CVST can present with a number of clinical symptoms ranging from only headache to coma.<sup>2,9</sup> The recorded symptoms of CVST are; headaches, increased intracranial pressure, seizures, aphasia, haemianopia, nystagmus, diplopia, focal neurological deficits such as sensory loss and hemiparesis, cranial nerve palsies, and changes in consciousness that can change from confusion to progressive coma.<sup>11</sup> Headache was the most frequent symptom in patients with CVST.<sup>1</sup> This symptom may be in acute, subacute, or chronic phase and can be in combination with other neurological complaints and findings. In two studies, headache was reported as the most frequent symptom (88.8%; 95%) in patients with CVT.<sup>1,5</sup> Similarly, the most frequently observed finding in our study was headache (80.4%). There was papilloedema in 23.5% of the cases, focal neurological findings like hemiparesis and/or hemihypoesthesia in 23.5%, and epileptic seizure in 19.6% of the cases. In the literature, while papilloedema was observed between 27-89%, focal or generalised seizures were observed between 35-40%, and this ratio increased in puerperium. The level of consciousness and focal neurological findings were seen in approximately one-third of the cases.<sup>12,13</sup> It was found that headache and papilloedema symptoms of our cases diagnosed with CVST were similar to the examples in the literature. However, seizure and changes in consciousness were rarely seen in our patient group. Although CVST has wide range of symptoms, but for most of the cases it should be noted that diagnosis can only be made with neuroimaging methods conducted after the clinician suspects that there is a more serious cause for the patient's symptom(s).

The seasonal variation in the occurrence of CVST has not been well investigated. Although the existing evidence is still controversial, but it is known that cardiovascular and

cerebrovascular events exhibit seasonal or monthly variations. Of the few studies related to seasonal variation,<sup>1,6,14</sup> Janghorbani et al., proved that cerebral vein and dural sinus thrombosis show seasonal variations and are seen most frequently in autumn and least frequently in summer.<sup>6</sup> Ferro et al. stated that prevalence of CVST increased in autumn and winter.<sup>1</sup> Slotz et al. reported that incidence of CVST rose in the summer and winter seasons.<sup>14</sup> In our study the cases were most frequently seen in the spring, and least frequently in the autumn. Therefore, our results differed from those in the literature.

In a study by de Bruijn et al., 84.7% cases were female.<sup>5</sup> In another study, the female percentage was 74.5%.<sup>1</sup> In a study conducted in Iran in 2008, the female/male ratio was 3.9.<sup>6</sup> Pregnancy and puerperium, the use of OCC, coagulation disorders, haematological diseases, systemic inflammatory diseases, infections, malignancy, severe dehydration, heart disease and trauma are shown to be among the predisposing factors. Despite this variety, any predisposing factor can be detected in 5-20% of the cases.<sup>15</sup> In the ISCVT study, Ferro et al., found that the genetic and acquired thrombophilia was the most frequent predisposing factor in CVST.<sup>1</sup>

De Bruijn et al. reported an increased risk of sinus thrombosis in women using OCCs.<sup>16</sup>

Terazzi et al. reported that OCC was the most frequent (47%) predisposing factor in CVST.<sup>17</sup> On the other hand, Nagara et al., emphasised the importance of postpartum period in CVST etiology.<sup>18</sup> In a prospective series of 59 patients with CVST, seven of the 50 (14%) female patients were in the puerperium and 35 (70%) were using OCCs.<sup>5</sup> In our study, compatible with the literature, 84.3% of the cases were female and it was detected that 33.3% of the patients were in the postpartum period, 15.7% were pregnant, and 5.9% were using OCCs. The fact that our results concerning predisposing factors are different from the literature can be explained by the lack of family planning practice in our region and high birth rates.

In our study, it was observed that the symptoms of 80.4% of the patients were subacute, for 11.76% they were acute, and 7.84% were in the chronic phase. The fact that our hospital is level 3, and neurologic deficit or its absence is among the reasons why most of the patients were in the subacute phase. This result differed from those of Terazzi et al., who stated that acute commencement was more frequent.<sup>17</sup> The health insurance features of patients with CVST admitted to our hospital were as follows: 2% had no insurance; 15.7% had full state medical insurance; and 82.3% had limited state medical insurance. The patients having limited insurance were not directly admitted to

our university hospital and were sent from a grade 2 hospital. For this reason most of these patients were diagnosed to be in a subacute or chronic state.

In the present study, transverse sinus thrombosis was observed most frequently with isolated and other sinus involvements. Superior sagittal was the second most frequent, while sigmoid was in the third place. Cavernous was the least frequently observed. These ratios differ from those of Terazzi et al., who found superior sinus involvement to be the most frequently seen thrombosis.<sup>17</sup>

MPV is a parameter widely used to measure the platelet volume.<sup>19</sup> It is able to efficiently estimate the activation of coagulation. Large platelets are both metabolically and enzymatically more active than small platelets and also produce more thromboxane A<sub>2</sub> and beta thromboglobulin that has prothrombotic features, including increased platelet activation, aggregation and adhesion molecule expression.<sup>20,21</sup>

In a literature search for venous vascular disorders, we found a few reports about MPV and venous thrombosis.<sup>8</sup> In a study, an increased MPV was identified as a predictor of venous thromboembolism such as deep vein thrombosis (DVT) and pulmonary embolism (PE). Kamisli et al. demonstrated that increased MPV and PDW were associated with brain lesions and severe neurological abnormalities in the acute phase of CVST.<sup>8</sup> However, the results obtained in the current study were not compatible with the results of Kamisli et al., because we found no association between the two parameters, and the phase of CVST.

Despite improvements in the recognition of CVST in recent years, diagnosis and treatment still may be difficult because of the variety of underlying risk factors and the number of different treatment methods.<sup>15</sup> Generally, treatment of CVST has included anticoagulation with heparin, and stabilising the patient's condition and preventing or reversing cerebral herniation.<sup>22</sup> However, some authors have emphasised the importance of thrombolytic therapy in CVST,<sup>23,24</sup> showing that thrombolysis was both safe and effective in comparison with anticoagulation with heparin.<sup>25</sup> Another study showed that anticoagulant treatment with low molecular-weight heparin for CVST was insufficient.<sup>26</sup> However, there is still no consensus regarding the efficiency and reliability of chemical thrombolysis and thrombectomy in the treatment of the disease. Tsai et al. applied chemical and mechanical thrombolytic treatment to 25 patients that had worsening haemorrhage and oedema despite heparin treatment.<sup>27</sup> On the other hand, Stam et al. stated that endovascular treatment can be beneficial although it

increases the risk of cerebral bleeding in patients with other serious diseases.<sup>28</sup> CVST is a clinical scheme in which mortality and morbidity may be very high if the condition is not diagnosed early and treated appropriately. In recently performed studies, mortality is reported to be between 6-10% in spite of the treatment.<sup>29</sup> Ferro et al. reported that the mortality rate was 3.4% over a period of 30-days.<sup>1</sup> In our study, the low molecular weight treatment was started for all patients in the acute phase, and no complications in connection with the treatment developed in any of the cases, and no patient died. Our results indicate that CVST is a disease which has a good prognosis.

CVST diagnosis has to be considered in young women who have a history of refractory headache not responding to analgesics, intracranial hypertension syndrome, focal neurologic deficit, sudden onset of seizure, being postpartum with changes in consciousness, pregnancy and the use of OCC. It should be noted that its prognosis is usually good in patients diagnosed with appropriate neuroimaging methods, treated with heparin in the acute phase and given anticoagulant in the follow-up period.

One of the limitations of the present study was its small sample size. A larger study might provide more accurate and reliable results. In order to obtain a larger sample, a multicentre approach might be used. Another limitation of our study is that our grade 3 university hospital has no obligation to admit 82.3% of patients owing to them having limited health insurance.

## Conclusion

Headache is one of the most frequent symptoms seen in CVST. Therefore, each patient presenting to ED with a headache should be carefully examined and this should be undertaken in cooperation with the medical staff from relevant departments. This multidisciplinary approach will ensure appropriate diagnosis and treatment for potential CVST cases.

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