

## Cerebral venous and sinus thrombosis in adult patient – Case report

### *Tromboza vena i venskih sinusa mozga – Prikaz slučaja*

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#### Summary

Cerebral venous and sinus thrombosis (CVST) is a rare type of cerebrovascular disease which accounts for <1% of all strokes. It can occur at any age and is characterized by thrombus within the cerebral venous and sinus system. The paper reviews the case of a 73-year-old woman hospitalized after the onset of severe headache, dizziness, nausea, vomiting and right-sided hemiparesis 4/5 degree. The suggestive signs of cerebral venous and sinus thrombosis (CVST) were hyperdense signal and empty delta sign on computed tomography (CT) image and the combination of the absence of a flow void with alternation of signal intensity in the dural sinus on magnetic resonance imaging (MRI). Except for the elevated D-dimer values, other laboratory findings were within reference range. Genetic disorders, acquired coagulation disorders and malignancies were excluded. The patient was treated with body weight-adjusted subcutaneous low-molecular-weight heparin (LMWH) with a good clinical response – disappearance of signs and symptoms and the absence of complications. She took oral anticoagulant therapy after the acute phase of the disease.

**Key words:** cerebral venous sinus thrombosis, headache, computed tomography, magnetic resonance imaging, anticoagulants

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#### Sažetak

Tromboza moždanih vena i venskih sinusa rijedak je oblik cerebrovaskularne bolesti koja čini <1% svih moždanih udara, a može se pojaviti u bilo kojoj dobi. Karakterizirana je stvaranjem tromba unutar vena i duralnih sinusa mozga. U radu je prikazan slučaj 73-godišnje bolesnice hospitalizirane nakon glavobolje jakog intenziteta, vrtoglavice, mučnine, povraćanja i kljenuti desnih udova 4/5 stupnja. Hiperdenzitet i „prazan delta znak“ na kompjutoriziranoj tomografiji (CT) mozga, te kombinacija odsutnosti protoka s promjenom intenziteta signala u duralnim sinusima na magnetskoj rezonanciji (MR) bili su znaci tromboze moždanih vena i sinusa. Osim povišenih vrijednosti D-dimera, ostali laboratorijski nalazi bili su unutar referentnih vrijednosti. Dodatnom obradom isključeni su genetski i stečeni poremećaji koagulacije, a rezultati laboratorijske i radiološke obrade u svrhu otkrivanja maligne bolesti bili su negativni. Bolesnica je liječena potkožnom primjenom niskomolekularnog heparina, nakon čega je došlo do nestanka simptoma i znakova bolesti. Tijek bolesti protekao je bez komplikacija. Nakon akutne faze bolesti nastavljena je oralna antikoagulantna terapija.

**Ključne riječi:** tromboza vena i venskih sinusa mozga, glavobolja, kompjutorizirana tomografija, magnetska rezonancija, antikoagulantna terapija

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## Introduction

Cerebral venous and sinus thrombosis (CVST) is a relatively rare cause and atypical form of cerebral stroke which accounts for < 1% of all strokes. It is characterized by thrombus within the cerebral venous and sinus system.<sup>1,2</sup> Cerebral venous and sinus thrombosis (CVST) can occur at any age, including the neonatal period. This type of cerebrovascular disease is more frequent in young adults. The incidence is 3-4 cases per 2 million per year in adult population, and 0.67 cases per 100 000 children below 18 years.<sup>2,3,4</sup> The predisposing factors include the use of oral contraceptives (OCC), pregnancy, childbirth, congenital and acquired coagulation disorders, neoplastic processes, cardiac defects, systemic diseases of the connective tissue, Behçet's disease, injuries, surgical procedures, inflammatory disease of the head and neck region, nephrotic syndrome, diarrhoea, dehydration, shock.<sup>2,5,6,7</sup> Risk factors cannot be identified in about 15% of the cases.<sup>5,8</sup> CVST are associated with accelerated coagulation and increased blood density, and occurs following endothelial damage and decelerated blood flow occur.<sup>2</sup>

Diagnosis is still frequently overlooked or delayed due to the wide spectrum of clinical symptoms and presentation. The clinical symptoms of CVST are non-specific, such as headache, symptoms associated with increased intracranial pressure without hydrocephalus, focal symptoms, epileptic seizures and consciousness disorders.<sup>1</sup> Headache is the most frequent symptom and occurs in about 90% of all the cases. Increased intracranial pressure occurs in almost 20-40% of CVST cases, focal and generalised seizures in 40% of the cases and focal neurological signs in 40-60% of the cases. Stupor or coma is found in 15-19% of patients at hospital admission and is usually seen in cases with extensive thrombosis.<sup>5</sup>

The diagnosis is based on neuroimaging – computed tomography (CT), magnetic resonance imaging (MRI), computed tomography angiography (CTA), magnetic resonance angiography (MRA), digital subtraction angiography (DSA), magnetic resonance venography (MRV). Computed tomography angiography (CTA) and magnetic resonance angiography (MRA) enable the characterisation of the blood flow in the pathologically affected vessels. Magnetic resonance imaging (MRI) provides better visualisation of the lesions than computed tomography (CT).<sup>9</sup> CTA or MRI is recommended for thrombosis detection, and CT can detect thrombosis in about 60% of the cases. MRI combined with MRA is especially sensitive.<sup>9</sup> In ambiguous cases, digital subtraction angiography (DSA) may be used for diagnosis.<sup>9,10</sup> MRI and MRV are

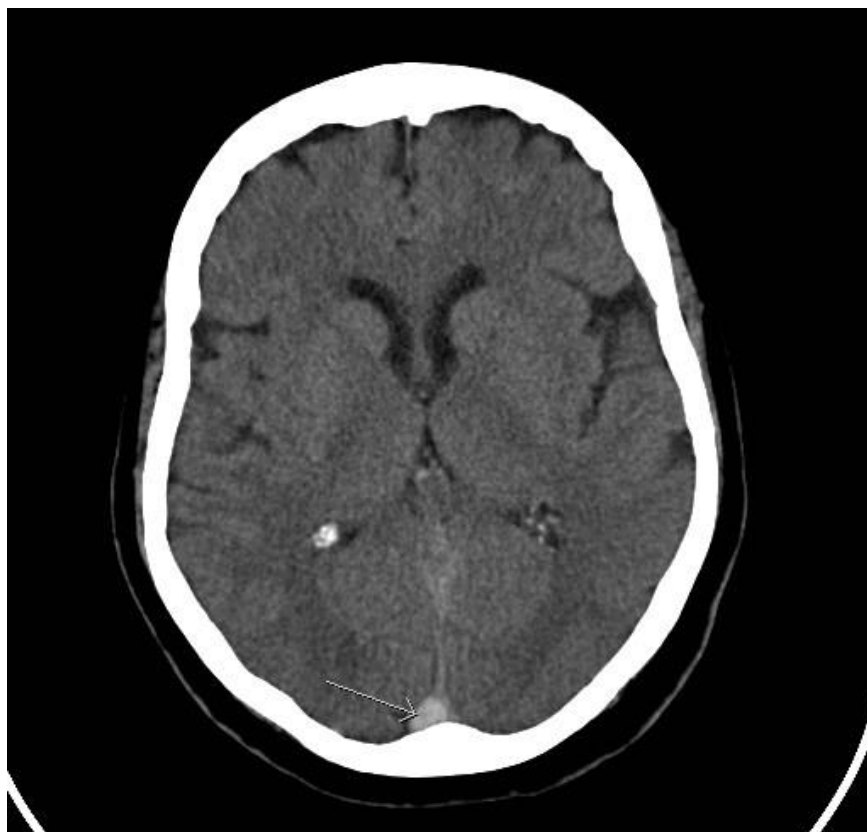
regarded the best methods for the diagnosis and follow-up of CVST.<sup>3,6,10</sup> MRI in combination with MRV have become the noninvasive imaging techniques of choice and are often used as the initial diagnostic methods for suspicious cases.<sup>10</sup> The T2-weighted -gradient-echo MRI and MRV sequence have a high diagnostic value for detecting both acute and subacute superior sagittal sinus, deep veins, and cortical veins thrombosis.<sup>11</sup>

The treatment consists of anticoagulants such as dose-adjusted intravenous heparin or body weight-adjusted subcutaneous low-molecular-weight heparin (LMWH), thrombolysis and symptomatic therapy of epileptic seizures and increased intracranial pressure.<sup>1,12</sup> The main intervention in the acute CVST is anticoagulation therapy (heparin or LMWH).<sup>1</sup> In patients in severe condition on admission or in those who deteriorate despite adequate anticoagulation therapy and in which the other causes of deterioration have been ruled out, systemic or local thrombolysis or thrombectomy is an option.<sup>1,3,6,13</sup> Decompressive surgery is the method in patients with large venous infarcts or haemorrhage.<sup>1,14</sup> After the acute phase of the disease, continued oral anticoagulant therapy (OAT) is recommended for a variable period of time, depending on the inherent thrombotic risk.<sup>1,2,13</sup> About 80% of cases have a good prognosis,<sup>15</sup> and around 15% of the patients remain disabled or die.<sup>5</sup> Recurrence of the disease affects approximately 15% of patients. The mortality rate in the first month after the onset of disease is up to 13%.<sup>16</sup> In a multinational multicentric prospective study of 624 adult patients with CVST, 8.3% had died.<sup>5</sup>

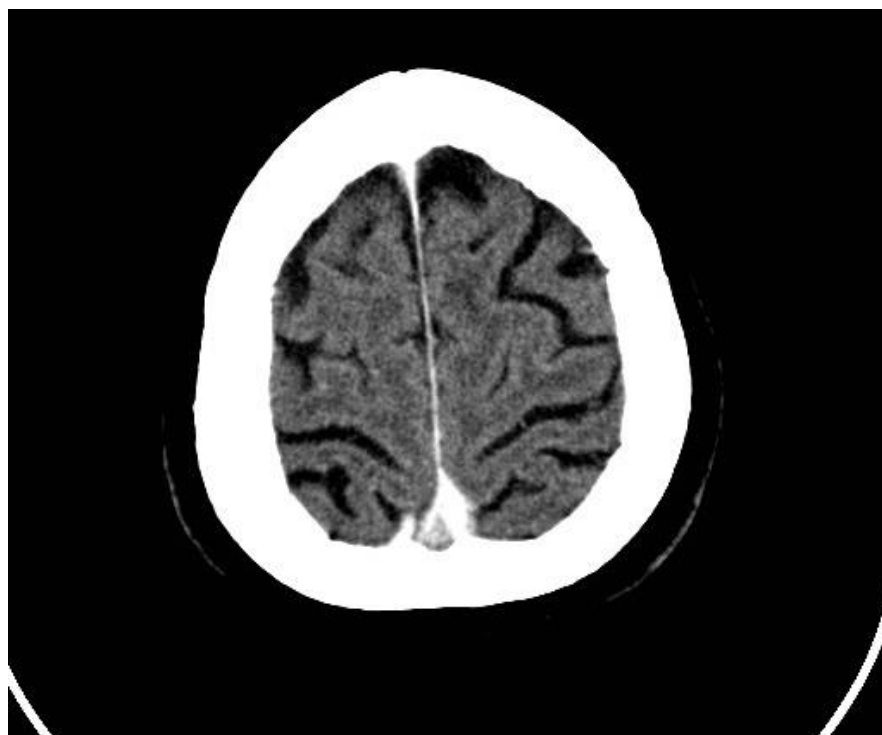
## Case report

A 73-year-old woman presented with a severe headache which started the night before medical examination and with dizziness, nausea and vomiting on the day of admission. She had no clinical or neurological disturbances at physical examination in the emergency room. High blood pressure was registered. During the day she developed right-sided hemiparesis 4/5 degree. Persistent headache was the dominant symptom. Five years earlier she was treated because of transient weakness of the left limbs. She had antihypertensive, statin, antidepressant and vitamin D in therapy.

The results of laboratory findings which were made in the emergency room were within reference values, except for elevated D-dimer. Unenhanced CT scan of the head demonstrated a hyperdense signal in the superior sagittal sinus (Picture 1), right transverse sinus, rectum sinus and in vena magnum Galeni. After intravenous contrast was given, the CT demonstrated an empty delta sign in the superior sagittal sinus which was indicative of CVST (Picture 2).



Picture 1 Unenhanced CT image show hyperdensity within superior sagittal sinus  
*Slika 1. Nepoboljšana slika CT pokazuje povećanu gustoću gornjeg sagitalnog sinusa*



Picture 2 Contrast enhanced CT image shows filling defect with enhancing rim (empty delta sign)  
*Slika 2. Kontrastom poboljšana CT pokazuje nedostatak punjenja s povećanjem ruba (prazan delta znak)*

In order to detect the cause of CVST, the patient underwent complete laboratory, clinical, ultrasound and radiological examination during the hospital stay in the Department of Neurology. Except for elevated D-dimer, laboratory findings were within reference range. Genetic and acquired coagulation disorders were excluded, as well as the existence of malignancies.

CTA registered a filling defect within the superior sagittal sinus which corresponded to thrombosis. MRI (1.5 T) of the brain without contrast showed hyperintensity at superior sagittal sinus, bilateral transverse sinus and rectum sinus on T1-weight gradient echo sequences, and MRI with contrast showed a visible filling defect within the venous sinuses. MRV using two-dimensional time-of-flight (2D TOF) technique showed a loss of flow in superior sagittal sinus and marginally maintained flow in bilateral transverse sinus. MRA using three-dimensional time-of-flight (3D TOF) technique showed reduced flow in the distal part and in M2 branches of the right arteria cerebri media (ACM).

The patient had no contraindications for anticoagulation (AC) therapy, so she was treated with body weight-adjusted subcutaneous LMWH with a good clinical response – disappearance of signs and symptoms and the absence of complications. She took warfarin after the acute phase of the disease.

### Discussion

In our patient, who was earlier treated because of hypertension, hypercholesterolemia, depression and osteoporosis, laboratory findings and neuroimaging methods were made because of sudden headache, dizziness, nausea, vomiting and weakness of the right limbs. She had elevated serum D-dimer values. Several studies have tested the value of D-dimer measurements. In most patients with recent CVST, D-dimer concentrations were elevated, so a negative D-dimer assay may make the diagnosis of CVST very unlikely.<sup>17,18,19</sup> In the study Crassard et al., in a series of 73 patients with CVST of less than 30 days duration, 26% of those who presented with isolated headache had normal D-dimer concentrations.<sup>20</sup> Thus, D-dimer concentrations are raised in most patients but normal D-dimer levels do not exclude the diagnosis of CVST, particularly in patients presented with isolated headache.<sup>20,21</sup> In our case the CT scan of the head showed multiple segmental cerebral sinovenous thrombosis. In the study of Wang et al. two or more sinus were affected in 78.9% cases,<sup>22</sup> which was also found in our patient. Headache was the first and dominant symptom in our patient. Headache is the most frequent symptom and occurs in about 90% of all

the cases,<sup>5,22</sup> and it is indicative of intracranial hypertension resulting from impaired venous drainage in patients with CVST.<sup>22</sup> Focal neurological signs occur in 40-60% of all the cases<sup>5</sup> and were registered on the second day of the onset of the disease in our patient. In patients with headache, focal deficit, epileptic seizures or an altered consciousness, CVST should always be considered.<sup>1,5</sup> In our paper diagnosis of CVST was made by using CT scan of the head. Unenhanced CT scan is the most frequent examination performed in emergencies. In CT imaging without contrast, thrombosis is manifested as hyperdensity,<sup>9,23</sup> and CVST may be detected in about 25% of the cases.<sup>24</sup> High density is a characteristic of the clot for the first week, and later it becomes iso- or hypodense.<sup>25</sup> Hyperdense thrombus in a sinus or a vein is a radiological sign of CVST,<sup>9,23,25</sup> as we found in our patient. Thrombosis is detected in about 60% of the cases in which contrast enhanced CT was used, and the false-negative rate can be as high as 40%.<sup>9</sup> Contrast enhanced CT reveals better modality for identifying dural venous sinus thrombosis and delta sign<sup>23,26</sup> which we registered in our patient. In patients in which CT of the brain without contrast is negative and there is a clinical suspicion of CVST, it is necessary to do CT with contrast. Empty delta sign on CT image and the combination of absence of a flow void with alternation of signal intensity in the dural sinus on MRI are the suggestive signs of CVST,<sup>26</sup> as we found in our patient. In MRV of our patient, we registered a loss of flow in superior sagittal sinus and maintained flow in bilateral transverse sinus. MRI in combination with MRV are the noninvasive imaging methods of choice for diagnosis suspicious cases.<sup>10</sup> The patient underwent extensive diagnostic procedures, but the cause of sinus thrombosis was not found and CVST from our paper is classified as an idiopathic encountered in about 15% of patients.<sup>5,8</sup> Despite good recovery after CVST,<sup>15</sup> about 50% of survivors may become depressed or anxious,<sup>27</sup> however, worsening of depression in our patient was not registered. Due to the recommended European Federation of Neurological Societies (EFNS) guidelines on the treatment of cerebral venous and sinus thrombosis,<sup>1</sup> our patient was treated with body weight-adjusted subcutaneous LMWH with the disappearance of symptoms and signs and the absence of complications. She took OAT after the acute phase of the disease. In previous studies CVST had a favourable outcome.<sup>15</sup> In our patient anticoagulant therapy led to complete recovery of neurological signs and symptoms. In the study by Ferro and contributors, in people aged 65 years and older CVST and isolated intracranial hypertension are less frequent than in young people. In elderly people decreased levels of

consciousness and mental status changes are more frequent than in younger people,<sup>27</sup> which was not the case with our patient. Carcinoma is more frequent as a cause of CVST in the elderly and an extensive search for cancer should be made to all the patients,<sup>25</sup> what we have done in our patient. There are insufficient data about the duration of OAT in patients with CVST. OAT is recommended for more than 6-12 months in patients with idiopathic CVST and for those with mild thrombophilia.<sup>1</sup> In the study Ferro and contributors, anticoagulant therapy is recommended for more than 6 months because of an increased risk of further thrombotic events.<sup>27</sup>

### Conclusion

In our report, we presented a case of multiple segmental sinovenous thrombosis with good prognosis. Early diagnosis and application of anticoagulant therapy affect the outcome of CVST. The aims of antithrombotic therapy in CVST are to recanalise the occluded sinus or vein, to prevent the propagation of the thrombus, and to treat the underlying protrombotic state in order to prevent venous thrombosis in other parts of the body and to prevent the recurrence of CVST.

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