



## A rare stroke: Cerebral Venous-Sinus Thrombosis; A Case Series Analysis Presented to Emergency Department and Review of the Literature

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### ABSTRACT

Cerebral venous sinus thrombosis (CVST) is a rare but acute and life-threatening disease. In this study, we present a case series of 10 patients with CSVT diagnosed in the emergency department of a tertiary hospital. Demographic characteristics, CVST etiologies, diagnostic characteristics in their history, radiological signs and prognosis were recorded during their hospitalization. The median age of the patients was 32 years. Half of the patients were women. It was known that three patients had otitis media, and the other three patients had pregnancy, puerperium and hormonal contraceptives. One patient had chronic inflammatory disease and one patient had idiopathic thrombosis. All but one of the patients had headache. The diagnostic tool was magnetic resonance venography and all patients had transverse sinus occlusion. All patients received anticoagulant treatment in the neurology department, 9 patients were discharged with good recovery, 1 patient died. Emergency clinicians should be more careful, especially in young patients and patients with thrombotic risk factors. Hormonal contraceptives are a major preventable risk factor. However, pregnancy and the postpartum period are thrombotic risk factors on their own. Intracranial infections such as otitis media may spread and cause cerebral vein thrombosis. Magnetic resonance venography is the most successful diagnostic tool for SSVT.

**Keywords:** Venous sinus thrombosis; emergency medicine; headache.

### Nadir bir İnme: Serebral Venöz-Sinüs Trombozu; Acil Serviste bir Vaka Serisi ve Literatür Derlemesi

#### ÖZ

Serebral venöz sinüs trombozu (SVST) nadir görülen ancak akut ve yaşamı tehdit eden bir hastalıktır. Bu çalışmada, üçüncü basamak bir hastanenin acil servisinde tanı alan 10 hastalık SVST vaka serisini sunuyoruz. Hastaların demografik özellikleri, SVST etiolojileri, özgeçmişlerindeki tanınan özellikler, radyolojik bulgular ve prognoz hastanede yattıkları süre boyunca kaydedildi. Hastaların ortanca yaşı 32 idi. Yarısı kadındı. Üç hastada orta kulak iltihabı, diğer üç hastada gebelik, lohusalık ve hormonal kontraseptif olduğu biliniyordu. Bir hastada kronik enflamatuvar hastalık mevcuttu ve bir hastada tromboz idiyopatiktir. Hastaların biri hariç tümünde baş ağrısı vardır. Tanı aracı manyetik rezonans venografi idi ve tüm hastalarda transvers sinüs tıkalıydı. Tüm hastalar nöroloji bölümünde yatarak antikoagülan tedavi aldı, 9 hasta şifa ile taburcu edildi, 1 hasta öldü. Özellikle genç hastalarda ve trombotik risk faktörleri olan hastalarda acil servis klinisyenleri daha dikkatli olmalıdır. Hormonal kontraseptif önenebilir bir majör risk faktörüdür. Ancak gebelik ve doğum sonrası dönem başlı başına bir trombotik risk faktörüdür. Otitis media gibi intrakraniyal enfeksiyonlar yayılarak serebral ven trombozuna neden olabilir. Manyetik rezonans venografi, SVST için en başarılı tanı aracıdır.

**Anahtar Kelimeler:** Sinüs ven trombozu; acil tıp; baş ağrısı.

#### INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is an acute and life-threatening condition. It is an uncommon medical condition compared to ischemic stroke and intracranial haemorrhage (1). Cerebral venous sinus thrombosis is responsible for 0.5-1% of all cerebrovascular diseases (2). Although the incidence of this disease is not certain, 0.22-1.32/100.000 patients per year are reported (3-5). A confidential data cannot be found about the rates of emergency department admissions. However, based on the case report series, a small number of patients are admitting every year (6). Although it is more common amongst women and between the ages 20-40, it can be seen at any age (2). Mortality rates are under 1% (7).

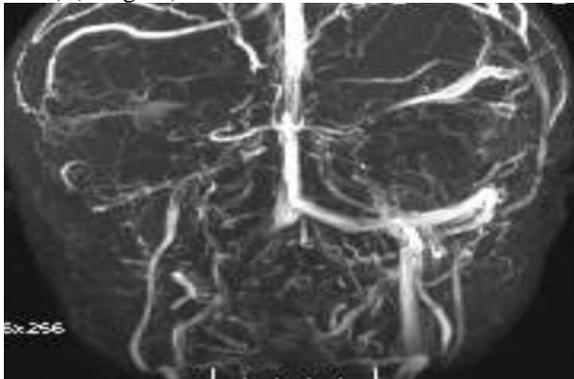
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In this study, 10 patients who are diagnosed as CVST between 01/11/2014 – 01/12/2016, in emergency department of a tertiary university hospital in Turkey, which is in a geographic location known to be that CVST is common. Demographic features of patients, etiologies of CVST, suggestive diagnostic features in patients' history, radiologic findings and prognosis had been evaluated. For the study, written permission was obtained from the institution where the patients were diagnosed and treated, and written consent was obtained from the patients or their legal guardians.

### CASE PRESENTATIONS

**Case 1:** A 30-year-old male patient presented to emergency department with 10 days of pain in right ear and nausea, vomiting and dizziness continuing for 3 days. In this medical history Behcet's Disease was diagnosed 3 years ago. With his history and physical examination, otitis media was the initial diagnosis. Analgesic therapy was given for symptomatic pain relief. Intracranial complication was suspected as the patients who had severe and analgesic-resistant headache. Cranial computed tomography (CT) was performed and inflammatory soft tissue mass in ethmoid cellular was seen. This was followed by a cranial magnetic resonance imaging (MRG), which showed soft tissue mass in tympanic cavity and right mastoid cellular, accompanying to abnormal signal intensity in right transverse sinus and sigmoid sinus. Suspected thrombosis in transverse and sigmoid sinuses leded us to further evaluation with magnetic resonance venography (MRV). It demonstrated increased signal intensity in right transverse sinus and sigmoid sinus with occlusion (thrombosis of right transverse and sigmoid sinuses) (Image-1).

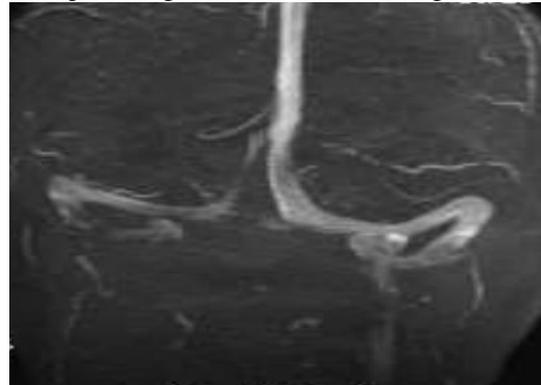


**Image-1:** MRV image of case 1; occlusion of right transverse and sigmoid sinuses

Considering the patients' clinical and radiological findings, he was diagnosed CVST secondary to acute otitis media. Antibiotherapy (ceftriaxone) and low molecular weight heparin (enoxaparin) therapy was given, and he was admitted to intensive care unit (ICU) of neurology department. During the following days, his antibiotherapy was switched to meropenem and linezolid as his infectious markers were still high. Also, acetazolamide was added to his medication for papilledema. Symptomatic treatment was given for his pain and fever during his hospitalization. After being treated for 24 days, he was in stable condition and discharged from hospital.

**Case 2:** 28-year-old male patient attended emergency department with complaint of headache and sense of fullness in ear for 4 days. His neurologic examination was completely normal. Symptomatic medication was given but his pain was resisting. A cranial CT was performed for his headache, and hyperintensity next to right cerebellar hemisphere was seen. Considering his clinical and radiological findings, lateral sinus thrombophlebitis was suspected and MRV was performed for differential diagnosis. It was reported as sinus venous thrombosis in right transverse sinus, sigmoid sinus and internal jugular vein. Antibiotherapy (ceftriaxone) and anticoagulation with low molecular weight heparin (enoxaparin) was initiated. He was admitted to neurology clinic, metronidazole was added to his therapy. After 21 days of treatment and complete resolution of symptoms he was discharged from hospital.

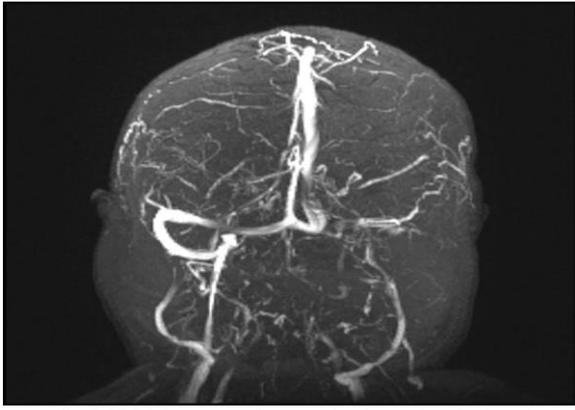
**Case 3:** 40-year-old female patient presented emergency department with loss of consciousness and whole-body contractions lasting for 1 minute. She had a caesarean section a week ago and she was complaining of tingling and pain on left upper extremity and left side of her face. Cranial CT was performed in emergency department and there were no pathological findings. As her complaints were persisting, cranial MRI and MRV were performed for further evaluation. There was no ischemic pathology detected, however, decreased venous flow was seen in the proximal part of right transverse sinus (Image-2).



**Image-2:** MRV image of case 3; decreased venous flow was seen in the proximal part of right transverse sinus

She was admitted to neurology clinic, antiepileptic therapy (levetiracetam), antibiotherapy (ceftriaxone) and anticoagulant therapy (enoxaparin) was initiated. After 10 days of hospitalization, she was discharged in stable condition.

**Case 4:** 67-year-old male patient attended emergency department with headache and abnormal walking. In cranial CT performed for acute cerebrovascular accident, there was no acute pathology. Cranial MRI and MRV were planned for further evaluation. In his medical history, he had ear pain for 5 months and he was diagnosed and operated for mastoiditis and deep neck abscesses, which were resistant to medical therapies. He was discharged from an otorhinolaryngology clinic, 2 weeks ago. Pathological examination of the surgical specimens was confirming mastoiditis and chronic inflammatory changes. In MRV thrombosis in left transverse sinus, sigmoid sinus and internal jugular vein (Image-3) was visualized.

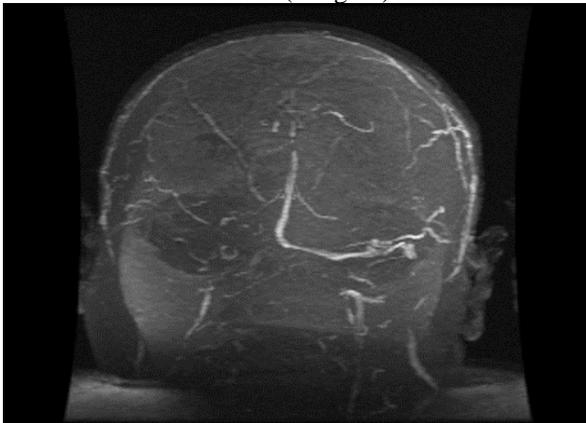


**Image-3:** MRV image of case 4; thrombosis in sigmoid and left transverse sinuses and internal jugular vein

He was hospitalized in neurology clinic, received antibiotherapy (meropenem) and low molecular weight heparin (enoxaparin), and surgical debridement for mastoiditis was performed by an otorhinolaryngologist. After 25 days of successful treatment, he is discharged from hospital.

**Case 5:** 32-year-old male patient presents emergency department with 6 days history of headache and transient vomiting. He had a cranial MRI 3 days ago, abnormal signal intensity suggesting thrombosis in superior sagittal sinus, right transverse sinus, sigmoid sinus and right internal jugular vein was seen. MRV was performed in our emergency department for further evaluation, and thrombosis was confirmed. Also, collateral venous flow of superior sagittal sinus was visualized. He is admitted to neurology clinic, received anticoagulant therapy. He is discharged after 25 days, with cure.

**Case 6:** 32-year-old female patient presented with gradually increasing headache and weakness in right upper and lower limbs for 3 days. In her history, she had a caesarean section 24 days ago. Cranial CT was performed for suspected cerebrovascular accident, no acute pathology is detected. Cranial MRI and MRV were performed for further evaluation and differential diagnosis. Abnormal signal intensity consistent with thrombosis in right transverse sinus, sigmoid sinus, superior sagittal sinus and confluens sinuum was seen (Image-4).



**Image-4:** MRV image of case 6; thrombosis in right transverse sinus, sigmoid sinus, superior sagittal sinus and confluens sinuum can be seen.

Imaging also demonstrated hemorrhagic venous infarct starting from area adjacent to thrombosed right transverse

sinus and subsequent in right temporal and occipital areas. Right lateral ventricle was also compressed due to hemorrhage. Moreover, hemorrhagic areas consistent with venous infarct were seen in left frontoparietal area. Patient was admitted to ICU of neurology clinic. Anticoagulant (enoxaparin) and antiepileptic (levetiracetam) therapy was initiated. Urgent cranial CT was performed as symptoms were not resolving with treatment and her mental status was deteriorating. Parenchymal hematoma, hemorrhagic transformation in infarct zone, and multiple hemorrhagic densities were seen. She was consulted to neurosurgery department for decompression surgery. Bilateral craniectomy and decompressive surgery were performed in order to reduce the increased intracranial pressure. Meanwhile, bacterial growth was detected in her blood culture and antibiotic therapy (meropenem) was started. She developed hypotension, vasopressor therapy has initiated, antibiotic regimens were changed as she was considered as in septic shock. On 7th day of her emergency department referral cardiopulmonary arrest has occurred, and she did not respond to resuscitative efforts.

**Case 7:** 31-year-old female patient presented with headache and numbness in left arm. There was no acute pathology in her cranial CT. For evaluating ischemic etiologies, cranial MRI and MRV were performed and thrombosis was seen in superior and inferior sagittal sinuses. Thrombosis was considered as a complication of her long term oral contraceptive usage. The patient was treated with low molecular weight anticoagulant (enoxaparin) and discharged after 13 days of hospitalization in neurology department.

**Case 8:** 63-year-old female patient presented emergency department with headache continuing for a month. She is known to have rheumatoid arthritis. Symptomatic therapy was given, but persistent symptoms lead us to further investigation with cranial CT. Hemorrhagic densities pointing venous infarction in right occipital lobe were seen. Cranial MRI and MRV were performed, thrombosis in superior sagittal sinus, right transverse sinus, confluens sinuum, sigmoid sinus and internal jugular vein were visualized. Under low molecular weight heparin (enoxaparin) treatment, she discharged from neurology clinic in a stable condition, after 17 days.

**Case 9:** 27-year-old female patient presented with weakness in left upper and lower limbs since 3 hours and transient hypoesthesia, lasting around 5 minutes. In her medical history, she had caesarean section with spinal anesthesia 3 days ago. She was also complaining of headache for a week. Cranial MRI and MRV imaging demonstrated thrombosis in superior sagittal sinus and right transverse sinus. She was admitted to neurology clinic, received low molecular weight heparin (enoxaparin) therapy and discharged after 16 days.

**Case 10:** 20-year-old male patient presented with severe headache that has started 2 days ago. He was known to be diagnosed otitis media of right ear 1 month ago. Persistent headache despite symptomatic treatment raised suspicion of intracranial pathology. Cranial MRI and MRV were performed, thrombosis in superior sagittal sinus and right transverse sinus were visualized. Low molecular weight heparin (enoxaparin) therapy administered in neurology clinic, and he was discharged after 25 days.

## DISCUSSION

CVST is a rare entity among all cerebrovascular diseases, though it is seen in a younger population. Coutinho et al. published a systematic review of 8829 CVST patients between 1942-2012; results of their study showed that the mean age of CVST patients is 32.9, and 64.9% of the patients are women (7). Zuluaga et al. studied 37 CVST patients retrospectively; emphasized that women and population between 20-40 age are at more risk (2). In our relatively smaller sized study, 8 of 10 patients are in this age interval. However, number of women and men are equal in our study. This finding can be explained by the small sample size, and it cannot be predictive for general population.

One of our cases resulted in demise. The systematic review of Coutinho et al. revealed that mortality of CVST is under 1%, whereas it was around 40% in 1940s (7). Decreased mortality can be related to improved medical cares within years (7). The pattern is also similar in ischemic strokes (8). Another reason that can be associated to decreased mortality is extensive usage of MRV (2, 7). Previously CVST was diagnosed in autopsy but now it can be rapidly diagnosed with MRV; therefore it is an acute pathology nowadays, whose incidence has increased and mortality has decreased (7). Diminish in traumatic and septic causes can be another reason of decreased mortality (7). Especially, broad usage of antibiotics dropped off septic causes (9).

Any kind of genetic or acquired prothrombotic state is a predisposing factor for CVST (1). Pregnancy, puerperium, some hormone replacement therapies, oral contraceptive usage, in vitro fertilization therapies are associated with higher incidence of CVST in women (2,10,11). Khan et al. acquired important data in their retrospective study of 110 patients with pregnancy and puerperium related CVST, across 5 Asian countries (10). According to this study almost half of the strokes that are seen in pregnancy and 1st month of postpartum stage are caused by CVST (10). It is also stated that puerperal strokes are mostly originated from venous structures (10). Similarly, in our case series 3 patients' etiologies are increased thrombosis risk in puerperal stage. A meta-analysis from Amoozegar et al. showed that 15-50 aged women using oral contraceptive have an increased risk of CVST by approximately 7.59 times (12). In our case series etiology of CVST of a 31-year-old female patient is oral contraceptive usage. Although hormonal contraceptives are clearly known to increase CVST risk, further studies are needed to determine which of them are causing greater risk and whether the duration of usage has an effect on increased risk (12). Another etiology of CVST is infections, and mastoiditis caused by otitis media is one of leading cause amongst them (13). Mastoiditis secondary to otitis media is a rare intracranial complication, which can occur either with direct invasion to mastoid bone or spreading through small vein thrombophlebitis (14). It is mostly caused by acute otitis media in paediatric population, whereas chronic otitis media is more likely to cause mastoiditis in adults (13). Among the cases we present, 3 patients have infection in etiology, and all are mastoiditis. Contradictory to common facts, all 3 of them had mastoiditis due to acute otitis media. Widespread usage of antibiotics diminished incidence and mortality of CVST secondary to mastoiditis,

likewise other infectious causes (14). Other prothrombotic factors blamed on etiology are malignancies, neurosurgeries, central venous catheterization, procedures like lumbar puncture and spinal anesthesia, dehydration, unregulated diabetes mellitus, hematologic diseases like polycythemia and thrombocytopenia, some inflammatory diseases including Behcet's disease (15). One of our cases also had rheumatoid arthritis in etiology. On the other hand, in 13-14% of CVST patients a risk factor cannot be identified (15,16). One of our patient's etiology also remains unknown.

CVST symptomatology varies widely according to patient's age, location of thrombus and duration of thrombotic process (1). In their case series with 17 patients, Cumurciuc et al. emphasized that headache is the most common symptom (17). Similarly, Zuluaga et al.'s study showed 86.5% of patients have headache (2). In our case series, all patients except one had headache. According to literature review and our study, CVST is in differential diagnosis of headache. Clinicians should suspect from CVST in patients with persistent headache, especially considering age and female gender. A recent review from Silberstein et al. stated that headache is the 5th most common complaint in emergency department admissions (18). Emergency physicians are in an important position to diagnose potentially lethal pathologies like CVST in patients presenting with such a common symptom. Ferro et al found the frequency of seizures to be 40% in CVST patients in their cohort of 624 patients. In the same study, the frequency of seizures in the first two weeks after the diagnosis was reported as 7%. Tadi et al. reported the frequency of seizures as 44 percent in their review (18). Seizures are more common in supratentorial lesions in their cohort (19). Focal seizures are the most common type of seizure in cvst patients (19). In 10 patients we presented, seizure was not seen before diagnosis or during follow-up. However, it may be possible to obtain data on seizures in CSVST patients with studies contains a much larger number of cases. Monoparesis or weakness accompanied by hemiparesis is the most common focal deficit in CVST (16,18). Ferro et al. reported the focal deficit frequency in CVST as 37% in their 89-centered prospective study (16). Focal deficits are less common in patients who are evaluated with MRI at an earlier stage and thus diagnosed early (20). Focal sensory or motor deficits were observed in 3 of the cases we presented. Although our findings are compatible with the literature, studies with larger patient groups are needed to gain statistical significance. Isolated intracranial hypertension syndrome (ie, headache associated with papilledema and visual impairment) is a common occurrence in CVST cases (21). It is observed more frequently in chronic cases. Papilledema is also more common in chronic cases than in acute cases (22). Cases resulting in coma or death may also occur among CVST patients (18).

In the diagnosis of CVST, imaging and laboratory findings are important along with clinically suspicious findings in risky patient groups. As laboratory parameters, complete blood count, coagulation panel, kidney and liver functions, and inflammatory markers such as sedimentation rate and C-reactive protein should be evaluated. D-dimer as an exclusion test is not as reliable as in deep venous

thrombosis so in risky patients, imaging should be performed regardless of the d-dimer result (18). Because it is faster and more accessible, non-contrast CT may be the first imaging tool to be considered (23). Cord sign may be seen as hyperdensity in the thrombosed part of the vein for a period of 2 weeks from the onset of thrombosis(18). In addition, indirect findings such as hemorrhagic infarct areas and multifocal hemorrhages can be observed with non-contrast cranial CT (23). Midline shift and focal edema have been reported due to hemorrhages and infarcts (23) In some cases, the empty delta sign is seen on contrast-enhanced CTs at the time of application (24). The empty delta sign is the most common direct imaging finding for contrast-enhanced CT (23). CT venography is a successful diagnostic tool to see the cerebral veins(25). However, the inability to distinguish bone structures and vein images is a disadvantage (23). Cranial MRI and MRV are major diagnostic tools for CVST, as they are superior in visualizing occlusion (1,19). They contain less artifacts than CT (23). In our cases all patients undergo MRI for definitive diagnosis. A retrospective study from Redd et al. demonstrated that hospitalization time of patients with cerebrovascular diseases significantly shortened after MRI become available at any time in emergency department, as unnecessary admissions to clinics are decreased (20). Although ever-ready MRI shortened hospital stay, larger studies or different methodologies are needed to determine the effect specifically on CVST.

Many intracranial events are included in the differential diagnosis of CVST such as pseudotumor cerebri, intracranial abscess, neurosarcoidosis, meningitis, abducens nerve palsy (18). Differential diagnoses, which are too many for clinicians, are also a challenge in making the true diagnosis.

In this case series treatment of patients started in emergency department, immediately after diagnosis. In CVST treatment, precautions should be initiated for patients with reversible aetiologies (1). After intracranial haemorrhage is ruled out, anticoagulants as an antithrombotic therapy should be given (21). If the patient's condition is worsening despite the treatment or intracranial haemorrhage occurs, patients should undergo mechanical or chemical thrombectomy (21). Both antithrombotic methods aim to resolve occlusion, prevent spreading of thrombus to adjacent intracranial veins, prevent thromboembolisms in other organ systems and reduce prothrombotic state (1, 22). All patients in our study received low molecular weight heparin. Except one of them, all other patients' thrombotic conditions become stable. If an infectious etiology is suspected admission of early and broad-spectrum antibiotherapy, accompanying to antithrombotic therapy, is critical for preventing both morbidity and mortality. Broad usage of antibiotics in recent years is known to reduce mortality of CVST, as well as permanent impairments (9). Our patients with infectious causes also received early antibiotherapy.

## CONCLUSION

Despite being a rare entity amongst all cerebrovascular diseases, CVST is more common in younger population. Its mortality gradually decreased within years, yet it is still a lethal disease. Emergency department presentations widely varies; however, headache is the most common

symptom and CVST must be kept in mind in these patients. There are multiple etiologic factors consisting preventable causes such as oral contraceptive usage, which also points out an important public health problem. MRI and MRV are powerful tools for definitive diagnosis, strengths of these imaging modalities also brings the discussion of any-time availability of MRI in emergency departments. Headache is one of the most common presenting symptoms and emergency physicians have a key role in recognizing CVST patients among them for prompt diagnosis and early treatment; which are critical steps for favourable patient outcomes.

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