Clinical Case Report

Medicine®

OPEN

# Oral contraceptives caused venous sinus thrombosis complicated with cerebral artery infarction and secondary epileptic seizures

## A case report and literature review

Feng Xu, MD, Cuifang Liu, MD, Xiaobo Huang, MD*

**Abstract**

**Rationale:** Venous sinus thrombosis is a special type of cerebrovascular disease. Its incidence is low and its symptoms are lack of specificity. And its early diagnosis and treatment are very difficult.

**Patient concerns:** This paper reported a rare case of a 43-year-old female who presented with cerebral venous thrombosis (CVT) complicated with cerebral artery infarction and secondary epileptic seizures due to oral contraceptives.

**Diagnoses:** The final diagnosis was intracranial venous sinus thrombosis, acute cerebral infarction in the left parietal lobe, intracranial hypertension syndrome, and continuous epilepsy.

**Interventions:** The patient recovered well after active treatment.

**Outcomes:** Three months after discharge, the muscle strength of the right limb of the patient was significantly increased, and no recurrence of neurological symptoms occurred.

**Lessons:** In conclusion, early diagnosis, correct evaluation, and standard treatment are still important challenges for CVT. Active treatment is recommended.

**Abbreviations:** CAI = cerebral artery infarction, CT = computed tomography, CVT = cerebral venous thrombosis, DR = digital radiography, DWI = diffusion-weighted imaging, MRI = magnetic resonance imaging, MRV = magnetic resonance venography, VST = venous sinus thrombosis.

**Keywords:** cerebral infarction, epilepsy, venous sinus thrombosis

## 1. Introduction

Cerebral venous thrombosis (CVT) is a group of special cerebrovascular diseases characterized by various causes of cerebral venous obstruction and cerebrospinal fluid malabsorption, and the incidence of CVT is about 0.5% of all strokes.[1] The clinical manifestations of CVT are complex, and lack of specificity, often subacute onset, and the course of the disease progresses slowly, may be manifested as headache, accompanied by nausea and vomiting. The onset of the disease is usually characterized by no obvious neurological symptoms, so CVT is easily confused with many diseases, its clinical diagnosis is difficult and easy to delay.

It was often seen in clinical reports that venous sinus thrombosis leads to thalamus infarcts or venous sinus thrombosis associated with hemorrhage after infarction.[2] However, venous sinus thrombosis complicated with cerebral artery infarction and secondary epileptic seizures has not been reported. In addition, oral contraceptive has been widely known as a risk factor for CVT.[3–5]

This paper reported a rare case of a patient who presented with CVT complicated with cerebral artery infarction and secondary epileptic seizures due to oral contraceptives.

## 2. Case report

A 43-year-old female continued oral contraceptive drugs (Marvelon, N.V. Organon) more than 20 days. There was sudden and persistent pain in the head and neck 5 days ago, but no obvious incentive. The neck digital radiography (DR) examination showed no obvious abnormality. The symptoms of occipital pain were progressively increased and she was treated in the local hospital. There was no obvious abnormality in cranial computed tomography (CT). The patient suffered from severe headache and nausea and ejection vomiting, followed by weakness in the right side of the body; she could not hold anything, unstable in standing, and was unable to walk, 1 day

Editor: N/A.

This study was approved by the institutional review board of Xuanwu Hospital Capital Medical University. Written informed consent was obtained from the patient for publication of this report.

The authors report no conflicts of interest.

Department of Traditional Chinese Medicine, Xuanwu Hospital Capital Medical University, Beijing, China.

* Correspondence: Xiaobo Huang, Department of traditional Chinese medicine, Xuanwu Hospital Capital Medical University, No. 45, Chang Chun Street, Xicheng District, Beijing100053, China (e-mail: huangxiaobo@xwh.ccmu.edu.cn).



Medicine (2017) 96:51(e9383)

Received: 15 November 2017 / Received in final form: 28 November 2017 / Accepted: 29 November 2017

http://dx.doi.org/10.1097/MD.0000000000009383

ago. Then, there was twitching of the lips and the right upper limb, and lasted 1 to 2 minutes, and her consciousness was clear when she was twitching. The interval of convulsions ranged from half an hour. The condition was getting worse, manifested as convulsions time gap significantly shortened, and then the patient was rushed into our hospital for treatment. Four hours after hospitalization, both eyes turned upward and limbs tetanic spasm occurred, which lasted for 3 minutes and could not be relieved.

The results of admission examination showed that the blood pressure was 120/82 mm Hg, the consciousness was clear, the cranial nerve examination showed no abnormalities, the optic disc edema was normal, the upper limb muscle strength of the right limb was 1, the lower limb muscle strength was 3-, and the right pathological sign was positive. No ataxia or sensory examination was performed, because the patient was uncooperative. Neck stiffness, the distance between the neck and chest is the length of 3 fingers, the result of kerniger sign was positive. In the past, there was no history of physical injury, no history of epilepsy, no history of heart disease, diabetes mellitus, hypertension, and so on. The patient was pregnant with 1 girl and she has 1 daughter before.

After admission, blood routine examination, physical examination, magnetic resonance imaging (MRI), and magnetic resonance venography (MRV) results showed that white blood cell count was $12.58 \times 10^9$/L, red blood cell count was $3.89 \times 10^{12}$/L, hemoglobin was 128 g/L, platelet was $223 \times 10^9$/L, and neutrophil percentage was 80.6%. The percentage of lymphocytes was 15.3% and in the normal range. The results of 3 rheumatic events showed that the C-reactive protein was 40.90 mg/L (0–8 mg/L), higher than the normal range. Four items of blood coagulation showed that fibrinogen concentration was 4.34 g/L (normal value: 2–4 g/L), prothrombin time, thrombin time, international normalized ratio activated partial prothrombin time, and prothrombin activity were all normal; thyroid hormone showed that the hypersensitive thyroid stimulating hormone (TSH3UL) was 0.284 mIU/L (0.35–5.5), and the rest were all normal. Electrolyte shows that sodium was 129.0 mmol/L, and the rest was normal. The renal function showed that urea was 1.33 mmol/L, uric acid was 36.30 μmol/L, and the others were normal. The results of Two D-dimer quantitative, heart function, liver function, electrocardiogram, blood lipid antinuclear antibody series, anticardiolipin antibody, homocysteine, and urine routine examination were all normal. MRV and MRI showed that the flow void signal of superior sagittal sinus and left transverse sinus disappeared, and irregular filling defect appeared. Diffusion-weighted imaging (DWI) showed that the large area signal of left parietal lobe was restricted, it showed high signal, and acute cerebral infarction occurred in the left parietal lobe (Fig. 1). The final diagnosis was intracranial venous sinus thrombosis, acute cerebral infarction in the left parietal lobe, intracranial hypertension syndrome, and continuous epilepsy.

Continuous infusion of midazolam micropump was performed and discontinued after 3 days. Meanwhile, 0.2 g intramuscular injection of phenobarbital every 8 hours, 5 days later, the patient convulsions symptoms disappeared, then disable phenobarbital, oral C Masi Bing once a day, 1 tablet each time. Subcutaneous injection of low-molecular-weight heparin sodium injection 4000 IU 2 times/day, mannitol 250 mL 1 time/day as intravenous dehydration treatment, Cefoperazone sodium and tazobactam sodium, and 2.5 g intravenous injection as anti-infection treatment.

In 5 days after the treatment, the convulsions stopped and the symptoms relieved after 13 days, with clear consciousness, clear speech, no abnormal sensation in the limbs, and the 5- of the

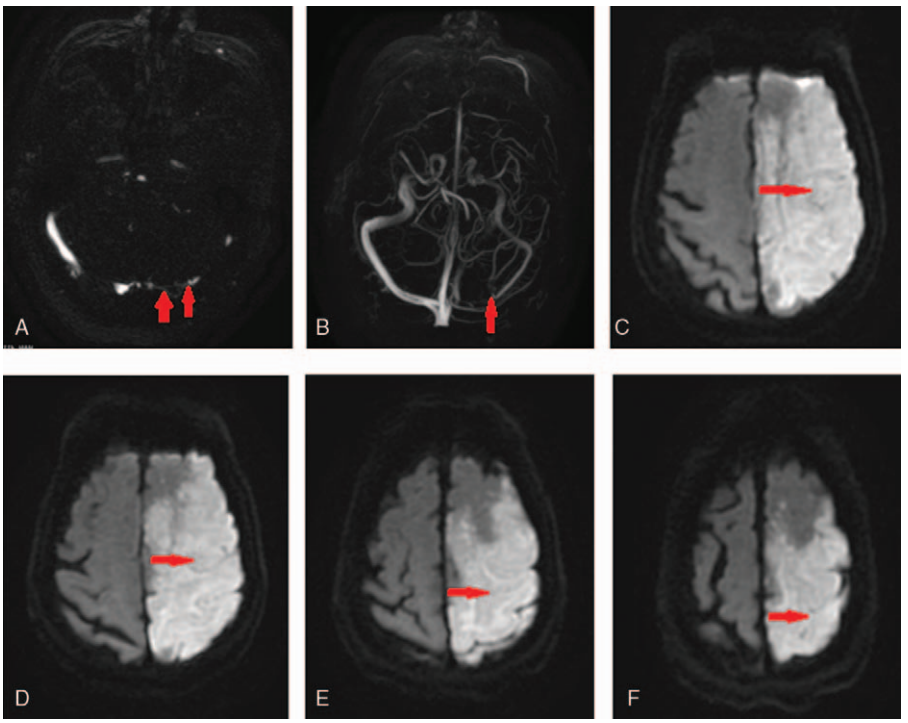


**Figure 1.** A-B: Magnetic resonance venography (MRV) and magnetic resonance imaging (MRI) showed that the flow void signal of superior sagittal sinus and left transverse sinus disappeared, and irregular filling defect appeared. C-F: Diffusion-weighted imaging (DWI) showed that the large area signal of left parietal lobe was restricted, it showed high signal, and acute cerebral infarction occurred in the left parietal lobe.

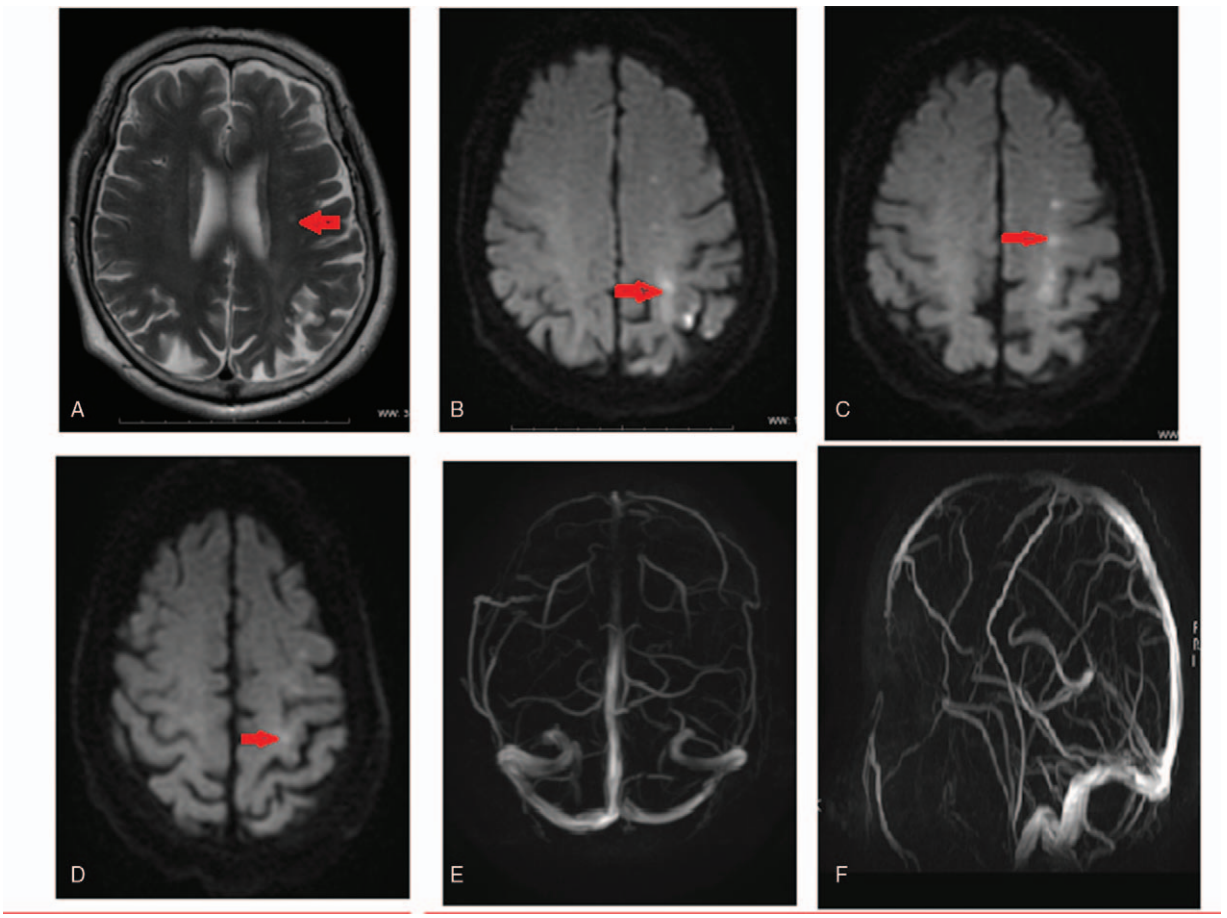


**Figure 2.** A: T2-weighted images (T2WI) showed punctate ischemic foci in the left corona radiata region. B-D Diffusion-weighted image (DWI) showed that the left frontal parietal cortex punctate restricted diffusion, which showed a high signal, suggesting subacute cerebral infarction; E-F: MRV showed superior sagittal sinus and left transverse running continuously, and no obvious abnormalities were observed.

upper and lower limbs. Discharge instruction was to continue to give C Masi Bing oral and warfarin oral medication, regular review of 4 blood coagulation, liver and kidney function, outpatient follow-up 3 months after discharge, the muscle strength of the right limb of the patient was significantly increased, and no recurrence of neurological symptoms occurred. T2-weighted images (T2WI) showed punctate ischemic foci in the left corona radiata region. DWI showed that the left frontal parietal cortex punctate restricted diffusion, which showed high signal, suggesting subacute cerebral infarction; MRV showed superior sagittal sinus and left transverse running continuously, and no obvious abnormality was observed (Fig. 2).

## 3. Discussion

CVT is an uncommon and difficult cerebrovascular disease identification; clinical lack of specificity in the early stages of the disease is often easily overlooked by patients and doctors, easily misdiagnosed as cerebral infarction, cerebral hemorrhage, or cerebral tumor. It was found that 37% of CVT patients were in the acute phase, 56% were in the subacute phase, and 7% were in a chronic phase. The average delay from symptom onset to admission was 4 days, with an average delay of 7 days from symptom onset to diagnosis.[6,7] There are CVT in infants and young and middle-aged men and women. The ratio of male to female is about 1:3, which is a potential threat to life safety.[8,9]

### 3.1. Etiology and pathogenesis

CVT causes are complex, common causes include tumor, trauma, infection, pregnancy and puerperium, blood system diseases, oral contraceptives, metabolic disorders, genetic dehydration, etc, but there are still 30% of CVT could not find obvious cause.[1,10,11] Risk factors for cerebral artery infarction include hypertension, diabetes mellitus, coronary heart disease, dyslipidemia, or the presence of various emboli leading to cerebral embolism. No other triggers were found in this patient except for oral contraceptives. The cause of CVT is likely to be that oral contraceptive drugs lead to the decrease of the anticoagulant function, and promoted the decrease of tissue plasminogen activator and plasminogen activator inhibitor, fibrinolytic function was decreased, and eventually lead to abnormal coagulation function.

### 3.2. Clinical manifestation

The incidence of venous sinus thrombosis is low. The clinical manifestation is affected by age, morbidity, and time of visit. It can be manifested as localized venous sinus thrombosis, such as intracranial hypertension and cerebral edema, or cerebral parenchymal injuries, isolated cortical vein obstruction, easily resulting in movement or sensory impairment or seizures.[1] A study of 220 cases of cerebral venous sinus thrombosis showed that, of the 220 patients, about 45% of patients had intracranial

hypertension, cerebral edema, cerebral venous infarction, and intracranial hemorrhage substantial injury, and there were 23% cases of nonhemorrhagic infarction, 20% cases of hemorrhagic infarction, and 12% patients with symptoms of cerebral hemorrhage.[12] It has been widely reported that epilepsy is one of the common clinical manifestations of CVT.[11–16] The imaging findings of this case suggest CVT, and the results of MRI and MRV scan show (Fig. 2) that there was no obvious abnormality in brain MRV, but there was acute cerebral infarction in the left frontal lobe. In combination with the prognostic features of CVT, CVT associated with arterial infarction and epilepsy grand mal were considered.

### 3.3. Diagnosis

Cranial CT is the most common method of examination in patients with CVT. CT venography has a useful value in the diagnosis of subacute or chronic cases of CVT, and MRI usually showed nonspecific lesions, such as hemorrhage, infarction and edema, and more different combinations,[17] as well as no specific marker for CVT. The presence of MRV allows the imaging of the venous system itself to show occluded blood vessels or intravascular thrombosis. Currently, the combination of MRI and MRV has largely replaced the minimally invasive cerebral angiography and CT diagnosis, becoming the gold standard of CVT.[1,18] In this patient, there were no significant abnormalities in the early CT examination. Then, the MRI combined with MRV indicated that the flow void signal of superior sagittal sinus and left transverse sinus disappeared, and irregular filling defect appeared. DWI showed that the large area signal of left parietal lobe was restricted, it showed high signal, and acute cerebral infarction occurred in the left parietal lobe, as shown in Fig. 1.

### 3.4. Prognosis

Unlike the type of arterial stroke, brain damage from venous thrombosis is largely reversible, because the cause of the development of venous infarction is due to venous reflux obstruction, increased intracranial pressure, decreased cerebral blood flow, decreased perfusion pressure, and finally leads to venous infarction.[19] At the same time, because of obstruction of vein and destruction of blood–brain barrier, the filtration of capillary network increases and leads to progressive cerebral edema. In the formation of venous thrombosis, blood flow can be established through the collateral pathway, cerebral perfusion may still be affected at low velocity, while in arterial thrombosis, blood flow was severely reduced, so that the brain tissue had rapid and irreversible damage, leading to ischemic necrosis of brain tissue.[20] Thus, despite of the absence of parenchymal lesions, increased venous congestion and elevated venous pressure resulting from perfusion failure may lead to brain dysfunction[21] and have a wide range of damage but reversible damage.

Arterial infarcts are usually hyperintense on T2WIs, whereas the T1-weighted images exhibit low signals, similar to venous edema or venous infarcts. DWI may help to distinguish between the 2. The first cranial MRI-DWI in this patient showed infarct in the parietal lobe, but exceeded the range of general arterial infarcts. The clinical outcome was rapid and complete, with only the left hemiparesis of the right limb, all of which were consistent with the characteristics of venous infarction. But the simple superior sagittal sinus thrombosis cannot produce venous infarction and hemorrhage, because of the superior sagittal sinus occlusion is not sufficient to induce cerebral venous circulatory disorders, and only cortical vein and bridging vein occlusion at the same time can lead to irreversible parenchymal damage on the basis of cerebral venous circulation, so the infarct in this patient was not confined to the vein alone.

The incidence of CVT was low and the majority of patients had a good prognosis. In 1 study, 79% of the patients recovered completely, with a total mortality rate of 8.3% and 5.1% who were unable to take care of themselves. The prognosis of poor prognosis usually occurs in the following situations: central nervous system infection, any malignant disease, deep vein thrombosis, admission CT, MRI showed intracranial hemorrhage, Glasgow Coma Scale score <9, mental state of disorder, older than 37 years, and male, etc.[5] In this case, the patient presented with cytotoxic brain edema despite the involvement of the arterial vessels, but this did not affect the prognosis of this disease. This may be related to the fact that active medical treatment has rapidly controlled the occurrence of complications.

Therefore, early diagnosis, correct evaluation, and standard treatment are still important challenges for CVT. Active treatment is recommended.

## References


[1] Bousser M-G, Ferro JM. Cerebral venous thrombosis: an update. Lancet Neurol 2007;6:162–70.

[2] Zhou G, Li M, Zhu Y, et al. Cerebral venous sinus thrombosis involving the straight sinus may result in infarction and/or hemorrhage. Eur Neurol 2016;75:257–62.

[3] Saadatnia M, Tajmirriahi M. Hormonal contraceptives as a risk factor for cerebral venous and sinus thrombosis. Acta Neurol Scand 2007;115: 295–300.

[4] Stegeman BH, de Bastos M, Rosendaal FR, et al. Different combined oral contraceptives and the risk of venous thrombosis: systematic review and network meta-analysis. BMJ 2013;347:f5298.

[5] Bousser MG, Crassard I. Cerebral venous thrombosis, pregnancy and oral contraceptives. Thromb Res 2012;130(Suppl 1):S19–22.

[6] Ferro JM, Lopes MG, Rosas MJ, et al. Delay in hospital admission of patients with cerebral vein and dural sinus thrombosis. Cerebrovasc Dis (Basel, Switzerland) 2005;19:152–6.

[7] Ferro JM, Canhao P, Stam J, et al. Prognosis of cerebral vein and dural sinus thrombosis: results of the international study on cerebral vein and dural sinus thrombosis (iscvt). Stroke 2004;35:664–70.

[8] Gulati D, Strbian D, Sundararajan S. Cerebral venous thrombosis: diagnosis and management. Stroke 2014;45:16–8.

[9] Krajíčková D, Klzo L, Krajina A, et al. Cerebral venous sinus thrombosis: clinical characteristics and factors influencing clinical outcome. Clin Appl Thromb Hemost 2016;22:665–72.

[10] Lee DJ, Ahmadpour A, Binyamin T, et al. Management and outcome of spontaneous cerebral venous sinus thrombosis in a 5-year consecutive single-institution cohort. J Neurointerv Surg 2017;9:34–8.

[11] Ichiyama T, Houdou S, Tomita Y, et al. Cerebral venous thrombosis associated with recurrent epilepsy-like attacks. Brain Dev 1989;11: 326–8.

[12] Oktar N, Dalbasti T. Protein s deficiency, epileptic seizures, sagittal sinus thrombosis and hemorrhagic infarction after ingestion of dimenhydrinate. Turk Neurosurg 2008;18:85–8.

[13] Shinoara Y, Hamaguchi K. [Cerebral venous and sinus thrombosis with temporal lobe epilepsy]. Rinsho Shinkeigaku 1973;13:718–25.

[14] Ho B, Huang P, Khor G, et al. Simultaneous thrombosis of cerebral artery and venous sinus. Acta Neurol Taiwan 2008;17:112–6.

[15] Ferro JM, Correia M, Rosas MJ, et al. Cerebral venous thrombosis Portuguese Collaborative Study Group[Venoport]. Seizures in cerebral vein and dural sinus thrombosis. Cerebrovasc Dis 2003;15: 78–83.

[16] Kumral E, Polat F, Uzunköprü C, et al. The clinical spectrum of intracerebral hematoma, hemorrhagic infarct, non-hemorrhagic infarct, and non-lesional venous stroke in patients with cerebral sinus-venous thrombosis. Eur J Neurol 2012;19:537–43.

[17] Sajjad Z. MRI and MRV in cerebral venous thrombosis. J Pak Med Assoc 2006;56:523–6.

[18] Bansal H, Chaudhary A, Mahajan A, et al. Acute subdural hematoma secondary to cerebral venous sinus thrombosis: case report and review of literature. Asian J Neurosurg 2016;11:177.
[19] Chatterjee S, Thomas B, Kesavadas C, et al. Susceptibility-weighted imaging in differentiating bilateral medial thalamic venous and arterial infarcts. Neurol India 2010;58:615–7.
[20] Ducreux D1 , Oppenheim C, Vandamme X, et al. Diffusion-weighted imaging patterns of brain damage associated with cerebral venous thrombosis. AJNR Am J Neuroradiol 2001;22:261–8.
[21] Murao K, Arakawa S, Furuta Y, et al. Cerebral venous thrombosis in the superior sagittal sinus as a rare cause of a paroxysmal kinetic tremor. Case Rep Neurol 2016;8:276–81.