

## A Short and Intermittent Course of Oral Contraceptive Pills and Risk of Cerebral Venous Thrombosis

### Kısa ve Aralıklı Oral Doğum Kontrol Hapları Kursu ve Serebral Venöz Tromboz Riski

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#### ABSTRACT

Cerebral venous sinus thrombosis is a rare disorder of cerebral vasculature. It can be presented by various clinical pictures depending on the site and extent of the thrombus. The risk factors are inherited or acquired. We describe a patient who used intermittent and short courses of oral contraceptive pills to postpone her periods to be able to fast for the holy month of Ramadan. She presented with status epilepticus. Investigations revealed cortical sinus thrombosis extending to the major cerebral venous sinus. She received optimal treatment for her seizure and cerebral venous sinus thrombosis. She was discharged in excellent condition. Users and the general public should be constantly reminded that OCP should only be used when directed by a physician, and should not be as over the counter medications

**Key Words:** Oral contraceptive pills, cerebral venous sinus thrombosis, intermittent use of oral contraceptive pills, misuse of oral contraceptive pills, short course use of oral contraceptive pills

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#### ÖZET

Serebral venöz sinüs trombozu, serebral damar sisteminin nadir görülen bir bozukluğudur. Trombüsün yeri ve yaygınlığına bağlı olarak çeşitli klinik tablolarla sunulabilir. Risk faktörleri kalıtsaldır veya edinilmiştir. Bu yazıda mübarek ramazan ayında oruç tutabilmek için aralıklı ve kısa süreli doğum kontrol hapları kullanarak adetini geciktiren bir hastayı anlatıyoruz. Status epilepticus ile başvurdu. Yapılan incelemelerde majör serebral venöz sinüse kadar uzanan kortikal sinüs trombozu saptandı. Nöbeti ve serebral venöz sinüs trombozu için optimal tedavi gördü. Mükemmel durumda taburcu edildi. Kullanıcılara ve halka sürekli olarak OCP'nin yalnızca bir doktor tarafından yönlendirildiğinde kullanılması ve reçetesiz satılan ilaçlar gibi olmaması gerektiği hatırlatılmalıdır.

**Anahtar Sözcükler:** Oral kontraseptif haplar, serebral venöz sinüs trombozu, oral kontraseptif hapların aralıklı kullanımı, oral kontraseptif hapların yanlış kullanımı, kısa süreli oral kontraseptif kullanımı

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## INTRODUCTION

Cerebral venous sinus thrombosis (CVST) is uncommon cerebrovascular accident disorder. Its incidence ranges from 2 to 5 per 1,000,000 annually<sup>1</sup>. It is three times more prevalent in women than men<sup>2</sup>. Thrombus in the cerebral sinuses can cause increased intracranial pressure, especially in the major sinuses, because of impaired cerebral spinal fluid absorption and local edema<sup>3</sup>. Many risk factors are responsible for thrombus formations. These are inherited or acquired. One acquired cause is drug use, including that of OCPs<sup>4</sup>. Clinical presentations vary among patients. Patients can present with signs of increased intracranial pressure such as headache and visual changes; however, they can also present with focal neurological deficits, seizures or changes in the level of conscious<sup>5</sup>. Diagnosis of this condition depends on patient history, clinical examination and appropriate imaging and blood tests. Magnetic resonance venography is the standard imaging choice for diagnosis; however, computed tomography (CT) brain scan and CT venography can be used if a magnetic resonance image (MRI) is not available or contraindicated. The main stay of treatment is an anticoagulation. The duration varies depending on the cause. In this report, we present a patient who intermittently used oral contraceptive pills for many years for a non-medical reason. She presented to us with status epilepticus and was found to have CVST.

## CASE REPORT

A 49-year-old female, right handed, who is healthy. The patient presented to the emergency department with her family with a seizure. She noticed left side upper limb weakness one day prior to presentation. She was taken to a nearby private clinic and was given unknown dose of aspirin and found to have high blood pressure. She was discharged to home. Her condition did not improve. On the day of presentation to us, her daughter found her unconscious on the ground having bitten her tongue. Upon arrival to ER, she developed continuous generalized seizure and was intubated and loaded with phenytoin by an

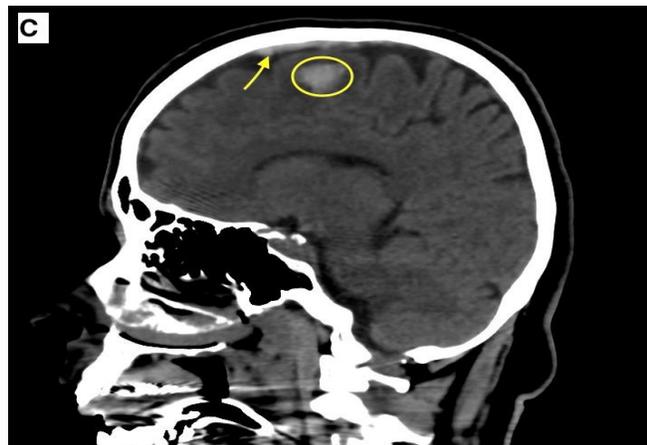
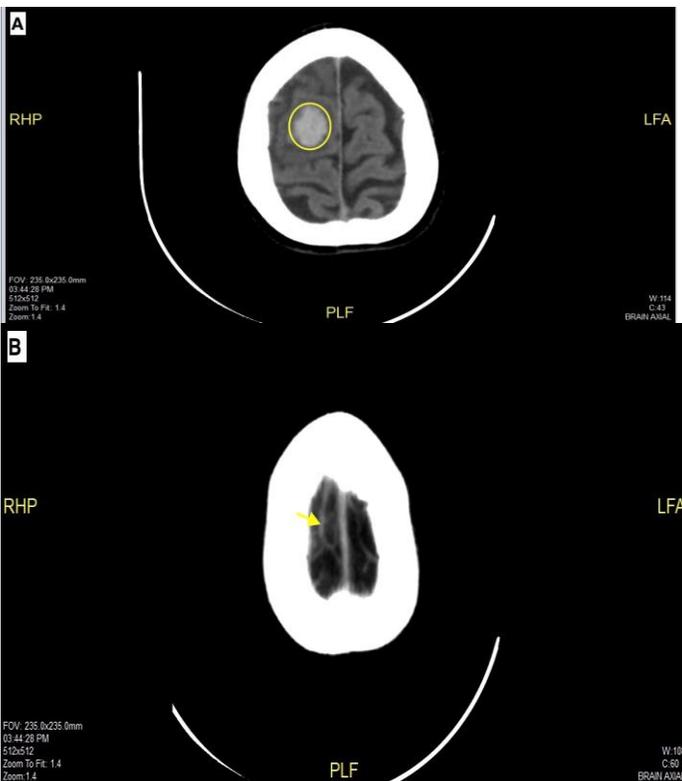
emergency physician. An urgent CT brain scan showed right subcortical frontal hematoma with cortical subarachnoid hemorrhage.

She denied any history of headache, fever or neck pain. She denied any skin rash, joint pain or previous venous thromboembolism (VTE) event. The patient has no history of miscarriage. She has a history of intermittent use of oral contraceptive during the holy month of Ramadan to stop menses so that she could fast for the whole month. She does not remember for how long she has followed this regimen. During the last Ramadan, she noticed some light bleed while using one OCP tablet, so she increased the dose to four tablets.

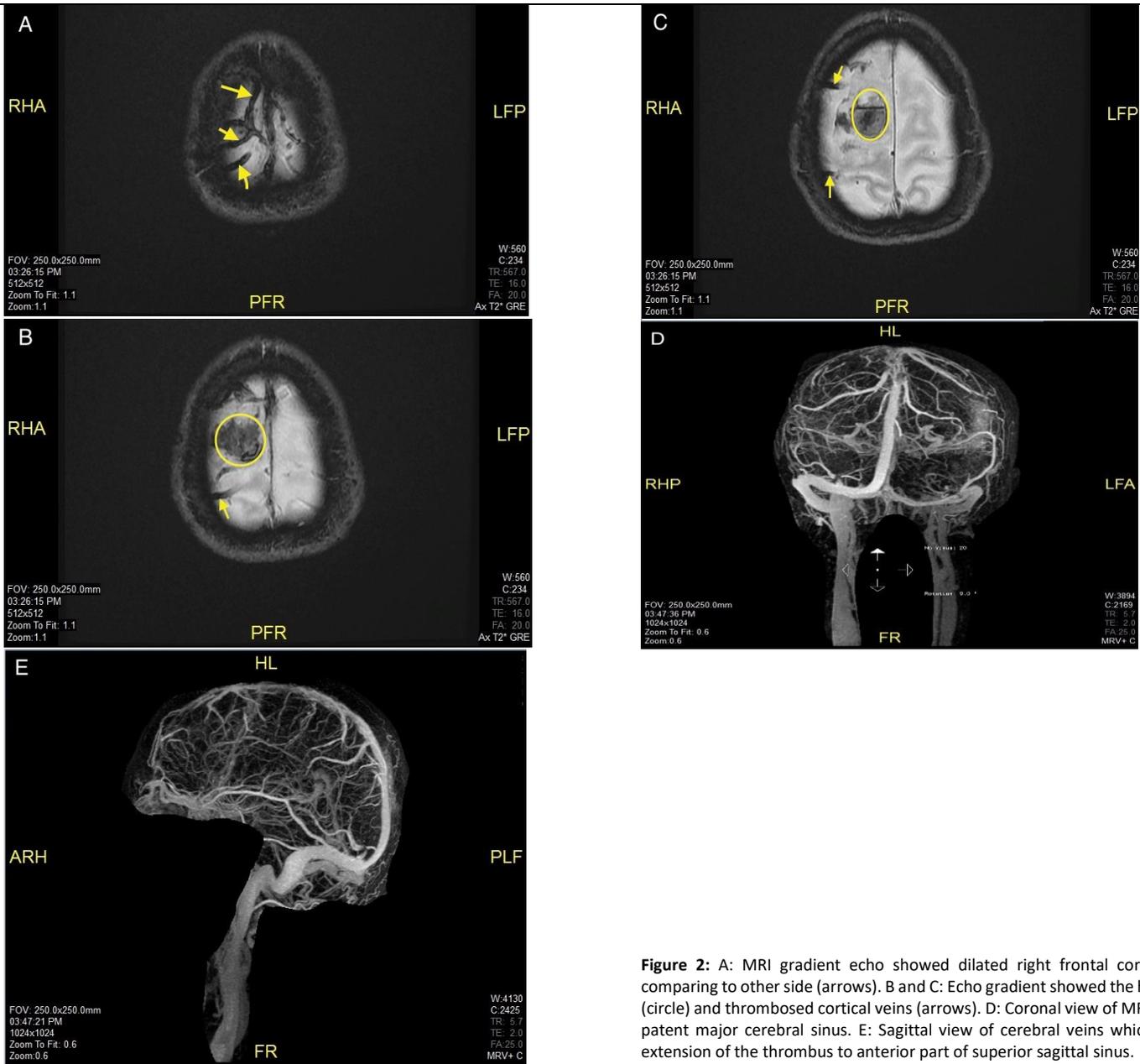
On examination, she was intubated and sedated on a mechanical ventilator. Vitals were stable. She could open her both eyes on verbal commands. She responded to single commands but could not move her left side; she could move only right side in response to painful stimuli, but could only slightly move her left hand. Her pupils were 3 mm, reactive and symmetrical. No abnormal movement was observed. Plantar response is extensor on the left side.

An urgent CT brain scan showed a right frontal lobe hemorrhage at the convexity with surrounding edema (Figure 1A). A dense cord sign was also noted on adjacent cortical veins (Figure 1B, arrow). There was a thrombus in the roof of the superior sagittal sinus (Figure 1C). An MRI/MRV brain scan (Figure 2) showed the presence of a superior right frontal lobe hemorrhage. The echo gradient sequence (Figure 2A, B and C) showed enlarged cortical veins in the right side compared with the left side. It also showed that cortical thrombosis extended to the anterior part of the superior sagittal sinus (Figure 2D and E). Thrombophilia work up was not done for two reason. First one because not available in our center and second reason there was no strong history supporting the thrombophilia with this age.

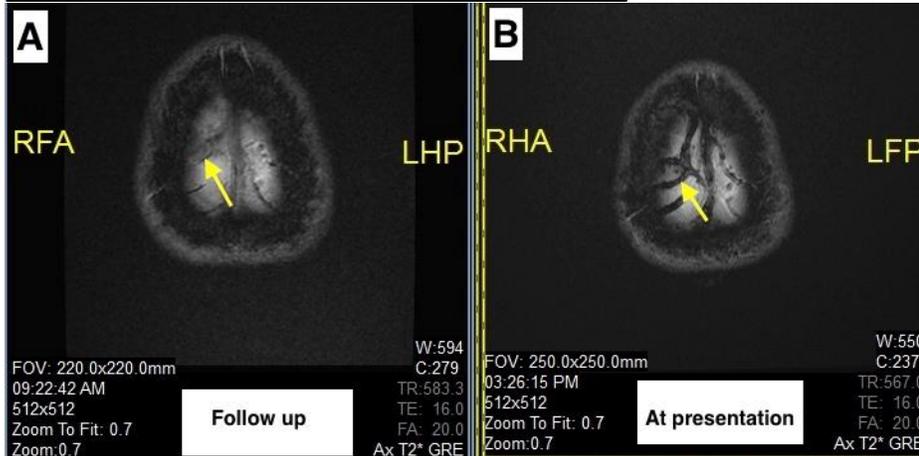
Cortical cerebral venous thrombosis was diagnosed. We started her on heparin infusion as CVST protocol. After three days, she was shifted to warfarin with a target international normalized ratio of 2 to 3. She was also started on antiepileptics for the seizure. The patient had three follow-up sessions in an outpatient clinic. Her condition remained stable with no headache or seizure. She has followed-up regularly in anticoagulation clinic with therapeutic international normalized ratio. Follow-up imaging showed reopening of the cortical veins (Figure 3).



**Figure 1.** A: Axial CT Brain showing right frontal hemorrhage (Circle). B: An axial CT brain showing cord sign on the right side (arrow). C: Sagittal view of CT brain showing subcortical frontal hematoma (Circle), with thrombus seen at superior sagittal sinus (arrow).



**Figure 2:** A: MRI gradient echo showed dilated right frontal cortical veins comparing to other side (arrows). B and C: Echo gradient showed the hematoma (circle) and thrombosed cortical veins (arrows). D: Coronal view of MRV showed patent major cerebral sinus. E: Sagittal view of cerebral veins which showed extension of the thrombus to anterior part of superior sagittal sinus.



**Figure 3:** A: Echo gradient MRI of the brain in follow up visit after three month showing normal caliber cortical veins. B: Echo gradient MRI of the brain at presentation showing dilated cortical veins (B).

**DISCUSSION**

We reported this case with cortical cerebral venous thrombosis to show that even short courses or intermittent use of oral contraceptive for various reasons can be a risk for CVST. As a Muslim country, we are required to fast for one month per the year during the holy month of Ramadan. Some people are exempt from this rule, including women during their menstrual period. Women are therefore required to make up these days by fasting after Ramadan. With the emerging and widespread use of oral contraceptive pills, women started to use it to postpone their menstruation until after Ramadan to be able to fast the whole month without interruption. Our patient used to use this short course of oral contraceptive for many years for that purpose. To date, there is no published case in Saudi Arabia for the short-term use of OCP to postpone menstruation in Ramadan. Two reports from Iran describe the same condition. One report is a cohort study conducted from October 2006 until October 2009<sup>6</sup>. Seventy cases were enrolled in this cohort with a diagnosis of cerebral venous thrombosis during Ramadan and other months (11 male and 59 female). Here, 19 out of 24 women with CVST during Ramadan had a history of short-term oral contraceptive use. The second report is a retrospective case series of nine patients with a diagnosis of cerebral vein thrombosis who has had used a short course of oral contraceptive during Ramadan in July and August of 2014 and 2015<sup>7</sup>. Our rationale with this paper is to increase awareness in the community that even short course use of OCP for any purpose can increase the risk of CVST. Our other rationale is to show the importance of medical images like MRI echo gradient in the diagnosis of cortical venous thrombosis when the large sinuses are patent on the image. This case has the advantage of demonstrating a novel way to using OCPs, which resulted in cerebral venous thrombosis and sequelae. The drawback is that OCPs have been linked to thrombosis.

The take-home message is to educate users and the general public that OCP should only be used under medical supervision and that it has a risk of VTE even with intermittent use or short courses.

**CONCLUSION**

Our experience taught us that using oral contraceptives for non-medical purposes, even for brief periods of time, can increase your risk of developing VTE. This is consistent with our understanding that taking oral contraceptives increases your risk of developing CVST and other VTEs.

**Conflict of interest**

No conflict of interest was declared by the author.

**REFERENCES**

1. Devasagayam S, Wyatt B, Leyden J, Kleinig T. Cerebral venous sinus thrombosis incidence is higher than previously thought: a retrospective population-based study. *Stroke*. 2016 Sep 1;47(9):2180-2.
2. Coutinho JM, Ferro JM, Canhao P, Barinagarrementeria F, Cantú C, Bousser MG, Stam J. Cerebral venous and sinus thrombosis in women. *Stroke*. 2009 Jul 1;40(7):2356-61.
3. Deveber G, Andrew M, Adams C, Bjornson B, Booth F, Buckley DJ, Camfield CS, David M, Humphreys P, Langevin P, macdonald EA. Cerebral sinovenous thrombosis in children. *New England Journal of Medicine*. 2001 Aug 9;345(6):417-23.
4. Saposnik G, Barinagarrementeria F, Brown Jr RD, Bushnell CD, Cucchiara B, Cushman M, Deveber G, Ferro JM, Tsai FY. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2011 Apr;42(4):1158-92.
5. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. *The Lancet Neurology*. 2007 Feb 1;6(2):162-70.
6. Sasanejad P, Ardekani AM, Velayati A, Shoeibi A, Saeidi M, Foroughipour M, Azarpazhooh MR. Cerebral vein thrombosis in women using short course oral contraceptive consumption. *Iranian journal of reproductive medicine*. 2012 Nov;10(6):537.
7. Khomand P, Hassanzadeh K. A case-series study of cerebral venous thrombosis in women using short course oral contraceptive. *Iranian journal of neurology*. 2016 Apr 3;15(2):92.