

Cerebral venous thrombosis following the use of oral contraceptive: A case report

Mehrafza Mir¹, Maryam Javadian^{2,*}, Mojgan Naeimi Rad³

¹Department of Anesthesiology, Babol University of Medical Sciences, Babol, Iran;

²Infertility and Reproductive Health Research Center, Health Research Institute & Department of Obstetrics & Gynecology, Clinical Research Development Unit of Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran;

³Clinical Research Development Unit of Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran;

Received: 23 May 2016

Accepted: 12 Jul 2016

Abstract

Cerebral Venous Thrombosis (CVT) is very rare. The most frequent risk factor for young women is the use of oral contraceptives.

A seventeen-year-old girl who had come down with a sudden onset of severe headaches, nausea, vomiting, and double vision referred to the emergency ward. She had been receiving combined oral contraceptive pill (OCP) in the past ten days for menometrorrhagia treatment. Computed Tomography (CT scan) proved normal, whereas Magnetic Resonance Venography (MRV) revealed evidence of sagittal sinus thrombosis and the patient was, as a result, treated with heparin. The patient's symptoms abated and the recovery began 48 hours after warfarin had been initiated. In five days, the patient was discharged with a good general health and without a headache or double vision.

Use of OCP is a major risk factor for CVT. In cases of headache in women taking OCPs, CVT should be considered among differential diagnoses. Physicians should take into account history of CVT and its risk factors when administering OCPs, and should inform patients of its symptoms.

Keywords: Cerebral Venous Thrombosis, Diagnosis, Risk factors, Oral contraceptive

Introduction

Cerebral Venous Thrombosis (CVT) is a rare lesion (1), which is more common among women than men by the ratio of 3:1 (2, 3). The increased risks in women can be attributed to such factors as pregnancy, postpartum, and oral contraceptive pills (OCPs) (4). Other main risk factors for CVT include prothrombin status, or genetic and acquired factors, malignancies, medications, infection, and head trauma (3). Cerebral and thrombosis of the sinus durae are less common than other types of stroke, and their diagnosis can be more challenging (5). However, the diagnosis of CVT is

now much easier and more frequent due to the use of magnetic resonance imaging (MRI) and the increased knowledge of its clinical symptoms (6). The symptoms and the signs of CVT include headaches with or without vomiting, papilledema, impaired vision, seizure, organ problems, or both, change in consciousness, numbness and coma (7, 8). This case report elaborates on how we diagnosed, managed, and treated a case of CVT in a girl.

The case report

The A 17-year-old woman was admitted to the emergency ward with severe headaches, nausea, and vomiting (5 days), and double vision in all directions (2 days). There were no history of traumatic brain injury, chest pain, severe hacking cough and fever. She had

*Corresponding author: Dr. Maryam Javadian, Infertility and Reproductive Health Research Center, Health Research Institute & Department of Obstetrics & Gynecology, Clinical Research Development Unit of Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran.
Tel: +989112142116, Email: javadianmaryam@yahoo.com

polycystic ovarian syndrome, which had been diagnosed three years earlier. She was on spironolactone for her hirsutism for two months, which caused the development of menometrorrhagia. The gynecologist advised her to take combined oral contraceptive pills (OCP) (Low dose) for her menometrorrhagia. Only ten days after the onset of OCP, she developed these symptoms. From the history and the clinical settings, a diagnosis of cerebral vein thrombosis (CVT) was suspected. On neurological examination, in addition to double vision, a severe bilateral papilledema, especially in the left eye, was observed, but there were no unilateral neurologic signs. Computed tomography (CT scan) of the cerebral proved normal, whereas MR venography revealed evidence of sagittal sinus thrombosis (Figure 1). After the diagnosis of CVT, a complete blood count, lupus anticoagulants (LA), protein C (PC), protein S, anti-dsDNA, anti phospholipid, anti-phospholipid, anti-cardiolipin antibodies, c-ANCA (Anti-PR3), P-ANCA, factor V Leiden, SGPT and SGOT were also conducted. The results of all the above-mentioned tests as well as the coagulation profile of the patient were normal (Table1).

The treatment of the patient started with low molecular weight heparin sodium 1000 international units, which was given intravenous infusion every hour for the duration of 48 hours. (Table1). In addition, valproic acid (Depacon) was also given to prevent any seizures. The patient's symptoms abated and the

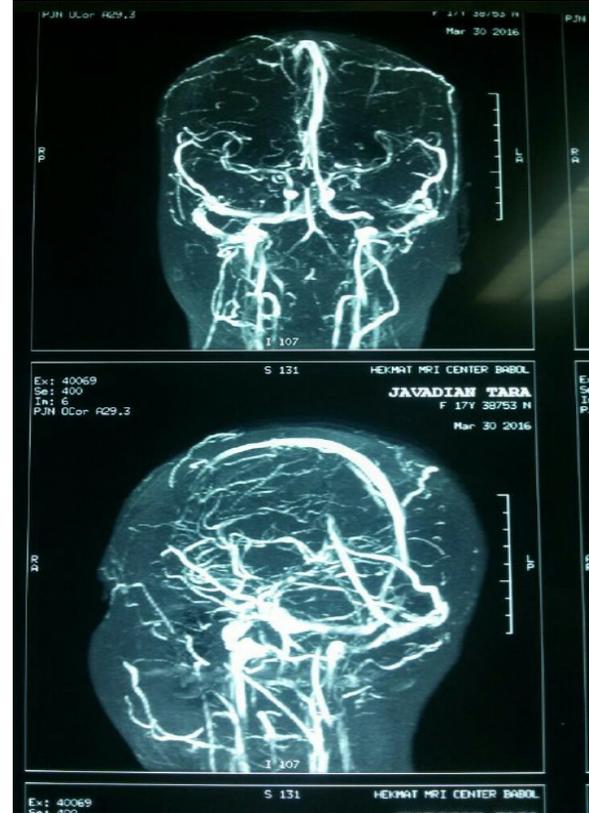


Figure 1. MR venography

recovery began after 48 hours. Then, simultaneously with heparin, warfarin was given to the patient and the dosage was titrated according to the international normalized ratio (INR). Warfarin (one pill a day) and coagulation tests were continued after the discontinuation of heparin and depacon. In five days, the patient was discharged with a good general health, without any headaches or double vision.

Discussion

The use of OCP is regarded as the main risk factor for CVT in young women, especially when they have a problem in prothrombin status. It is worth mentioning that in more than 85% of adult patients, at least one risk factor is diagnosed for CVT, which is often related to their prothrombin status (9). Physicians may often find it very challenging to diagnose CVT, and may mistake it for other types of stroke. The most frequent symptom for CVT patients is headache (like the case of our patient), which is present in 80% to 90% of adult patients. It is, however, the least specific symptom in young patient. The most present symptom is the

Table 1: Description of laboratory variables of the case

Variables	Results
Hemoglobin (Hb)(mg/dl)	12.3
Mean corpuscular volume (MCV) (femtoliters/cell)	82.6
Lupus anticoagulants (LA) (%)	45
Protein C (PC) (IU/dL)	88
Protein S (IU/dL)	75
Anti-dsDNA (IU/dL)	2
Antinuclear antibodies (ANA)	Negative
Anti phospholipid(Gplu/ml)	2
Anti-cardiolipin antibodies (U/ml)	0.9
c-ANCA (Anti-PR3) (U/ml)	1.2
P-ANCA(U/ml)	0.3
Factor V Leiden (Ratio)	3.2
SGPT(U/L)	190
SGOT(U/L)	46

unusual headache with stroke-like symptoms (9, 10). Similarly, our patient had an unusual headache with double vision. In patients with suspected CVT, MR and MR venogram can usually help confirm the diagnosis of sagittal sinus thrombosis and is usually more sensitive than CT (1). It is difficult to rule out other possible diagnoses, however. The CT scan of the head has been reported to be normally used in more than 30% of CVT cases, and its results are rather unspecific. Therefore, CT scan has a greater role in other acute and sub-acute cerebral disorders (5). In the case of our patient, the CT scan of the cerebral was normal; therefore, we decided to request MR venogram for the patient. Doppler ultrasound (with or without contrast) is also a non-invasive technique, used for both diagnosis and follow-up of CVT, but requires further assessment (11, 12). Angiography may also be useful for the diagnosis of CVT (5). The meta-analysis of 14 studies conducted to measure D-dimer in 1134 patients showed that there was an increased D-dimer in 7 studies (13). In a study conducted on 233 patients, the D-dimer showed 94% of sensitivity and 98% of specificity in the diagnosis of CVT within the first seven days of the emergence of symptoms (14). In order to explore the genetic and acquired factors, all patients should be assessed for their anti-thrombin, protein C, protein S, leiden 7 factor, prothrombin G20210A mutation, lupus anticoagulant, anti-cardioleptin, and anti-beta2 glycoprotein 1 (15). It should be mentioned that in our study, we did not apply all these tests for our patient. For children and adults, anticoagulant therapy with low molecular weight heparin is recommended. After the acute phase of CVT, anticoagulant plus warfarin should be continued for 3 to 12 months for adults and 3 to 6 months for children (INR=2 to 3) (16). The results obtained from a study conducted on 124 patients (70.16% female) showed that headache, papilledema and seizure were the most common symptoms of CVT, and that 65.51% of women had been using OCPs prior to the development of the symptoms (17). In another study conducted on 15 patients with CVT, MRI was helpful in 14. It was also found that the most important risk factor for CVT was the use of OCPs, followed by the history of CVT (40%) in patients and their families. Of the 15 patients, only 5 had headaches, and 13% of them had thrombophilia (18).

Conclusion

The use of OCP is regarded as a major risk factor for CVT. In case a woman taking OCPs suffers from headaches, CVT should be suspected among different possible diagnoses. Physicians should take the history of CVT and its risk factors into account when the prescribe OCPs, and should let patients know about its symptoms.

Acknowledgements

We would like to thank the clinical research development unit of Rouhani Hospital in Babol.

Conflict of interest

The authors declare that there is no conflict of interests.

References

1. Patel SI, Obeid H, Matti L, Ramakrishna H, Shamoun FE. Cerebral Venous Thrombosis: Current and Newer Anticoagulant Treatment Options. *Neurologist*. 2015 Nov;20(5):80-88.
2. Coutinho JM, Ferro JM, Canhao P, Barinagarrementeria F, Cantu C, Bousser MG, et al. Cerebral venous and sinus thrombosis in women. *Stroke*. 2009;40(7):2356-2361.
3. Ferro JM, Canhao P, Stam J, Bousser MG, Barinagarrementeria F. Prognosis of cerebral vein and dural sinus thrombosis: results of the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT). *Stroke*. 2004;35(3):664-670.
4. Stam J. Thrombosis of the cerebral veins and sinuses. *The New England journal of medicine*. 2005 Apr 28;352(17):1791-1798.
5. Bousser MG, Ferro JM. Cerebral venous thrombosis: an update. *Lancet Neurol*. 2007;6(2):162-1670.
6. Tsai FY, Nguyen B, Lin WC, Hsueh CJ, Yen A, Meng K, et al. Endovascular procedures for cerebrovenous disorders. *Acta Neurochir Suppl*. 2008;101:83-86.
7. Leker RR, Steiner I. Isolated intracranial hypertension as the only sign of cerebral venous thrombosis. *Neurology*. 2000 May 23;54(10):2030.
8. Zuurbier SM, Coutinho JM. Cerebral Venous Thrombosis. *Adv Exp Med Biol*. 2017;906:183-1893.
9. de Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Case-control study of risk of

cerebral sinus thrombosis in oral contraceptive users and in [correction of who are] carriers of hereditary prothrombotic conditions. The Cerebral Venous Sinus Thrombosis Study Group. *BMJ (Clinical research ed)*. 1998 Feb 21;316(7131):589-592.

10. Terazzi E, Mittino D, Ruda R, Cerrato P, Monaco F, Sciolla R, et al. Cerebral venous thrombosis: a retrospective multicentre study of 48 patients. *Neurol Sci*. 2005;25(6):311-315.

11. Stolz E, Kaps M, Dorndorf W. Assessment of intracranial venous hemodynamics in normal individuals and patients with cerebral venous thrombosis. *Stroke*. 1999;30(1):70-75.

12. Valdueza JM, Hoffmann O, Weih M, Mehraein S, Einhaupl KM. Monitoring of venous hemodynamics in patients with cerebral venous thrombosis by transcranial Doppler ultrasound. *Arch Neurol*. 1999;56(2):229-234.

13. Dentali F, Squizzato A, Marchesi C, Bonzini M, Ferro JM, Ageno W. D-dimer testing in the diagnosis of cerebral vein thrombosis: a systematic review and a meta-analysis of the literature. *J Thromb Haemost*. 2012;10(4):582-589.

14. Meng R, Wang X, Hussain M, Dombos D, 3rd, Meng L, Liu Y, et al. Evaluation of plasma D-dimer plus fibrinogen in predicting acute CVST. *Int J Stroke*. 2014;9(2):166-173.

15. Nakashima MO, Rogers HJ. Hypercoagulable states: an algorithmic approach to laboratory testing and update on monitoring of direct oral anticoagulants. *Blood Res*. 2014;49(2):85-94.

16. Einhaupl K, Stam J, Bousser MG, De Bruijn SF, Ferro JM, Martinelli I, et al. EFNS guideline on the treatment of cerebral venous and sinus thrombosis in adult patients. *Eur J Neurol*. 2010;17(10):1229-1235.

17. Ashjazadeh N, Borhani Haghghi A, Poursadeghfard M, Azin H. Cerebral venous-sinus thrombosis: a case series analysis. *Iran J Med Sci*. 2011;36(3):178-182.

18. Christo PP, Carvalho GM, Gomes Neto AP. [Cerebral venous thrombosis: study of fifteen cases and review of literature]. *Rev Assoc Med Bras*. 1992;56(3):288-292.