



# Dural sinus thrombosis due to hormonal contraception

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Headache is a common complaint encountered in outpatient clinics and emergency rooms. It can be due to a wide variety of diseases, ranging from a simple tension headache to more serious intracranial pathologies. Dural sinus thrombosis is an uncommon cause of headache that can rarely complicate the use of hormonal contraception. Herein, we present a 42-year-old woman with a 2-month history of headache resistant to usual treatment regimens. The recent introduction of monthly injections of combined estrogen and progesterone for contraception provoked further workup that confirmed the presence of dural sinus thrombosis. Warfarin therapy was initiated and the patient later required a ventriculoperitoneal shunt for symptom relief. Clinicians should maintain a high index of suspicion when evaluating a patient with resistant headache while

## Case presentation

A 42-year-old woman with no past medical history began experiencing recurrent headaches for 2-month duration. She described the headache as frontal, dull aching, 6/10 in severity, and associated with nausea and vomiting. Acetaminophen and various NSAIDs provided no relief, which prompted her to seek medical advice. She had no history of smoking, diabetes mellitus, hypertension, or prior blood clots. Six months earlier, she began receiving monthly injections of combined estrogen and progesterone for contraception. On examination, her BMI was 25 kg/m<sup>2</sup>, blood pressure was 130/80 mmHg, pulse regular at 80/min, and she was afebrile. There was no nuchal rigidity, and neurological examination was unremarkable. Ear, nose, and throat examination were normal and fundoscopic examination was negative for papilledema. A noncontrast computed tomography (CT) scan of the brain was normal.

The patient continued to experience worsening symptoms. A repeat fundus examination 1 week later revealed bilateral papilledema and was admitted to the hospital for further workup. MRI with and without contrast of the brain and magnetic resonance venogram with contrast revealed extensive thrombosis affecting multiple cerebral veins, both superficial and deep (Fig. 1). The workup for prothrombotic states was nonrevealing. Therapeutic anticoagulation with heparin followed by warfarin to achieve a target international normalized ratio of 2–3 was instituted. Because of the persistence of symptoms, it was decided to perform a ventriculoperitoneal shunt for cerebrospinal fluid drainage and relief of intracranial tension. The patient then became symptom free and was discharged 1 week later.

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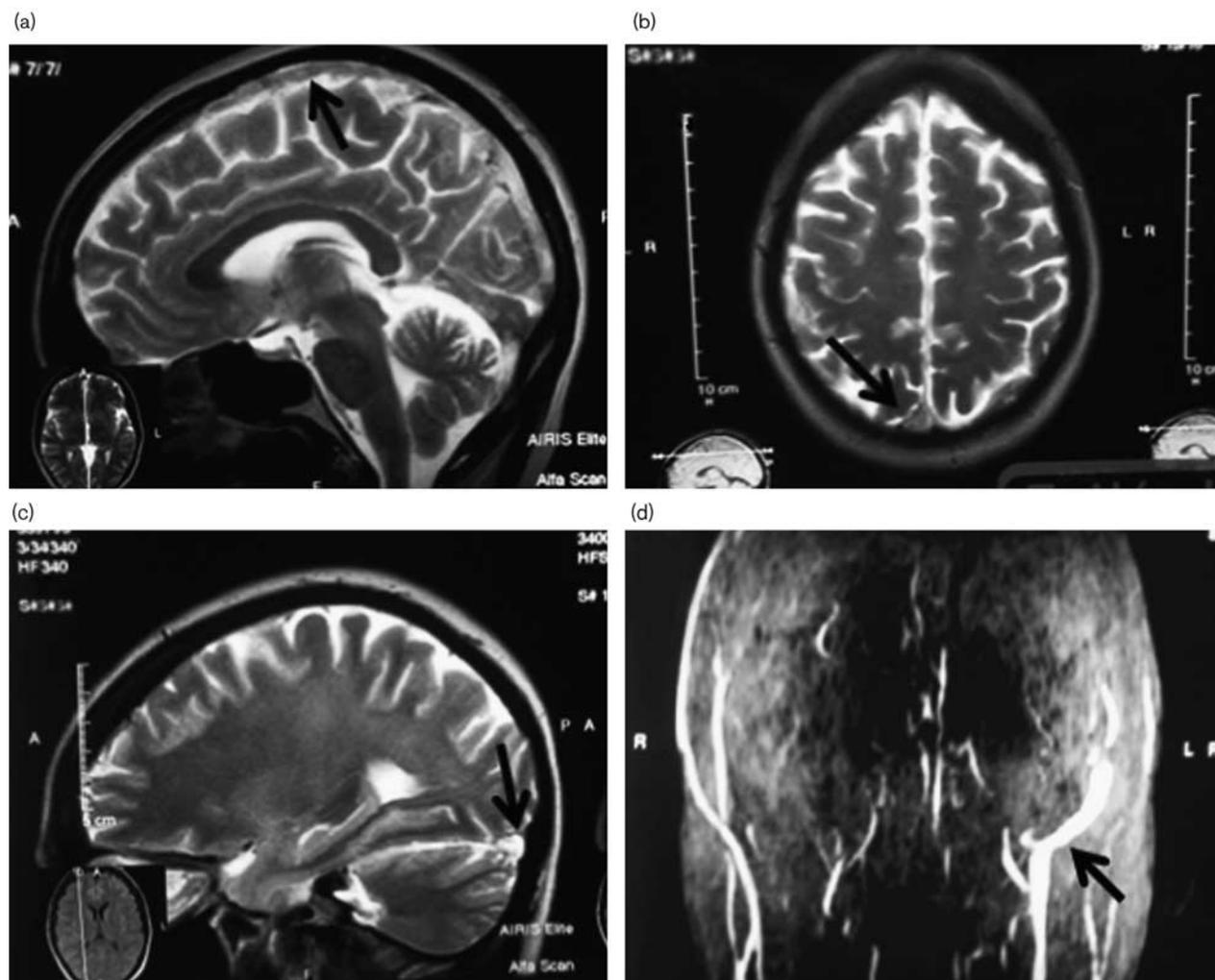
## Discussion

Dural sinus thrombosis is an uncommon condition with varied clinical presentation usually affecting middle-aged women. It has acquired attention recently because of improved imaging techniques and better awareness among physicians, particularly neurologists. Although more than 100 causes [1] have been described in the literature, pregnancy and puerperium are the most frequent risk factors [2]. A study in the USA, based on the data from the 1993–1994 healthcare cost and utilization project, estimated that dural sinus thrombosis complicated 11.6 in every 100 000 deliveries, and that increased maternal age was a major risk factor [3]. Prothrombotic states are another important cause for dural sinus thrombosis.

Since the introduction of hormonal contraception in the early 1960s, case reports emerged describing its association with increased risk of thrombosis [4]. This has been presumed to be because of the estrogenic component irrespective of the route of administration. More recent data showed a higher incidence of venous thrombosis with third-generation (desogestrel and gestodene) rather than second-generation progestins (e.g. levonorgestrel and norgestrel), with an estimated risk of 1.4–4 times as high as that associated with second-generation preparations [5,6]. The procoagulant effect of oral contraceptive pills (OCPs) is due to the resultant increase in the levels of coagulation factors and decreases in the levels of the anticoagulant proteins: antithrombin and protein S [7].

Despite a low absolute risk (15 cases per 100 000 cardiovascular events per year), women who are taking

Fig. 1



(a) Sagittal T2-weighted MRI brain through the midline showing hyperintense signal throughout the superior sagittal sinus (arrow) corresponding to sinus thrombosis. (b) Axial T2-weighted MRI brain illustrating the classic delta sign of hyperintense thrombosis in the superior sagittal sinus. (c) Sagittal T2-weighted MRI brain demonstrating absence of the flow void on the right transverse sinus (arrow). (d) Cerebral magnetic resonance venography with contrast venogram demonstrates the absence of flow in bilateral transverse sinuses, right sigmoid, and internal jugular veins. There is reconstitution of flow into the left sigmoid and internal jugular (arrow). Deep veins are also noted to have abnormal filling.

OCP have a 3–6 times greater risk of venous thromboembolism than women who do not [8]. The risk is highest during the first year and increases with age (> 35 years), obesity, recent surgery, and some forms of thrombophilia, especially factor V Leiden mutation [9]. For this reason, some experts believe that all first-time OCP users should be screened for factor V Leiden mutation [10]. Women with prothrombotic defects and concomitant oral contraceptive use had an increased odds ratio of 30 to develop cerebral sinus thrombosis, relative to women that did not carry this defect [11]. The most common sites of thrombosis associated with OCP are the deep veins, which may be complicated by pulmonary embolism. Arterial thrombosis is less frequent and is usually predisposed by other concomitant risk factors, such as smoking [12].

It is generally accepted by medical authorities that the health risks of OCP are lower than those from pregnancy and birth. However, complications are still possible in a certain category of high-risk patients. For this reason the WHO has created a graded scheme of precautions when considering which patients should not use hormonal contraception. Women identified with WHO category 4 diagnoses should not be given OCP [11]. Category 4 includes patients with a history of venous thromboembolism, cerebrovascular or coronary artery disease, patients whose age is greater than 35 years and smoke 20 or more cigarettes per day, patients with history of headache with focal neurological symptoms, prior history of diabetes mellitus with complications, hypertension (blood pressure of >160/100 mmHg or with concomitant vascular disease), patients with liver disease, patients with breast

cancer, and patients undergoing major surgery with expected prolonged immobilization. In an attempt to reduce the risk of thrombosis, products with lower dosage of estrogen should be utilized (e.g. Alesse, Loestrin 1/20, Levlite, and Mircette).

Headache resistant to treatment in middle-aged women taking OCP should not be taken lightly, especially when the more common causes of headache are excluded. Two serious conditions must be promptly ruled out: benign intracranial hypertension and dural sinus thrombosis. Fundoscopic examination should be performed looking for signs of increased intracranial pressure. Papilledema can be a latent sign of increased intracranial tension and its absence does not rule out intracranial hypertension. Benign intracranial hypertension is characterized by the presence of slit-like ventricles on the CT brain and increased cerebrospinal fluid pressure greater than 25 mmHg. Dural sinus thrombosis, which has a worse prognosis, is not evident on noncontrasted brain CT, and MRI/venogram with and without contrast is necessary to confirm the diagnosis. Although CT contrast venography remains popular in some centers and may be a superior technique in certain cases [13], the classic empty delta sign is present in only 20% of the cases [14].

### Conclusion

Dural sinus thrombosis is a rare and under-recognized cause of headache that should be considered in women with recent introduction of hormonal contraception. The absence of papilledema and a negative CT brain should not halt further workup. MRI/venogram is mandatory to confirm the diagnosis.

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### Conflicts of interest

There are no conflicts of interest.

## References

- 1 Bousser MG. Cerebral venous thrombosis: nothing, heparin, or local thrombolysis? *Stroke* 1999; **30**:481–483.
- 2 Cantú C, Barinagarrementeria F. Cerebral venous thrombosis associated with pregnancy and puerperium. Review of 67 cases. *Stroke* 1993; **24**: 1880–1884.
- 3 Lanska DJ, Kryscio RJ. Risk factors for peripartum and postpartum stroke and intracranial venous thrombosis. *Stroke* 2000; **31**:1274–1282.
- 4 Vessey MP. Thrombosis and the pill. *Prescr J* 1970; **10**:1–7.
- 5 Jick H, Jick SS, Gurewich V, Myers MW, Vasilakis C. Risk of idiopathic cardiovascular death and nonfatal venous thromboembolism in women using oral contraceptives with differing progestagen components. *Lancet* 1995; **346**:1589–1593.
- 6 [No authors listed]. Effect of different progestagens in low dose oestrogen oral contraceptives on venous thromboembolic disease. World Health Organization Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception. *Lancet* 1995; **346**:1582–1588.
- 7 Middeldorp S, Meijers JC, van den Ende AE, van Enk A, Bouma BN, Tans G, et al. Effects on coagulation of levonorgestrel- and desogestrel-containing low dose oral contraceptives: a cross-over study. *Thromb Haemost* 2000; **84**:4–8.
- 8 Chasen-Taber L, Stampfer MJ. Epidemiology of oral contraceptives and cardiovascular disease. *Ann Intern Med* 1998; **128**:467–477.
- 9 Vandenbroucke JP, Koster T, Briet E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral-contraceptive users who are carriers of factor V Leiden mutation. *Lancet* 1994; **344**:1453–1457.
- 10 Vandenbroucke JP, van der Meer FJ, Helmerhorst FM, Rosendaal FR. Factor V Leiden: should we screen oral contraceptive users and pregnant women? *BMJ* 1996; **313**:1127–1130.
- 11 De Bruijn SF, Stam J, Koopman MM, Vandenbroucke JP. Case-control study of risk of cerebral sinus thrombosis in oral contraceptive users who are carriers of hereditary prothrombotic conditions. *BMJ* 1998; **316**:589–592.
- 12 WHO. *Improving access to quality care in family planning: medical eligibility criteria for contraceptive use*. Geneva: World Health Organization 1996. pp. 13–26.
- 13 Vogl TJ, Bergman C, Villringer A, Einhüpl K, Lissner J, Felix R. Dural sinus thrombosis: value of venous MR angiography for diagnosis and follow-up. *Am J Roentgenol* 1994; **162**:1191–1198.
- 14 Ameri A, Bousser MG. Cerebral venous thrombosis. *Neurol Clin* 1992; **10**: 87–111.

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