CASE REPORT

Throbbing headache is not always migraine; it can be serious

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Cerebral venous thrombosis (CVT) is a rare but serious venous thrombotic disorder in the general population. It has an estimated annual incidence of about 4–5 cases per 1 million persons. It is more common in females than males. We describe below a case of a 49-year-old female patient who presented to the emergency room with 1 day history of right-sided throbbing headache associated with vomiting. Computed tomography (CT) scan of the head without contrast showed venous sinus thrombosis involving the posterior sagittal sinus, extending into the dominant right transverse sinus, which was confirmed by CT head with intravenous contrast. The patient was immediately started on anticoagulation with therapeutic low-molecular-weight heparin that was transitioned to warfarin. Follow-up CT head 3 months later showed resolution of the thrombus and recanalization of the affected veins. A high level of suspicion for a rare disorder like CVT should be considered as part of the differential diagnosis of headache, which is a commonly encountered problem, because immediate anticoagulation treatment can prevent fatal complications.

Keywords: cerebral venous thrombosis; headache; oral contraceptive pills; sinus infection; anticoagulation

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Cerebral venous thrombosis (CVT) is a rare disorder that involves thrombosis of the veins and sinuses of the brain. It most commonly involves the superior sagittal sinus. The annual incidence is estimated to be approximately 5 cases per 1 million persons in western countries. CVT causes 0.5% of strokes (1, 2).

Case presentation

A 49-year-old Caucasian woman presented to emergency department with sudden onset of right fronto-temporal throbbing headache for 1 day. It started as 3/10 in severity and then progressed to 10/10 in about half hour. The headache was associated with right eye pain, nausea, multiple episodes of vomiting, photophobia, and phonophobia as well as chills but no fever. She denied any vision changes, dizziness, speech difficulty, focal weakness, rash, joint pains, neck pain, or rigidity. The patient was previously healthy with no history of chronic medical problems except recurrent sinus infections as well as environmental allergies. Her medications included fexofenadine and oral combined contraceptive pills (CCPs), which she has been taking regularly for 10 years for menorrhagia. She had neither personal nor family history of blood clots, bleeding disorders, or any malignancy. She never smoked but used to drink alcohol socially. The patient had no history of abortion or difficulty getting pregnant. She had three pregnancies; last one was at the age of 35 with no complications. Her mother had three miscarriages while being on phenobarbital for epilepsy. Physical examination showed normal vital signs with blood pressure of 127/70 mm Hg, pulse 88 beats/min, temperature 98.2 °F (36.8 °C), respiratory rate 14 per min, and oxygen saturation 99% on room air. She was alert, oriented to time, place, and person, and in no distress; cardiopulmonary examination revealed clear breath sounds bilaterally without wheezes or rhonchi, and normal heart sounds with no murmurs, gallops, or rubs. Abdominal exam showed no tenderness, masses, or organomegaly, and she had no edema of the lower extremities. Detailed neurological examination showed intact cranial nerves 2–12 and round, reactive pupils to light and accommodation with normal fundi. She had normal and symmetric motor power in both upper and lower extremities, intact sensation, and no focal neurologic deficit.

Complete blood count was abnormal for leukocytosis of 18.6 K/µL with higher lymphocyte differential count of 21% and no bands. Complete metabolic panel and
Coagulation studies were within normal limits. Infectious workup including blood cultures was negative. The patient was given ketorolac and hydromorphone, but failed to relieve her headache; so computed tomography (CT) of the head without contrast was done that showed venous sinus thrombosis involving the posterior sagittal sinus and extending into the dominant right transverse sinus (Fig. 1). CT head with contrast was done for confirmation (Fig. 2); it showed occlusive thrombus within the posterior superior sagittal sinus, extending inferiorly into the dominant right transverse sinus, sigmoid sinus, and superior right internal jugular vein. The diagnosis of cerebral venous sinus thrombosis was made based on the patient’s presentation and CT findings. Her OCPs were stopped. Anticoagulation was started with low-molecular-weight heparin (LMWH) that was switched to warfarin with an international normalized ratio (INR) target range of 2.0 to 3.0. She received warfarin for 3 months and then switched to low-dose aspirin. Further workup during her hospital stay including carotid artery Doppler and transthoracic echocardiogram was negative. Follow-up CT head 3 months after the initial diagnosis showed complete recanalization of the occluded cerebral sinuses and veins.

Three weeks after completion of anticoagulation, the patient underwent testing for prothrombotic conditions, including protein S, protein C, and antithrombin deficiency; antiphospholipid syndrome; prothrombin G20210A mutation; and factor V Leiden; all were negative.

Discussion
CVT is a rare disorder that occurs more commonly in pregnant women, women on hormonal contraceptives, patients younger than 40 years of age, and patients with thrombophilia. The incidence of 5 cases per million persons per year goes up to 12 cases per 100,000 women annually during pregnancy and puerperium (3). So, it is more common in women than men, with a ratio of 3:1 (4). Thrombophilia is the most common risk factor of CVT (5); in the International Study on Cerebral Vein and Dural Sinus Thrombosis (ISCVT) cohort, prevalence of thrombophilia was 34%, and inherited thrombophilia was 22% (6). Acquired thrombophilias associated with CVT include antiphospholipid antibodies and hyperhomocysteinemia. Antithrombin III deficiency, protein C and protein S deficiency, factor V Leiden mutation, and the prothrombin gene mutation 20210 are inherited thrombophilias associated with CVT. Testing for these prothrombotic conditions is indicated 2–4 weeks after completion of anticoagulation (7).

Other risk factors include, but are not limited to, pregnancy, postpartum state, hormonal contraceptive therapy, and localized infections, such as otitis media, mastoiditis, sinusitis, and meningitis as well as systemic...
Causes of CVT. Laboratory studies are useful for determining the possible clinical evaluation and on imaging studies, while clinical diagnosis of CVT is based on clinical evaluation and on imaging studies, while clinical laboratory studies are useful for determining the possible causes of CVT.

Head CT is the most frequently performed imaging study, but it has the disadvantage of poor sensitivity (12) as it shows direct signs of CVT in just a third of patients. Magnetic resonance imaging of the head combined with a magnetic resonance venography is the recommended study for CVT by the American Heart Association and the American Stroke Association (AHA/ASA) 2011 Scientific Statement as it is the most sensitive study (12).

Treatment acutely is focused on anticoagulation and amelioration of hypercoagulable factors to the extent possible. The role of anticoagulation is to avoid thrombus spread, recanalize thrombosed sinuses and cerebral veins, and stop complications of deep vein thrombosis and pulmonary embolism. The duration of anticoagulation depends on the underlying risk factor according to the AHA/ASA guidelines (7). In patients with provoked CVT (associated with a transient risk factor), vitamin K antagonists (VKA) should be continued for 3 to 6 months, with a target INR of 2.0 to 3.0 (7). In patients with unprovoked CVT, VKA may be continued for 6 to 12 months, with a target INR of 2.0 to 3.0. Indefinite anticoagulation with a target INR of 2.0 to 3.0 should be considered in patients with recurrent CVT, venous thromboembolism (VTE) after CVT, or first CVT with severe thrombophilia (including homozygous prothrombin G20210A; homozygous factor V Leiden; deficiencies of protein S, protein C, or antithrombin; combined thrombophilia defects; or antiphospholipid syndrome). In pregnant women with CVT, full anticoagulant doses of LMWH, rather than unfractionated heparin, should be continued throughout pregnancy, and LMWH or VKA with a target INR of 2.0 to 3.0 should be continued for a minimum of 6 weeks after delivery (for a total duration of therapy of 6 months at least). It is recommended to advise women with a history of CVT that future pregnancy is not absolutely contraindicated, but they should be aware that prophylaxis with LMWH during future pregnancies and the postpartum period is advisable (7).

While non-VKA oral anticoagulants (NOACs) have intuitive appeal given their ease of use and apparent superiority to warfarin in VTE, Marshall and Connors caution that the lack of reversibility of the NOACs may be problematic in CNS-related thrombotic issues (13). On the contrary, a small study was done in Germany that involved seven patients treated with rivaroxaban, who were compared to nine patients treated with VKA. Oral anticoagulation was started 5 days after bridging with heparin. It concluded that factor Xa inhibitor showed a similar clinical benefit as VKA in the treatment of CVT (14). However, specific guidelines in this setting are not yet available.

Close clinical follow-up is strongly advised, and according to the AHA/ASA 2011 Scientific Statement, follow-up imaging is recommended in 3 to 6 months after diagnosis to look for recanalization (12).

Early recognition and proper treatment are essential as CVT can result in serious complications including venous infarction, subarachnoid hemorrhage, pulmonary embolism, dural AV-fistula, and epilepsy (15).

We believe that the precipitating factor in our case was the use of oral contraceptive pills superimposed on a recurrent sinus infection treated with several courses of antibiotics; hence, the patient was instructed to stop hormonal contraceptives. On clinical follow-up, her headache had completely resolved, and she had no recurrence of CVT on follow-up imaging.

Conclusion
CVT is a very serious condition that should never be missed in patients who present with acute or subacute headache with unusual features. Although headache is the main presenting complaint, it remains to be a challenging diagnosis due to its wide range of clinical pictures and different risk factors. If it occurs in women taking oral contraceptive pills, they should receive no estrogen-based therapies in the future. This unusual case report emphasizes the significance of timely diagnosis of CVT through neuroimaging and the necessity of immediate anticoagulation as the most crucial step in patient management. Such case is unique in how a fatal condition may masquerade in a common migraine picture and be easily missed if high degree of vigilance is lacking.

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