Transgender venous thrombosis

Amanda Opaskar, MD; Eugene L. Scharf, MD; Michael W. Chilungu, MD; Adam G. Kelly, MD

A 53-year-old male-to-female transgender patient on cross-sex hormone replacement therapy (CSHT), estradiol 8 mg daily, presented to the emergency department (ED) with acute-onset headache and left visual field disturbances after a recent mechanical fall with head trauma. The medical history was notable for hyperlipidemia. There was no personal or family history of clotting disorders and no history of tobacco use.

In the ED, the patient experienced a generalized tonic-clonic seizure characterized by forced left gaze deviation lasting 1 minute. Neurologic examination was notable for left inferior quadrantanopia. Noncontrast CT of the head showed a right parietal hypodensity. MRI revealed infarction involving the left parietal-occipital cortex in a nonarterial distribution suggesting venous infarction. Magnetic resonance venography (MRV) confirmed a cortical vein thrombosis with cortical microhemorrhage (figure).

Hospital management included cessation of CSHT and initiating systemic anticoagulation with heparin as a bridge to warfarin with goal international normalized ratio 2–3.

Laboratory evaluation for hypercoagulability was negative. The patient's headache and visual field deficits improved and she was discharged home without functional deficit.

At 90-day follow-up, the patient's headache and vision continued to subjectively improve. Interval MRV showed recanalization of the cortical vein (figure). Repeat serologic evaluation for hypercoagulability was negative. With resolution of the thrombus, anticoagulation was discontinued, aspirin 81 mg daily was started for antithrombotic effect, and CHST with lower dose estradiol 4 mg daily was resumed.

DISCUSSION

While cerebral venous thrombosis (CVT) is an uncommon cause of stroke, comprising 0.5–1% of all strokes, it is potentially serious and associated with mortality close to 10% in observational studies.¹

Risk factors for CVT are inherited or acquired hypercoagulable states including head injury, cancer, infection, pregnancy, autoimmune conditions, and inherited thrombophilia.² Hormonal medications including oral contraceptives, hormone replacement therapy (HRT), CSHT, and other hormonal therapy have also been associated with venous thromboembolic events (VTE).^{2,3}

We report a case of CVT in a male-to-female transgender patient on CSHT for over 20 years, without undergoing gender reassignment surgery, who achieved favorable outcome. In this patient, a history of recent head trauma was believed to precipitate the formation of venous thrombosis. We discuss the treatment options including timing of resuming HRT.

There are a growing number of patients identified as transgender in the United States, with estimates of about 150,000 youth age 13–17 and 1.4 million adults.⁴ CSHT, pursued by many transgender patients, allows individuals to develop secondary sex characteristics that conform to their gender identity.⁵ CSHT has been shown to improve transformation satisfaction, psychological profile, cognitive function, emotional repercussions, and quality of life

Practical Implications

Cerebral venous thrombosis is a rare complication in transgender patients on cross-sex hormone therapy.

From the Department of Neurology, University of Rochester, NY.

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Correspondence to: Amanda_opaskar@urmc.rochester.edu

Figure Neuroradiologic features of cerebral venous thrombosis

Magnetic resonance venography shows cortical venous filling defect consistent with a venous thrombosis (A) that reconstitutes on surveillance imaging (E, red arrows). Susceptibility-weighted sequencing shows hypointensity of the right cortical vein consistent with thrombosis (B, blue arrow) with interval resolution of blooming artifact (F, blue arrow). Sagittal noncontrast T1-weighted sequencing shows hyperintensity in the region of the cortical vein suggestive of acute thrombus (C, gold arrow) with interval resolution (G). Diffusion weight sequence shows parieto-occipital restricted diffusion outside of conventional arterial vascular distribution suggestive of venous infarction (D) with interval cystic encephalomalacia on surveillance imaging consistent with chronic infarct (H).

in these patients and is typically continued lifelong.⁶ Major or life-threatening complications of CSHT are rare and include VTE, early coronary artery disease, ischemic stroke, and cancer.^{2,5}

In the United States, standard CSHT regimens include a combination of low-dose oral estradiol with the antiandrogen spironolactone.⁵ European regimens contain cyproterone, a high-potency progesterone not readily available in the United States. Transdermal estrogens have lower VTE risk but are less efficacious, requiring multiple patches in order to obtain the desired serum estrogen level.⁵

Retrospective studies of VTE risk of transgender patients on CSHT have estimated a 2%–6% lifetime risk of VTE although with current lower dose estrogen regimens the risk has been even less.⁵ One previous case of an unprovoked CVT in a male-to-female transgender patient on long-term CSHT after gender reassignment surgery has been reported that identified risk factors of older age and seropositive lupus anticoagulant.

Optimal timing of repeat imaging, anticoagulation vs antiplatelet therapy, and when to consider resuming CSHT are open questions. Multiple studies have demonstrated that recurrent VTE/CVT is highest within the first year.^{1,3} The current American Heart Association/American Stroke Association guidelines recommend anticoagulation for 3–6 months in patients with provoked CVT. One study of women on estrogen therapy (oral contraceptive pills or HRT) with previous VTE showed a low likelihood of recurrent VTE of <10% within 5 years in patients who had resumed hormonal therapy after treatment with anticoagulation. In transgender patients, due to the potential negative quality of life effect of cessation of CSHT, timing of resuming therapy is of particular importance.⁶

In our patient, withholding CSHT had a negative quality of life effect. At 90 days, repeat imaging showed complete recanalization, and after discussion with the patient, who was accepting of the risks, anticoagulation was discontinued and CSHT was resumed with low-dose antiplatelet therapy.

Further study is needed to investigate the optimal anticoagulation duration, timing of CSHT resumption, and role of antiplatelet therapy.

REFERENCES

1. Saposnik G, Barinagarrementeria F, Brown RD, et al. Diagnosis and management of cerebral venous thrombosis: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2011;42:1158–1192.
2. Oster JM, Shastri P, Geyer C. Cerebral venous sinus thrombosis after gender reassignment surgery. *Gender Medicine* 2010;7:270–275.
3. Eischer L, Eichinger S, Kyrle PA. The risk of recurrence in women with venous thromboembolism while using estrogens: a prospective cohort study. *J Thromb Haemost* 2014;12:635–640.
4. Herman J, Flores AR, Brown TNT, et al. Age of Individuals Who Identify as Transgender in the United States. Los Angeles: The Williams Institute: UCLA School of Law; 2017.
5. Arnold JD, Sarkodie EP, Coleman ME, Goldstein DA. Incidence of venous thromboembolism in transgender women receiving oral estradiol. *J Sex Med* 2016;13:1773–1777.
6. Gorin-Lazard A, Baumstarck K, Boyer L, et al. Is hormonal therapy associated with better quality of life in transsexuals? A cross-sectional study. *J Sex Med* 2012;9:531–541.

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AUTHOR CONTRIBUTIONS

A. Opaskar: study design/conceptualization, data gathering, analysis or interpretation of the data, drafting/revising the manuscript for intellectual content. E. Scarf: analysis or interpretation of the data, drafting/revising the manuscript for intellectual content. M. Chilungu: analysis or interpretation of the data, drafting/revising the manuscript for intellectual content. A. Kelly: study design/conceptualization, analysis or interpretation of the data, drafting/revising the manuscript for intellectual content.

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A. Opaskar, E. L. Scharf, and M. W. Chilungu report no disclosures. A. Kelly serves as CME editor for *Neurology*[®] and writes questions for American Academy of Neurology educational activities including *Continuum* and the Self-Assessment Examination. Full disclosure form information provided by the authors is available with the **full text of this article at Neurology.org/cp**.

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