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Syncope in a Transsexual Male

Case Report

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At some centers, endocrinologists are seeing a high number of patients with transgender disorders. Men trying to achieve feminization are on high-dose estrogen therapy that results in a prothrombotic state. We describe a case of a transsexual man who developed pulmonary embolism on high-dose estrogen therapy.

Case Report

A 35-year-old transsexual male was admitted to the hospital after transiently losing consciousness. Prior to his fall, he felt lightheaded. On admission, he denied chest pain, dyspnoea, cough, hemoptysis, or incontinence. He was not intoxicated and did not smoke. The patient had been taking high-dose oral estrogen (2 mg) for 1 year to achieve feminization. The estrogen dosage was increased 3 months ago to 3 mg daily. He had not yet undergone gonadectomy. His heart rate was 101 beats per minute, blood pressure 147/95 mm Hg, respiratory rate 18 breaths per minute, and room air oxygen saturation 97%. Physical examination was only significant for gynecomastia. Electrocardiogram showed regular sinus rhythm, T-wave inversion in V1, and biphasic P-waves in V1, V2, and V3. Chest radiograph demonstrated peripheral patchy airspace density in the right middle lobe and left lower lobe consistent with pulmonary infarcts. Arterial blood gas showed pH of 7.32, pO_2 of 72, and pCO_2 of 43. D-dimer was normal. Ventilation-perfusion scan was high probability revealing wedge-shaped perfusion defects in the right middle lobe and left lower lobe. Lower extremity Doppler did not show deep vein thrombosis. The risks of estrogen therapy were reviewed with the patient; however, he decided to continue hormonal therapy. The patient was started on anticoagulation.

The increased risk of venous thrombosis has been well established in women on hormone replacement (Grodstein et al, 1996). Men with gender identity disorder are typically treated with estrogen doses that are 2 to 3 times (or higher) the recommended dose for hormone replacement in postmenopausal women. These high doses are given to achieve feminization and to suppress endogenous testosterone secretion. The incidence of cardiovascular side effects is increased on these doses. In the Coronary Drug Project (1970), men with established coronary artery disease showed significantly increased incidence of nonfatal myocardial infarction, pulmonary embolism, and thrombophlebitis when treated with 5 mg of conjugated estrogen compared to placebo. Similarly, retrospective studies in transsexual males have documented 20-fold to 45-fold increases in thromboembolic events (Asscheman et al, 1989; van Kesteren et al, 1997). Anecdotal evidence indicates that transdermal estrogen preparations may be less thrombogenic than oral estrogen, presumably secondary to lack of first pass metabolism (van Kesteren et al, 1997).

One of the mechanisms by which estrogen results in a hypercoagulable state is by inducing resistance to activated protein C (Rosing et al, 1997). In a recent study of transsexual males, patients treated with oral estrogen had a significant increase in resistance to activated protein C compared to patients treated with cyproterone acetate (Toorians et al, 2003). This leads to a thrombophilic state. Hence, there is a tremendous need to study the safety and efficacy of various hormonal preparations and the role of routine anticoagulation in this patient population.

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