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Case Report / Olgu Sunumu

A Stroke Case Associated with Tibolone Intake in a Male-to-Female Transgender Patient: A Case Report and Review of Literature

Genetik Olarak Erkek Transeksüel Hastada Tibolon İlişkili İnme Olgusu: Olgu Sunumu ve Literatür Taraması

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Abstract

Hormone replacement therapies (HRT) are known to increase the incidence of thromboembolic events. HRT-related thromboembolic events are mainly related to the estrogen dosage and route of administration. Necessary dosage in transgender individuals is higher than those in postmenopausal women. Tibolone is a specific drug, which has estrogenic, progesterogenic, and androgenic properties and is used in HRT. Many studies reported its effect on the incidence of thromboembolic events in postmenopausal women; however, studies on the possible complications of higher dosage in transgender patients are limited. Therefore, transdermal therapies should be considered due to lower incidence of complications, especially in patients with risk factors for thromboembolic events. Necessary detailed information about the possible complications should be addressed and patients should be followed up closely.

Keywords: Stroke, ischemic stroke, tibolone, transgender individuals, IV thrombolysis, hormone replacement therapies

Öz

Hormon replasman tedavilerinin (HRT) tromboembolik olay insidansını artırdığı bilinmektedir. HRT ilişkili tromboembolik olaylar kullanılan östrojen dozu ve kullanım yolu ile ilişkilidir. Transseksüel bireylerde kullanılan östrojen dozu postmenapozal kadınlarda kullanılan dozlardan yüksektir. Tibolon; östrojenik, progesterojenik ve androjenik özelliklere sahip olan ve HRT'de kullanılan özel bir ilaçtır. Postmenapozal kadınlarda tromboembolik olay insidansı üzerine etkisini gösteren farklı çalışmalar vardır ancak daha yüksek dozların kullanıldığı transeksüel bireylerle alakalı olarak literatürde yeterli çalışma yoktur. Bu nedenle, özellikle tromboembolik olaylar için risk faktörleri olan hastalarda, daha düşük komplikasyon insidansı nedeniyle transdermal tedaviler seçilmelidir. Ayrıca muhtemel komplikasyonlar açısından hastalar bilgilendirilmeli ve yakın takip edilmelidir.

Anahtar Kelimeler: İnme, iskemik inme, tibolone, transseksüel bireyler, IV tromboliz, hormon replasman tedavisi

Introduction

Hormone replacement therapies (HRT) are known to increase the incidence of thromboembolic events. HRT-related thromboembolic events are mainly related to the estrogen dosage and route of administration. Necessary HRT dosage in transgender individuals is higher than those in postmenopausal women. The choice of treatment is important to prevent possible complications in these individuals, who have additional risk factors.

Herein, we present a case of acute ischemic stroke in a transgender woman and its association to high dosage HRT.

Case Report

A 36-year-old genetically male transgender patient presented unconscious to the emergency department. Witnesses stated that she had been unresponsive for 2 hours. It was found that she used tibolone at 2.5 mg orally eight times daily, but the length of consumption was not disclosed. In addition, she was a smoker but without other conventional vascular risk factors such as hypertension, diabetes, or dyslipidemia. The physical and neurological examination was limited due to the patient's confused state, but it revealed the left arm and leg weakness and dysarthria.

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The patient's National Institutes of Health Stroke Scale (NIHSS) score was 11 (Figure 1). Intravenous alteplase was administered at 0.9 cc/kg 3 hours after symptom onset. Right middle cerebral artery M1 segment occlusion was observed on craniocervical computed tomography (CT) angiography and mechanical thrombectomy was performed (Figure 2). No hemorrhage was observed in the cranial CT obtained 24 hours after the treatment (Figure 3). The patient's NIHSS score regressed to 4. Acetylsalicylic acid at 100 mg (1x1) and clopidogrel at 75 mg (1x1) were started.

The lipid profile and HbA1c values were within normal limits. During the admission, repeated testing for anti-nuclear antibodies and cytoplasmic anti-neutrophil cytoplasmic antibodies yielded negative results. The protein C, protein S, anti-thrombin activity, and factor V were within normal limits. Factor V Leiden, methylenetetrahydrofolate reductase, and prothrombin gene mutations were not tested due to economic concerns. Electrocardiography (ECG) demonstrated normal sinus rhythm. No cardiac pathology was discovered in the echocardiography. She refused a 24-hour rhythm Holter test due to her poor socioeconomic status; however, serial ECGs, which were obtained during her hospital admission, revealed no sign of arrhythmia. The patient avoided providing further information about the sex reassignment surgery. The patient was discharged with acetylsalicylic acid at 100 mg and clopidogrel at 75 mg. On the 3-month follow-up, the patient's NIHSS was 0 and mRS was 0.

Discussion

The dosage of HRT therapies used in transgender women is higher than other treatments. HRT-related thromboembolic events are known to be related to the estrogen dosage and route of administration (1). For ductal growth and suppression of endogenous testosterone, E2 is administered orally and frequently up to 6-10 mg/day. The dosing with sublingual administration is 2-4 mg/day and in transdermal applications, the same dosage corresponds to approximately 4 of 0.1 mg patches. These estrogen levels have increased the incidence of all vascular events in the short term, especially coronary artery disease, stroke, and pulmonary embolism (2). This increase is observed less in transdermal administration compared to other administration routes (1).

Tibolone is a specific drug, which has estrogenic, progesterogenic, and androgenic properties and is used in HRT. It is preferred in postmenopausal women because it has fewer side effects

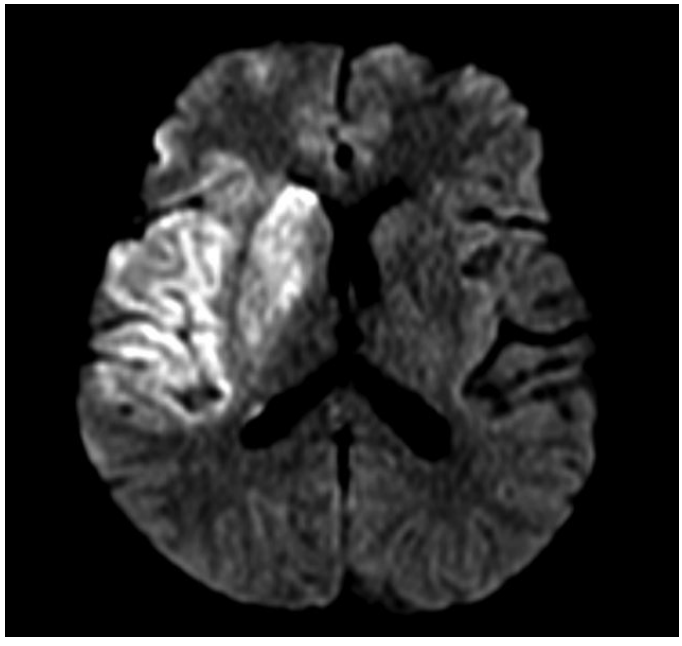

Figure 1. The diffusion-weighted MRI shows the right middle cerebral artery area of acute restriction

MRI: Magnetic resonance imaging

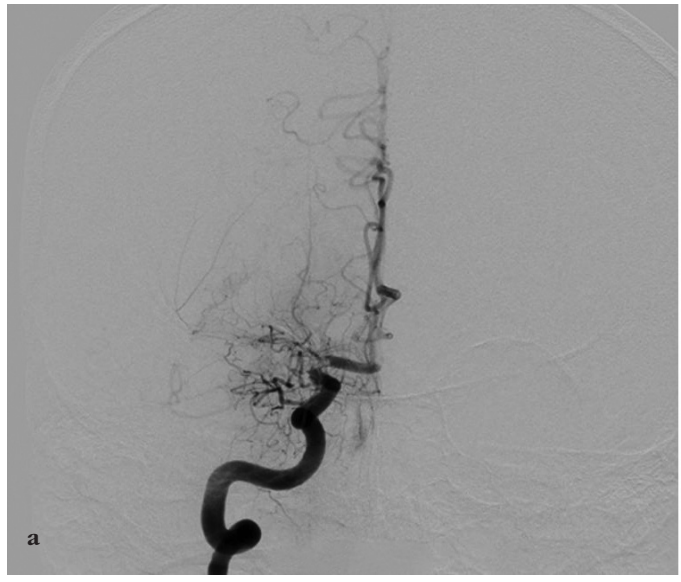

Figure 2a. Carotid artery angiography showed M1 segment occlusion of the right middle cerebral artery

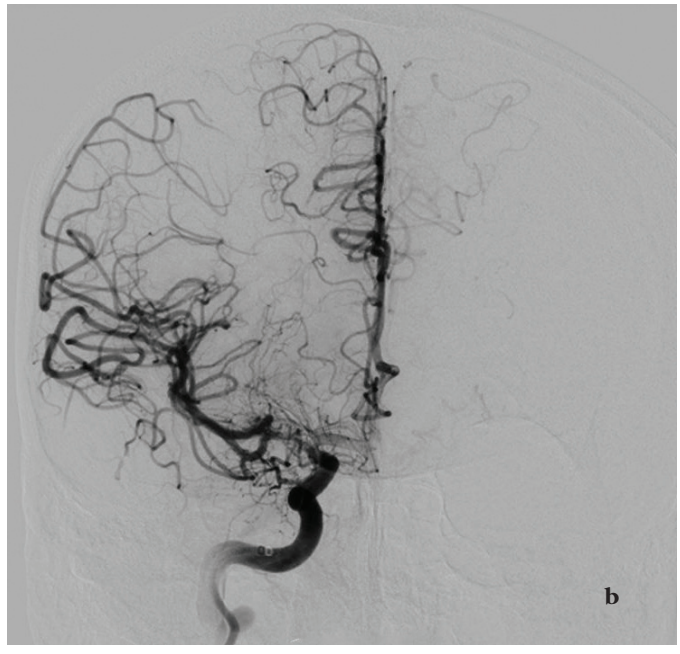

Figure 2b. The blood vessels were recanalized 4 hours after admission

on the endometrium and breast tissue and is good at controlling postmenopausal symptoms, such as osteoporosis and hot flashes. The first studies that were conducted to show tibolone's effect on the coronary arteries showed that tibolone and its metabolites reduce the frequency of coronary artery disease via its anti-mitotic activity on smooth muscle cells in the artery walls (3). In addition, by lowering lipoprotein (a) and triglyceride levels in the blood, tibolone has positive effects on the atherosclerotic process and negative effects on the lipid profile by lowering high-density lipoprotein levels (4). Another study revealed that both tibolone and other HRT contribute to the atherosclerotic processes by increasing the thickness of the intima-media of the carotid arteries (5). Contrary to previous studies that showed tibolone reduces the incidence of thromboembolic events, new studies have shown an increased incidence of stroke and cardiovascular events, especially in women over 60 years of age (6). Its biological mechanism is unclear; however, it is thought to increase the susceptibility to cerebrovascular disease by increasing the C-reactive protein levels and carotid intima-media thickness (7).

However, all these are the results of studies conducted on postmenopausal women. Studies in the literature, which inquire into the effects of tibolone in transgender individuals who require high-dose HRT, are insufficient. Therefore, patients who are over 40 years old, smokers, and who have obesity, migraine with aura, and history of thromboembolic events should be informed in detail and should be closely monitored in terms of complications. Transdermal preparations should be selected in these patients, if possible. They should also be encouraged to make lifestyle changes to reduce such risks. Thorough studies must be conducted with higher dosages to provide patients who are transgender with safer treatments and attention for the removal of social and bureaucratic barriers that prevent transsexual people from taking advantage of the healthcare system facilities.

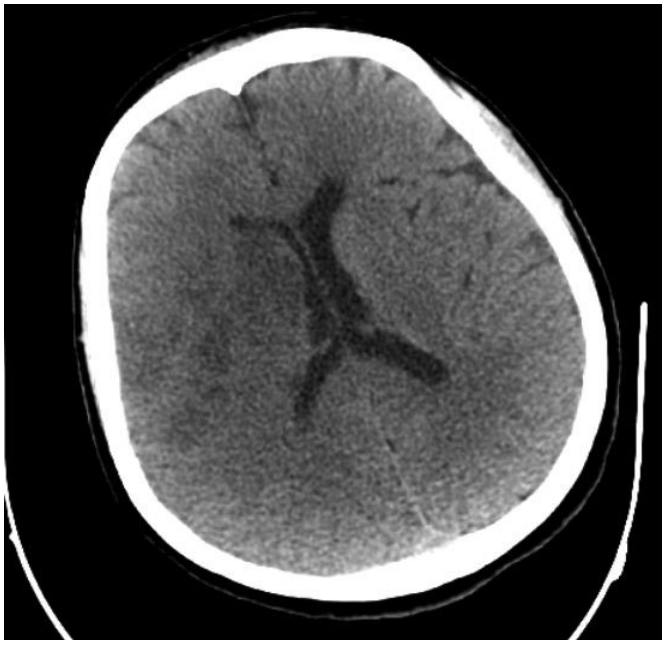

Figure 3. Cranial CT obtained at the 24th hour of treatment

CT: Computed tomography

Ethics

Informed Consent: Consent was taken from the patient for publication.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A., K.İ.C., I.K.A., Concept: E.G., Design: I.S., E.G., Data Collection or Processing: I.S., K.İ.C., Analysis or Interpretation: A.A., Literature Search: A.A., L.R., Writing: A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

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