



Cerebral Venous Sinus Thrombosis Associated with Dutasteride Use

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Cerebral venous thrombosis (CVT) is an uncommon cause of stroke that mainly affects young adults with known risk factors of prothrombotic conditions, pregnancy, infection, malignancy, and drugs. Dutasteride is a 5α -reductase inhibitor that is used for benign prostate hypertrophy and androgenetic alopecia. To date, CVT caused by dutasteride use has not been reported. A 25-year-old male presented with headache and diplopia. He had taken 0.5 mg of dutasteride every other day for 9 months to treat alopecia. A headache developed 7 months after he started taking medication, and horizontal diplopia occurred 1 month after the onset of headache. Fundus examination showed bilateral papilledema. Brain magnetic resonance imaging showed thrombosis in the left sigmoid and transverse sinuses. Headache and diplopia improved after discontinuing dutasteride and starting anticoagulation. The results from this case report indicated dutasteride as a potential cause of CVT. Presumably, the increased estrogen level due to dutasteride use caused the formation of a thrombus.

Key Words: Alopecia, venous thrombosis, 5-alpha reductase inhibitors

INTRODUCTION

Cerebral venous thrombosis (CVT) is less frequent than other types of strokes and has a different clinical presentation and etiologies.

Numerous conditions are known to cause CVT, such as prothrombotic conditions, infection, inflammatory disease, hematologic disease, malignancy, pregnancy, puerperium state, and drugs.¹ Therefore, thorough etiologic investigations are needed to determine the cause of CVT. However, its underlying risk factors are not found in approximately 13% of adult patients with CVT.² Finasteride, a 5α -reductase inhibitor, is used to treat benign prostate hypertrophy as well as androgenetic alopecia,

and it has been reported to induce CVT as a complication.³ Dutasteride is a new 5α -reductase inhibitor with the same indication as finasteride. Herein, we report a case of CVT caused by dutasteride use. Informed consent was obtained from the patient.

CASE REPORT

A 26-year-old male was admitted to the neurology department due to headache and horizontal diplopia. He had no previous illness or trauma history and was non-smoker. The patient had been taking 0.5 mg of dutasteride every other day for 9 months to treat alopecia. He did not take any medication except dutasteride. A headache developed 7 months after he began taking the medication, and horizontal diplopia occurred 1 month after the onset of headache. Pulsatile headache with dizziness initially started from the occipital area and progressed to the bi-frontal and temporal areas. The patient complained of horizontal diplopia when he looked laterally to either side. Neurologic examination showed no weakness, ataxia, sensory disturbance, or visual field defect.

Initial fundus examination showed bilateral papilledema and retinal hemorrhage (Fig. 1A). To determine the cause of intra-

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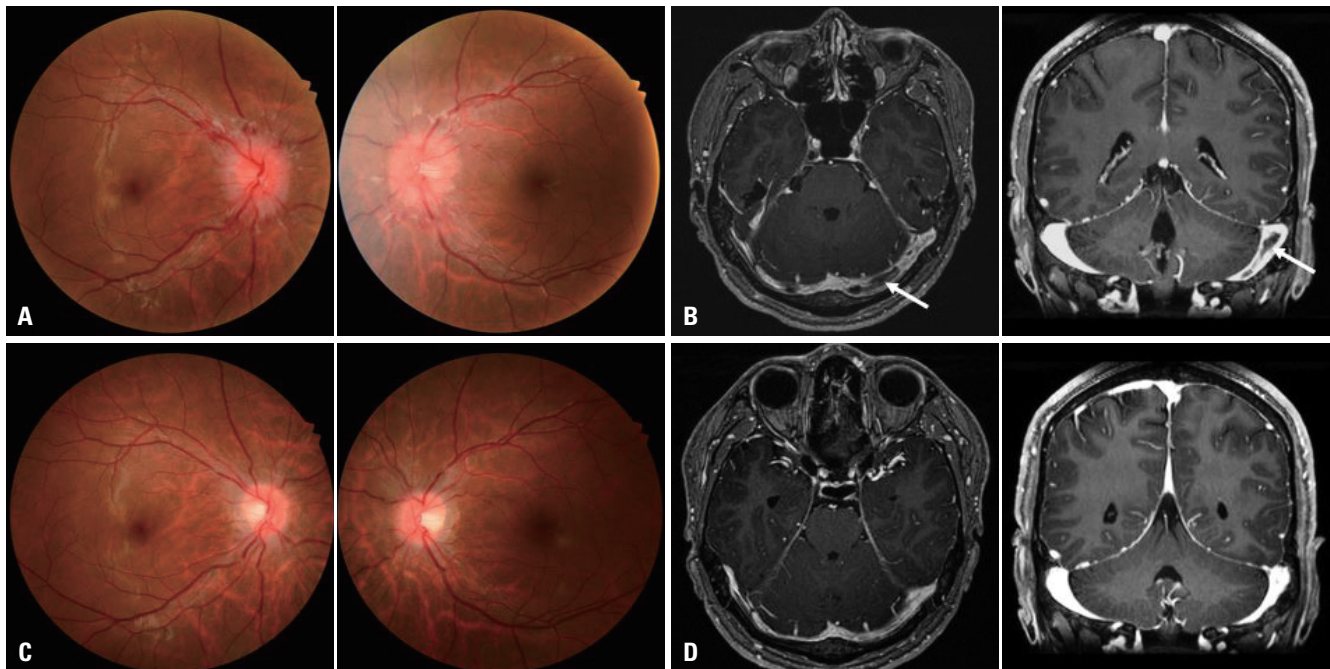


Fig. 1. (A) Initial fundus photograph shows bilateral papilledema and retinal hemorrhage. (B) Initial brain magnetic resonance imaging (MRI) shows thrombosis (arrows) in the left jugular vein, sigmoid, and transverse sinuses. (C) The papilledema is apparently improved after 6 weeks of anticoagulation treatment. (D) Follow-up MRI performed after 9 months of anticoagulation treatment shows resolution of sinus thrombosis in the left sigmoid and transverse sinuses.

cranial hypertension, brain magnetic resonance imaging (MRI) was performed on the day of admission, and it revealed thrombosis in the left jugular vein, sigmoid, and transverse sinuses (Fig. 1B). The patient showed no fever or specific findings based on blood tests for infectious conditions, including white blood cell count, erythrocyte sedimentation rate, and C-reactive protein. In addition, autoimmune antibodies, D-dimer, fibrinogen, antithrombin III, protein C, protein S, prothrombin time, activated partial thromboplastin time, and platelet count were normal. Serum estradiol level, which was measured 4 days after the discontinuation of dutasteride, was 14.2 pg/mL (normal range for male, 11.3–43.2).

There was no specific drug history to explain cerebral venous thrombosis other than dutasteride use. Therefore, dutasteride was discontinued, and intravenous anticoagulation was started to treat CVT. In addition, mannitol was used due to the bilateral papilledema for 10 days. We also used 250 mg of acetazolamide twice a day to alleviate intracranial hypertension for 5 months. After 1 week of intravenous anticoagulation, 7.5 mg of warfarin was given daily. After 6 weeks of oral anticoagulation treatment, the patient’s symptoms were relieved, and bilateral papilledema was improved (Fig. 1C). Follow-up brain MRI performed at 9 months after anticoagulation treatment showed resolution of sinus thrombosis in the left sigmoid and transverse sinuses (Fig. 1D). Oral anticoagulation treatment was discontinued after follow-up MRI, and the patient had no symptoms since then.

DISCUSSION

Several types of drugs can cause CVT. Oral contraceptives are known to increase the risk of sinus thrombosis due to their prothrombotic effects. In addition, asparaginase, cisplatin, methotrexate, lithium, and steroids can cause CVT.⁴ In several case reports, finasteride was found to cause CVT. Finasteride is a competitive inhibitor of type II 5 α -reductase and an intracellular enzyme that converts the androgen testosterone into 5 α -dihydrotestosterone. As a result of this mechanism, finasteride could increase serum estrone and estradiol levels and elevate the risk of CVT.^{5,6}

In the present case, the patient also took dutasteride, a selective inhibitor of the type I and II isoforms of 5 α -reductase, which is more widely expressed and found in the skin, liver, and kidneys. The patient did not have other prothrombotic conditions, such as infection, inflammatory disease, malignancy, or hematologic disease, and was not using any medications that could cause CVT, except dutasteride. Previous studies did not show consistent evidence of a significant association between dutasteride therapy and risk of cardiovascular adverse events.^{7,8}

In this case, symptoms including headache, dizziness, and horizontal diplopia, which indicate intracranial hypertension, occurred progressively and were relieved with anticoagulation treatment, as in the previously reported CVT cases. Although there have been several studies that reported cases of CVT caused by specific drugs, dutasteride has not yet been reported to cause CVT. The present case indicates that the risk of

CVT should be considered when dutasteride is prescribed for alopecia, benign prostate hyperplasia, or prostate cancer. In addition, a detailed history should be taken for patients who present with headache and other neurologic symptoms.

AUTHOR CONTRIBUTIONS

Conceptualization: Kyung-Yul Lee. **Data curation:** Bo Kyu Choi, Jae Wook Jung, and Kyeongyeol Cheon. **Investigation:** Bo Kyu Choi. **Methodology:** Bo Kyu Choi. **Supervision:** Bang-Hoon Cho, and Kyung-Yul Lee. **Validation:** Bo Kyu Choi, Bang-Hoon Cho, and Kyung-Yul Lee. **Writing—original draft:** Bo Kyu Choi. **Writing—review & editing:** Kyeongyeol Cheon, Bang-Hoon Cho, Jae Wook Jung, and Kyung-Yul Lee. **Approval of final manuscript:** all authors.

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