Brief Communication

Cerebral venous sinus thrombosis following tamoxifen prescription

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The first detailed explanation of cerebral venous sinus thrombosis (CVST) appeared in 1825 in France. Until recently, CVST was largely an autopsy diagnosis. However, with the introduction of magnetic resonance and angiography, it is now reliably detected during life. The day-by-day list of CVST causes is increasing. There are rare reports of tamoxifen therapy in patients suffering from cancer and further development of arterial stroke as well as CVST.[1-3] Herein, we describe a patient with CVST using tamoxifen as a drug for hormone replacement therapy without any history of malignancy. The reason for presenting this case is to enhance physicians' awareness of this unusual but serious side effect of tamoxifen.

A 58-year-old female underwent hysterectomy due to massive abnormal uterine bleeding to control hemorrhage. Afterwards, she had been prescribed tamoxifen by a gynecologist, 20 mg per day for preventing osteoporosis. Three months later, she was hospitalized in Alzahra Hospital of Isfahan University of Medical Sciences, Isfahan, Iran due to severe headache followed by tonic clonic seizure and right-sided weakness. On initial examination, she was in the post ictal phase and slightly confused. On cranial nerve examination, only bilateral papilledema was attained. There was right-sided weakness (MRC grade 3 strength) in the upper and lower limbs. Other neurological examinations were normal. On initial brain CT scan, left frontal and parietal infarcts was apparent and further brain MRI and MRV revealed superior sagittal sinus thrombosis (**Figure 1**). Therefore, heparin was prescribed with a diagnosis of CVST. She discharged one week later in good condition. When discharging, her weakness was improved and the force of her right limbs was increased to MRC grade 4. During hospitalization, tests for vasculitis workup including antinuclear antibody, antineutrophilic cytoplasmic antibody, and antiphospholipid and anticardiolipin antibody were sent. Tests for thrombophilia including homocysteine level, protein C, antithrombin III and S were sent as well, but they were all within normal limits.

Women with breast cancer who were treated with tamoxifen have an 82% increased risk of ischemic stroke, and a 29% increased risk of any stroke.[2] Tamoxifen is associated with a 2-3 fold increased risk of venous thromboembolism in 3 of the 4 prospective randomized trials for breast cancer prevention. Venous thromboembolism occurred mostly in women over 50 years of age.[4] Raizer et al[5] reported 20 patients

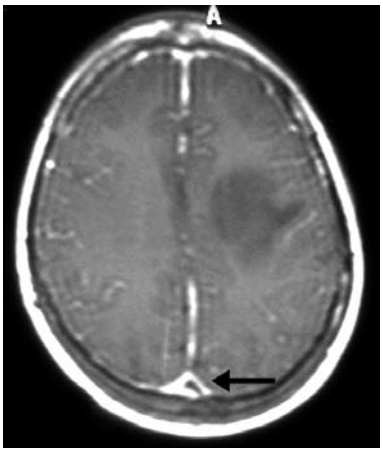

Figure 1 - Brain MRI with contrast demonstrating left frontal and parietal venous infarction and empty delta sign (arrow).

with cancer who developed cerebral sinus thrombosis. Three patients out of 20 were receiving antiestrogen therapy. Although in previous reports cancer and tamoxifen therapy coexisted as a cause of CVST, in this report tamoxifen on its own was detected as a risk factor. It is important to remember that malignancy is a known etiology for developing CVST and systemic thrombosis is well recognized in cancer patients, however, our patient was prescribed tamoxifen only for preventing osteoporosis and no other underlying cause for developing CVST such as coagulopathies, oral contraceptives, and systemic diseases was found.

In conclusion, physicians should be aware of this infrequent but grave side effect of tamoxifen therapy, particularly with the more extensive use of tamoxifen.

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References

1. Bushnell C. The cerebrovascular risks associated with tamoxifen use. ***Expert Opin Drug Saf*** 2005; 4: 501-507.
2. Bushnell CD, Goldstein LB. Risk of ischemic stroke with tamoxifen treatment for breast cancer: a meta-analysis. ***Neurology*** 2004; 63: 1230-1233.
3. Vogel VG, Costantino JP, Wickerham DL, Cronin WM, Cecchini RS, Atkins JN, et al. Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP Study of Tamoxifen and Raloxifene (STAR) P-2 trial. ***JAMA*** 2006; 295: 2727-2741.
4. Kujovich JL. Hormones and pregnancy: thromboembolic risks for women. ***Br J Haematol*** 2004; 126: 443-454.
5. Raizer JJ, DeAngelis LM. Cerebral sinus thrombosis diagnosed by MRI and MR venography in cancer patients. ***Neurology*** 2000; 54: 1222-1226.