Unilateral Internal Carotid Artery Occlusion After Letrozole Treatment in a Postmenopausal Woman with Breast Cancer

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To the Editor: Letrozole, a third-generation aromatase inhibitor (AI), is a relatively newer class of endocrine agents used in hormone-receptor-positive breast cancer.[1] Vascular thrombotic events, such as acute myocardial infarction and acute cerebral infarction, in patients with breast cancer after initiation of letrozole therapy have been documented in the literature.[2,3] However, the impact of this adjuvant endocrine therapy on increasing the risk of developing vascular thrombotic events has been a controversial issue. Here, we report a rare case of a woman with breast cancer developing unilateral internal carotid artery (ICA) occlusion after letrozole treatment.

On October 9, 2015, a 56-year-old postmenopausal woman with 2 years history of hypertension was admitted to the Second Affiliated Hospital of Nanchang University with dizziness for 4 days. She had suffered once transient numbness of the right limbs 1 week previously. Except for diagnosed with breast cancer (infiltrative ductal carcinoma) 2 years ago, her previous medial history was unremarkable. She had been treated with modified radical mastectomy, adjuvant radiotherapy, and chemotherapy (5-fluorouracil, doxorubicin, and cyclophosphamide). No evidence of breast cancer recurrence had been verified by follow-up imagings with computerized tomography (CT) and mammography during 1 year follow-up. One year before admission, brain magnetic resonance (MR) angiography (Figure 1a) and Doppler ultrasonography examination did not reveal any severe stenosis or occlusion of cerebral arteries. At the same time, lipid profiles and estrogen levels showed total cholesterol (6.16 mmol/L), triglycerides (1.56 mmol/L), low density lipoprotein (3.94 mmol/L) and estradiol (43.2 pmol/L). Subsequently, an AI of letrozole 25 mg/d was initiated until admission. On admission, right superficial temporal artery pulse could be touched obviously. The rest of neurological examination was normal. On day 2 after admission, brain MR imaging on admission showed normal signal intensity. However, MR angiography revealed homolateral occlusion of ICA and middle cerebral artery [Figure 1b]. CT angiography showed occlusion of the entire right ICA as well as the patency of anterior communicating artery [Figure 1c]. Meanwhile, Doppler ultrasonography examination detects no blood flow signals of right ICA. In addition, multifocal atherosclerotic plaques formation could be found in common carotid arteries, external carotid arteries, and subclavian arteries bilaterally. Electrocardiogram showed a normal sinus rhythm. Laboratory studies revealed increased total cholesterol (6.93 mmol/L), triglycerides (3.36 mmol/L), and low-density lipoprotein (3.44 mmol/L) after hospitalization. Letrozole was stopped on day 3 and our patient was administrated with aspirin (100 mg/d) and atorvastatin (20 mg/d). After her dizziness symptom was improved moderately, she was discharged on day 10.

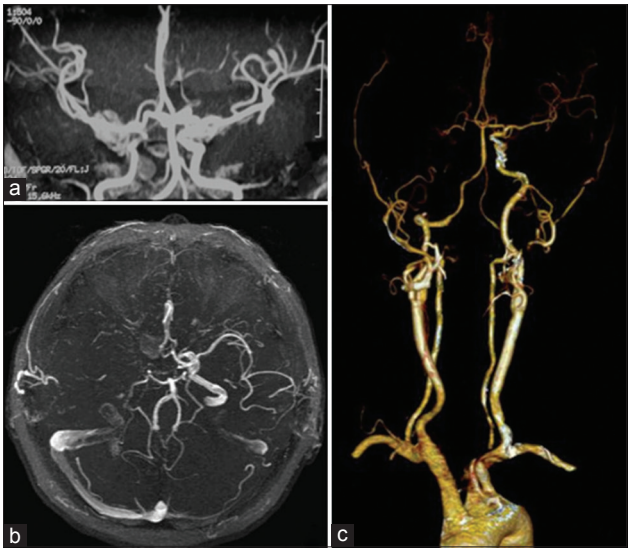

Figure 1: (a) Brain magnetic resonance angiography 1 year before admission did not reveal any severe stenosis or occlusion of right internal carotid artery; (b) brain magnetic resonance angiography on admission showed complete occlusion of right internal carotid artery; (c) computerized tomography angiography on day 2 after admission demonstrated occlusion of the entire right internal carotid artery as well as the opening of anterior communicating artery.

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Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.176079

Received: 27-10-2015 **Edited by:** Xin Chen
How to cite this article: Shen YY, Xiong J, Wang Y, Chai YX, Dai TM, Zhang WJ, Tu JL. Unilateral Internal Carotid Artery Occlusion After Letrozole Treatment in a Postmenopausal Woman with Breast Cancer. Chin Med J 2016;129:494-5.

Third-generation AIs, as their superior efficacy and lower risk of recurrent disease compared to tamoxifen, have become important agents for postmenopausal women with hormone-receptor-positive breast cancer. AIs inhibit the activity of estrogen by competitively binding to the estrogen receptor, thereby blocking the conversion of androgens to estrogens, which may finally result in estrogen levels decreasing in tissue and plasma. Moreover, the decreased estrogen levels play a key role in inhibiting the growth of breast tumors.[4] However, the Breast International Group 1-98 study shows that AIs therapy can also be accompanied by adverse events, such as thromboembolic events, cardiac events, and cerebrovascular accidents accounting for nearly 1%.[1] At present, whether AIs treatment can increase risk of cerebrovascular or cardiovascular accidents in patients with breast cancer is not clear in the literature.

Although several cerebrovascular risk factors including postmenopausal state, hyperlipidemia, and hypertension are found in this patient, 1-year adjuvant letrozole therapy was to some extent blamed for changing of the right ICA from normal blood flow to total occlusion in short time. Comparing the variation of lipid profiles and estrogen levels between pre- and post-letrozole administration in plasma, it indicates that letrozole may increase the production of lipid profiles (especially triglycerides). In addition, Doppler ultrasonography examination demonstrates increased quantity and size of atherosclerotic plaques in cerebral arteries. We, therefore, speculate that letrozole may play an important role in aggravating atherosclerosis formation by regulating lipid profiles. Combining with above cerebrovascular risk factors, letrozole makes for unilateral ICA occlusion within such a short time. Previous studies investigating the effects of different AIs on lipid profiles have demonstrated mixed results. Because of the intricate biological relationship of estrogen with lipid profiles and metabolism, the mixed results from previous studies may be explained by heterogeneity in genes involved in estrogen signaling and estrogen and AI metabolism.[5] However, our study was limited to a case report. We expect more, larger sample clinical studies will be devoted to exploring the correlation between letrozole therapy and cerebrovascular adverse events. Efforts should be made, if possible, to avoid the occurrence of adverse event in patients with breast cancer after initiation of letrozole therapy, such as controlling risk factors actively and oral administration with aspirin and statin agents routinely.

In conclusion, letrozole therapy causing ICA occlusion is extremely rare. It may increase the production of lipid profiles, and then play an important role in aggravating atherosclerosis formation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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