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Case Report

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A Case Report of Cerebral Venous Thrombosis after Taking Tamoxifen in Breast Cancer Patient

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Abstract

Background: *Tamoxifen is commonly used in adjuvant treatment in hormonal receptor positive breast cancer patients. Cerebral venous thrombosis is one of the rare adverse events from tamoxifen.*

Report of the case: *A 52-year-old lady was diagnosed right breast cancer (stage T3N3M0). She was undergone right modified radical mastectomy. The pathological results revealed invasive lobular carcinoma, size 6x2.3x2 cm. , grade 2, negative resected margin, ten out of fifteen lymph nodes were positive for malignancy. The immunohistochemistry was ER 90%, PR 25%, Her2 negative, and Ki67 10%. She obtained adjuvant chemotherapy, 4 cycles of Doxorubicin and cyclophosphamide followed by 4 cycles of paclitaxel every 3 weeks. She was prescribed tamoxifen during adjuvant radiation to her chest wall and regional lymph nodes. Approximately 8 months after taking tamoxifen, she complained progressive headache, dizziness, nausea and vomiting.*

Emergency CT brain with Contrast was done to rule out brain metastases. The scan revealed hyper dense lesion at temporal area with vasogenic edema, focal filling defect at left transverse sigmoid junction and upper portion of internal jugular vein. There was no demonstrable parenchymal metastasis. MRI and MRV of the brain showed acute dural venous sinus thrombosis of the lateral aspect of the left transverse sinus, left sigmoid sinus, left upper internal jugular vein as well as cortical venous thrombosis in the left vein of Labbe. Venous infarction in the left temporal lobe and left superior cerebellar hemisphere.

Causing intraparenchymal hematoma in the left lobe. Laboratory analysis was done. Protein C/S, Lupus anticoagulant, ant thrombin, homocystein, anticardiolipin IgG/IgM, anti B2 glycoprotein I-IgG/IgM was normal. She was given enoxaparin 0.6 ml SC every 12 hours and tamoxifen was off. The scan of CT brain 6 days later showed interval decreased attenuation intraparenchymal hematoma at left posterior temporal lobe. Her headache was improved and no neurological deficit was detected. Ultrasonography of both lower extremities showed no evidence of deep vein thrombosis. She then switched to aromatase inhibitors.

Discussion: *Clinical risk factors for venous thromboembolism are major general or orthopedic surgery, paralysis, pelvic fracture, trauma, cancer previous venous thromboembolism, cancer, major surgery, trauma, obesity, varicose veins, cardiac disease, pregnancy and nephritic syndrome. Our patient had none of these risk factors. Although it is quite rare, cerebral venous thrombosis must be kept in mind of possible adverse effect from tamoxifen.*

Keywords: Cerebral Venous Thrombosis, Tamoxifen, Breast Cancer

Introduction

Tamoxifen is a selective estrogen receptor modulator and has been introduced for breast cancer treatment since early 1970s. The efficacy and safety of tamoxifen has been studied in many trials and the results showed that tamoxifen improved disease free survival and overall survival [1-13]. Tamoxifen has approved to use for adjuvant and metastatic setting in estrogen receptor positive breast cancer [14]. However, tamoxifen has some side effects such as hot flashes, flushing, cramping which are common. The rare side effect including thromboembolic events venous thrombosis, pulmonary embolism and ischemic stroke is also known from tamoxifen treatment. Cerebral venous thrombosis is a condition that there is an acute thrombosis in dural sinuses or cerebral veins in the brain. This condition can lead to hemorrhagic or infarction and cause symptoms such as headache, motor weakness, seizure or abnormal visions [15-18]. We present a case of a breast cancer patient who developed cerebral venous thrombosis while taking tamoxifen treatment.

Report of the case

A 52-year-old lady was diagnosed right breast cancer (stage T3N3M0). She was undergone right modified radical mastectomy. The pathological results revealed invasive lobular carcinoma, size 6x2.3x2 cm. , grade 2, negative resected margin, ten out of fifteen lymph nodes were positive for malignancy. The immunohistochemistry was ER 90%, PR 25%, Her2 negative, and Ki67 10%.

She obtained adjuvant chemotherapy, 4 cycles of Doxorubicin and cyclophosphamide followed by 4 cycles of paclitaxel every 3 weeks. She was prescribed tamoxifen during adjuvant radiation to her chest wall and regional lymph nodes. The dose of tamoxifen was 20 mg per day.

Approximately 8 months after taking tamoxifen, she complained progressive headache, dizziness, nausea and vomiting. Emergency MRI and MRV of the brain were done to rule out brain metastases.

MRI and MRV of the brain showed acute dural venous sinus thrombosis of the lateral aspect of the left transverse sinus, left sigmoid sinus, left upper internal jugular vein as well as cortical venous thrombosis in the left vein of Labbe. Venous infarction in the left temporal lobe and left superior cerebellar hemisphere, causing intraparenchymalhematoma in the left lobe. There was no demonstrable parenchymal metastasis (Figure 1, 2).

Laboratory analysis was done. Protein C/S, Lupus anticoagulant, ant thrombin, homocystein, anticardiolipin IgG/IgM, anti B2 glycoprotein I-IgG/IgM was normal. The laboratory examination was shown in (Table 1).

A B C

Figure 1: demonstrates MRI and MRV of the brain
A: venous infarction in the left temporal lobe and left superior cerebellar hemisphere, causing intraparenchymal hematoma in the left lobe.
B-C: acute dural venous sinus thrombosis of the lateral aspect of the left transverse sinus, left sigmoid sinus left upper internal jugular vein

Table 1: demonstrated the laboratory results on the first day before the treatment

LAB	Results	normal value
Prothrombin time	13.6	10.8-14.6
Normal plasma	12.7	-
INR	1.07	1.03
APTT	26.1	22.3-35.3
Normal plasma	28.5	-
Lupus anticoagulant	Negative on APTT	Negative
Protein C	Func 75	Func 70-140% - Ag 65-153%
Protein S	Free Ag 104	Free Ag 57-158%
antithrombin	80	75-125
homocystein	3.8	0-15
anticardiolipin IgG	<12	<12
anticardiolipin IgM	<12	<12
anti B2 glycoloprotein I IgG	<20	<20
anti B2 glycoloprotein I IgM	<20	<20

She was given enoxaparin 0.6 ml subcutaneous every 12 hours and tamoxifen was off. The scan of CT brain 6 days later showed interval decreased attenuation intraparenchymal hematoma at left posterior temporal lobe as shown in (Figure 2). The 2 month follow-up MRI Brain and MRV Brain was presented in (Figure 3), showing interval much resolution of venous infarction and sub-acute hematoma in left temporal lobe and at superior aspect of left cerebellar hemisphere with interval improvement of thrombosis involving left transverse sinus, left sigmoid sinus and upper left internal jugular vein.

Her headache was improved and no neurological deficit was detected. Ultrasonography of both lower extremities showed no evidence of deep vein thrombosis. She then switched to aromatase inhibitors.

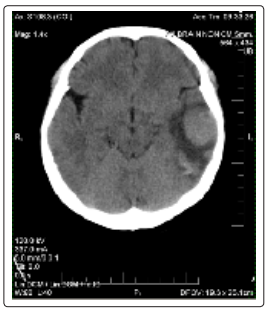
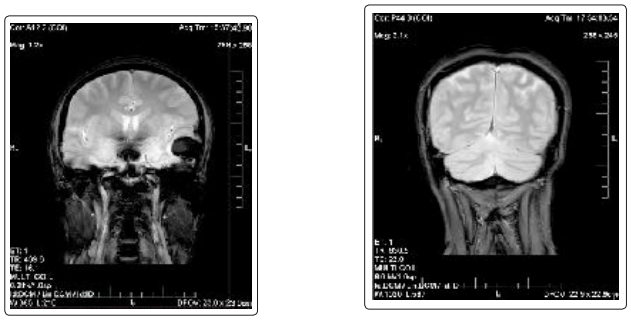


Figure 2: shows non-contrast CT brain after 6 days of treatment



A B

Figure 3: shows the follow-up MRI and MRV of the brain

Discussion

The higher risk of developing venous thromboembolism during tamoxifen treatment in breast cancer was reported in many studies [19-22]. The International Breast Cancer Intervention Study (IBIS) which is a prevention study using tamoxifen have revealed a 2 fold increased risk of venous thromboembolism [21]. Some studies have shown the factors associated with venous thromboembolism such as age or other factors that involved the past history of coronary heart disease including high blood pressure, high cholesterol level [23-26]. The explanation of tamoxifen effect has been discussed in many plausible mechanisms because the incidence of thromboembolism is unpredictable. Many studies have shown the prothrombic estrogenic effect of tamoxifen [27-29]. Or tamoxifen might trigger some pathways as in coronary heart disease; therefore women with prior coronary heart disease have a higher risk of thromboembolism. Also, the hypothesis that tamoxifen could induce an acquired hypercoagulable state by reducing the levels of natural anticoagulant proteins. It arises in close association with hypercoagulable states, puerperium, oral contraceptives, and malignancy [30-31].

The greatest risk of thromboembolic event was reported in the first 2 years after initiation of tamoxifen therapy [32].

In conclusion, although it is quite rare, cerebral venous thrombosis must be kept in mind of possible adverse effect from tamoxifen. Risk and benefit need to be evaluated before prescribing the treatment. Further understanding of the mechanism in presenting thromboembolism is needed to develop other pharmacological agents or the prevention treatment.

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