Acute coronary syndrome in a breast cancer patient treated with tamoxifen

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Abstract

Tamoxifen is a non-steroidal antioestrogen widely used in the treatment of breast cancer. Prolonged exposure to this therapy may result in cardio vascular undesirable events particularly thrombotic events. Arterial effects are rare. We report a case acute coronary syndrome in a locally advanced post menopausal breast cancer treated with neoadjuvant chemotherapy, surgery, adjuvant chemotherapy, radiotherapy and tamoxifen for 2 years. Then we discuss the controversial protective effect of tamoxifen against myocardial infarction.

Introduction

Tamoxifen is a non-steroidal antioestrogen and is considered to be the front line endocrine treatment for breast cancer. It was approved in 1978 by the US Food and Drug Administration for treatment of advanced postmenopausal breast cancer. Subsequently it was widely used in postmenopausal and premenopausal women both as adjuvant treatment for early disease and for advanced disease. Toxicity is known to be low. Nevertheless, the possibility that prolonged exposure may result in premature osteoporosis, endometrial adenocarcinoma and thrombotic events. Most cases reported are of venous thromboembolism; arterial events are rare. In this article, we report a case of an acute coronary syndrome in a post menopausal woman treated with tamoxifen for breast cancer.

Case report

A 46 years old woman with no history of vascular disease or source of cardiac emboli had a history of a locally advanced breast cancer diagnosed five years ago. Biopsies revealed an invasive ductal carcinoma grade 3. Immunocytochemical staining was positive for hormonal receptors and negative for c-erb B2. The staging of the neoplastic disease, revealed a IIIB stage according to AJCC breast staging 7th edition. The patient undergone 4 cycles of neoadjuvant chemotherapy (AC60 regimen) modified radical mastectomy and axillary lymph node curage. Macroscopic examination of the resection has revealed a single tumor nodule measuring 30x32 mm. Histologically, the tumor was classified as grade 4 according to Chevallier's classification. Two lymph node metastases were detected. Post operatively, the investigations didn't reveal any metastatic localization. The patient received adjuvant chemotherapy (4 Docetaxel), external beam radiation and hormonotherapy with tamoxifen. She has received 2 years of tamoxifen 20 mg/day when she developed an acute coronary syndrome. The patient presented to the department of emergencies with chest pain. There was no evidence of ST segment elevation on the electrocardiogram. Troponin was positive and urgent coronary angiography revealed a stenosis of 40% of the anterior interventricular (AIV) artery. A medical treatment based on aspirin, clopidogrel, β Blockers, and statin was carried out. Tamoxifen was stopped. As the patient was in amenorrhea for almost three years, we discussed with her benefice and cardio vascular risks of the treatment with aromatase inhibitors. The estimate survival gain calculated with Adjuvant online scoring system was almost 12% at 10 years. The patient preferred this therapeutic option with cardiovascular examination, electrocardiogram and biological lipid assessment every 3 months. After 3 years of follow up, she remains disease free without any cardio-vascular event.

Discussion

Tamoxifen is the endocrine treatment of choice for selected patients with all stages of breast cancer. In post menopausal women, five years of adjuvant tamoxifen reduces the 15-year risk of breast cancer recurrence by approximately 40 percent and breast cancer mortality by 35 percent [1].

Tamoxifen is a selective estrogen receptor modulator (SERM) with both agonist and antagonist properties, depending on the individual target organ. The adverse effects associated with tamoxifen, including hot flashes, vaginal discharge, thromboembolic events, and endometrial cancer.

Therefore, A number of studies, including the Early Breast Cancer Trialists Collaborative Group (EBCTCG) overview analysis and the large Breast Cancer Prevention Trials, have demonstrated that tamoxifen use is associated with an increased rate of venous thromboembolic events (2.8 percent), especially within the first two years of tamoxifen use, in elderly women, and that there is a significant additional procoagulant effect when tamoxifen is added to chemotherapy [2]. Additionally, this risk was increased in patients who had

surgery, immobilization, or fracture in the month prior to the event.

In contrast, arterial events particularly myocardial infarction, as shown in our case report is rare in women treated with tamoxifen. In fact, several studies have reported a significant reduction in myocardial infarction events among the tamoxifen-treated group. MacDonald and Stewart showed a 50% reduction in events among women treated with 20 mg/d tamoxifen for 5 years [3]. This beneficial effect may be due to the favorable effect of tamoxifen on lipid profiles. In a randomized trial in 57 normal postmenopausal women, tamoxifen in a dose of 20 mg/day led to significant reductions in total and LDL-cholesterol (12 and 19 percent, respectively) and an 18 percent fall in fibrinogen levels without any change in HDL-cholesterol. Moreover, Tamoxifen also has weak antioxidant properties, protecting LDL cholesterol from potentially harmful oxidation at least in vitro [5].

Tamoxifen is a coronary vasodilator in a porcine in vitro model and substantially increases endothelial function. Other mechanisms, such as anti-inflammatory effect and effects on insulin metabolism, should not be overlooked [6].

While these data suggest a potential protective effect against myocardial infarction, the available data from clinical suggest that in postmenopausal women both with and without cardiac heart disease, the use of tamoxifen is **not** associated with either a beneficial or adverse cardiovascular effect. Otherwise, other data suggest that the use of tamoxifen is not associated with a beneficial cardiovascular effect.

Finally, in all these trials, there were relatively few events reported, and myocardial infarction was not a prospective endpoint in any. Further studies are required to better define the effect of tamoxifen on cardiac risk.

References

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Davies C, Godwin J, Gray R, Clarke M, Cutter D and al (2011). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 378(9793):771.
2. Cuzick J, Powles T, Veronesi U, et al (2003). Overview of the main outcomes in breast-cancer prevention trials. Lancet 361:296–300.
3. McDonald CC, Stewart HJ (1991). Fatal myocardial infarction in the Scottish adjuvant tamoxifen trial. The Scottish Breast Cancer Committee. BMJ 24:435–7.
4. Grey AB, Stapleton JP, Evans MC, Reid IR (1995). The effect of the anti-estrogen tamoxifen on cardiovascular risk factors in normal postmenopausal women. J Clin Endocrinol Metab 80(11):3191
5. Wiseman H (1995). Tamoxifen as an antioxidant and cardioprotectant. Biochem Soc Symp 61:209 –219.
6. David J. Grainger and Peter M. Schofield (2005). Tamoxifen for the Prevention of Myocardial Infarction in Humans: Preclinical and Early Clinical Evidence. Circulation 112:3018-3024

Conflict of interest: None

The manuscript has never been presented before in another journal