

Tamoxifen Induced Pancreatitis in Eu-lipidemia: A Case Report

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Case Report

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Abstract

Tamoxifen is used as hormonal therapy in the treatment of breast cancer patients. Tamoxifen tablet is a well tolerated and generally devoid of any life threatening adverse drug reaction. Pancreatitis is a rare but life threatening adverse drug reaction of tamoxifen. Rare side effects of drugs are usually missed. Previous case reports and review discussions are available and argue that tamoxifen leads to dyslipidemia and pancreatitis is mostly related to development of hypertriglyceridemia. Here we are reporting a case where patient developed pancreatitis after short term use of tamoxifen (only 1 month). To our knowledge this is a first case report where no dyslipidemia was detected prior to development of pancreatitis and, thus, such short term presentation may be linked to immunologic or idiosyncratic reaction to tamoxifen. Gynecologists are routinely referred patients on tamoxifen therapy for abnormal endometrial thickness and, thus, any patient with acute abdominal pain on tamoxifen therapy should be thoroughly investigated for pancreatitis too. From our case it comes to light lipid derangements may not be always associated with such event and discontinuation of tamoxifen is recommended.

Keywords: Tamoxifen; Pancreatitis; Eu-lipidemia

Introduction

Tamoxifen is the most widely used anti-estrogen in adjuvant endocrine treatment of primary breast cancer, as well as leading hormonal therapy in receptor positive metastatic breast carcinoma. The adverse effects of tamoxifen are generally mild and do not induce serious complications even after extended periods of administration. Most of the adverse effects include hot

flushes, vaginal discharge, menstrual changes, bone pain and fatigue. Previous reports are available that state pancreatitis to be rare adverse drug reaction of tamoxifen. Among these reports 3 months is the earliest onset of pancreatitis. So far, tamoxifen induced lipid derangement (hypertriglyceridemia) has been labelled as the culprit for developing pancreatitis. We are here reporting a patient who developed pancreatitis following short term therapy (1 month) with tamoxifen and that too without any lipid

derangement. All other possible causes were ruled out. Therefore, pancreatitis in context of newly prescribed drug (i.e. tamoxifen) with short span of history points to possible immunologic injury of drug.

Case Report

A 36 year old female with no co morbid illness presented to our hospital with complaints of lump in right breast and cough along with breathlessness (NYHA grade 3). On examination she had lump in the lower inner quadrant of right breast which was non mobile and firm in consistency with palpable right axillary lymph node. Mamography showed a speculated mass in the lower inner quadrant of right breast with ipsilateral axillary lymphadenopathy. Trucut biopsy was performed from breast lesion which showed invasive duct carcinoma (ER, PR: positive and Her-2-neu: negative). A HRCT chest revealed interstitial lung disease with multiple nodular lesions in bilateral lungs. PET-CT was done that showed FDG avid lesions in right breast, right axilla, bilateral lungs, liver, and multiple bony sites. Liver and renal function tests, lipid profile and amylase were normal. In view of metastatic disease she was treated with palliative chemotherapy consisting of nano-particle albumin bound paclitaxel (260mg/m²/cycle) and Carboplatin (AUC=5). Post 5 cycles she presented with complaints of severe headache and vomiting. MRI brain was done that revealed multiple enhancing lesions in brain suggestive of metastatic. She was treated with palliative WBRT brain (30 GY/10#). FDG PETCT was done that revealed progression in liver, right adrenal and new pleural deposits. In view of ECOG PS of 3 she was treated with tamoxifen. After 1 month of starting tamoxifen she presented with complaints of severe abdominal pain (left hypochondriac that radiated to back) along with tenderness, nausea and vomiting. CT scan showed peripancreatic inflammation and edematous pancreas. Serum amylase was 624 U/L. Her lipid profile was normal with serum cholesterol 160mg/dl, serum triglyceride 155mg/dl, serum LDL 106mg/dl, serum HDL 23 and serum VLDL 31 mg/dl. With suspicion of tamoxifen as cause for her pancreatitis it was discontinued. By 2nd day patient was free of abdominal pain and 10th day serum amylase was 57 U/L. Patient was further treated with palliative chemotherapy (Gemcitabine and Carboplatin) and was not re-challenged with tamoxifen. Nine cycles have been completed. Patient has not developed any other episode of pancreatitis over this 12 months period.

Discussion

Hormonal manipulation is an easy and simple way to treat cancers which are hormone responsive. The main

cancers where hormonal treatment is of proven value are breast and prostate. Tamoxifen, Raloxifen, Anastrozole, Letrozol, Exemestane and Fulvestrant are the important anticancer hormonal agents used in cases of breast malignancies. Tamoxifen is a non steroidal hormonal therapy that is classified as selective estrogen receptor modulator. Differential action on different tissues has been described. It acts as a competitive antagonist of estrogen receptor in breast tissue. In contrast, it behaves as agonist in endometrial tissue [1].

Tamoxifen has been established as the main adjuvant hormone therapy in premenopausal women (ER-positive) after surgical resection of breast cancer for prevention of recurrence [2]. The recommended dose is 20 mg daily for 10 years [3]. It has been the among the choice of therapies for non florid metastatic breast cancer in premenopausal patients with 50% response rate and 12 to 18 months of median duration of response [4]. Tamoxifen is usually well tolerated even over long period of time. Hot flushes, vaginal discharge, menstrual changes, bone pain and fatigue are the common adverse drug reactions but don't warrant disruption of treatment and can be managed symptomatically.

Here we have described a rare but life threatening adverse drug reaction of Tamoxifen. Our patient is a de novo metastatic breast carcinoma and thus was treated with palliative chemotherapy, radiotherapy (WBRT) and sequentially with tamoxifen monotherapy. She developed acute pancreatitis after 1 month of tamoxifen that was diagnosed owing to typical pain of acute pancreatitis described.

Majority of cases of acute pancreatitis occur due to gall stones, heavy alcohol intake, viral infections, and trauma, and hypertriglyceridemia, autoimmune or interventional procedures like endoscopic retrograde cholangio-pancreatography [5]. Only 1 to 2% are drug related [6,7].

The possible etiologic factors in our patient may be metastasis to pancreas, dyslipidemia, hypercalcaemia (owing to skeletal metastasis and, thus, tamoxifen flare), viral infection, or drug related. She didn't develop hypertriglyceridemia, calcium dysmetabolism and fever. CT scan didn't point out to any metastatic lesion in the pancreas. So the most possible reason stands out to be drug related and in this case tamoxifen.

Various case reports of post tamoxifen use pancreatitis have been explained in the past. Elisaf, et al. and Lin, et al. reported their cases and reviewed the development of acute pancreatitis after tamoxifen use in association with dyslipidemia [8,9]. All the cases had hypertriglyceridemia in common. Kanel and Thompson described the effect of

tamoxifen on lipid metabolism as paradoxical estrogen agonistic action. Sakhri, et al. have demonstrated positive rechallenge for the recurrence acute pancreatitis with the reintroduction of tamoxifen and, thus, suggested to prohibit the re-use of tamoxifen if it is the suspected causative agent [10,11]. Three months is the earliest onset of pancreatitis that has been reported [12]. Since Tamoxifen is continued for longer duration (10 years) in adjuvant setting, therefore fasting lipid profile should be monitored.

Our patient developed acute pancreatitis within 1 month of tamoxifen use. She did not have hypertriglyceridemia. She was never re-challenged with Tamoxifen. There is no further episode of pancreatitis. This may be explained as an idiosyncratic or immunologic reaction to Tamoxifen as the pancreatitis resolved soon within 2 days of discontinuing the same.

Adverse reaction to tamoxifen in the form of purpuric vasculitis and acute inflammatory arthritis has been described in the past [13]. In contrast, Boyd and King described a patient who achieved remission for psoriasis upon tamoxifen administration [14]. Though tamoxifene induced inflammatory reactions and clinical effectiveness in such case reports suggest the possible role of tamoxifen as immunomodulator, owing to rarity of incidents the differential inflammatory and anti-inflammatory role of anti-estrogen is topic of debate. The other serious complications of Tamoxifen that have been explained are thrombosis and endometrial carcinoma [15,16].

Conclusion

Though tamoxifen is a safe and well tolerated drug, any unwarranted symptom should not be ignored and patients should be investigated for the possible reasons. Acute abdominal pain should be looked upon with high index of suspicion for pancreatitis. Tamoxifen therapy may cause pancreatitis even with short term therapy (in our case it was only one month). Though previous case reports suggest tamoxifen induced dyslipidemia that causes pancreatitis, here in our case there was no alteration in the lipid profile of patient. Thus, tamoxifen may cause pancreatic damage either indirectly (via dyslipidemia) or directly (as in our case).

Clinical Practice Points

Patients being treated with tamoxifen should undergo fasting lipid profile periodically. Besides, patients who complain of new onset abdominal pain after initiation of tamoxifen therapy should be investigated for pancreatitis as this is a life threatening complication and timely

discontinuation of the drug will prevent morbidity and possible mortality.

References

1. Fugh-Berman A, Epstein S (1992) Tamoxifen: disease prevention or disease substitution? *Lancet* 340(8888): 1143-1145.
2. Colleoni M, Gelber S, Goldhirsch A, Aebi S, Castiglione-Gertsch M, et al. (2006) Tamoxifen after adjuvant chemotherapy for pre-menopausal women with lymph node positive breast cancer: International Breast Cancer Study Group Trial 13-93. *J Clin Oncol* 24(9): 1332-1341.
3. Davies C, Pan H, Godwin J, Gray R, Arriagada R, et al. (2013) Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 381(9869): 805-816.
4. Burstein HJ, Harris JR, Morrow M (2011) Malignant Tumors of the Breast. In: De Vita, Hellman, and Rosenberg's Cancer Principles & Practice of Oncology. 9th (Edn.), pp: 1441.
5. Gardner TB, Berk BS, Yakshe P (2006) Acute Pancreatitis. *eMedicine*.
6. Sekimoto M, Takada T, Kawarada Y, Hirata K, Mayumi T, et al. (2006) JPN guidelines for the management of acute pancreatitis: epidemiology, etiology, natural history, and outcome predictors in acute pancreatitis. *J Hepatobiliary Pancreat Surg* 13(1): 10-24.
7. Lankisch PG, Droge M, Göttesleben F (1995) Drug induced acute pancreatitis: incidence and severity. *Gut* 37(4): 565-567.
8. Elisaf MS, Nakou K, Liapis G, Pavlidis NA (2000) Tamoxifen-induced severe hypertriglyceridemia and pancreatitis. *Ann Oncol* 11(8): 1067-1069.
9. Lin, Hsu CH, Chao (2004) Tamoxifen Induced Severe Acute Pancreatitis: A Case Report. *Dig Dis Sci*. 49(6): 997-999.
10. Kanel KT, Wolmark N, Thompson PD (1997) Delayed severe hypertriglyceridemia from tamoxifen. *N Engl J Med* 337(4): 281.
11. Sakhri J, Ben Salem C, Harbi H, Fathallah N, Ltaief R (2010) Severe acute pancreatitis due to tamoxifen-

- induced hypertriglyceridemia with positive rechallenge. JOP 11(4): 382-384.
12. Kim YA, Lee S, Jung JW, Kwon YJ, Lee GB, et al. (2014) Severe pancreatitis due to tamoxifen-induced hypertriglyceridemia with diabetes mellitus. Chin J Cancer Res 26(3): 341-344.
 13. Drago F, Arditit M, Rebora A (1990) Tamoxifen and purpuric vasculitis. Ann Intern Med 112 (12): 965-966.
 14. Boyd AS, Shyr Yu, King LE (2002) Basal cell carcinoma in young women: An evaluation of the association of tanning bed use and smoking. Journal of the American Academy of Dermatology 41(5): 887-889.
 15. Hernandez RK, Sørensen HT, Pedersen L, Jacobsen J, Lash TL (2009) Tamoxifen treatment and risk of deep venous thrombosis and pulmonary embolism. A Danish population-based cohort study. Cancer 115(19): 706-709.
 16. Swerdlow AJ, Jones ME (2005) For the British Tamoxifen Second Cancer Study Group Tamoxifen Treatment for Breast Cancer and Risk of Endometrial Cancer: A Case-Control Study J Natl Cancer Inst 97(5): 375-384.