



A Case Report of Endometrial Carcinoma in a Patient Treated with Tamoxifene and Letrozole for Carcinoma Breast

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Abstract

The risk of endometrial cancer and breast cancer are increased by higher endogenous estrogen levels. Tamoxifene is a selective estrogen receptor modulator used for treatment and prevention of estrogen receptor positive breast cancer. However it increases the risk of endometrial cancer. Letrozole an aromatase inhibitor reduces breast cancer incidence but their influence on endometrial cancer is uncertain.

Keywords: Endometrial cancer, Tamoxifene, Breast cancer, Letrozole, Aromatase inhibitor.

Introduction

Selective estrogen receptor modulators (SERM) and aromatase inhibitor have shown to reduce the risk of developing ER positive breast cancer. Tamoxifene, a potent SERM has been successfully used as adjuvant therapy for breast cancer. However the effect of tamoxifene as both an agonist and antagonist of estrogen may cause pathologic changes in uterus. The agonist effect may stimulate endometrial proliferation leading to endometrial hyperplasia, endometrial polyp and rarely endometrial cancer. Letrozole, a potent aromatase inhibitor work by inhibiting aromatase enzyme leading to decreased peripheral conversion of estrogen. It has favourable action on uterus. It does not stimulate endometrial proliferation and thus is preferred as hormonal therapy in post menopausal women.

Case Report

A 56 year old woman presented with right breast lump on 11.2.10. FNAC from breast lump was done

and it showed invasive ductal carcinoma. Core biopsy for IHC was done and it showed ER positive PR positive Her2neu negative. She underwent Right Modified Radical Mastectomy with axillary node dissection. Surgical pathology report showed T3 lesion with 4 out of 10 lymph node positive. She received 6 cycle of FEC last on 19.5.10. She received adjuvant radiotherapy 50 Gy in 25 fractions between 21.6.10 and 23.7.10. She was put on adjuvant hormonal therapy with tab tamoxifene 20 mg per day from 7.11.10. She continued Tamoxifene for 1 year and 2 months. Her ultrasonography abdomen done on 23.1.12 showed thickened endometrium (14.1mm). She was switched to tab letrozole 2.5 mg. She took tab letrozole for 5 yrs and was discontinued on 28.5.17. Thereafter she was on 6 monthly follow up and she was doing well. She had complained of abnormal uterine bleeding in nov 20. Her ultrasonography abdomen showed endometrial thickening with focal lesion. She underwent abdominal hysterectomy on 2.2.21. Her surgical

pathology report showed endometroid carcinoma with pathological T3 lesion. She is now on post op radiotherapy.

Discussions

Tamoxifene is SERM that block the signalling of endogenous estrogen receptor in normal and malignant breast tissue. It is a reasonable option for prevention of recurrence in non metastatic hormone positive breast cancer. It has estrogen like effect on uterus, bone, liver and coagulation system. It is associated with increased risk of both uterine cancer and uterine sarcoma. Duration of treatment should also be taken in account. The ATLAS trial showed a reduced risk of breast cancer recurrence but an increased risk of endometrial cancer among patient taking tamoxifene for more than 5 years. Risk of endometrial cancer is also higher in post menopausal women and older patients than premenopausal and younger patients. Letrozole is a non steroidal competitive inhibitor of aromatase. It inhibits synthesis of estrogen by inhibiting conversion of adrenal androgen to estrogen. It has no estrogen agonist effect. It has favourable effect on endometrium. In study conducted by Crawford et al the sustained effect of aromatase inhibitor on endometrial histology in 8 patients with endometrial hyperplasia (EH), 4 patient with localised endometrial carcinoma and 4 with mets endometrial carcinoma were examined. The result showed decrease in mean endometrial thickness both in women with EH and localised EA. In 2015 Chlebowski et al demonstrated in a cohort of 17064 women who were diagnosed with hormone positive breast cancer that incidence of endometrial cancer was 48 percent lower in aromatase inhibitor group vs tamoxifene group. Endometrial cancer were 29 percent lower in aromatase inhibitor group vs the no endocrine therapy group.

There is no evidence based recommendation for uterine malignancy screening for patients on tamoxifene. Current recommendations are annual gynaecological examination and evaluation for any AUB. The value of tras vaginal sonography (TVS) in asymptomatic patients on limited tamoxifene

treatment (<5 yrs) is unproven. The abnormal endometrial thickness >9 mm is acceptable in studies but further investigation like D & C are not recommended in absence of vaginal bleeding.

Conclusions

Tamoxifene can induce endometrial cancer during chronic exposure (adjuvant or preventive therapy) at a low frequency, preferably in postmenopausal women and those with typical risk factor for endometrial cancer. This risk can be minimized by detecting and treating endometrial pathology before the initiation of tamoxifene treatment. For patients taking tamoxifene, irregular vaginal bleeding should be evaluated via hysteroscopy and if etiology remain unclear, a biopsy should be done.

Conflict of Interest: None

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