April 2009

Spectrum of tamoxifen associated endometrial pathology in breast cancer patients

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Short Report

Spectrum of Tamoxifen Associated Endometrial Pathology in breast cancer patients

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Abstract

The objective of the study was to determine the incidence and type of endometrial abnormalities in long term users of tamoxifen with breast cancer. All patients with a diagnosis of Oestrogen Receptor positive breast cancer on Tamoxifen therapy who had also undergone endometrial biopsy for abnormal bleeding or other symptoms were included. Among the 37 cases that had long term follow up available, 21(57%) had evidence of endometrial pathology. There were seven cases of simple hyperplasia and thirteen of endometrial polyp. Only one case of endometrial carcinoma was seen. These findings support the association between prolonged tamoxifen therapy and endometrial pathology of possible neoplastic potential. Endometrial pathology is dependent on duration of exposure to Tamoxifen, therefore, close follow up of such patients is recommended.

Introduction

Tamoxifen is a non steroidal anti-oestrogen and widely used as an effective hormonal therapy in breast cancer patients. Long term tamoxifen has been shown to increase the disease free survival and prevent the relapse of disease and reduce risk of malignancy in the contra lateral breast.[1]

Several factors are known to affect endometrial cancer risk, including reproductive characteristics, obesity, use of steroid hormone preparations and certain medical conditions and smoking.[1] Exposure to unopposed oestrogen stimulus whether endogenous or exogenous, substantially increases women's risk of this disease. Use of combination contraceptive preparation substantially lowers the risk. Obesity a source of endogenous (unopposed) oestrogen among post menopausal women, also increases endometrial cancer risk.[1,2]

Oestrogen promotes the growth of breast cancer cells. Tamoxifen works against the effects of oestrogen on these cells. While Tamoxifen acts against the effects of oestrogen on breast tissue, by competitively displacing estrogen, it does have weak intrinsic oestrogenic activity. Tamoxifen has been used for more than 20 years to treat patients with advanced breast cancer.

There has always been concern regarding the long term use of tamoxifen therapy and a number of reports have been published describing tamoxifen use and spectrum of associated endometrial pathology including endometrial hyperplasia, endometrial polyps and carcinoma.[3]

The present study describes endometrial pathology in 37 breast cancer patients on long term tamoxifen treatment that underwent dilatation and curettage (D& C) for diagnostic purposes.

Patients, Methods and Results

This case controlled study describes 37 breast cancer patients treated at Aga Khan University Hospital from 1994 to 1999 who received adjuvant tamoxifen therapy. These patients underwent sampling by dilatation and curettage for diagnostic purposes as they presented with either irregular or post menopausal bleeding per vaginum. These patients were identified by the indexing and coding unit of the medical record department of the Aga Khan University.

One patient underwent subsequent hysterectomy one year after the initial endometrial sampling and the hysterectomy sample was also available for histological evaluation.

The ages of the patients ranged from 25 to 54 years with a median age of 52 years. The medical charts of all these patients were reviewed to collect data regarding age, date and stage at diagnosis of breast cancer, primary therapy instituted, estrogen receptor status of primary tumour, dose and duration of tamoxifen treatment. All the patients' received tamoxifen in a dose of 20 mg daily. The range of Tamoxifen used was 2-5 years. Median duration of tamoxifen treatment was 22 months. History of any other hormonal therapy, complaint for which endometrial sampling was performed and any other risk for endometrial malignancy was also identified.

Histo-pathological findings of 21 cases that developed endometrial pathology were compared to 16 cases that did not develop any pathology.

The histological findings in all the cases are shown in the table. Among women taking tamoxifen, 57% had evidence of abnormal endometrium. Tamoxifen treatment was discontinued after diagnosis of simple hyperplasia and subsequent hysterectomy done one year later, exhibited normal secretory endometrium.

All the cases of simple hyperplasia did not reveal atypia.

The polyps identified ranged in size 4-6 cms. Histologically they were composed of hyperplastic endometrial glands and thick walled vascular channels. Only one case of endometrial carcinoma was diagnosed.

Table: Histological findings of patients with endometrial pathology.

Type of uterine pathology	No of cases	Percentage
Endometrial Polyp	13	62%
Simple Hyperplasia	07	33%
Complex Hyperplasia	0	0%
Carcinoma	1	3%
Total Abnormal Cases	21	100%

Conclusion

Adequate clinical follow up of these patients with hysteroscopy and endometrial sampling may help in preventing or assist in early diagnosis of pre neoplastic or neoplastic processes in the endometrium even in asymptomatic patients.

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