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Endometrial polyps in obese asymptomatic pre and postmenopausal patients with breast cancer: Is screening necessary?

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HIGHLIGHTS

- Obese asymptomatic postmenopausal women with breast cancer have a very high prevalence of subclinical endometrial polyps.
- In premenopausal women with estrogen receptor positive breast cancer, obesity is not a risk factor for endometrial polyps.
- Pre-tamoxifen endometrial assessment could be a rational option in postmenopausal ER(+) breast cancer, obese and elderly patients.

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ABSTRACT

Objective. To evaluate the prevalence of endometrial polyps in obese asymptomatic pre and postmenopausal patients with breast cancer and to know if a baseline pretamoxifen endometrial assessment should be taken into consideration in these women at high risk.

Methods. A cross-sectional study was carried out with 201 women with breast cancer. A diagnostic hysteroscopy was performed in all women. All formations suspected as polyps were removed. The prevalence of endometrial polyps was analyzed in all patients (n = 182) and in premenopausal (n = 49) and postmenopausal (n = 118) women with estrogen receptor (ER) positive breast cancer (BC) according to their body mass index (BMI) and other risk factors.

Results. Hysteroscopic evaluation was possible in 182 cases (90.5%). Of the total of women, 160 (87.9%) were ER(+)BC patients, 133 (73.1%) postmenopausal women and 41.5% were obese (BMI ≥ 30 kg/m^2). Endometrial polyps were found in 52 cases (28.5%) (3 cases of simple hyperplasia harbored within a polyp). In premenopausal patients with ER(+)BC, there were no statistical differences in endometrial polyps according to their BMI (22.3% in non-obese women vs 31.7% in obese) while in all patients (26.4% in non-obese vs 44.0% in obese) and in postmenopausal women with ER(+)BC (25.9% in non-obese vs 48.6% in obese) there were statistical differences. In all women the relative risk (RR) of endometrial polyps in obese patients was 2.24 (1.01–4.83), in obese postmenopausal women with ER(+)BC was 2.75 (1.01–7.40) and in obese premenopausal patients with ER(+) BC was 1.42 (0.80–3.29).

Conclusions. Asymptomatic women with breast cancer have a high prevalence of baseline subclinical endometrial polyps and it is very high in obese postmenopausal patients with estrogen receptor positive breast cancer. Therefore, there may be a future role for baseline pretamoxifen screening of some sort for the obese asymptomatic postmenopausal patient, especially if they are elderly and ER positive.

Introduction

Breast cancer patients also have a higher risk of endometrial pathology [1] because many individual and environmental risk factors (nulliparity, early onset of menarche, late age at menopause, obesity, etc.) are shared in both endometrial pathology and breast cancer promotion [2,3].

Although the American College of Obstetricians and Gynecologists [4] in 2006 stated that in asymptomatic women using tamoxifen (TAM), screening for endometrial cancer has not been shown to be effective; emerging evidence based on the presence of benign endometrial polyps before therapy suggests the existence of high and low-risk groups for the development of atypical hyperplasias with tamoxifen treatment in postmenopausal women [5,6]. Cancer risk in an endometrial polyp is low (3–10.7%) but the risk of these polyps becoming malignant after tamoxifen treatment, even in asymptomatic patients, is considerably

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higher than the risk observed in the general population [7]. Moreover, in premenopausal women, tamoxifen has no known increased risk of uterine cancer [4] but probably does increase the risk of uterine bleeding [8–11].

Obesity is a very well known important risk factor for endometrial polyps in pre and postmenopausal women [12,13]. Few studies provide a reliable systematic pretreatment endometrial assessment both in the general and in the obese population [14–22]. In all studies, transvaginal ultrasonography (TVUS) has been used as a screening method and most of them used an endometrial thickness (ET) >4 mm to indicate a hysteroscopic evaluation in postmenopausal patients.

Hysteroscopy is the most reliable method of endometrial disease diagnosis and the available hysteroscopes have made it possible to remove polyps as outpatient surgery with few complications and a high degree of user satisfaction. This has made hysteroscopy the gold standard for diagnosing and the treatment of endometrial polyps [23].

On the other hand, a new option in postmenopausal women with ER positive breast cancer is third generation aromatase inhibitors (AIs) (letrozole, anastrozole and exemestane). Current studies found less rate of emerging endometrial pathology during AIs therapy [24] than tamoxifen use.

To the best of our knowledge, no other study has investigated the prevalence of endometrial polyps by systematic hysteroscopy in all these patients, regardless of hormonal status, hormonal receptor positivity and BMI. It is very important to know if there are endometrial polyps not only in postmenopausal women with ER-positive breast cancer (potential endometrial side effects of tamoxifen use), but also in premenopausal women because of increased uterine bleeding risk, which creates a consequent need for many diagnostic tests, subsequent treatment and a high burden of anxiety in women with cancer. Therefore, the diagnosis and resection of endometrial polyps prior to hormonal treatment would be a very reasonable option in these patients, especially those at high risk for them.

The goal of our study was to estimate the true prevalence of endometrial polyps in obese asymptomatic pre and postmenopausal patients with breast cancer, before any treatment at the moment of their diagnoses.

Patients and methods

Inclusion criteria

A cross-sectional study was carried out on 294 pre and postmenopausal women suffering infiltrating breast cancer who were treated in the Unit of Gynecologic Oncology of the Puerto Real University Hospital from January 2008 to January 2012. Before surgical treatment, patients were eligible for the hysteroscopic endometrial assessment if they had an intact uterus (no previous hysterectomy, no previous TAM, and no previous endometrial ablation), in the case of premenopausal women had not reported genital bleeding or hormonal therapy use (including contraceptives) during the previous year and in the case of postmenopausal women had not received, from the previous year, or were not receiving any hormonal therapy (HT), had no postmenopausal genital bleeding, or had not been submitted to an endometrial biopsy or to a diagnostic–therapeutic curettage in their post-menopausal period.

Patients were defined as postmenopausal by amenorrhea ≥1 year and had FSH ≥ 40 mIU/mL. Women must be asymptomatic from a gynecologic standpoint and informed consent was obtained from each patient after the nature of the study was fully explained. Inclusion criteria were carried-out by 201 women. An approved protocol was obtained from the local ethics committee, and this study was conducted according to the guidelines of the Helsinki Declaration and resolution 196/96 of the National Health Council on Research Involving Human Subjects [25].

Methods

Anthropometric parameters were measured in all women. Obesity was defined as a BMI ≥ 30 kg/m^2. A detailed gynecologic history and a TVUS evaluation of the endometrium were performed. In premenopausal women, the endometrial thickness was measured in the early follicular phase.

In women with amenorrhea ≥1 year FSH levels were determined. A diagnostic hysteroscopy without anesthesia was done in each woman before any treatment for their breast cancer, independent of the ultrasonography findings. Hysteroscopic evaluation was done in the outpatient clinic by two experienced gynecologists (DLL and RCD) using a 5-mm sheathed hysteroscope (Bettocchi Office Hysteroscope, Karl Storz, Tuttlingen, Germany) and physiological saline as the distension medium.

At the hysteroscopic finding of polyps and, based on the hysteroscopist's judgment, an immediate outpatient polypectomy was done with scissors or with a bipolar electrode (Versapoint Bipolar Electrosurgery System, Ethicon, Somerville, NJ, USA). In the cases of polyps larger than 3 cm in diameter, severe endocervical stenosis or when the patient was unable to tolerate the procedure, a deferred inpatient resectoscopic polypectomy under general anesthesia was accomplished. In all cases, polyps were sent for histological examination. The findings were classified according to the WHO histopathological criteria [26]. This classification is based on the morphological features of glands and stroma in the polyps. Size was estimated by the hysteroscopist using the largest polyp as the reference. The gold standard for calling something a true endometrial polyp was the histology report.

Endometrial polyp prevalence was analyzed in all patients (Group 1), in premenopausal ER(+) breast cancer patients (Group 2) and in postmenopausal ER(+) breast cancer patients (Group 3) according to their body mass index (BMI) and other risk factors. Analyses were performed only in pre and postmenopausal ER(+) breast cancer patients because these are the potential users of adjuvant hormonal treatment.

Statistical analysis

The data were collected and analyzed using SPSS 15.0 for Windows (version 11.5, SPSS Inc., USA). Clinical and demographic variables of patients (age, parity, breast feeding, age at menarche and menopause, time since menopause, body mass index, previous hormone replacement therapy, breast tumor size, and endometrial thickness) were compared in all groups of women. Prevalence of endometrial polyps in the different groups was calculated. Statistical analysis was carried out by calculating frequencies, means and standard deviations. A Chi-square test was adopted for comparison of frequencies and Student's t test was used for means comparisons. In a second time, obesity and other risk factors associated with endometrial polyps were analyzed. In order to evaluate these risk factors, prevalence ratios with their respective 95% confidence intervals were calculated using Pearson's Chi-square or Fisher's exact test. Statistical significance was set at $p < 0.05$.

Results

Principal demographic and clinical characteristics of patients in all groups are shown in Table 1. Among the initial 294 women who had been diagnosed with breast cancer and before any treatment, 201 were eligible for the endometrial hysteroscopic evaluation and finally, it was possible in 182 patients (90.5%). In 9 cases (4.4%), after being informed about the procedure, the patient refused the consent and in 10/182 cases (5.4%) hysteroscopy was not possible because a firm endocervical stenosis was present or the patient was unable to tolerate the procedure.