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Endometrial Cancer and Tamoxifen

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Your patient has a new or unusual symptom. What tests would you request first, and how are they interpreted? This column, dedicated to advanced practice nurses and experienced oncology nurses, will discuss a variety of assessment and diagnostic techniques to help in the evaluation and management of clinical problems. If you are interested in writing for this column, contact Associate Editor Catherine Burke, MS, APRN, BC, ANP, AOCN®, via e-mail at cburke@mdanderson.org.

Chief Complaint

Marie is a 64-year-old woman with a history of estrogen receptor-positive breast cancer. She has been taking tamoxifen for four years, and her chief complaint is new vaginal bleeding. What are the diagnostic possibilities, and how would you work her up?

Discussion

Tamoxifen therapy in women with breast cancer clearly has been shown to reduce the development of both recurrent and new contralateral cancers. Tamoxifen acts as an antiestrogen in breast tissue by blocking the estrogen receptor and preventing cell growth. A compilation of data from published trials indicates that adjuvant tamoxifen therapy reduces the incidence of contralateral breast cancers by 40% and recurrence by 25% ("Systemic Treatment of Early Breast Cancer," 1992). This effect was observed in women with estrogen receptor-positive tumors and was significant enough to justify trials using tamoxifen therapy to prevent breast cancer in high-risk women (Dunn & Ford, 2001). Consequently, millions of women are taking tamoxifen for either the treatment or prevention of breast cancer.

Fornander et al. (1989) provided early evidence that tamoxifen is a causal agent in the development of endometrial cancer, where it has weak estrogenic properties. This study found a 6.4-fold increase in the relative risk of developing endometrial cancer in a group of postmenopausal women with early breast cancer who were treated with adjuvant tamoxifen. The greatest risk occurred after five years in women who received 40 mg per day of tamoxifen. Fisher et al. (1994) confirmed these findings when they reported the results of the National Surgical Adjuvant Breast and Bowel Project B-14 trial involving receptor-positive, node-negative postmenopausal patients with breast cancer. Twenty-three cases of endometrial cancer were found in women who received 20 mg per day of tamoxifen, compared with two cases in placebo-treated women. Calculated rates for developing endometrial cancer were two to three times greater than those of the general population. The risk of developing endometrial cancer is dose and time dependent, with higher cumulative doses and exposures producing a greater relative risk. However, the beneficial effect of tamoxifen for breast cancer prevention far exceeded the relative risk for developing endometrial cancer.

Primary Diagnostic Possibility: Endometrial Cancer

Because the presenting sign of endometrial cancer is new vaginal bleeding and a history of tamoxifen use is considered to be a risk factor, the advanced practice nurse should consider this to be the primary possible diagnosis. Endometrial cancer is the most common gynecologic cancer in the United States. In 2004, Jemal et al. estimated 40,320 new cases of the disease and 7,090 deaths as a result of endometrial cancer. Most cases of endometrial cancer are diagnosed at an early, favorable stage when cure rates are high. Abnormal bleeding is the most common early symptom of the disease. Most endometrial cancers are associated with unopposed estrogenic stimulation of either endogenous or exogenous origin (Barakat, 1998). Obesity is a major risk factor, especially for women more than 50 pounds overweight, because obese women have chronic levels of circulating estrone produced by the aromatization of androstenedione in adipose tissue. Other estrogen-related risk factors include nulliparity, late menopause (after age 55), and unopposed oral estrogen intake. The relative risks for these factors range from 2–10 times more than in the general population. The magnitude of the tamoxifen-associated risk falls within the lower limits of these risk profiles. In standard doses, tamoxifen may be associated with endometrial proliferation, hyperplasia, polyp formation, and invasive cancer (Committee on Gynecologic Practice, the American College of Obstetricians and Gynecologists, 2001), all of which produce a thickening of the uterine lining. Lahti et al. (1993) and Exacoustos et al. (1995) found that women who had received tamoxifen had a thicker endometrium and a higher incidence of endometrial polyps when compared with women who had not received the drug.

Which tests should be ordered for this patient?

Routine screening tests, including transvaginal ultrasound and endometrial biopsy, have been used to triage asymptomatic

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