Detection of Endometrial Cancer in Asymptomatic Postmenopausal Breast Cancer Patient Treated with Tamoxifen : A Case Report

SUPAT SINAWAT, M.D. (HONS), M.Sc.*,
TAWEESILP CHIYABUTRA, M.D.*,
PILAIWAN KLEABKAEW, M.D.*

Abstract

Breast cancer is among the commonest malignancies in women and tamoxifen has been widely used for more than two decades for treatment of breast cancer. It has been known that long term use of tamoxifen significantly increases the risk of endometrial cancer but there is no generally accepted recommendation regarding the surveillance of endometrial pathologies in breast cancer patients taking tamoxifen. Although the incidence of endometrial cancer associated with tamoxifen use is not high, the risk is true and these patients could be helped by screening methods such as transvaginal ultrasonogrphy. We report here a case of endometrial cancer detected by transvaginal 2D scan in an asymptomatic postmenopausal woman taking tamoxifen.

Key word : Tamoxifen, Endometrial Cancer

SINAWAT S, CHIYABUTRA T, KLEABKAEW P
J Med Assoc Thai 2001; 84: 1033-1036

Tamoxifen, a nonsteroidal anti-estrogen, has been used as an endocrine therapy of choice in treatment of all stages of breast cancer for over two decades(1). Although tamoxifen seems to have only a few adverse effects, several studies have shown that postmenopausal breast cancer patients who have been treated for more than 12 months with tamoxifen are at increased risk for endometrial pathologies such as endometrial hyperplasia(2-4), endometrial polyp(5-8), and endometrial carcinoma(9-12). Up to date, there is no consensus regarding surveillance for endometrial cancer in women receiving tamoxifen. Most centers tend to perform aggressive evaluation of the endometrium only in patients presenting with symptoms such as abnormal vaginal bleeding or discharge(13). Some reports, however,

* Department of Obstetrics and Gynaecology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand.

revealed that endometrial carcinoma could arise in those treated with tamoxifen who exhibit no symptoms[14,15].

A 53 year old, G4 P3-0-1-3, woman was diagnosed with breast cancer of her left breast eight years previously. Her menstrual periods ceased about one year before she was found to have breast cancer. After modified radical mastectomy with axillary lymph nodes resection were performed she was given 6 courses of chemotherapy and five year-duration of tamoxifen treatment. During the five year period of tamoxifen treatment she experienced no gynecologic symptoms such as abnormal vaginal discharge or bleeding, thus was not referred to the gynecologist for gynecologic check up or endometrial evaluation. Three years previously she was instructed by her physician to discontinue tamoxifen and has been well ever since. At the beginning of the year 2000 she received an invitation letter from our group to come for a gynecologic check up and decided to participate in the screening program. Upon pelvic examination, no gross abnormalities of pelvic organs were found. We, therefore, performed a transvaginal ultrasonography in order to evaluate her endometrium. The results of transvaginal scan revealed a slightly enlarged uterus (3.4 x 5.6 x 8.7 CM) and thickened endometrium (endometrial thickness measured 28 mm) with multiple small hypoechogenic areas within the thickened endometrium. After detailed and informative counseling was given the patient agreed to proceed with uterine curettage to determine the cause(s) of the thickened endometrium. Fractional curettage was performed and the pathological results later on demonstrated grade III endometriod adenocarcinoma of the endometrium extending to the endocervix. One month after uterine curretage, she was found to have ascites and decided to have an exploratory laparotomy. The intra-operative findings showed involvement of carcinoma at the serosal surface of the uterus, right adnexa and omental surface. Total abdominal hysterectomy with bilateral salpingooophorectomy and omentectomy were done. Histological evaluation of operative specimens revealed poorly differentiated adenocarcinoma of the endometrium involving the serosal surface of the uterus and endocervix. Omental metastasis was also histologically confirmed. After cytoreductive surgery she was given adjuvant chemotherapy which comprised of taxol and carboplatin. Unfortunately, she died after the second course of chemotherapy due to advanced metastasis and multiple organ failure.

DISCUSSION

Breast cancer is one of the commonest malignancies found in women. In the western world it accounts for approximately one-third of all cancers in women and the incidence has been found to be increasing worldwide[16]. Since the early 1980s, tamoxifen has become the standard adjuvant therapy for patients with breast cancer and it is estimated that over one million women worldwide are using tamoxifen to reduce the risk of the recurrence of breast cancer[17]. Although tamoxifen was thought to have only a few side effects, reports have indicated that it is associated with an increased incidence of proliferative and neoplastic changes in the endometrium, with a 1.3 to 7.5 relative risk of developing endometrial carcinoma[18]. This carcinogenic effect has been attributed to estrogenic stimulation and/or to a genotoxic effect of this agent[19,20]. The increased risk of endometrial carcinoma following the use of tamoxifen has stimulated studies on endometrial diagnostic methods. During the past decade several reports have shown the benefits of transvaginal ultrasonography in detecting endometrial pathologies in patients receiving tamoxifen[6, 21,22]. Sonohysterography has been claimed to be a useful diagnostic tool in differentiating a space-occupying lesion, eg. endometrial polyp, from abnormal endometrial-myometrial junction[23] while the contribution of pulsed doppler flow in the diagnosis of endometrial pathologies seems to be inconclusive [22]. So far there is no general agreement regarding surveillance of endometrial pathologies in breast cancer patients receiving tamoxifen. The American College of Obstetricians and Gynecologists recommended prompt endometrial evaluation only in patients who presented with gynecologic symptoms such as abnormal vaginal bleeding[13]. The case reported here, however, demonstrated that, at least to some extent, endometrial cancer could be detected earlier by transvaginal ultrasonography even in asymptomatic patients. Further study in this aspect, thus, is needed to evaluate the benefit of transvaginal ultrasound scan in detecting endometrial pathologies in breast cancer patients taking tamoxifen in the hope that this will provide us with early detection or even prevention of endometrial cancer associated with the use of tamoxifen.

(Received for publication on August 25, 2000)

REFERENCES

1. Early Breast Cancer Trialists' Collaborative Group. Systemic treatment of early breast cancer by hormonal, cytotoxic, or immune therapy. Lancet 1992; 339: 1, 71-6.
2. Cohen I, Rrosen DJD, Shapira J. Endometrial changes in postmenopausal women treated with tamoxifen for breast cancer. Br J Obstet Gynaecol 1993; 100: 567-71.
3. Lahti E, Blanco G, Kauppila A. Endometrial changes in postmenopausal breast cancer patients receiving tamoxifen. Obstet Gynecol 1993; 81: 660-4.
4. Kedar RP, Bourne TH, Powels TJ. Effects of tamoxifen on uterus and ovaries of postmenopausal women in a randomixed breast cancer prevention trial. Lancet 1994; 343: 1318-23.
5. Cohen I, Altaras MM, Shapira J. Time-dependent effect of tamoxifen therapy on endometrial pathologies in asymptomatic postmenopausal breast cancer patients. Int J Gynecol Pathol 1996; 15: 152-5.
6. Hann LE, Giess CS, Bach AM. Endometrial thickness in tamoxifen-treated patients: Correlation with clinical and pathologic findings. AJR 1997; 168: 657-62.
7. Cohen I, Beyth Y, Altaras MM. Value of sonohysterography in asymptomatic, postmenopausal tamoxifen-treated patients. Gynecol Oncol 1997; 64: 386-9.
8. Corley D, Rome J, Curtis MT. Postmenopausal bleeding from unusual endometrial polyps in women on chronic tamoxifen therapy. Obstet Gynecol 1992; 79: 111-5.
9. Killackey MA, Hakes TB, Pierce VK. Endometrial adenocarcinoma in breaset cancer patients receiving antiestrogens. Cancer Treat Rep 1985; 69: 237-9.
10. Hardell L. Tamoxifen as a risk factor for carcinoma of corpus uteri. Lancet 1988; 3: 563-7.
11. Malfetano JH. Tamoxifen-associated endometrial carcinoma in postmenopausal breast cancer patients. Gynecol Oncol 1990; 39: 82-5.
12. Robinson DC, Bloss JD, Schino MA. A retrospective study of tamoxifen and endometrial cancer in breast cancer patients. J Natl Cancer Inst 1995; 59: 189-93.
13. ACOG committee opinion. Tamoxofen and endometrial cancer. Number 169, February 1996. Committee on Gynecologic Practics. American College of Obstetricians and gynecologists. Int J Gynaecol Obstet 1996; 53: 197-9.
14. Fisher B, Constanantino JP, Redmond CK. Endometrial cancer in tamoxifen treated breast cancer patients. Findings from the national Surgical adjuvant Breast and bowel project. J Natl Cancer Inst 1994; 86; 527-37.
15. Ismail SM. Pathology of endometrium treated with tamoxifen. J Clin Pathol 1994; 47: 827-33.
16. Parker SL, Tong T, Bolden S, Wingo PA. Cancer Statistics, 1996. CA Cancer J Clin 1996; 46: 5-27.
17. Fisher B, Costantino J. A randomized clinical trial evaluating tamoxifen in the treatment of patients with node-negative breast cancer who have estrogen receptor positive tumors. N Eng J Med 1989; 320: 479-84.
18. Daniel Y, Inbar M, Bar AmA, Peyser MR, Lessing JB. The effects of tamoxifen treatment on the endometrium. Fertil Steril 1996; 65: 1083-9.
19. Hachisuga T, Hideshima T, Kawarabayashi T. Expression of steroid receptors, Ki-67, and epidermal growth factor receptor in tamoxifen-treated endometrium. Int J Gynecol Pathol 1999: 18: 297-03.
20. Shibutani S, Suzuki N, Terashima T. Tamoxifen-DNA adducts detected in the endometrium of woman treated with tamoxifen. Chem Res Toxicol 1999; 12: 646-53.
21. Bese T, Kosebay D, Demirkiran F. Ultrasonographic appearance of endometrium in postmenopausal breast cancer patients receiving tamoxifen. Eur J Obstet Gynecol Reprod Biol 1996; 67: 157-62.
22. Elizabeth J, Suh B, Goodman A. Surveillance for endometrial cancer in women receiving tamoxifen. Ann Internal Med 1999; 131: 127-35.
23. Achiron R, Lipitz S, Sivan E, Goldenberg M, Mashiach S. Sonohysterography for ultrasonographic evaluation of tamoxifen-associated cystic thickened endometrium. J Ultrasound Med 1995; 1499: 685-8.

รายงานผู้ป่วย : การตรวจวินิจฉัยมะเร็งเยื่อบุโพรงมดลูกด้วยการตรวจคลื่นเสียงความถี่สูงทางช่องคลอดในผู้ป่วยมะเร็งเต้านมวัยหมดระดูที่ได้รับการรักษาด้วยยาทาม็อกซิเฟน

สุพัชญ์ สีนะวัฒน์, พ.บ., วท.ม.,*
ทวีศิลป์ ไชยบุตร, พ.บ., พิไลวรรรณ กลีบแก้ว, พ.บ.**

มะเร็งเต้านมเป็นมะเร็งที่พบบ่อยเป็นอันดับต้น ๆ ในสตรี และทาม็อกซิเฟน (Tamoxifen) เป็นยาที่ใช้เพื่อป้องกันการกลับเป็นซ้ำของมะเร็งเต้านมมาเป็นเวลาเกือบสองทศวรรษ มีการศึกษาหลายรายงานที่ระบุว่าการใช้ยาทาม็อกซิเฟนในสตรีวัยหมดระดู เพิ่มความเสี่ยงของการเกิดมะเร็งเยื่อบุโพรงมดลูก แต่ก็ยังไม่มีข้อสรุปที่ชัดเจน ถึงแนวทางในการเฝ้าระวังพยาธิสภาพของเยื่อบุโพรงมดลูกที่อาจเกิดขึ้นในสตรีวัยหมดระดูที่ได้รับทาม็อกซิเฟน คณะผู้ศึกษาได้รายงานผู้ป่วยมะเร็งเต้านม 1 ราย ซึ่งได้รับการรักษาด้วยทาม็อกซิเฟนในช่วงหลังหมดระดูเป็นเวลา 5 ปี ผู้ป่วยไม่มีอาการใด ๆ ทางนรีเวช การตรวจคลื่นเสียงความถี่สูงทางช่องคลอดพบการหนาตัวผิดปกติของเยื่อบุโพรงมดลูก ผลการขูดมดลูกพบว่าเป็นมะเร็งเยื่อบุโพรงมดลูกชนิด endometrioid adenocarcinoma ผู้ป่วยได้รับการผ่าตัดเอามดลูก ท่อนำไข่ รังไข่ และ omentum ออกทางหน้าท้อง และเสียชีวิตในเวลา 3 เดือนต่อมาเนื่องจากความล้มเหลวในการทำงานของระบบหายใจ

คำสำคัญ : ทาม็อกซิเฟน, มะเร็งเยื่อบุโพรงมดลูก

สุพัชญ์ สีนะวัฒน์, ทวีศิลป์ ไชยบุตร, พิไลวรรรณ กลีบแก้ว
จดหมายเหตุทางแพทย์ ฯ 2544; 84: 1033-1036

* ภาควิชาสูติศาสตร์-นรีเวชวิทยา, คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น, ขอนแก่น 40002