Case Report

Uterine Fibroid in Breast Cancer Patients receiving Tamoxifen Therapy

Mioma Uteri pada Penderita Kanker Payudara dengan Terapi Tamoksifen

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Abstract

Objective: Selective estrogen receptor modulators (SERMs) such as tamoxifen play a role in increasing the risk of developing uterine Fibroid.

Methods: Case report.

Case: Mrs. 47 years old, Para 6, presented with chief complaints of vaginal bleeding since a year ago. The patient was diagnosed with breast carcinoma 4 years ago and has had a right mastectomy followed by 6 cycles of chemotherapy which is then continued with tamoxifen treatment for 4 years, USG examination revealed uterine myoma to which we performed bilateral salphingoophorectomy hysterectomy, with anatomic pathology results of a uterine Fibroid and chronic endometritis.

Conclusions: Selective estrogen receptor modulators (SERMs) such as tamoxifen exhibit antagonistic reactions in breast tissue which makes it appropriate to be used in the treatment of breast cancer. However, they can also be potentially agonistic on estrogen receptors in the uterus, which can cause the growth of uterine Fibroid. Nevertheless, the benefits of adjuvant tamoxifen for breast cancer outweighs its potential for developing uterine Fibroid and endometrial carcinoma, because metastatic breast cancer will always be fatal, whereas uterine myoma and endometrial cancer caused by the effects of tamoxifen can be prevented by regular evaluation and total hysterectomy.

Keywords: breast cancer,tamoxifen, uterine fibroid.

Abstrak

Tujuan: *Selektif estrogen reseptor modulator (SERMs) seperti tamoksifen berperan dalam meningkatkan risiko mengembangkan mioma uteri.*

Metode: *Laporan Kasus.*

Kasus: *Ny 47 tahun Para 6, datang dengan keluhan perdarahan dari jalan lahir yang dirasakan ibu selama 1 tahun ini, pasien telah menderita kanker payudara 4 tahun yang lalu dan telah dilakukan mastektomi mammae dextra dilanjutkan kemoterapi 6 siklus kemudian dilanjutkan dengan pengobatan tamoksifen selama 4 tahun ini, dari pemeriksaan USG didapatkan adanya mioma uteri kemudian dilanjutkan dengan tindakan histerektomi salphingooforektomi bilateral, dengan hasil patologi anatomi suatu mioma uteri dan endometritis kronis.*

Kesimpulan: *Selektif estrogen reseptor modulator (SERMs) seperti tamoksifen merupakan reaksi antagonis reseptor estrogen pada jaringan payudara yang digunakan dalam pengobatan kanker payudara, tetapi dapat berpotensi agonis pada reseptor estrogen pada uterus sehingga dapat menyebabkan pertumbuhan mioma uteri. Tetapi penggunaan tamoksifen ajuvan untuk kanker payudara lebih bermanfaat dibandingkan dengan potensinya untuk mengembangkan mioma uteri dan karsinoma endometrium, karena kanker payudara metastatik akan selalu berakibat fatal, sedangkan mioma uteri dan kanker endometrium yang ditimbulkan oleh efek tamoksifen dapat dicegah dengan evaluasi teratur dan dilakukan tindakan total histerektom.*

Kata kunci: *kanker payudara, mioma uteri, tamoksifen.*

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INTRODUCTION

Uterine fibroid occurs in 20-25% of women of reproductive age.[1] According to a study conducted in the United States, the incidence of uterine Fibroid cases occurring in Caucasians is 8.9 / 1000 wheras the incidence of people of color is 30.9 / 1000. The prevalence of uterine Fibroid increases with age, peaking in women in their 40s. A study found that 77% of cases requiring hysterectomy revealed uterine Fibroids.[2]

Breast cancer accounts for 30% of all cancers in women and causes about 20% of all cancer deaths, second only to lung cancer. Since the beginning of its incident in the 1980s, cases of breast cancer has increased 3% per year in the western world, and it is estimated that cancer will overtake cardiovascular disease as the leading cause of death in the early twenty-first century. Tamoxifen is the endocrine treatment of choice for selected patients with all stages of breast cancer.[3] Tamoxifen has been known to reduce the incidence of contralateral cancer by 40%.[4]

It is estimated that 2 out of 1000 women / year develop endometrial carcinoma while receiving tamoxifen therapy, compared with 1 in 1000 women reported by SEER in the general population. For breast cancer patients who already have a high risk for endometrial cancer, the added risk of long-term tamoxifen therapy is miniscule compared to its known benefits.[5]

The factors causing uterine Fibroid are unknown, but there are 2 theories. Stimulation theory argues that estrogen is an etiological factor, this is further supported by the following facts : Uterine Fibroid grows faster during pregnancy,this neoplasm has never ovured before menarche, uterine Fibroid usually atrophies after menopause, endometrial hyperplasia is found with uterine myoma. Cellnest Theory states that the occurrence of uterine Fibroids depends on immature muscle cells contained in the Nest cell which can then be stimulated continuously by estrogen.[6,7]

Selective Estrogen Receptor Modulators (SERMs) such as tamoxifen are nonsteroidal hormones that act as antiestrogens in breast tissue.[8] They were first approved by the US Food and Drug Administration for the treatment of breast cancer in 1978 and until now, tamoxifen is used among women of all ages for the treatment of all stages of breast cancer. Tamoxifen reduces the risk of subsequent contralateral breast cancer and also its recurrence and risk of mortality. Upon further investigation, it was discovered that tamoxifen is associated with the development of endometrial cancer. Tamoxifen has a complex mechanism of action including anti-estrogenic activity in the breast and estrogenic effect on other tissues, including endometrium.[9]

Tamoxifen is a first generation breast cancer drug, developed in the 1970s, and is currently designed for the treatment of breast cancer. Tamoxifen acts as an estrogen receptor antagonist in breast tissue, but in bone and uterine tissue Tamoxifen acts as an estrogen receptor agonist, so as to maintain bone mineral density in postmenopausal women. Therefore tamoxifen is also considered for the treatment of osteoporosis.[10] Tamoxifen can act as an agonist for uterine endometrial hyperplasia and polyp production, thus possibly increasing the risk of endometrial cancer.[3]

Tamoxifen has a complex mechanism of action including anti-estrogenic activity in the breast and estrogenic effects on other tissues, including the endometrium.[9] Women taking tamoxifen must be informed of the risk of endometrial proliferation, endometrial hyperplasia, endometrial cancer, and uterine sarcoma, and any effects caused during tamoxifen therapy such as abnormal vaginal bleeding, vaginal discharge. An encounter with any of the mentioned symptoms warrant an immediate full examination. Postmenopausal women taking tamoxifen should be monitored for symptoms of endometrial hyperplasia or cancer, premenopausal women treated with tamoxifen who are not at risk for uterine cancer do not need additional monitoring outside of routine gynecological care, unless the patient has been identified as having a high risk of endometrial cancer. Routine endometrial surveillance has not been proven effective in increasing early detection of endometrial cancer in women using tamoxifen and is not recommended. If atypical endometrial hyperplasia develops, appropriate gynecological management must be performed, and the use of tamoxifen must be reassessed.[11]

Before conducting tamoxifen therapy, initial gynecologic screening should be done, these include transvaginal ultrasonography, sonohysterography and hysteroscopy to assess endometrial conditions. The level of endometrial cancer risk in women treated with tamoxifen depends on dose and time. Studies show that at an early stage, the degree of histology and biology of tumors that develop in individuals treated with tamoxifen 20 mg / day are no different from

those that appear in the general population. Some reports have indicated that women who are treated with tamoxifen doses higher than 40 mg / day are more likely to develop tumors that are more biologically aggressive.

Women who take tamoxifen must be informed of the potential for endometrial proliferation, endometrial hyperplasia, dometrial cancer, and uterine sarcoma, they must be educated to immediately report abnormal symptoms such as vaginal bleeding, spotting, or leukorrhea. The ability of tamoxifen to induce endometrial malignancy and other histopathological conditions seems to differ between premenopausal and postmenopausal women.

Women with endometrial lesions such as polyps diagnosed before tamoxifen treatment have a higher risk of developing atypical endometrial lesions. Therefore, these patients require annual gynecological examinations such tranvaginal ultrasound and even hysteroscopy. These examinations must be carried out even when patients present without symptoms. Hysterectomy can be considered in women with atypical endometrial hyperplasia. Tamoxifen can be used again after hysterectomy in endometrial carcinoma, this requires a consult with a doctor who has experience treating breast cancer.

CASE

A 47-year-old female, Para 6, presented with chief complaints of vaginal since a year ago, bleeding was found in the form of spotting and the patient has been menopausal since 4 years ago. The patient was diagnosed with breast carcinoma 4 years ago and right mastectomy has been performed, followed by 6 cycles of chemotherapy which is then continued with tamoxifen treatment for 4 years. Results of a physical examination revealed a BMI of 31.25 (class 1 obesity). Our patient also suffered from hypertension since undergoing tamoxifen therapy with a dose of 20 mg twice a day and routinely consumes 10 mg of amlodipin to treat this hypertension. Gynecological examination found normal inspection of urethra and vulva, In examinations with speculum, portio was slippery, external uterine ostium was closed, fluor albus was negative, fluxus was positive. Upon bimanual examination, we found a slippery portio, closed uterine externum, uterine cavities enlarged as big as a swan's egg, closed uterine ostium, negative fluor albus and positive flux.

There was no mass felt in both adnexas and parametrium was limp. Laboratory examination results reveal Hb: 13.4 gr / d, Ca 125: 16.28 U / mL, CEA: 1.64 U / mL, GDS: 148 gr / dl. From ultrasound examination, we found an enlarged uterus with size 13x12x11 cm, and a hyperechoic mass 5x4x3 cm in size was seen in the myometrium with a clear boundary. In the Doppler picture was an appearance of feeding arteries which is suggestive of uterine myoma. We then proceeded with bilateral salphingoophorectomy hysterectomy then the results of PA revealed a uterine Fibroid and chronic endometritis.

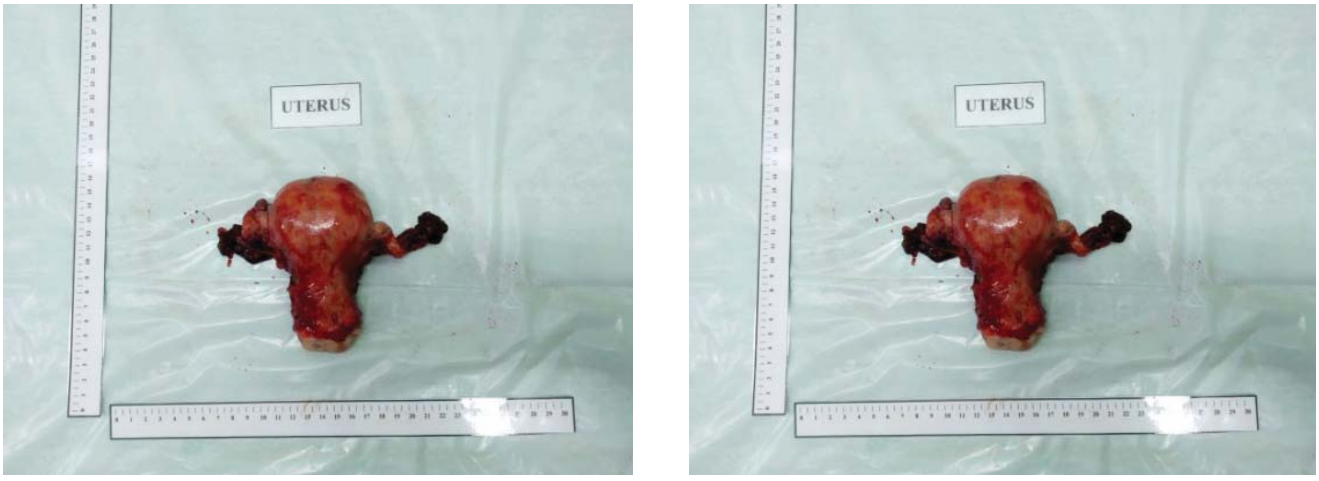

Figure 1. Uterine Fibroid in a patient receiving Tamoxifen

DISCUSSION

In this patient, the uterine fibroid she suffered has caused symptoms, namely bleeding and pain. This complaint has disturbed the patient's quality of life and interferes with her daily activity due to constant menstruation and pain that does not go away with analgesics. Thus, operative management is indicated in this patient.

Considering that this patient no longer has a need for her reproductive function, is undergoing tamoxifen therapy for breast cancer for four years and that tamoxifen increases the risk of endometrial malignancy as much as 1.3 to 7.5, we have decided to perform Salphingoophorectomy hysterectomy on this patient. Another factor which made us favour this decision is that salphingooforectomi aims to increase the efficacy of tamoxifen therapy against breast cancer.

Patients are given an explanation that surgical removal of the uterus and ovaries will be performed to remove uterine myoma and to prevent endometrial cancer that can be caused by tamoxifen therapy and to also increase the efficacy of tamoxifen therapy against breast cancer.

Salphingoophorectomy hysterectomy can solve the patient's problem and reduce the side effects caused by tamoxifen therapy on the risk of endometrial cancer.

Tamoxifen is an effective treatment in reducing the recurrence rate and mortality for breast cancer patients, on the other hand, the undesirable side effects of this treatment are an increased risk of endometrial cancer and changes to the genitals. The benefits of tamoxifen treatment for breast cancer outweigh the toxicity it causes, because metastatic breast cancer is always fatal, whereas the effects of endometrial cancer and changes in gynecological components can still be evaluated periodically and treated more quickly.

CONCLUSION

Uterine fibroid can occur due to estrogen stimulation caused by the use of tamoxifen which is an estrogen receptor agonist in uterine and endometrial tissue. Nevertheless, Tamoxifen treatment is urgently needed in these patients to prevent contralateral metastases. For this patient, it was decided to perform HTSOB to remove uterine myomas and to prevent endometrial cancer and to also increase the effectiveness of tamoxifen therapy.

REFERENCES

1. Unit G, Teaching A. Unaware of a large leiomyoma : A case report with respect to unusual symptoms of large leiomyomas. 2015; 4: 431–3.
2. Vilos GA, Allaire C, Laberge P, Leyland N, Vilos AG, Murji A et al. The Management of Uterine Leiomyomas. J Obstet Gynecol Can. 2015; 37: 157–78.
3. Kim KH, Lee S, Lee KS, Joo JK, Kim SC, Kim YH et al. The effect of tamoxifen therapy on the endometrium and ovarian cyst formation in patients with breast cancer. Obstet Gynecol Sci. 2018; 61: 615.
4. Chen JY, Kuo SJ, Liaw YP, Avital I, Stojadinovic A, Man YG et al. Endometrial cancer incidence in breast cancer patients correlating with age and duration of tamoxifen use: A population based study. J Cancer. 2014; 5: 151–5.
5. Craig V. Endometrial Tamoxifen : Up a Controversy. 1995; 1: 467–72.
6. Coakley F V., Foster BR, Farsad K, Hung AY, Wilder KJ, Amling CL et al. Pelvic applications of MR-guided high intensity focused ultrasound. Abdom Imaging. 2013; 38: 1120–9.
7. Jiang N, Xie B, Zhang X, He M, Li K, Bai J et al. Enhancing Ablation Effects of a Microbubble-Enhancing Contrast Agent ("SonoVue") in the Treatment of Uterine Fibroids With High-Intensity Focused Ultrasound: A Randomized Controlled Trial. Cardiovascul Intervent Radiol. 2014; 37: 1321–8.
8. Reuben Peyser M, Inbar M, Lessing JB, Bar-Am A, Wallach EE, Daniel Y. The effects of tamoxifen treatment on the endometrium. Fertil Steril 2016; 65: 1083–1089. Howell A, Johnston S. Selective estrogen receptor modulators (SERMs). Endocrinol Manag Breast Cancer. 2013; : 45–62.
9. Polin SA, Ascher SM. The effect of tamoxifen on the genital tract. Cancer Imaging 2008; 8: 135–145.
10. 10. Howell A, Johnston S. Selective estrogen receptor modulators (SERMs). Endocrinol Manag Breast Cancer. 2013; : 45–62.
11. Litigation L. Committee opinion. Obstet Gynecol. 2011; 118: 389–391.