Role of Ultrasound in Diagnosis of Endometrial and Ovarian Changes Asscoiating Adjuvant Hormonal Therapy in Breast Cancer Patients

Alaa Eldin Mohamed Abdelhamid, Heba Allah Hassan Mamdouh, Samar Mohamed Abdelhamid Eshiba, Mohamed Latif Abouegylah, Menatallah Mohamed Osama Hegazy

Department of Radiodiagnosis, Faculty of medicine, Alexandria University

Introduction

Several hormonal therapy strategies are available for premenopausal women with breast cancer. Tamoxifen, a selective estrogen receptor modulator (SERM), is one of the most commonly prescribed adjuvant endocrine therapies for ER-positive breast cancer. It has proven effective in reducing both recurrence and mortality.

Tamoxifen acts as an ER-α antagonist in breast tissue but exerts an ER-β agonist effect in the endometrium, which can lead to a spectrum of uterine pathologies, including endometrial polyps, hyperplasia, adenocarcinoma, sarcoma, and cyst formation. Zoladex (goserelin), an LHRH agonist, may be used in combination with tamoxifen as adjuvant therapy. This approach helps lower estrogen levels and reduces tamoxifen-induced endometrial thickening. Third-generation non-steroidal aromatase inhibitors, such as letrozole (Femara), are approved for the treatment of hormone receptor-positive breast cancer in postmenopausal women. These agents reduce estrogen synthesis by inhibiting the aromatase enzyme responsible for converting androgens into estrogens. Unlike tamoxifen, aromatase inhibitors do not directly interact with estrogen receptors, and therefore are associated with fewer gynecological side effects.

Aim of the work

The aim of this study is to identify the role of ultrasound in detection of endometrial and ovarian changes that are associated with adjuvant hormonal therapy in management of ER positive breast cancer patients.

Patients and Methods

PATIENTS: This study was carried on 100 female patients with estrogen receptor (ER) positive breast cancer in both pre-menopausal and post-menopausal women. Ultrasound assessment was done at the beginning of the study, after 6 months follow-up and another ultrasound follow-up after 1 year.

METHODS: All patients were subjected to: Detailed personal, medical, and surgical history, clinical examination focused on gynaecological complaints. Histopathological examination with immunohistochemistry was included for all biopsy samples. Pelvis ultrasound was done (either transabdominal or transvaginal ultrasound) including baseline examination at beginning of hormonal therapy, follow-up after 6 months and another US follow-up after 1 year.

Results

The study included 100 female patients with estrogen receptor (ER) positive breast cancer managed by surgery, chemo/radiotherapy and hormonal therapy. All patients were receiving various hormonal therapy regimens, including tamoxifen alone (n=17), tamoxifen combined with Zoladex (n=55), Femara (n=24), or Femara in combination with Zoladex (n=5).

The endometrial thickness ranges on ultrasound examination in the current study; 32 patients (32%) had thickened endometrium with endometrial thickness ranging from 8 to 32mm. At baseline US, the mean endometrial thickness was 6.05 ± 4.38 across the different groups. US follow-up after 6 months of hormonal treatment revealed significant differences in endometrial thickness between the groups taking nolvadex (±zoladex) and femara.

The highest mean endometrial thickness was observed in the tamoxifen group (8.39 ± 5.05) followed by tamoxifen and zoladex group (mean thickness was 7.88 ± 5.31). No significant increase in endometrial thickness was observed among the femara and femara plus zoladex groups. These results indicate that tamoxifen lead to increased endometrial proliferation.

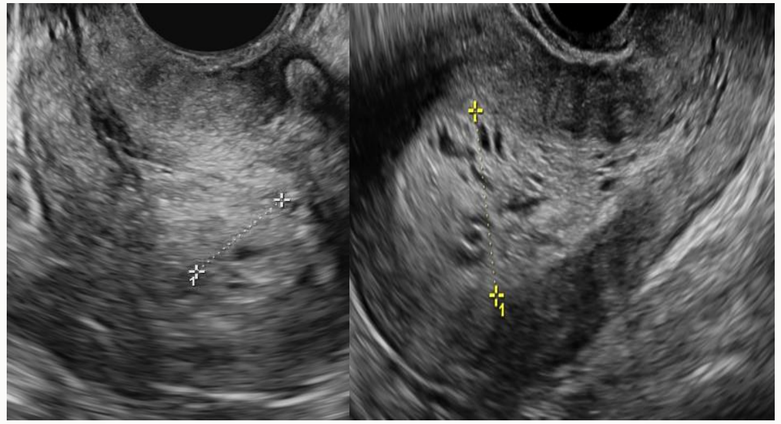

Figure 1: grey scale US of uterus of patient taking tamoxifen reveals thickened endometrium recaching 18mm, Figure 2: grey scale US of uterus of patient taking tamoxifen and zoladex showing thickened endometrium reaching 12mm.

Table (1) :Comparison between the different type of hormonal therapy to endometrial thickness

Endometrial thickness (mm)	Type of hormonal therapy				p
	Nolvadex (n = 17)	Nolvadex and Zoladex (n = 54)	Femara (n = 24)	Femara and Zoladex (n = 5)	
Baseline					
Min. – Max.	3.0 – 16.0	2.0 – 23.0	2.0 – 15.0	2.0 – 12.50	0.039*
Mean ± SD.	6.41 ± 4.04	6.76 ± 4.97	4.17 ± 2.55	6.20 ± 4.04	
Median (IQR)	5.0 (4.0 – 7.50)	4.75 (4.0 – 8.0)	3.75 (3.0 – 5.0)	6.0 (3.50 – 7.0)	
Sig. bet. type	p_1=0.874,p_2=0.025*,p_3=0.880,p_4=0.006*,p_5=0.944,p_6=0.196				
6 months					
Min. – Max.	3.0 – 18.0	2.0 – 25.0	2.0 – 10.0	2.0 – 12.0	0.001*
Mean ± SD.	8.39 ± 5.05	7.88 ± 5.31	4.17 ± 1.79	5.80 ± 4.15	
Median (IQR)	7.0 (4.0–12.70)	6.0 (4.0 – 10.0)	3.75 (3.0 – 5.0)	4.0 (3.0 – 8.0)	
Sig. bet. type	p_1=0.787,p_2=0.002*,p_3=0.205,p_4<0.001*,p_5=0.222,p_6=0.511				
Z(p_0)	-1.575 (0.115)	-2.843*(0.004*)	-0.398 (0.690)	-0.184 (0.854)	
1 years					
Min. – Max.	3.0 – 20.0	2.0 – 20.0	2.0 – 10.0	3.0 – 11.0	0.001*<
Mean ± SD.	8.35 ± 4.81	7.87 ± 4.56	4.13 ± 1.53	5.80 ± 3.11	
Median (IQR)	8.0 (4.0 – 10.0)	6.0 (4.0 – 10.0)	4.0 (3.0 – 4.50)	5.0 (4.0 – 6.0)	
Sig. bet. Type	p_1=0.867,p_2=0.001*,p_3=0.378,p_4<0.001*,p_5=0.390,p_6=0.223				

Conclusion

- Transvaginal ultrasonography is employed as a non-invasive modality for assessing and monitoring endometrial thickness in breast cancer patients undergoing hormonal therapy .
- The use of tamoxifen hormonal therapy is associated with increased endometrial thickness, which progressively rises in proportion to duration of treatment.
- The combination of tamoxifen and zoladex results in a reduced incidence of increased endometrial thickness.
- Ovarian cysts which develop in association with hormonal therapy rarely progress to invasive neoplastic behavior. Therefore, most ovarian cysts in women receiving tamoxifen can be safely managed with regular US follow-up rather than immediate surgical intervention.
- Femara can be used safely without any gynecological side effects. Furthermore, it can be used as an alternative to tamoxifen in patients who develop tamoxifen-induced endometrial thickening