Transvaginal sonographic study of uterine changes in breast cancer patients treated with TAMOXIFEN

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Aim

The aim of this work is to study the various pathological uterine changes occurring in breast cancer patients treated by tamoxifen as hormonal therapy using the transvaginal ultrasound.

Methods and materials

The study was performed upon 76 female patients (ages ranging between 36 and 58 years), originally managed for cancer breast and receiving Tamoxifen therapy or planned to start their Tamoxifen therapy in the time period between September 2010 and August 2011. 66 patients were post-menopausal (86.8%), while only 10 were still menstruating (13.2%).

17 patients were symptomatic (22.3%), including 14 having one or more attack of frank bleeding and 3 patients complaining from vaginal spotting.

All patients were subjected to full history taking, clinical examination and trans-vaginal ultrasound using endo-vaginal probe with 4-9MHz frequency). Virgin patients were excluded from the study.

For patients who were still going to start their treatment with Tamoxifen, a baseline study was performed followed by a second (follow up) study 6 months later.

For each patient, the uterus was examined in both axial and sagittal planes. The maximum thickness of the endometrium was measured in the longitudinal mid-sagittal plane at the widest point between the endometrial-myometrial interfaces.

Symptomatic patients were further assessed by dilatation and curettage (D&C) and histopathological assessment. Also patients, in whom the endometrium was found markedly thickened (above 15 mm), histopathological assessment after D&C was performed.

Results
The endometrial thickness was correlated with the duration of treatment at the time of examination and proved to be statistically significant; the longer the duration of treatment with Tamoxifen, the thicker the endometrium at the time of examination (Table 1).

Table (1): Relation between duration of treatment and endometrial thickness.

<table>
<thead>
<tr>
<th>Duration</th>
<th>&lt; 10</th>
<th>10 - &lt;20</th>
<th>20 - &lt;30</th>
<th>30+</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>%</td>
<td>No</td>
<td>%</td>
<td>No</td>
</tr>
<tr>
<td>&lt;1</td>
<td>14</td>
<td>34.1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&gt;1- &lt;2</td>
<td>19</td>
<td>46.3</td>
<td>3</td>
<td>12.0</td>
</tr>
<tr>
<td>2 - &lt;3</td>
<td>7</td>
<td>17.1</td>
<td>14</td>
<td>56.0</td>
</tr>
<tr>
<td>3- &lt;4</td>
<td>0</td>
<td>0.0</td>
<td>6</td>
<td>24.0</td>
</tr>
<tr>
<td>#4</td>
<td>1</td>
<td>2.4</td>
<td>2</td>
<td>8.0</td>
</tr>
</tbody>
</table>

MCp: p value for Monte Carlo test

*: Statistically significant at p # 0.05

The presence of endometrial cystic changes was also assessed for every patient with 42.1% of patients having positive cystic changes on ultrasound basis.

Other findings were found in 14 cases representing 18.4% of studied cases; these included the presence of uterine fibroids (5 cases), retained fluid within the endometrial cavity (4 cases), suspected focal endometrial pathology (2 cases), associated ovarian cysts (2 cases) and in 1 case an indistinct endometrial myometrial interface was suspected.

From the 76 examined cases, 14 patients came just before starting Tamoxifen treatment. The endometrial thickness was measured both in the baseline study and on follow up. The endometrial thickness being almost doubled from the baseline after tamoxifen treatment (table 2) with only four cases having endometrial cysts at follow up, representing 28.6% of the followed up cases.

Table (2): Comparison between thickness at baseline and after 6 months for the followed up cases (14 cases)
Out of the 76 patients, 25 have undergone pathological assessment, out of which 15 were symptomatic and 10 had no symptoms but their endometrial thickness was markedly increased.

Out of the 25 patients who went for pathology; **8 patients had simple hyperplasia, 5 had cystic hyperplasia, 2 had complex cystic hyperplasia, 5 had polyps either alone or on top of other endometrial pathology (either hyperplasia or atrophy) and 5 had early signs of neoplasia (atypia/intra-epithelial neoplasia).**

Correlation between the results of histopathology and trans-vaginal sonographic findings was performed; any irregularities of the endometrial myometrial interface or inability to adequately distinguish between them should alert the patient and the treating physician to go for histopathology even in the absence of any symptoms (Table 3).

<table>
<thead>
<tr>
<th>Findings at histopathology</th>
<th>Thickness</th>
<th>Cysts</th>
<th>Other findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple hyperplasia (8 cases)</td>
<td>27.5</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>16.8</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.1</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>18.7</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td></td>
<td>8.0</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12.9</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td>15.4</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td></td>
<td>28.3</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Cystic hyperplasia (5 cases)</td>
<td>14.5</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>Number of Cases</td>
<td>Findings 1</td>
<td>Findings 2</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>-----------------</td>
<td>------------</td>
<td>------------</td>
</tr>
<tr>
<td>Complex cystic hyperplasia (2 cases)</td>
<td>18.6</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Simple hyperplasia with polyp (2 cases)</td>
<td>14.6</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Cystic hyperplasia with polyp (1 case)</td>
<td>17.4</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Cystic atrophy with polyp (1 case)</td>
<td>9.3</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Polyp (1 case)</td>
<td>24.5</td>
<td>no</td>
<td></td>
</tr>
<tr>
<td>Complex hyperplasia with atypia (3 cases)</td>
<td>26.7</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Cystic hyperplasia with atypia (1 case)</td>
<td>34.0</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>Atypical hyperplasia with focal intraepithelial neoplasia (1 case)</td>
<td>27.4</td>
<td>yes</td>
<td></td>
</tr>
</tbody>
</table>

Images for this section:
Fig. 1: 42 years old menopausal asymptomatic patient, on Tamoxifen treatment for 2 years, coming for routine follow up. The endometrium is seen mounting to 10.4 mm with few cystic changes; being within the average thickness and ultrasound appearance for her clinical status.
Fig. 2: 50 years old menopausal asymptomatic patient, coming before starting tamoxifen treatment, with the endometrium mounting to 3.7 mm on the baseline study. 6 months later the patient came back for reassessment, still asymptomatic, the endometrium was 7.5 mm. (A) baseline study. (B) Follow up after 6 months.

Fig. 3: 40 years old asymptomatic patient, still menstruating at presentation time, coming before starting tamoxifen treatment and for follow up after 6 months. (A) Baseline study
with endometrium measuring 2.5 mm. (B) After 6 months, the endometrium mounting to 5.8 mm.

**Fig. 4:** 40 years old menopausal patient presenting after 1 attack of severe vaginal bleeding after 1 year of Tamoxifen treatment. (A) Shows the total endometrial thickness (12.1 mm), (B) and (C) shows the presence of retained blood mounting to 5.2 mm. The patient went for D&C and histopathology proved to be simple endometrial hyperplasia having no signs of atypia.
Fig. 5: 43 years old menopausal patient presenting with recurrent attacks of vaginal spotting after 2 years of Tamoxifen therapy. Transvaginal U/S revealed focal endometrial pathology mounting to 9mm in diameter (A) and (B) associated with small endometrial cysts (C). Histopathology proved to be cystic endometrial atrophy with focal adenomatous hyperplasia.
Conclusion

conclusions

• Transvaginal ultrasound is a simple, non-invasive technique, widely accepted by patients with no major complication.
• Transvaginal ultrasound can be used as a 1st line investigation in patients receiving tamoxifen.
• Tamoxifen therapy is associated with increased endometrial thickness, which might reflect a wide range of histopathological findings.
• Some of the pathological entities associated with tamoxifen intake include simple hyperplasia, cystic hyperplasia, complex cystic hyperplasia, polyps either alone or on top of other endometrial pathology (hyperplasia or atrophy), cellular atypia and neoplasia.

Recommendations

• A baseline study is advised to rule out the presence of any pathology prior to starting tamoxifen therapy.
• A second examination should be performed for all patients after 3 years of tamoxifen treatment to search for malignancy.
• A third examination after completion of the five years of tamoxifen treatment is advised even if the patient is asymptomatic.
• An endometrial thickened above 10 mm needs further evaluation by other modalities (such as hysterosonography or hysteroscopy) and/or short term follow up.
• Any patient with an endometrial thickness above 15 mm should go for histopathology.
• Inability to adequately assess a well defined endometrial-myometrial interface should be further investigated.
• Any patient presenting with abnormal vaginal bleeding while on tamoxifen therapy should be evaluated; transvaginal ultrasound represent an easy technique to start with, any suspicious finding should be adequately assessed.

Personal information

Professor Dr Mohamed Hamdy Mahmoud Zahran
Professor of Radiodiagnosis & Medical Imaging
**Nationality**: Egyptian

**Date & Place of birth**: 6 July 1942, Alexandria- Egypt.

**Social Status**: Married and has two children.

**Scientific Certificates**:

1) Bachelor of Medicine, M.B-CH.B (June 1965)


3) Diploma of Medicine " DM" (1971)

4) Doctor degree of Radiodiagnosis "M.D" (1974). Discussed Ph.D thesis before on 1973 and its title was "The Radiological Study of Lower Urinary tract in Health & Disease of Egyptian Infants & Children with Special Reference to Vesicoureteric Reflux"

5) BA degree in Law and Sharia. Oct. 2004

6) High Diploma of Law and Sharia. Oct. 2005


**Scientific Experience**:

1) Staff member- Radiology Department- Faculty of medicine- Alexandria University since 1965 till present.

2) Worked as senior consultant radiologist in ministry of public health in Kuwait for seven years and General Secretary of the medical discipline committee of Radiology (1980-1987).

3) Professor of Radiodiagnosis in radiology department- Faculty of medicine- King Abdul Aziz university- Jeddah- Kingdom of Saudi Arabia for two years (1996-1998)


7) Visiting professor in CTO (central hospital for Traumatology and Orthopedics) Torino-Italy. 2003
8) Visiting professor in CHEO (Children hospital of Easter Ontario) Canada, 2007

9) Member of the permanent committee for promoting Professors and assistant professors (one of fifteen) .. for over 15 years.

Scientific Activities: (For more information refer to the attached detailed C.V)

1)

**Faculty of Medicine, Alexandria University**

Published 36 papers in local, national and international journals.

2) Member in different scientific societies.

3) General secretary of Egyptian society of radiology & nuclear medicine for three years.

4) Member of the Egyptian board of professors of radiology "consists of 15 members only" for promoting the university staff allover Egypt to obtain and achieve professor and assistant professor title.

5) Shared in more than 98 meetings & congresses "national & international" (Active participation)

6) Supervised about 50 theses (Master & Doctorate).

7) Shared in the discussion and assessment of 50 thesis (Master & Doctorate).

Constructive Activity:

1) Initiated the first ultrasound centre in Egypt 1974.

2) Initiated the radiology department in "Alexandria Medical Centre". Biggest private hospital in Alexandria (270 beds capacity).

Languages:

1) Arabic: Native language.

2) English: Excellent (Speaking, writing and reading)

3) French: Fair.

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Images for this section:
Fig. 6: Professor Dr Mohamed Hamdy Mahmoud Zahran Professor of Radiodiagnosis & Medical Imaging
References

REFERENCES


