TSH receptor antibodies in breast cancer and benign breast disease: a hospital based study

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INTRODUCTION

Breast cancer is the most frequent malignant tumour in women worldwide with about 1 million women being affected.1 Breast cancer is a hormone dependent malignancy. Thyroid hormone receptors affect both the normal breast cell differentiation and breast cancer cell proliferation, with effects of thyroid hormones similar to those caused by estrogens.2,3 Some studies have indicated thyroid autoimmune changes as prognostic factors in breast cancer.4 Relationship between thyroid diseases with breast cancer was demonstrated in several studies.5-8 Some of the studies showed higher incidence of breast cancer in patients with thyroid dysfunction compared to healthy controls.9-13

TSH Receptor Antibodies is present in thyroid autoimmune diseases. The ligand for TSH Receptor Antibody (i.e.) TSH Receptor, is also present in breast cancer tissue.14 Only limited aspects of potential association between TSHRAb and breast cancer have been postulated, whereas the exact mechanism has not
been identified. Genetic, environmental and molecular pathways of both female predominant diseases have been described, and integrated analysis of the above entities provides opportunity to identify the potential relevant common etiological mechanism.

The potential relationship between TSH Receptor antibodies and breast cancer has not been clearly documented, as the elevated serum levels of TPO Ab and Tg Ab in patients with breast cancer, detected in some studies, have not been confirmed elsewhere. Furthermore, no conclusive research has been undertaken concerning significance of TSHRAb in patients with breast cancer and benign breast tumours. The aim of this prospective study is to determine the presence of TSH Receptor antibodies in women with breast cancer or benign breast tumours, and to analyse a possible relationship between TSH Receptor antibodies and these two groups of breast diseases with emphasis to laboratory findings.

METHODS

The study was carried out in Saveetha medical college and hospital, Chennai, India. The study included healthy controls (Group 1, n=29), women with benign breast tumours (Group 2, n=29), and women with breast cancer (Group 3, n=29).

All patients were without any known thyroid disease, and studied before any radio or chemotherapy. Breast cancer patients, women with benign breast tumours and healthy controls gave formal consent for participation in the study. Signed informed consent was obtained from all participants, allowing analysis of all clinical and laboratory data mentioned in this paper.

All patients underwent serological determination of TSH Receptor antibodies based on electro chemiluminescence immune assay. The normal ranges were <1.22 IU/L for TSH receptor antibody. Those women without any breast or thyroid disease were the control group. The clinical and laboratory details of 87 women hospitalized were prospectively analyzed, using a post hoc Tukey HSD for normally distributed continuous data, chi-square test for comparers.

RESULTS

Table 1: Mean age of all three groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>Control group</th>
<th>Benign tumours</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>45.14±13.58</td>
<td>31.25±8.61</td>
<td>51±14.29</td>
</tr>
</tbody>
</table>

A total number of 87 patients were included in this study. Out of this, 29 women were healthy controls, 29 women with benign breast tumours and 29 women with breast cancers.

The age of the patients ranged from 20 years to 92 years (Table 1).

Table 2: Parameters of the study population.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Controls mean±SD (group i)</th>
<th>Benign tumours mean ± SD (group ii)</th>
<th>Breast cancer mean ± SD (group iii)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSHRAb (&lt;1.22IU/L)</td>
<td>0.75±0.53</td>
<td>0.59±0.33</td>
<td>0.71±0.49</td>
<td>0.403 (NS)</td>
</tr>
</tbody>
</table>

Table 3: TSH receptor antibody values within study population.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Control group</th>
<th>Benign tumours</th>
<th>Breast cancer</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal range</td>
<td>27 (93.1%)</td>
<td>29 (100.0%)</td>
<td>23 (79.3%)</td>
<td>79 (90.8%)</td>
</tr>
<tr>
<td>Elevated</td>
<td>2 (6.9%)</td>
<td>0 (0%)</td>
<td>6 (20.7%)</td>
<td>8 (9.2%)</td>
</tr>
<tr>
<td>Total</td>
<td>29 (100.0%)</td>
<td>29 (100.0%)</td>
<td>29 (100.0%)</td>
<td>87 (100.0%)</td>
</tr>
</tbody>
</table>

All patients were without any known thyroid disease are studied. TSHR Ab were determined in healthy controls, women with benign breast tumours and breast cancer (Table 2).

Those women without any breast or thyroid disease were the control group. Out of these 29 patients in control group, 2 had elevated TSH Receptor antibody level.

Among the 29 patients with benign breast tumours there was no elevation of TSHR Ab (Table 3), which indicated no association of TSHR Ab with benign breast tumours.

Out of 29 patients with breast cancer, 6 had elevated levels of TSH Receptor antibodies, which indicated TSH Receptor antibodies are statistically significant in breast cancer (Table 3), (Figure 1), and association of TSH Receptor antibodies with breast cancer.
DISCUSSION

TSHR Ab is a positive determinant of breast cancer. The prevalence of TSHR Ab in breast cancer is 20.7%. In the present study, among 29 patients with breast cancer, 6 patients were found positive for TSHR Ab. TSHR Ab levels were significantly higher in our series in patients with breast cancer, comparing to controls and to patients with benign breast tumors.

Mammary gland is derived from iodide-concentrating ectoderm. Increased intake of iodine is considered as a protective factor against the occurrence of breast cancer. The incidence of breast cancer has been attributed to differences in dietary iodine intake, and an effect of iodine on breast has been postulated (Mittra I, 1976). Uptake of iodine in to the breast alveolar and ductular cells happens in the mechanism of active transport via the glycoprotein - Na+/I-symporter (NIS). The expression of NIS occurs in 80% to 90% breast cancer cases. TSH receptors are present in fatty tissue, which is abundant in mammary gland (Davies et al., 1994). Additionally, some endocrine stimuli identified in thyroid products exert a simultaneous action on the breast and the various thyroid antibodies which could also interact with receptors on breast tumours. Thyroid antibodies could interact with the receptors on breast tumours. Interaction between TSHR Ab and breast Cancer can occur, common in the adipose tissue. TSH Receptor expression is common in breast cancer, with higher prevalence in low-grade breast cancer.

In our study, TSHR Ab levels were significantly higher in breast cancer comparing to benign breast tumours and controls. They are positive determinants of breast cancer. Therefore, we suggest that TSHR Ab can be called a positive predictor for the subsequent development of breast cancer.

However, further research is needed to elucidate the mechanism linking Breast cancer and TSHR Ab. The major limitation of our study was the small sample size. Further studies including a larger group of patients are necessary to confirm the results. (Ditsch et al., 2010; Szychta et al., 2013).

CONCLUSION

The present study indicates that the serum levels of TSH Receptor Antibody are significant higher in patients with Breast cancer. These results have implications not only for the screening of patients but also for the development of new prognostic markers. Further high-quality prospective studies are needed to explore whether TSH Receptor Antibodies are potential prognostic markers for patients with Breast cancer.

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REFERENCES

9. Rasmussen B, Feldt-Rasmussen U, Hegedus L, Perrild H, Bech K, Hoier-madsen M. Thyroid...