ER-β Expression in Different Thyroid Carcinomas: Immunohistochemical Study

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Abstract

Background: Thyroid diseases are more prevalent in females particularly between puberty and menopause and carcinomas of the thyroid are three-times more frequent in females than in males. This suggest a role of estrogen in the pathogenesis of thyroid diseases.

Objective: To evaluate the presence of estrogen receptor beta in different thyroid carcinomas. And to detect if there is differences in expression of ER between different diagnoses.

Material and Methods: In this retrospective and immunochemical study 41 cases of thyroid carcinomas were obtained from files of Pathology Department, Faculty of Medicine, Cairo University between January 2013 and December 2015. Paraffin-embedded tissue sections fixed in formalin were used. Two sections were prepared from each paraffin block; one of them stained with Hematoxylin and Eosin (H & E) for histological re-evaluation, while other was subjected to the immunohistochemical marker (ER-β).

The (Allred) score method was used to evaluate immunohistochemical staining and the cases were considered positive if showing nuclear immunoreactivity and with score more than 2.

Results: This study was carried upon 41 selected cases including 12 follicular carcinoma, 16 papillary carcinoma, 3 poorly differentiated carcinoma, 3 anaplastic carcinoma and 7 medullary carcinoma. The ER-β positive cases were 37/41 (90.2%) cases. On comparing of both positivity and Allred scoring between the different malignant pathological diagnoses, p-value was (<0.05) for both which was statistically significant. The expression is observed more in well differentiated malignant tumors than higher grade tumors. On contrary there were no significant correlation between ER-β expression and age, sex or menopausal status.

Conclusion: ER-β is detectable in different thyroid carcinomas with more expression in well differentiated malignant tumors than higher grade tumors.

Recommendations: These findings entail evaluation of the possible therapeutic usefulness of an anti estrogen therapy in thyroid carcinoma cases.

Key Words: Estrogen receptors – Thyroid gland – Malignant tumors – ER-β.

Introduction

THYROID cancer is uncommon tumor representing 1.48% of total malignant cases in Egypt [1]. But it is three-times more frequent in females than in males, and the peak rates occur earlier in females [2]. All this epidemiological data suggest a role of estrogen in the pathogenesis of thyroid diseases.

ER has been identified, for instance in a wide range of human neoplasms, including carcinoma arising in breast [4] and in endometrium [5]. Also in colon [6], lung [7], pancreas [8], and other organs classically considered not to be targets for estrogens.

Material and Methods

A total of 41 thyroid carcinoma cases; 12 follicular carcinoma, 16 papillary carcinoma, 3 poorly differentiated carcinoma, 3 anaplastic carcinoma and 7 medullary carcinoma were obtained from files of Pathology Department, Faculty of Medicine, Cairo University between January 2013 and December 2015. Selection was both consecutively and according to the availability of adequate tissue and clinical data.
Immunohistochemistry:

Formalin-fixed Paraffin-embedded tissue sections were used. Two (5 microns thick) sections were prepared from each paraffin block; one of them stained with Hematoxylin and Eosin (H & E) for histological re-evaluation, while other subjected to the immunohistochemical marker (ER-β). Immunohistochemical staining in this study was automated.

Positive control: Normal breast was used as a positive control for ER-β.

Assessment of ER-β: The (Allred) score method was used to evaluate immunohistochemical staining for the estrogen receptors. The Allred score is the sum of two component scores: proportion and intensity of staining, gives us a score in the range 0-8 (excluding score=1) [9]. Intensity score: No staining of any nuclei at high magnification=0, weak (only visible at high magnification)=1, moderate (readily visible at low magnification)=2, strong (strikingly positive at low magnification) =3. While proportion score: 0%=0, <1%=1, 1-10% =2, 11-33%=3, 34-66%=4, 67-100%=5. Scoring of ER-β in tumor cells was performed on high power field (400X) using a standard light microscope. The cases were considered positive if their score was more than 2, and showing nuclear immunoreactivity.

Statistical analysis: Data were statistically described in terms of mean ± Standard Deviation (± SD), or frequencies (number of cases) and percentages when appropriate. Comparison of numerical variables between the study groups was done using Mann Whitney U-test for independent samples for comparing two groups and Kruskal Wallis test for comparing more than two groups. For comparing categorical data, Chi-square (χ²) test was performed. Exact test was used instead when the expected frequency is less than 5. Correlation between various variables was done using Spearman rank correlation equation. p-values less than 0.05 was considered statistically significant. All statistical calculations were done using computer program SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) release 15 for Microsoft Windows (2006).

Results

41 thyroid carcinoma cases ranging in age from 17 to 72 years with mean 42.1 ± 10.88 years. 35 were females (85.4%) ranging in age from 17 to 72 years with mean 40.4 ± 11.7 years. And 6 males with age ranging from 45 to 57 years with mean 50.7±4.96 years. The distribution of cases in Charts (1,2).

In thyroid carcinoma cases 37/41 (90.2%) were ER-β positive, they were 31 females (27 premenopausal and four postmenopausal) ranging in age from 17 to 72 years with mean age 38.3 ± 10.58 years, and 6 males ranging in age from 45 to 57 years with mean age 50.7±4.96 years. According to Allred scoring the cases were as follows: One case=3, four cases=4, one case=5, six cases=6, fourteen cases=7, eleven cases=8. Most of positive cases were females (31/37) (83.8%), and most of them were premenopausal 27/31 (87%).

Analysis of different malignant diagnoses Chart (3) revealed: Positive papillary carcinoma cases were 16/16 (100%); they were thirteen females (all were premenopausal) ranging in age from 26 to 47 years with mean age 33.3 ± 5.92 years and three males ranging in age from 45 to 57 years with mean age 49.3 ± 6.65 years. Allred score were: Three cases=4, one case=5, six cases=6, four cases =7 and two cases=8.

Positive Follicular carcinoma cases were 12/12 (100%); ten females (7 premenopausal and 3 postmenopausal) ranging in age from 34 to 72 years with mean age 46 ± 11.33 years and two males 50 and 56 years with mean age 53 ± 4.24 years. Allred score were: One case=3, nine cases=7 and two cases=8. Positive poorly differentiated carcinoma cases were 1/3 (33.3%); one female 33 years old (premenopausal). Allred score=8. Anaplastic carcinoma cases were 1/3 (33.3%); one female 17 years old (premenopausal). Allred score=4. Medullary carcinoma cases were 7/7 (100%); six females (5 premenopausal and one postmenopausal) ranging in age from 31 to 55 years with mean age 41.16 ± 8.20 years and one male (50 years old). Allred score were: One case=7 and six cases=8.

Analysis of age with sex of ER-β positive cases within the different pathological diagnoses revealed that mean of age of females was lower than males in all types of carcinomas.

On comparing of both positivity and Allred scoring between the different malignant pathological diagnoses, using Pearson Chi-Square and Kruskal-Wallis Test respectively, p-value was (<0.05) for both which was statistically significant and ER-β expression is observed more in well differentiated malignant tumors than higher grade tumors.
Figs. (1,2): Follicular thyroid carcinoma, capsular invasion (H & E X100 & ER-β, positive cytoplasmic and nuclear X100).

Figs. (4,5): Medullary thyroid carcinoma; amyloid deposits (H & E X100 & ER-β, positive cytoplasmic and nuclear X100).

Fig. (3): Follicular thyroid carcinoma (ER-β, positive cytoplasmic and nuclear membrane X400).

Fig. (6): Medullary thyroid carcinoma (ER-β, positive, cytoplasmic and nuclear X400).

Fig. (7): Poorly differentiated thyroid carcinoma (H & E X100).

Fig. (8): Poorly differentiated thyroid carcinoma (ER-β, positive nuclear and cytoplasmic X400).

Chart (1): Pathological diagnoses distribution.
In this retrospective and immunohistochemical study, we investigated the expression of ER-β in 41 cases of thyroid carcinoma cases. Most of cases were females (31 out of 37) (83.8%) with age mean 38.3±10.58 years and most of them were premenopausal 27 (87%). While male cases age mean was 50.7±4.96 years. In Vaiman et al., study [10] females age mean=29 years and according to menopausal state were 189 premenopausal (81.81 %) and 42 postmenopausal (18.18%), while male age mean was 37 years. In another study done by Huang et al., [11] cases were all females, 80 were premenopausal (67.2%) and 39 were postmenopausal (32.8%). In our study the age means for both females and males were higher but distribution of cases according to menopausal status were close.

ER-β expression was detected in 37/41 carcinoma (90.2% of carcinomas). While in Vaiman et al., study [10] ER-β was detected in carcinoma; follicular, papillary, medullary and anaplastic (70/103; 67.96%), so incidence was lower than that in our study. In Bléchet et al., study [12] ER-β was detected in 26/28 medullary carcinoma (92.85%) which is almost the same result of our study where all medullary carcinoma cases were 7/7 (100%) expressing ER-β.

And on comparing positivity in the different malignant pathological diagnoses (papillary carcinoma, follicular carcinoma, poorly differentiated carcinoma, anaplastic carcinoma and medullary carcinoma), p-value=0.001 which was statistically highly significant. On contrary in Vaiman et al., 2010 [10] no significant difference was found between the various thyroid lesions (p-value >0.05).

Conclusion:
ER-β is detectable in different thyroid carcinomas with more expression in well differentiated
malignant tumors than higher grade tumors. Further investigations are necessary to explain discrepancy between different studies, which might be explained by technical factors such as use of monoclonal or polyclonal antibodies or various staining procedures.

References


