

Steroidal Hormone Receptor Expression in Male Breast Cancer

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Background & aim: Although the etiology of male breast cancer is unclear, hormonal levels may play a role in the development of this disease. It seems that reduced androgen or increased estrogen stimulation can promote the risk of breast cancer in men. The aim of this study was to investigate the expression of steroid hormone receptors including estrogen receptor (ER) and progesterone receptor (PR) in Iranian male subjects with breast cancer.

Methods: This prospective review was conducted on 18 male cases with breast cancer in Omid Hospital, Mashhad, Iran (Oct. 2001-Oct. 2006). ER and PR were measured by immunohistochemistry, and clinicopathologic features and family history were obtained via interviews. Data were analyzed with SPSS Version 13, and using descriptive statistics.

Results: The median age was 63.2 years, and all cases presented with infiltrating ductal carcinoma. The results revealed a high rate of ER (88.8%) and PR (66.6%) expression.

Conclusion: Male breast cancer is significantly more likely to express hormonal receptors in comparison with female breast cancer.

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Introduction

Male breast cancer typically occurs at a much lower rate, compared with female breast cancer; however, its prevalence varies depending on geographical location. Similar to female breast cancer, the risk of male breast cancer appears to be related to increased lifelong exposure to estrogen or reduced androgen. Klinefelter's syndrome, history of mumps orchitis, undescended testis, or testicular injury are among the risk factors in men, perhaps due to an imbalance in the estrogen-testosterone ratio. Feminization, whether genetically or due to environmental exposure, appears to increase the risk of this cancer, as reported in transsexuals receiving exogenous estrogens. The majority of male breast cancers are ER positive, and a few studies have examined the contribution of markers such as HER2/*neu* and p53 (1).

This prospective study investigates the expression of steroid hormone receptors (estro-

gen receptor (ER) and progesterone receptor (PR)) in male breast cancer in Mashhad, Iran.

Materials and Methods

Specimens were collected from 18 patients with male breast cancer in Omid University Hospital, between October 2001 and October 2006. The steroid hormone receptors (ER and PR) were measured by immunohistochemistry, and the patients' clinicopathologic characteristics, especially their family history were recorded via interviews. Results were analyzed using SPSS Version 13.

Results

During the study, of 803 patients with mammary carcinomas who referred to Radiation Oncology Department of Omid Hospital, 2.24% (18 cases) presented with male breast cancer. The characteristics of patients with breast

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cancer are presented in Table 1.

Table 1.

Researcher	Number	Marker Expression (%)				
		ER α	ER	PR	AR	HER2 ^a
Rayson ⁵	77	91	ND	96	95	29
Munoz de toro ⁶	18	61	ND	72	38	ND
Pich ⁷	47	51	ND	47	34	ND
Pich ⁸	50	57	ND	50	36	56
Andre ⁹	90	75	ND	74	0	12
Mourao-Necto ²	48	75	ND	69	ND	62
Wany-Rodriquez ¹¹	65	95	ND	79	ND	9
Muir ¹²	59	81	ND	63	ND	5
Barlund ¹³	129	72	ND	70	ND	4
Rudlowski ¹⁴	99	87	ND	65	ND	15
Murphy ¹⁵	16	80	93	87	93	ND
Benchellal ¹⁶	19	92	ND	100	ND	ND
This article	18	88.8	ND	66.6	ND	ND

ND: non diagnosed HER2: c-erb-2

The median age was 63.2 years, and all cases had infiltrating ductal carcinoma. The family history of breast cancer was negative in 17 cases, and in one case, the sibling (sister) suffered from breast cancer. Staging was compared with TNM (Tumor, Node, Metastasis) system, and the most frequent stages were II and III.

The mean of metastatic axillary lymph nodes was 4.74 nodes (from 0 to 17).

*Among 18 subjects, 2, 7, 4, and 3 patients were in stages I, II, III, and IV, respectively; however, the stages of two patients were unknown.

ER and PR were positive in 88.8% and 66.6% of the patients, respectively (ER and PR were negative in base on 0% of IHC staining).

Discussion

In 2005, an estimated number of 1600 new cases of male breast cancer were diagnosed in U.S.A (3). The mean age for diagnosis of male breast cancer is 67 years, which is 5 years more than the average in women (2). In this review, the median age of diagnosis was reported as 63.2 years old.

Breast cancer affects Iranian women at least one decade earlier than their counterparts in developed countries (4); though, this has not been proven for male patients.

Data show that 93.7% of male breast cancer are ductal or unclassified carcinomas; 2.6%, 1.8% and 1.5% are papillary, mucinous and lobular, respectively (2). In the present review, 100% of cases present with ductal carcinoma.

Although the etiology of male breast cancer is unclear, hormonal levels may play a role in the development of this disease.

Male breast cancer has a high rate of hormone receptor expression, and approximately 90 % and 81% of male breast cancers express the estrogen and progesterone receptors, respectively (2). In this review, 88.8 % of male breast cancers express ER, and 66.6.% express PR. Male breast cancers are significantly more likely to express hormonal receptors in comparison with female breast cancers (2).

The presented data in this review add to the body of information regarding steroid receptor expression in male breast cancer.

Males have lower circulating levels of estradiol than females. The extremely-high level of hormone receptor expression observed in male breast cancer is quite intriguing. Without sufficient legend to bind to and activate their cognate receptors, it seems that there is no selective advantage for male breast tumors to express hormone receptors. This might be explained considering the hormonal environment in post-menopausal women, where the production of ovarian hormones has virtually ceased.

The in situ production of estrogens in breast carcinoma is considered to play an important role in the proliferation of breast cancer cells, as it has been demonstrated that breast tumors possess enzyme systems required to produce bioactive estrogens in situ from circulating precursors androstenedione or oestrone sulphate (16). In post-menopausal women, these systems are active, and the same might be expected in males.

Male breast cancers are known to over-express intratumoral aromatase (18), which is likely to contribute to in situ estrogen biosynthesis. Thus, the availability of bioactive estrogens in a male environment, characterized by relatively low serum levels of estrogen will presumably provide a growth advantage for ER-positive tumors (15).

Finally, due to the rarity of male breast cancer, a significant problem in studying this disease is finding sufficiently large numbers to allow multivariate analysis of possible prognostic markers.

Conclusion

In our study, expression of hormone

receptors in male breast cancer was high, like to the others studies.

Conflict of Interest

No conflict of interest exists.

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