

The Role of Estrogen and Progesterone Receptors in Epithelial Ovarian Tumors and Its Importance as a Prognostic Indicator

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Abstract:

Introduction: Ovarian carcinomas are one of the most common causes of death among women. Presently so many biomarkers are available for the early detection of the ovarian carcinomas like P53, EGFR, Ki67, CK, HER 2/ Neu. In the present study we analyze the expression of estrogen and progesterone receptor status in various epithelial ovarian tumors as prognostic indicators.

Aim of the study: To study the expression of estrogen and progesterone receptor in the surface epithelial tumors of ovary in assessing its role as prognostic marker.

Materials and Methods: The Present study was conducted at Department of Pathology and 30 cases of ovarian tumour that occurred from May 2013 to April 2018 were randomly selected. Immunohistochemical analysis was carried out with estrogen and progesterone receptor marker for the 30 cases.

Conclusion: In the present study serous tumours had more positive expression for both estrogen and progesterone receptors than the mucinous tumours.

Keywords: Ovarian tumors, Surface epithelial tumors of ovary, Estrogen and Progesterone receptor.

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Introduction

Tumors arising from the female reproductive tract are the most common cancers affecting women. Among them, ovarian cancer is one of the leading causes of cancer deaths because of its gradual onset and relatively late diagnosis [1]. At the time of diagnosis, 70% of ovarian tumors have already spread to adjacent pelvic organs and 60 % of the tumors with metastasis beyond pelvic organs. Ovarian neoplasms are a heterogeneous group of malignant tumors originating from different ovarian counterparts like surface epithelium, sex cord stromal cells and germ cells [2]. Surface epithelial tumors of the ovary are the most common cause of death among the ovarian tumors [3].

Estrogen and progesterone are steroid hormones and the expression of these hormone receptors in surface epithelial ovarian tumors has a therapeutic and prognostic significance. Cytosolic estrogen and progesterone receptors are present in many organs like breast, uterine endometrium, myometrium, cervix, fallopian tubes and ovaries.

Since 70% of ovarian cancers express estrogen receptors (ERs), the main source for ovarian cancer development is considered to be estrogen; whereas progesterone and its receptor are considered to be protective against the development of ovarian

cancers [4,5]. However the clinical importance of estrogen and progesterone receptor expression in ovarian carcinomas is yet to be established. Nulliparity, early menarche, late menopause and long estimated number of years of ovulation are the main risk factors for epithelial tumors of the ovary [6]. The Present study was carried out to know the "Role of estrogen and progesterone receptor expression in surface epithelial tumours of ovary" in assessing its prognosis.

Materials and Methods

The present study was undertaken in the Department of Pathology and we have randomly selected 30 cases of epithelial ovarian tumours that occurred from May 2013 to April 2018. Immunohistochemical analysis was performed using estrogen and progesterone receptor marker.

Technique of Analysis Used:

1. Paraffin blocks were prepared from the ovarian neoplasm specimens.
2. Sections from blocks were used for hematoxylin and eosin staining and for immunohistochemistry.
3. Immunohistochemical analysis was performed using estrogen and progesterone receptors.

The stained slides were given score by two separate observers and the average score was calculated. The interpretation and scoring was done by Allred scoring system [10].

Allred scoring system considers only the invasive tumor cells to be assessed. The normal breast duct epithelial cells are taken as internal positive control. As they stain positive for ER/PR markers generally. Positive test result for ER, PR, or both have to be considered "hormone-receptor-positive" in ovarian cancer. Hormone therapy either lowers the estrogen levels or blocks the effects of estrogen and thereby helps to slowdown or stop the growth of the hormone receptor-positive ovarian tumors.

Result

Totally 30 cases [Benign Serous – 12, Benign Mucinous –12, Borderline Serous -3, Malignant Mucinous cystadenoma -3] of various types of surface epithelial ovarian tumours from different age group of women were subjected to estrogen and progesterone receptor immunohistochemical study. All 12 cases of benign serous tumours shows positive expression for both estrogen and progesterone receptor, out of 12 benign mucinous tumour 3 cases showed positive expression for progesterone receptor alone. Remaining 15 cases did not show any expression of both estrogen and progesterone receptor.

Table 1: correlation between the ER and PR

ER/PR Expression	PR +VE	PR –VE	Total
ER +VE	12(40%)	0 (0%)	12(40%)
ER –VE	3(10%)	15(50%)	18(60%)
TOTAL	15 (50%)	5(50%)	30 (100%)

Table 2: Expression of ER and PR in different epithelial tumours

Receptor / Types	Serous	Mucinous	Total
ER+/PR + ve	12	0	12
ER+/PR - ve	0	0	0
ER-/PR + ve	0	3	3
ER-/PR - ve	3	12	15
TOTAL	15	15	30

Table 3: Correlation of ER and PR expression with size of the tumour

Type / Size	< 10cm	> 10cm	Total
Serous	9 ER+/PR+&3 ER-/PR-	3 ER+/PR+	15
Mucinous	3 ER-/PR+	12 ER-/PR-	15
Total	15	15	30

Discussion

The surface epithelial ovarian cancers are one of the leading cause of the cancer death in women. Malignant ovarian tumours are usually detected clinically at a very advanced stage. The steroid hormones play an important role in determining the prognosis and to decide hormonal treatment in different epithelial ovarian cancers. Hence it is important to identify the type of steroid receptor expressed in the ovarian neoplasm to render hormonal therapy for the benefit of patients [11].

The two important steroid hormones secreted by the ovaries are estrogen and progesterone. These two hormones act through specific receptors in maintaining the normal menstrual cycle, they also act as important risk factors in stimulating gynecologic malignancies. The prognostic value of the estrogen and progesterone receptor expression is well understood in breast and endometrial cancers. The expression of these two receptors in the epithelial ovarian tumours is under the scope of ongoing recent research studies. Positive expression in this study was 40% for both estrogen

receptor and progesterone receptor; 10% for progesterone receptor alone, 50% cases showed negative for both estrogen and progesterone receptor. We observed expression of ER in 40% cases and expression of the PR in 10% of the cases. These figures are agreed with a study by Siriwan et al., [12] Highest expression of the ER is generally seen in the serous tumours and lowest expression is seen in the mucinous tumours.

The present study has documented the expression of the ER to be 40% in serous carcinomas and 0% in mucinous tumours. The expression of the ER and PR were significantly associated with each other. About 40% cases showed positivity for both ER and PR expression; 50% cases show negativity for both ER and PR.

The Present study correlated receptor positivity with the size of the tumours. In serous tumours of < 10 cm, 30% cases were ER positive and tumors >10cm, 10 % cases were positive. Regarding the mucinous tumours only 10% shows PR positive expression and are <10cm; >10cm size lesions shows negativity for PR expression in 40%.

FIGO staging is the only universally accepted system for assessing prognosis in patients with ovarian carcinoma; it is a powerful prognostic predictor while most other putative prognostic factors are of little importance compared to stage [13].

The study have shown PR positive combination patterns such as ER+/PR+ or ER-/PR+ to be positively correlated with benign tumors ($P < 0.01$) and low stage. PR negative patterns such as ER+/PR- or ER-/PR- were associated with higher stage tumors, our findings were concordant with other studies. Iversen et al [14] in his study he found that significantly lower survival in patients who were ER+/PR+ compared to ER-/PR-, however they did not evaluate survival of patients with ER-/PR+ expression. Munsted et al [15]. used immunohistochemistry and observed a positive survival influence in patients with ER-/PR+ tumors along with a significant association with other prognostic factors such as low stage, lower grade and minimal ascites at primary surgery. Siriwan et al [16]. Found good prognosis in ER-/PR+ cases.

We could not evaluate the association of ER/PR expression with survival rates because of failure of follow up of patients.

Conclusion

The expressions of the estrogen and progesterone receptors in ovarian tumors are variable in nature. The Progesterone receptor expression was associated with favorable prognostic factors that included younger age, benign tumor and low FIGO stage. No such association was observed with expression of estrogen receptor.

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