Section: Pathology

Original Research Article

A STUDY ON EVALUATION OF IMMUNOEXPRESSION OF ER, PR AND Ki67 IN OVARIAN EPITHELIAL TUMORS

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ABSTRACT

Background: Ovarian epithelial tumors represent a diverse group of neoplasms arising from the surface epithelium of the ovary. They encompass a spectrum of histological subtypes, ranging from benign to borderline to malignant tumors. Identifying the immunochemical markers, the molecular and histological characteristics of these tumors is crucial for accurate diagnosis, prognostication, and treatment planning.

Materials and Methods: A total of 100 patients with epithelial ovarian tumors were included in the study and assessed for immunoexpression of estrogen receptors (ER), progesterone receptors (PR) and Ki67 levels using ALLRED scores and Ki67 proliferative index respectively.

Results: Majority of the tumors were benign (60%). Malignant tumors had higher scores of ER, PR and Ki67 expression.

Conclusion: Expression of different markers (ER, PR, and Ki-67 index) in different types, stages, and grades of tumors has significant role in management of tumors and predicting treatment response.

Keywords: Malignancy, Epithelial tumors, estrogen receptor, progesterone receptor, Ki67.

INTRODUCTION

Ovarian epithelial tumors account for the vast majority of ovarian neoplasms (90%). They arise from the epithelial cells covering the ovary and its cortical surface. These tumors can be broadly classified into several histological subtypes, including serous, mucinous, endometrioid, clear cell, and transitional cell (Brenner) tumors.[1]

Serous tumors are the most common subtype and can be further classified as serous cystadenomas, serous borderline tumors, and serous carcinomas. Mucinous tumors are characterized by the presence of mucin-producing epithelial cells and can be benign, borderline, or malignant. Endometrioid and clear cell tumors often arise from endometriotic cysts and are associated with endometriosis. Brenner tumors, also known as transitional cell tumors, are rare and typically benign, composed of transitional-like epithelial cells.[2]

The exact etiology of ovarian epithelial tumors remains unknown, but several risk factors have been hypothesized such as, age, nulliparity, family history of ovarian cancer, and mutations in genes such as BRCA1 and BRCA2. The incidence rates of ovarian epithelial tumors vary with geographical boundaries, age, with higher rates reported in developed countries and in older.

Estrogen receptors (ER-alpha and ER- beta) and progesterone receptor expression in epithelial ovarian tumors can vary among different histological subtypes and can guide in treatment decisions, particularly hormone therapy which target ER or PR (Selective estrogen receptor modulators (SERMs) and selective progesterone receptor modulators (SPRMs) respectively).[5,6]

Markers of proliferation (e.g., Ki-67) can provide information about the proliferative activity of tumor cells, which may correlate with tumor aggressiveness and prognosis.[7]

The present study was conducted to evaluate the significance of estrogen receptors (ER), progesterone receptors (PR), and Ki67 expression by immunotyping in epithelial ovarian tumors.

MATERIALS AND METHODS

This observational study was conducted in the department of Pathology, Malla Reddy Medical College for Women, Jeedimetla, over a period of one year from

October 2023 to September 2024. All patients with histopathological diagnosis of surface epithelial tumors who underwent abdominal hysterectomy with bilateral / unilateral oophorectomy in the institution were included. Patients with non-neoplastic lesions or non-epithelial tumors, patients who underwent resection outside the institution and patients with metastatic tumors were excluded from the study.

Informed consent was taken from all study participants and ethical committee approval was also taken. A total of 100 cases with surface epithelial ovarian tumors were included in the study.

The specimens were fixed using 10% neutral buffered formalin solution and paraffin embedded tissue blocks were prepared. Each block was divided into sections which were stained using H & E stains.

Immunotyping was done for ER, PR and Ki67. PR and ER immunoexpression levels were evaluated using ALLRED score and that of Ki67 was evaluated using Ki67 proliferation index.[8,9]

The ALLRED system of scoring ranges between 0-8 and consists of 2 components, ie proportion score (assesses the percentage of tumor cell with positive staining; 0-5) and intensity score (assess the intensity of staining – 0-3). Greater the score, greater levels of immunoexpression. ALLRED score of 0-2 is considered negative while score of 3-8 is considered positive.[10,11]

Ki67 expression levels were scored according to the proliferative index: no cells positive = 0; 1+ = when <1 % of cells are positive; 2+ = when 1-5 % of cells are positive; 3+ = when ≥5–10 % of cells are positive; 4+ = when ≥10–20 % of cells are positive and 5+ = when ≥20 % of cells are positive.

Statistical analysis was done using SPSS software. Descriptive statistics and tests such as the $\chi 2$ test, Fisher's exact test, and the independent sample T-test were used to analyze the data. Descriptive statistics were used to determine the frequency, mean, and standard deviation of different demographic variables and IHC markers. P value of < 0.05 was considered statistically significant.

RESULTS

100 patients with histopathological diagnosis of surface epithelial tumors were included in the study. Amongst the 100 patients, 35 cases (35%) were malignant, 60 cases (60%) were benign and rest of the 5 cases (5%) were borderline.

The age of study population ranged from 15 to 72 years with a mean of 44.6 years. Most of the patients with malignant tumors were aged above 45 years. The mean age of patients with malignancy was 51.5 years, 35.4 years for benign and 42.8 years for patients with borderline tumor.

Serous tumours were the most common type, while mucinous tumors were the second most common.

All the cases were subjected to IHC staining. All tumors showed positivity for ER, PR and Ki67 markers.

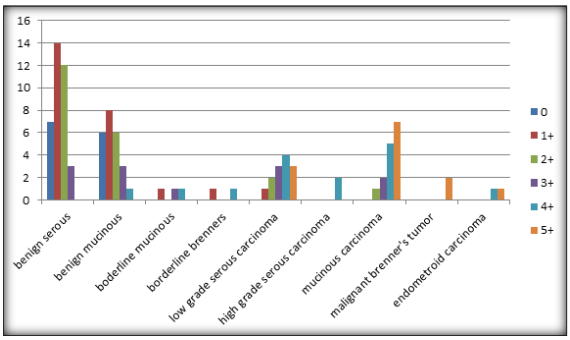

Figure 1: Expression of Ki67 in histological subtypes of surface epithelial ovarian tumors

ER and PR expression was noted in all the tumors. Benign tumours had lower ALLRED scores while patients with malignant tumors had higher ALLRED scores.

Majority of the benign tumor have Ki67 proliferative index < 3+ and majority of the malignant tumors have Ki67 proliferative index >4+. The present study shows significantly higher proliferation index (PI) in malignant tumors followed by borderline tumors and lowest in benign tumors (P < 0.05).

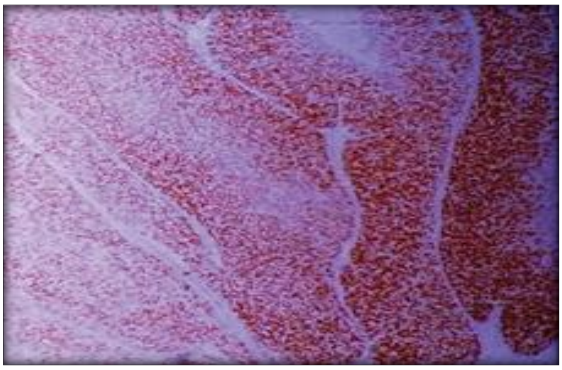

Figure 2: Malignant Brenner tumor with ER positivity

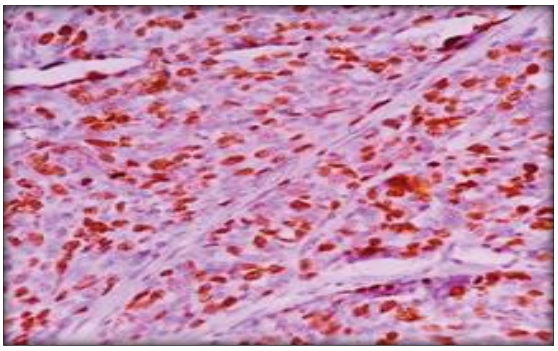

Figure 3: High grade serous carcinoma with PR positivity

Table 1: Expression of ER & PR in histological subtypes of surface epithelial ovarian tumors.

Tumor type		No of cases	ALLRED score for PR		ALLRED score for ER	
			0-2	3-8	0-2	0-2
Benign	Benign serous	36	25	11	28	8
	Benign mucinous	24	18	6	19	5
Borderline	Borderline mucinous	3	1	2	2	1

	Borderline Brenner's tumor	2	0	2	1	1
Malignant	Low grade serous carcinoma	14	2	12	1	13
	High grade serous carcinoma	2	0	2	0	2
	Mucinous carcinoma	15	1	14	3	12
	Malignant Brenner's tumor	2	0	2	1	1
	Endometroid carcinoma	2	0	2	0	2
	Total	**100**	**47**	**53**	**55**	**45**

DISCUSSION

Ovarian tumours are the commonest cause of cancer related morbidity and mortality in women. Immunoexpression of various markers like estrogen receptors (ER), progesterone receptors (PR) and Ki67 can aid in evaluating the aggressiveness of tumor and can predict the response to treatment.

In present study a total of 100 cases with epithelial ovarian tumors were included. There were 60% benign, 5% borderline and 35% malignant cases.

Higher expression of ER and PR (scores 3-8) were seen in malignant tumors, which is in accordance with the study done by Verma et al.12 In present study ER expression was seen in all subtypes of tumors, unlike the study done by Kriplani and Patel et al,[13] where ER expression was absent in mucinous tumours.

Comparison of ER and PR expressions of endometrioid carcinoma in the present study was found similar to study done by Sutton et al.[14] ER and PR expressions were highest in high grade serous carcinoma and similar to the studies done by Sylvia et al,[15] and Lindgren et al.[16]

The Ki67 index was of higher grade in malignant tumors signifying the higher level of proliferation. This is similar to studies done by Gursan et al,[17] Naik et al.[18]

CONCLUSION

The ALLRED scores and Ki-67 index is often incorporated into prognostic and predictive assessments, helping to stratify patients into different risk categories and guide treatment decisions, particularly regarding the use of chemotherapy and endocrine therapy.

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Conflicts of interest: Nil

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