



Histopathology

HISTOPATHOLOGICAL PATTERNS OF OVARIAN TUMORS AND THE ROLE OF ER, PR AND HER2/neu IN SURFACE EPITHELIAL TUMORS OF OVARY

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ABSTRACT Ovaries have a capacity to give rise to a variety of neoplasms. Ovarian cancers pose one of the greatest challenges to the clinicians and pathologist worldwide because they exhibit heterogenous clinical behavior and wide range of histopathological patterns. The aim of this study is to study the various patterns of ovarian tumors by histopathological examination and the expression of ER, PR and HER2/neu in surface epithelial tumors of ovary. **Materials and methods.** A total of 108 specimens of ovarian tumors were studied in this cross-sectional study. Histopathological examination was done followed by Immunohistochemical studies with ER, PR and HER2/neu in surface epithelial tumors of ovary as per standard protocol. Result: Among the 108 number of ovarian tumors, 97 were benign, 2 were borderline and 9 were malignant. Surface epithelial tumors was the commonest (64.81%), followed by germ cell tumors (30.56%), sex cord stromal tumors (1.85%) and collision tumor (2.78%). IHC studies with ER was expressed in 54.84% of the benign, 100% in borderline and 50% in malignant surface epithelial tumors of ovary. PR was expressed in 54.84% of the benign, 100% of the borderline and in only 1 malignant case. HER2/neu was only expressed by malignant surface epithelial tumors in 66.67% cases. **Conclusion.** Benign tumors of ovary are common than the malignant. Surface epithelial tumors are the commonest of all the histological types. A significant association was found between ER, PR and HER2/neu expression and the tumor type.

KEYWORDS : Ovarian tumors, surface epithelial tumors, ER, PR, HER2/neu.

INTRODUCTION

Ovaries have a capacity to give rise to a diverse variety of neoplasms. Histogenesis of individual tumor varies widely and each of the subtypes is derived from different components of the organ.⁽¹⁾ The morphology-based classification system and demonstrating that it accurately reflects both histogenesis/cell of origin, and the underlying molecular abnormalities of the different ovarian tumor subtypes.⁽²⁾ Ovarian cancer is the seventh most common type of malignancy in women. According to the ethnic groups, the highest prevalence is between Caucasian women, followed by, African-American and Asian women.⁽³⁾ It is the 5th cause of death and morbidity in females worldwide.⁽⁴⁾ The World Health Organization categorized ovarian neoplasms on the basis of tissue of origin: Surface epithelial-stromal tumors (65%), Germ cell tumors (15%), Sex cord-stromal tumors (10%), Metastatic ovarian tumor (5%), and Miscellaneous ovarian tumor (5%).⁽⁵⁾ Ovarian cancer is a complex neoplastic assembly, usually affecting women over the age of 65 years.⁽⁵⁾

Ovarian cancers pose one of the greatest challenges to the clinicians and pathologists worldwide because they exhibit heterogenous clinical behavior and wide range of histopathological patterns. Early ovarian cancers might go undetected because they cause minimal or no symptoms.⁽⁶⁾ It is now recognized that the histotype represents distinctions in cell of origin and molecular abnormalities. Within each histotype, tumors are further subclassified as benign, borderline, or malignant. Benign neoplasms of ovary are more common than the malignant neoplasms.⁽³⁾ Malignant surface epithelial tumors are the most common tumors among the other histomorphological types of malignant ovarian tumors.⁽⁷⁾ Serous neoplasm is the most common and together with benign, borderline and malignant comprises about 30% of all ovarian tumors.⁽⁸⁾

Serous cystadenocarcinoma is the most common malignant tumor, followed by mucinous cystadenocarcinoma and granulosa cell tumors.⁽⁷⁾ Mucinous neoplasms are less common than serous neoplasms and are bilateral in less than 10% of cases. As with their serous counterparts, ovarian mucinous tumors have been divided into benign (mucinous cystadenoma), borderline, and malignant (mucinous carcinoma). Endometrioid carcinoma and clear cell carcinoma comprises 10% of all primary ovarian carcinomas. Brenner tumors constitute between 1% to 2% of all ovarian neoplasm.⁽²⁾

Cytosolic estrogen and progesterone receptors are present in ovaries. The ovaries in addition to being a source of estrogens and progesterone are also the targets for these hormones.⁽⁹⁾ ER is a group of proteins found inside cells which are activated by the hormone estrogen.

Estrogen receptors belong to the nuclear transcription factors superfamily and represent the classical pathway of estrogen-dependent action. ER is overexpressed in about 70% of the ovarian cancers. ER positivity may be seen in nucleus and cell membrane.⁽¹⁰⁾ The biological actions of progesterone are mediated by two natural PR isoforms, PR-A and PR-B. PR is a protein found in the nucleus of a cell and its expression shows nuclear positivity.⁽¹¹⁾ HER2 is a member of the epidermal growth factor receptor (EGFR) family of molecules and is encoded by the HER2 proto-oncogene on the long arm of chromosome 17. The staining with HER-2/neu is seen as a cell membrane with continuous brown colour depicting as membrane positivity. HER-2/neu is overexpressed in ovarian carcinomas and indicates a poor prognosis.⁽¹²⁾ Immunohistochemical study with ER, PR, and HER2/neu helps to know the biological behavior, treatment outcome and predicting prognosis of ovarian tumors.⁽⁹⁾

AIMS AND OBJECTIVES

To study the various patterns of ovarian tumors by histopathological examination and the expression of ER, PR and HER2/neu in surface epithelial tumors of ovary.

MATERIALS AND METHODS

The study included 108 resected specimens of ovarian tumors, submitted for histopathological examination to the Department of Pathology, Fakhruddin Ali Ahmed Medical College and Hospital, Barpeta, Assam. After proper fixation with 10% formalin detailed gross examination was done and processed routinely. Following the standard protocol, blocks were prepared and serial sections from the block were obtained. The sections are mounted on a glass slide and are stained with Haematoxylin and Eosin stain and are studied under light microscope. Thereafter, immunohistochemistry with ER, PR, and HER2/Neu was done on the diagnosed case of surface epithelial tumors of ovary as per IHC protocol. Duration of the study was 1 year, from July 2021 to August 2022.

RESULTS

The age group ranged from 18 to 77 years. The mean age was 37.06 years. The most prevalent age group was found to be 38-47 years.

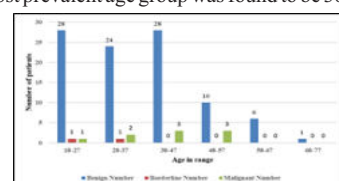


Figure 1: Bar diagram showing age distribution of the patients with ovarian tumors.

Out of 108 cases, 89.81% (97 cases) were benign, 1.85% (2 cases) were borderline, and 8.33% (9 cases) were malignant tumors. Surface epithelial tumors comprised of 70 cases (64.81%), germ cell tumors contributed 33 cases (30.56%), sex cord stromal tumors 2 cases (1.85%) and collision tumors 3 cases (2.78%).

Table 1: Distribution of percentage of ovarian tumors as per histological classification.

	No. of cases	Percentage (%)
Surface Epithelial tumors	70	64.81%
Germ cell tumors	33	30.56%
Sex cord stromal tumors	2	1.85%
Collision tumors	3	2.78%
Total	108	100%

Among the surface epithelial tumors, most common tumor was serous cystadenoma with 40 cases (37.03%). The distribution of the cases is shown in the bar diagram in Figure 2.

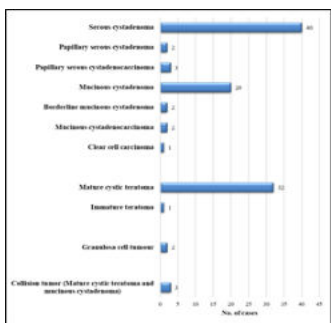


Figure 2: Bar diagram showing the distribution of spectrum of ovarian tumors.

Immunohistochemical study with ER showed positivity in 34 cases (54.84%) of benign, 2 cases (100%) of borderline tumors and 3 cases (50%) of malignant surface epithelial tumors of ovary.

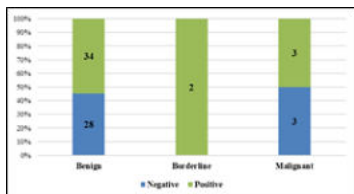


Figure 3: Bar diagram showing ER expression in surface epithelial tumors of ovary.

PR expression was found positive in 34 cases (54.84%) of benign, 2 cases (100%) of borderline and 1 case (16.67%) of malignant surface epithelial tumor of ovary.

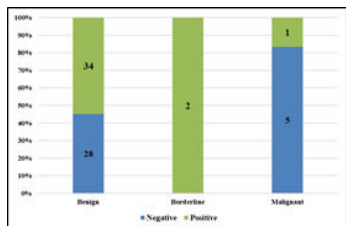


Figure 4: Bar diagram showing PR expression in surface epithelial tumors of ovary.

HER2/neu expression was found positive only in 4 cases (66.67%) of malignant surface epithelial tumors. The benign and borderline tumors had negative expression for HER2/neu.

Figure 5: Bar diagram showing HER2/neu expression in surface epithelial tumors of ovary.

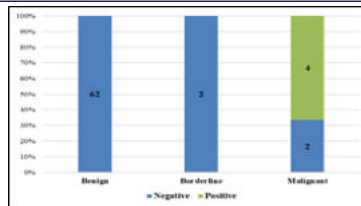


Figure 6: Photomicrograph showing cyst wall lined by multilayer mucin filled tall columnar epithelium in a case of borderline mucinous cystadenoma.(H&E)

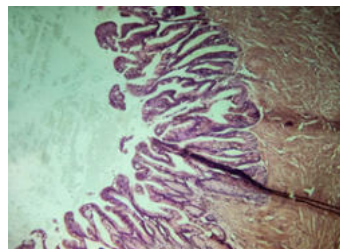


Figure 7: Photomicrograph showing ER positivity in a case of borderline mucinous cystadenoma; 10x.

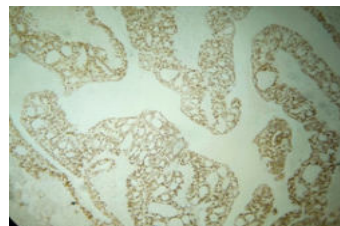


Figure 8: Photomicrograph showing PR positive in a case of borderline mucinous cystadenoma; 10x.

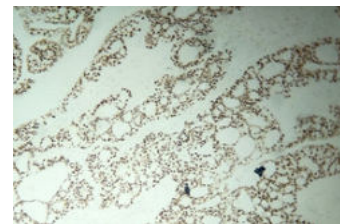


Figure 9: Photomicrograph showing papillary growth pattern invading the stroma in papillary serous cystadenocarcinoma. (H&E)

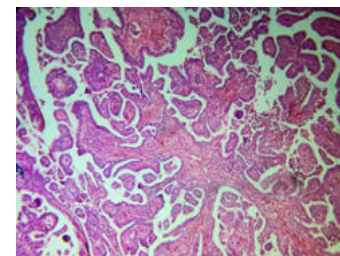


Figure 10: Photomicrograph showing HER/2Neu positivity in papillary serous cystadenocarcinoma; 40x

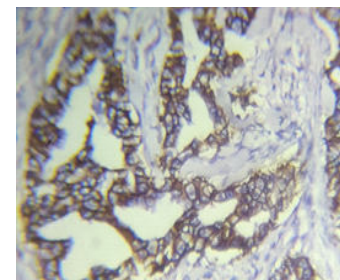


Figure 11: Photomicrograph showing complex intestinal type glands with loss of glandular architecture. The neoplastic glands are seen invading the stroma. (H&E stain); 10x

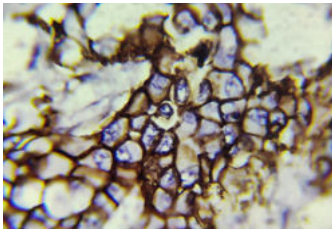


Figure 12: Photomicrograph showing HER2/Neu positivity in a case of mucinous cystadenocarcinoma; 100x

DISCUSSION

Ovarian tumors are a heterogeneous group of neoplasms with variable clinical, morphological, and histological features.(13) There is inherent variability even within a single class of tumor, with biological behaviour ranging from benign to the extremely aggressive malignant tumor.(14) Due to the totipotent and multipotent nature of ovarian germ cells and mesenchymal cells, a wide variety of neoplasms can develop in the ovary.(15) Identification of various histological patterns of ovarian tumors is important for diagnosis as well as prognosis.(16) Better clinical outcomes in ovarian cancer are positively correlated with the presence of the estrogen (ER) or progesterone (PR) receptors. Therefore, estimating estrogen and progesterone levels may be used to help select ovarian cancer patients for hormone therapy, which is more likely to enhance both response and prognosis.(17) HER2/neu may be a potential marker to predict the poor prognosis of ovarian cancer patients.(18)

Age is an important factor in ovarian tumors. In the present study the cases were in the age range from 18-77 years with a mean age of 37.06 years. Similar age range were also observed by Garg S. et al.(2014)(19), Agrawal P et al. (2015)(14) and Birare S D et al.(2018)(15).

The tumors were categorised based on their histomorphological features into benign, borderline and malignant. Benign tumors were common comprising of 89.81% cases, borderline tumors were 1.85% and malignant tumors were 8.33% observed in the present study. Studies done by Kumar V et al. (2015)(20) and Birare S D et al.(2018)(15) had similar findings. The former observed benign ovarian tumors in 91.25% and malignant tumors in 8.75% cases and the later found 85.71% benign tumors, 5.26% borderline and 8.57% malignant surface epithelial tumors of ovary.

In the present study, the ovarian tumors were classified broadly as surface epithelial tumors, germ cell tumors and sex cord stromal tumors. Among these the majority of the cases were surface epithelial tumors comprising of 64.81%. Germ cell tumors contributed 30.56% of the cases and sex cord stromal tumors were found to be in 1.85% in the present study. Birare S D et al.(2018)(15), Gupta N.et al.(2019)(21) and Sampurna K. et al.(2022)(13) found similar data in their studies.

Immunohistochemical study with ER, PR and HER2/neu were done in 70 cases of surface epithelial tumors of ovary in the present study. ER expression was found in maximum number of cases in our study (55.71%), which was close to the study conducted by Tangitgamol S. et al. (2009)(22). Expression of PR was found in 37 cases (52.86%) which was close to the findings of Sylvia M T et al.(2016).(23) HER2/neu were expressed in 5.71% cases similar to the findings by Atla B.et al.(2016)(24) where they found HER2/neu expression in 7.14%.

CONCLUSION:

The most common clinical presentation in the study population was pain abdomen. Among the ovarian tumors, surface epithelial tumors were found to be more common. Benign surface epithelial tumors were the commonest. Benign and borderline ovarian tumors showed negative expression for HER/2neu. ER, PR positivity in ovarian cancers was found to have better clinical outcome on follow up. HER2/neu expression is a potential marker which indicates poor prognosis of ovarian cancer. Immunohistochemical study with ER, PR and HER2/neu in ovarian tumors should necessarily be done to guide therapy for a favourable outcome.

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