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Role of Her-2 Neu as Prognostic Indicator in Surface Epithelial Tumors of Ovary

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Abstract
Introduction: *Ovarian carcinomas are the chief cause of death among women. Presently so many biomarkers are accessible for the early detection of the ovarian carcinomas like P53, EGFR, Ki67, CK, HER 2/ Neu. In this study we analyze the prognostic significance of HER 2/Neu in various surface epithelial ovarian tumors.*
Aims of the study: *To know the prognostic significance of HER-2/Neu in surface epithelial ovarian tumor.*
Materials and Methods: *The Present study was conducted in Rajah Muthiah Medical College and Hospital, Chidambaram.10 cases were randomly selected. Ovarian tumour that occurred from May 2013 to April 2018. Immunohistochemical analysis was done with HER2/Neu receptor marker for the 10 cases.*
Conclusion: *HER 2 /Neu expression is significantly not associated with tumor grade, tumor type and patient's age.*
Keywords: *Surface epithelial ovarian tumours, HER 2/Neu, Cystic ovarian tumours.*

Introduction

Among women, Gynecological malignancies are the chief cause of death. In this, ovarian neoplasms is the prime cause of death because of its gradual onset and delayed diagnosis[1]. Ovaries are located in the capacious pelvic cavity where it can enlarge without producing any significant symptoms. When the diagnosis is made, 70% of tumors have by then spread far away from the ovary and 60 % of the tumors are spread far away from the pelvis[2]. Ovarian carcinomas are heterogeneous group of malignancies that originate from various cell types of the ovary like epithelial, sex cord stromal and germ cell tumours[2].

The human epidermal growth factor receptor (HER) has an important role in the development of many carcinomas in human beings. It regulates the differentiation, survival and cell growth through numerous signal transduction pathways and participates in differentiation and cellular proliferation[4]. Presently so many markers are used to foresee the prognosis and designing for better management of the surface epithelial ovarian tumors.

Materials and Methods

The Present study was conducted in Rajah Muthiah Medical College and Hospital, Chidambaram. We have randomly selected 10 cases of ovarian neoplasms that occurred from May 2013 to April 2018. Immunohistochemical analysis was done with HER2/Neu receptor marker.

Technique of Analysis Used:

1. Paraffin blocks were prepared for histopathological examination.
2. Blocks were put through haematoxylin & eosin staining.
3. Immunohistochemical analysis was done in automated machine in the Doctor's Diagnostic Laboratory in Trichy.

The interpretation and scoring was done by Allred scoring system[9].

Result

Totally 10 cases of various types of surface epithelial ovarian neoplasms belonging to different age group of women were subjected to HER2/ Neu immunohistochemical study in which all the 10 cases showed negativity for HER 2/ Neu expression.

Discussion

HER 2/Neu is an oncogene. It is of epidermal growth factor receptor family. It is implicated in malignant transformation. It plays an important role in the development of various carcinomas in humans including ovarian carcinoma. The prognostic importance of the HER 2 /Neu expression on ovarian carcinoma was examined by several studies, but the role of expression of HER2/Neu on surface epithelial ovarian carcinomas is still not clear[5, 6].

The prognostic value of the HER 2 /Neu expression in surface epithelial ovarian carcinomas is yet controversial, because the expression is considerably variable among different individual studies dealing with different samples[7].

In this assessment of expression of HER 2 /Neu in surface epithelial ovarian carcinomas and its association with tumor type and its clinicopathological correlation with the patient's age, histological type of the tumor and tumour size. This study is to analyze the expression of HER2/Neu in surface epithelial ovarian cancer, to know if it has a considerable amount of prognostic importance or not.

The role of expression of HER2/Neu in surface epithelial tumours of ovary is even today controversial because various studies have reported that the expression it's in ovarian cancer is between 5% and 30% (Hellstrom I et al 2001)[8].

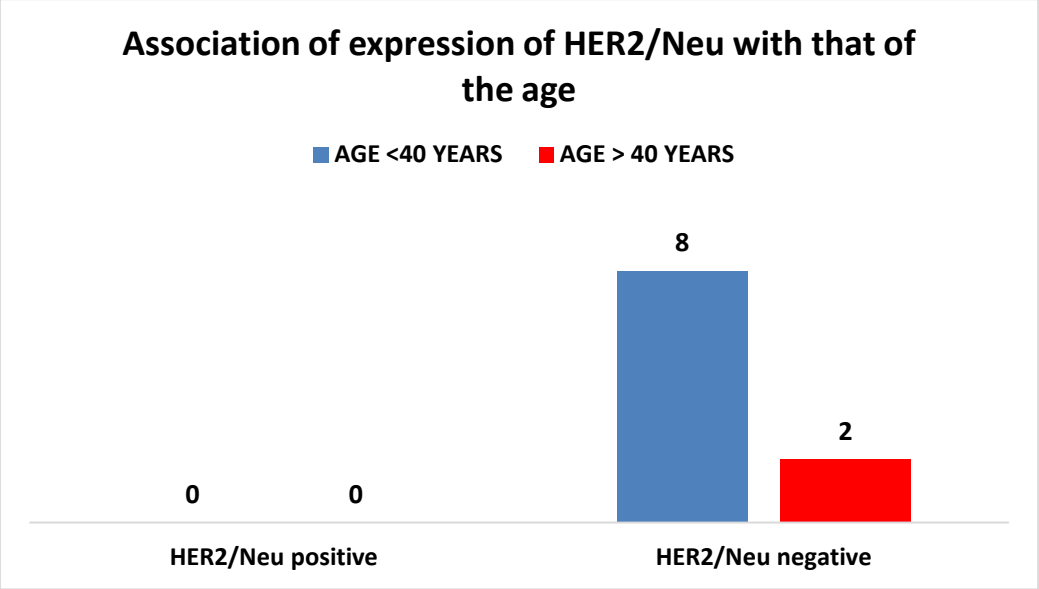
The study done by Sapna et al concluded that among 24.3% HER2/Neu positive cases, 66.7% were less than 50 years of age and 33.3% were above 50 years of age and among 75.7% of negative cases, 67.9% were below 50 years of age and 32.1% were more than 50 years of age.

In this study, among the 10 cases the expression of HER 2 /Neu is negative irrespective of the age. Among these cases, 8 cases were less than 40 years and 2 cases were greater than 40 years of age. But all 10 cases show negative expression on HER2/Neu. Thus we come to a conclusion that HER2/Neu expression on surface epithelial ovarian neoplasms has no relevance with the age group. [Table 1]

Table: 1 Association between of expression of HER2/Neu with that of the age.

HER 2/Neu status	Age <40 years	Age > 40 years
Positive	0 (0%)	0 (0%)
Negative	8 (80%)	2 (20%)

Graph 1: Association between of expression of HER2/Neu with that of the age



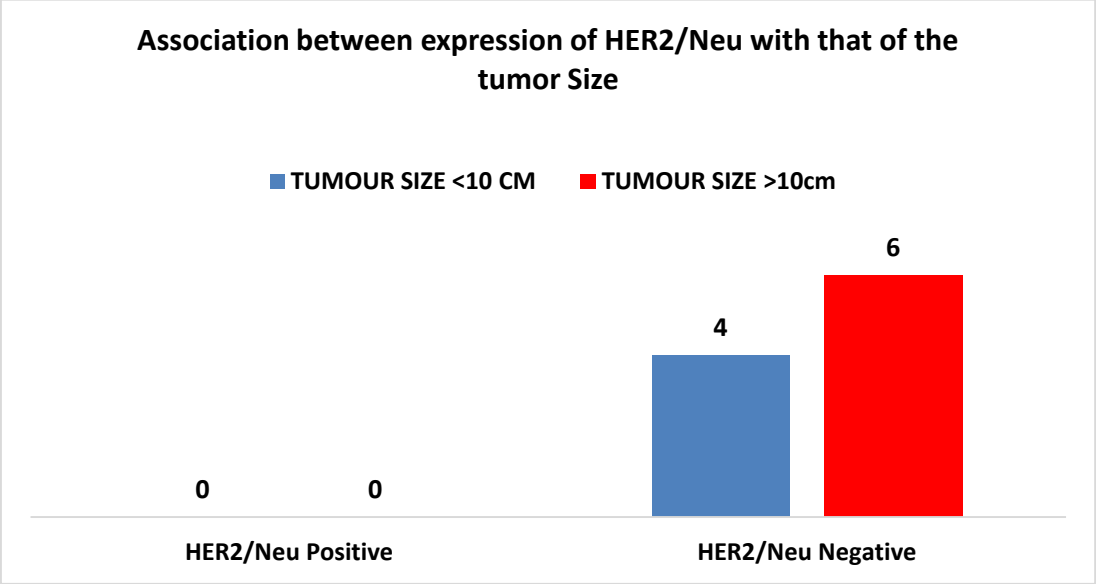
The study done by Sapna et al study concluded that among 24.3% tumors which were HER2/Neu positive, 50% had size below 10 cm and 50% had size above 10 cm. Among 75.7% cases which were HER2/Neu negative, 39.3% cases had size below 10 cm and 60.7% had size above 10 cm.

In this study, among the 10 cases, tumor which were below 10 cm are 4 in number and tumors above 10 cm are 6 in number but all have negative expression for HER2/Neu. Hence, we come to a conclusion that there is no association between the tumor size and expression of HER2/Neu. [Table 2]

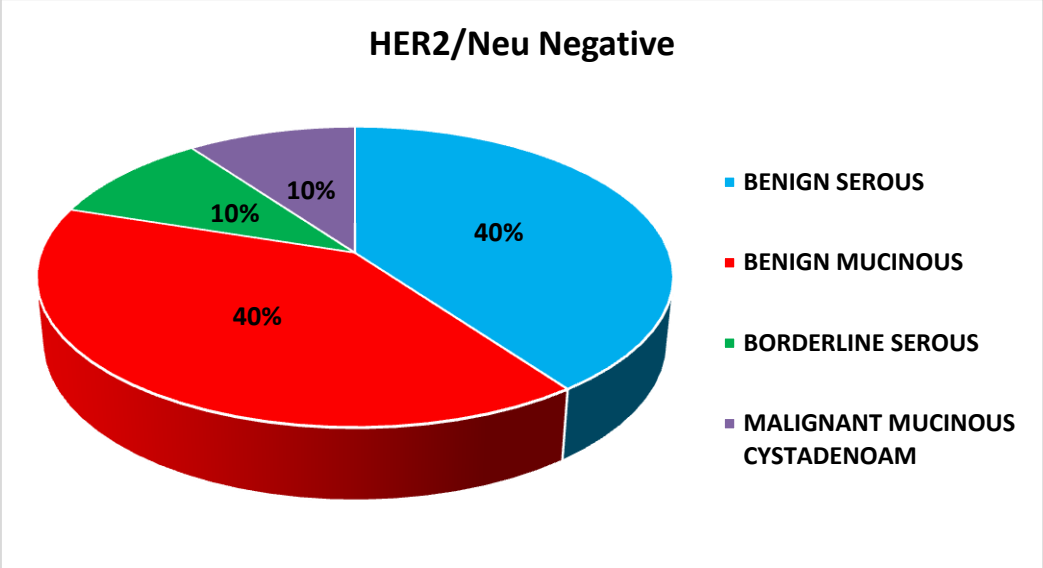
Table 2: Association between expression of HER2/Neu with that of the tumor Size

HER2/Neu status	Size < 10 cm	Size > 10cm
Positive	0 (0%)	0 (0%)
Negative	4 (40%)	6 (60%)

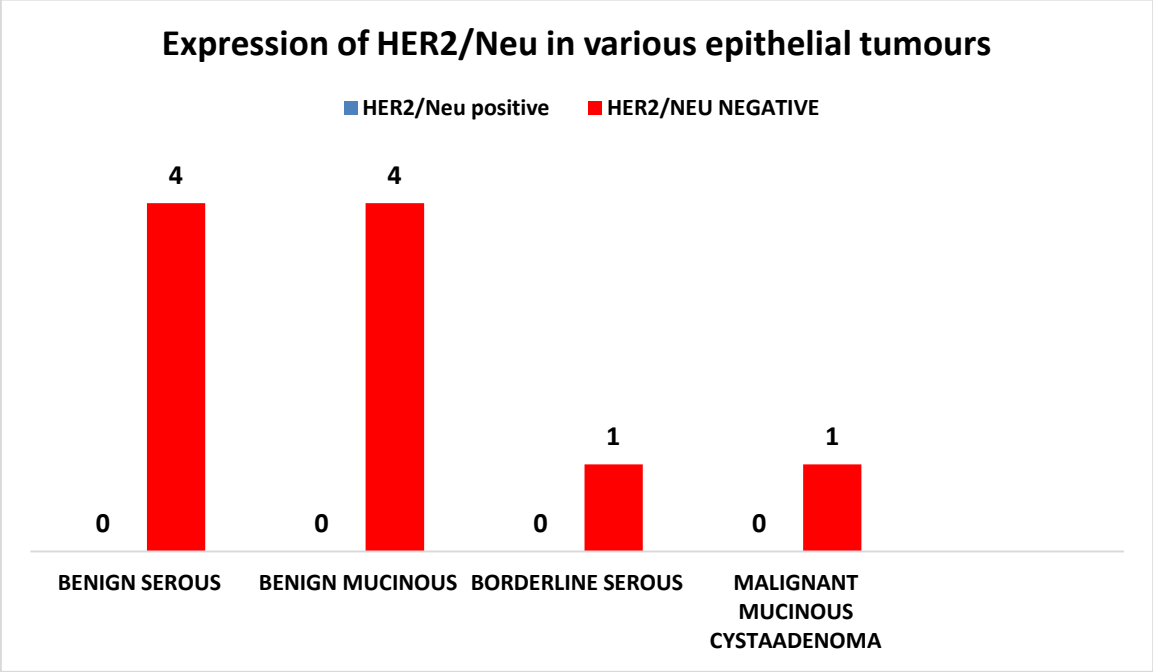
Graph 2: Association between expressionof HER2/Neu with that of the tumor Size



Graph 3: Negative expression of HER2/Neu in Ovarian Epithelial tumors



Graph 4: Expression of HER2/Neu in various epithelial tumors



There were similar results found by Sueblinvong T et al 2007, who found nil association between expression HER2/Neu and clinic-morphological features analyzed among 74 cases of surface malignant ovarian tumors.

Many other studies revealed various degrees of detection rate for HER2/Neu immunostaining such as Berchuch et al 1990 (32%), Salmon et al 1989 (26%), Bookman et al 2003 (11%), Dimova et al 2006 (11%), Nielsen JS et al 2004. (35%), and Malamou-Mitsi V 2007 (18%).

The positive expression of the HER 2 /Neu had very vast range of variation in various studies i.e. 2% to 100%. The intensity of the staining also does not associatetumour grade in various studies.

After revising all the studies stated above, finally we deduce that expression of HER2/Neu does not have any remarkable correlation with clinicopathological prognostic indicators like patient's age, tumour grade and tumor size. It still needs further assessment as a prognostic factor in ovarian neoplasms.

Conclusion

The analysis of the immunoexpression of HER2/Neu among the surface epithelial ovarian

carcinomas showed negative expression in all 10 cases selected for immunostaining. In this study- benign serous, borderline serous, benign mucinous and malignant mucinous cystadenocarcinoma, all show negative expression for HER2/Neu immunostaining. In this assessment there is no marked correlation observed between expression of HER2/ Neu and clinicopathological factors like patient's age, tumor grade and tumor size. Hence we propose that HER2/Neu needs further evaluation for being a prognostic marker in surface epithelial ovarian neoplasms. Additional studies are warranted to ascertain the value of HER2 as a prognostic marker of ovarian neoplasms that is either resistant or responsive to specific chemotherapeutic agents or high-dose chemotherapy.

Summary

In this study the independent expression of HER2/Neu in the surface epithelial ovarian tumours was assessed. As expression of HER2 / Neu is predominantly seen in surface epithelial tumors of the ovary, we selected 10 cases of various types of surface epithelial tumors out of 149 cases from the period of May 2013 to April 2018 and found out that all showed HER2/Neu negative expression.

Though the tumour grade and its stage are the main prognostic indicators in surface epithelial tumors of ovary, the HER2/Neu positivity does not significantly correlate with grade and stage of the tumor or other prognostic markers like patient's age, tumor size. Hence we propose that HER2/Neu needs further assessment as a prognostic marker in epithelial ovarian cancers.

Reference

1. Luo H, Xu X, Ye M, Sheng B, Zhu X (2018) the prognostic value of HER2 in ovarian cancer: A meta-analysis of observational studies. PLoS ONE 13(1): e0191972
2. Tavassoli FA, Devilee P. Pathology and genetics of tumors of breast and female genital organs. World Health Organisation classification of tumors .IARC Press, Lyon, 2003; 123-24.
3. Hanna L, Adams M. Prevention of ovarian cancer. Best Practical Residents Clinical Obstetrics Gynaecology 2006; 20: 339-62.
4. Nida Iqbal and Naveed Iqbal, "Human Epidermal Growth Factor Receptor 2 (HER2) in Cancers: Overexpression and Therapeutic Implications," Molecular Biology International, vol. 2014, Article ID 852748, 9 pages, 2014.
5. Goel, et al.: Study of HER2/Neu Oncogene in Benign and Malignant Ovarian Tumors, International Journal of Scientific Study |July 2014 | Vol 2 | Issue 4.
6. M.C. Marinas et al. EGFR, HER2/Neu and Ki 67 immunoexpression in serousovarian tumours. Rom J Morphol Embryol 2012; 53(3):563-567.
7. Hadeel A. Kerbel, Rehab H. Abdul Saheb and Dhafer S. Alabbasi, Expression of p53 and HER2/Neu in serous ovarian carcinoma with different grades of differentiation (immunohistochemical study) .
8. Hellstrom I, Goodman G, Pullman J, Yang Y, Hellstrom KE. Overexpressionof HER2 in ovarian carcinomas. Cancer Res. 2001;61:2420-2423
9. Allred DC, Bustamante MA, Daniel CO, Gaskill HV, Cruz AB Jr. Immunocyto-chemical analysis of estrogen receptors in human breast carcinomas. Evaluation of 130 cases and review of the literature regarding concordance with biochemical assay and clinical relevance. Arch Surg 1990;125:107-13.