



ORIGINAL RESEARCH PAPER

Pathology

CORRELATION OF HISTOLOGICAL TYPE, GRADE OF CERVICAL MALIGNANCY WITH AGE AND HER2/ NEU EXPRESSION

KEY WORDS: Age , Her2/neu, Cervical carcinoma, post menopausal bleeding

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ABSTRACT

OBJECTIVES: To correlate age of patient with Histological type, grade and stage of cervical malignancy and with HER2/ neu expression.

METHODS: Sixty five samples of cervical tumour tissue received at Pathology Department of our hospital and diagnosed as carcinoma cervix were included in the study.

RESULT: The mean age of the study group was 51.89 +/- 12.18 years and range between 41-60 years. Most of the patients presented with complaints of bleeding (post-menopausal/ irregular/ post coital bleeding) and/ or PV discharge. Out of total 65 cases, 58 (89.23%) cases were diagnosed as Squamous cell carcinoma, while 05 (07.69%) were Adenocarcinoma and 02 (3.07%) cases were of Adenosquamous carcinoma. HER2/neu status was positive for over expression in 23 out of 65 cases, thus accounting for 35.38% of cervical carcinoma.

RESULT: Maximum number of cases were observe and the mean age was 51.89+/-12.18 years. Most of patients with carcinoma cervix were married out of 65 cases, 63 (96.55%) cases were married. Out of total 65 cases of our study, 23 (35.38%) cases were positive for HER2/neu protein over expression.

INTRODUCTION

Carcinoma cervix is one of the common malignancy in women in India with an incidence of 9 to 44 per 100,000 women.⁽¹⁾

Invasive cervical carcinoma has been divided into various categories based on their histological appearance and staining characteristics.⁽²⁾ Most common histological subtype of carcinoma cervix is Squamous Cell Carcinoma 80% followed by Adenocarcinoma 15%. Adenosquamous and Neuroendocrine tumors account for remaining 5%.⁽³⁾

Mortality due to cervical cancer is also an indicator of health inequities.⁽⁴⁾ In India peak age for cervical cancer incidence is 55-59 years.⁽⁵⁾ Current data from National Cancer Registry Program (NCRP) indicates that the most common sites of cancer among women are the breast and the cervix.⁽⁶⁾

Carcinoma of cervix may have a variety of clinical presentation. It may be discovered on routine PAP smear in any asymptomatic women, patient with irregular vaginal bleeding or in late stage patient may present with symptoms of a mass lesion or metastatic disease.⁽⁷⁾

New techniques in diagnosis have helped to modify histological classification in particular the use of immunohis to chemistry has improved diagnostic accuracy.⁽⁷⁾ There is now a general agreement that the membranous IHC staining pattern of HER-2/neu correlates with receptor protein expression and prognosis.⁽⁸⁾ There are variable reports on expression of HER-2/neu in cervical carcinoma either due to heterogeneity of the lesion or due to antigen retrieval.^(9,10)

More studies are required in India to assess correlation of over expression of HER-2/neu with various histological subtypes and stage of carcinoma cervix, as it is the leading cause of death. The logical step to follow is the testing of molecular targeted therapies trying to improve the prognosis of cervical cancer patients.⁽¹¹⁾

Material And Methods

This study was carried out in Department of pathology, Mahatma Gandhi Medical College and Hospital, Sitapura, Jaipur (Rajasthan). Sixty five samples of cervical tumour tissue received at Pathology Department of our hospital and diagnosed as carcinoma cervix were included in the study.

The type of specimen received were: Hysterectomy specimen (Figure1), Cervical biopsies

The tumour were cut at various levels depending on the individual cases and they were allowed to fix in 10% formalin for 24-48 hrs. After fixation multiple bits were taken from the representative areas of tumour and accompanying tissues. Special attention was given to the margin of the tumour, invasion in surrounding tissue in case of hysterectomy specimen. Immunohistochemical staining for HER2/neu receptor was done in each and every case of cervical carcinoma.

Detailed microscopic examination of the tumour was done to arrive at a histopathological diagnosis. The lesions were classified as per the WHO/FIGO classification of cervical carcinoma. Immunohistochemical scoring was done for HER2/neu staining using ASCO/CAP guidelines update 2018. The data compiled were analysed for various parameters like age, clinical symptoms, signs, location of tumour, gross features of the tumour, grading of tumour, WHO/FIGO classification and HER2/neu over expression.

RESULTS

The mean age of the study group was 51.89 +/- 12.18 years and range between 41-60 years. According to age distribution, in age group 21-30- years – 2 cases (3.07%), 31-40 years – 13 cases (20%), 41-50 years – 18 cases (27.69%), 51-60 years – 18 cases (27.69%), 61-70 years – 11 cases (16.92%), 71-80 years – 3 cases (4.61%).

Most of the patients presented with complaints of bleeding (post-menopausal/ irregular/ post coital bleeding) and/ or PV discharge. In this study 12 cases presented with as only bleeding, 7 cases complained of PV discharge. Majority of cases i.e. 44 presented with complaints of bleeding and discharge. 20 cases were found to have bleeding and/or discharge with other complaints such as weakness, bachache and pain abdomen.

Out of 65 (100%) cases, 58 (89.23%) cases were labelled Squamous cell carcinoma, out of which 53 (91.37%) were moderately differentiated (Figure2) and 05 (08.62%) were poorly differentiated. 05 (7.69%) were labelled as Adenocarcinoma out of which 3(60%) cases were moderately differentiated and 02(40%) cases were labelled as poorly

differentiated. Only 02 cases (03.07%) were labelled as Adenosquamous.(Table 1)and (Figure3)

100% cases in which adenocarcinoma (5 cases) and adenosquamous carcinoma (2 cases) were married and 96.55% (56 cases) of squamous cell carcinoma were diagnosed in married females. Only 2 cases of squamous cell carcinoma were observed in unmarried females.

Out of 58 cases of squamous cell carcinoma, 14 were less than 40 years of age and 44 were more than 40 years of age. Out of 5 cases of adenocarcinoma(Figure4), 01 case was less less than 40 years and 04 cases were more than 40 years. 2 cases of adenosquamous were more than 40 years of age. Total number of 50 cases were above 40 years of age. HER2/neu status was positive for over expression in 23 out of 65 cases(Figure 5,6), thus accounting for 35.38% of cervical carcinoma. 5 cases were HER2/neu positive before 40 years of age and 18 case were HER2/neu positive which were more than 40 years of age.

Out of 58 cases of squamous cell carcinoma 20 were positive for HER2/ neu marker, in 5 cases of adenocarcinoma 2 were positive for HER2/ neu staining and out of 2 cases of adenosquamous cases 1 was positive for HER2/neu staining.(Table 2)

DISCUSSION

In present study total 65 cases clinically diagnosed and/or suspected of having carcinoma cervix were evaluated histologically and immunohistochemically. The largest study concluded is by Doo – yi oh et al (2015)⁽¹²⁾they studied 412 cases of cervix. R J Hale et al (1991)⁽¹³⁾reported a study of 62 cases. Our study has nearly the same number of cases as given in the above study. However Pramod Sarwade et al (2016)⁽¹⁴⁾ has done the similar study on 58 cases.

In present study the mean age of ca cervix was 51.89+/-12.18 years and ranges from 20-80 years and maximally distributed in the 41-60 years (55.38%).Michael J Costa et al (1995)⁽¹⁵⁾ observed the mean age of ca cervix cases was 51 years. This was in accordance to our study.(Table 3)

Tessa Joseph et al (2015)⁽¹⁶⁾ observed the mean age of ca cervix cases was 53.75 years.

According to a study conducted by Doo-Yi Oh et al (2015)⁽¹²⁾ the mean age of presentation of ca cervix is 49 years.

In the present study 67.69% of cases presented with bleeding (postmenopausal/ post coital bleeding/ irregular bleeding) and foul smelling vaginal discharge , which is well correlated with the study ofNimisha Sharma et al (2016).⁽¹⁷⁾

A close association of carcinoma cervix with the marital status was observed in the present study. 63 cases of ca cervix were married and only 2 cases of SCC was diagnosed in an unmarried female. It strongly favours the role of HPV virus in the development of carcinoma cervix.

In the present study out of 65 cases Squamous cell carcinoma forms the major proportion of cases number being 58 (89.23%). Adenocarcinoma was second in the list accounting to 5 (7.69%) and Adenosquamous 2(3.07%) was the least common. These carcinoma were further subclassified into well, moderate and poorly differentiated categories. Moderately differentiated SCC 53 (81.53%) forms the most common category of carcinoma cervix.

As considering the histological grading of ca cervix, the study conducted by Swasti Bajpai et al (2017)⁽¹⁸⁾ stated that 40 cases out of total 43 cases were squamous cell carcinoma were the most common histological grade of ca cervix reported by Christopher M Lee et al (2004)⁽¹⁹⁾ and Pramod

Sarwade et al (2016)⁽¹⁴⁾.

In studies carried out by Nimisha Sharma et al (2016)⁽¹⁷⁾ squamous cell carcinoma (72%) was the most common grade of ca cervix. HER2 positive staining in invasive ca cervix ranged from 14-100% in various studies. Out of total 65 cases of our study, 23(35.38%) cases were positive for HER2/neu protein over expression.(Table 4)

R J Hale et al (1991)⁽¹³⁾ reported HER2/neu over expression in cervical cancer. In their study 38.7% cases showed evidence of HER2/neu protein over expression. Swasti Bajapai et al (2017)⁽¹⁸⁾ showed 35.7% percentage of HER2/neu over expression in carcinoma cervix.

The positivity rate in present study is close to that reported by Sharma N et al (2016)⁽¹⁷⁾ and Sarwade et al (2016)⁽¹⁴⁾, who reported positivity rate of 36.6% and 44% respectively. Costa et al (1995)⁽¹⁵⁾ and Ndubisi et al (1997)⁽²⁰⁾ observed HER2/neu over expression of 77% and 22% respectively.

Table 1; Showing Histological Grading Of Carcinoma Cervix.

Type of Tumor	Tumor differentiation	No. of Cases	Percentage (%)
Squamous cell carcinoma		58	
	Well Diff.	0	0%
	Mod. Diff.	53	91.37%
	Poorly Diff.	5	8.62%
Adenocarcinoma		5	
	Well Diff.	0	0%
	Mod. Diff.	3	60%
	Poorly Diff.	2	40%
Adenosquamous		2	

Table 2; Distribution Of Histological Type Of Carcinoma CervixWith Her2/neu Status

Type of Tumor	No. of cases	HE R2/neu status	
		Positive	Negative
SCC	58	20	38
Adenocarcinoma	5	2	3
Adenosquamous	2	1	1
Total	65	23	42

Table 3; Summary Of Mean Age And Range Found In Ca Cervix By Various Authors

Author	Mean Age (Years)	Age Range (Years)
Michael J Costa et al (1995)	51	19 – 81
Tessa Joseph et al (2015)	53.75	40 – 70
Doo – Yi Oh et al (2015)	49	27 - 67
Present Study	51.89	20 - 80

Table 4; Her2/neu Over Expression In Various Studies

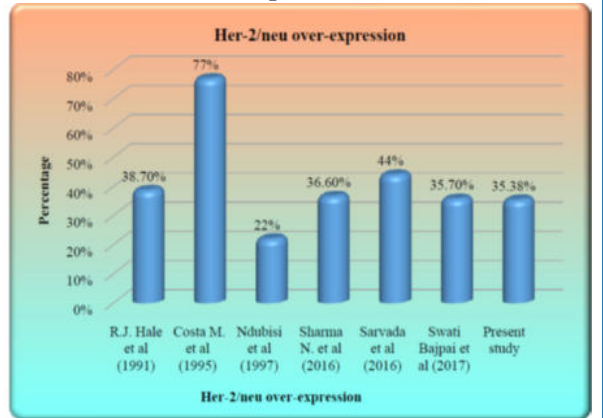




Figure 1: Hysterectomy Specimen With Bilateral Adnexa

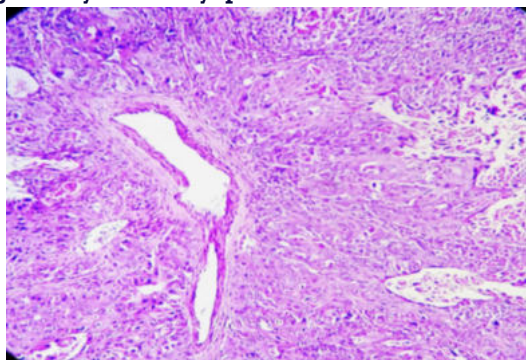


Figure 2; Moderately Differentiated Squamous Cell Carcinoma (keratinizing, H&E, 10x)

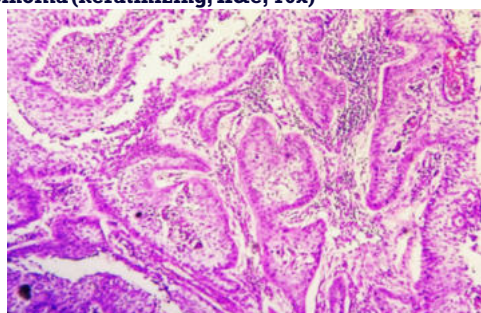


Figure 3; Adenosquamous Carcinoma (H&E, 10x)

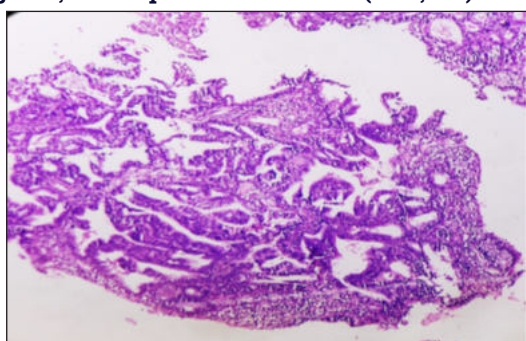


Figure 4; Moderately Differentiated Adenocarcinoma (h&e, 10x)

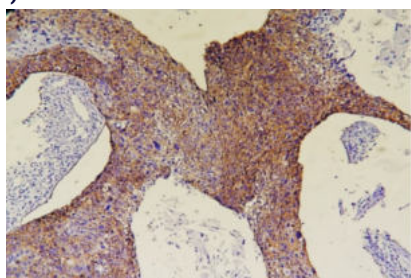


Figure 5; Section Showing Immunohistochemical

Staining For Her2/neu Receptor With Ihc Score Of +3 (10x)

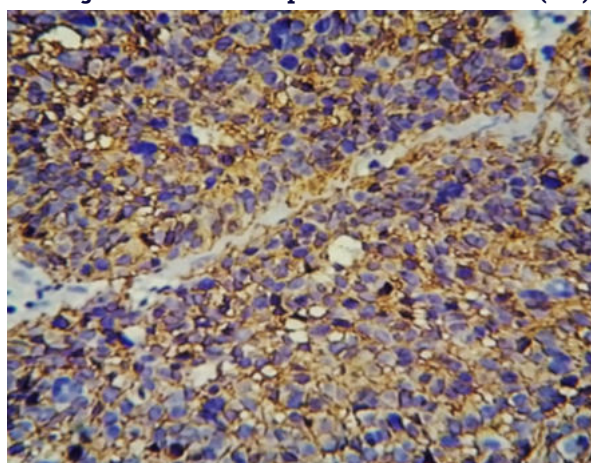


Figure 6; Section Showing Immunohistochemical Staining For Her2/ne Receptor With Ihc Score Of +3 (10x)

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