

RECLASSIFICATION OF CA CERVIX USING MUCIN STAINS AND ITS CLINICAL RELEVANCE

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ABSTRACT:

Background: Carcinoma cervix is the most common genital cancer encountered in clinical practice in India. The categorization of cervical carcinoma in terms of only their morphological appearance, in Hematoxylin and Eosin stained sections, yields incomplete and often erroneous diagnosis. Recategorisation of ca cervix based on Mucin characteristics is of academic, as well as prognostic importance. The study was conducted with the objective demonstrating mucin in cervical Carcinomas, that were originally classified as squamous cell carcinomas, and to reclassify and modify their histological diagnosis. **Methods:** The study was conducted by staining sections from cervical biopsies of 551 patients that were clinically suspected and/or diagnosed as having carcinoma cervix, and subsequently confirmed histopathologically by Hematoxylin and Eosin staining, received at the Histopathology section of Department of Pathology, Mahatma Gandhi Medical College, Jaipur. PAS and Alcain-blue Mucin stains were used. **Results:** Majority of these patients(62%), were in the age group of 41 to 60 years. 80% of the patients came with the complaints of bleeding and discharge per vaginum (PV). 10.91% mucin secreting neoplasms were falsely classified as squamous cell carcinoma by Hematoxylin and Eosin method. **Conclusions:** Mucin histochemistry should be carried out routinely in all the cases of carcinoma cervix.

Key Words: CA Cervix, Adenosquamous carcinoma, Mucin stains

INTRODUCTION:

Carcinoma cervix is the most common genital cancer encountered in clinical practice in India (80%). The death toll is around 70,000 cases every year (1). India accounts for about 20% of cervical cancer cases reported from the world

(2). The high prevalence and mortality, therefore, makes the study of ca cervix essential. No form of cancer better documented the remarkable effects of prevention, early diagnosis and curative therapy on mortality and morbidity rate

than carcinoma cervix, because carcinoma cervix follows a progressive course from dysplasia to carcinoma in situ and eventually, to invasive carcinoma (3).

Worldwide, high risk type HPV-16 and 18 contribute over 70% of all cervical cancer cases. Most common in India are also type 16 and 18 (4).

Most cervical carcinoma arises at the squamo-columnar junction of the cervix, which represents the labile transformation zone. Invasive cervical carcinoma has been divided into various categories based on their histological appearance and staining characteristics (5).

Squamous cell carcinomas account for about 80% of cancers of the uterine cervix, and the majority of the remainder are adenocarcinomas (6).

The categorization of cervical carcinoma in terms of only their morphological appearance, in Hematoxylin and Eosin stained sections, yields incomplete and often erroneous diagnosis. In reality, only about 70% of cervical carcinomas are purely squamous. Many Mucin Secreting cancers escape detection unless a mucin stain (PAS and Alcian Blue) is applied (5,7,8).

It has been shown in various studies that adenosquamous carcinomas often pursue an aggressive course and are associated with worse prognosis, than the purely adeno or squamous counterparts, because most of them are poorly differentiated (9). Also, these covert mucus secreting tumors occur with undue frequency in women less than 40 years, and accounts to significant extent of poor prognosis in young patients, who present with rapidly metastasizing tumors and respond poorly to conventional treatment (10,11,12,13). Hence, recategorisation of carcinoma cervix based on Mucin characteristics is of academic, as well as prognostic importance.

The study was conducted with the objective demonstrating mucin in cervical Carcinomas, that were originally classified as squamous cell carcinomas, and to reclassify and modify their histological diagnosis.

MATERIAL & METHODS

The study was conducted by staining sections from cervical biopsies of 551 patients that were clinically suspected and/or diagnosed as having carcinoma cervix of epithelial origin, and subsequently confirmed histopathologically by Hematoxylin and Eosin staining, received at the Histopathology section of Department of Pathology, Mahatma Gandhi Medical College, Jaipur from Feb 2014 to Jan 2015.

Consent was taken from the ethics committee of the institute and the patients participating in the study.

The material consisted of two main groups of specimens:

1) Control group :-

A) Sections from kidney - Periodic Acid Schiff's method.

B) Sections from colon - Orcein Alcian Blue [OR/AB (pH2.5)]

2) Cervical biopsies:- 3 paraffin sections, 4µi thick, stained with-

(A) Hematoxylin and Eosin

(B) Periodic Acid and Schiff: for demonstration of neutral mucin.

(C) Orcein-Alcian Blue (pH 2.5): for demonstration of acidic mucin.

The data collected were analysed using SPSS software.

RESULTS

In the present study, a total of 55 cases were studied. Majority of these patients(62%), were in the age group of 41 to 60 years. 29% of the

patients were less than 41 years of age, and 9% were more than 61 years old.

80% of the patients came with the complaints of bleeding and discharge per vaginum (PV). Remaining either had isolated discharge or bleeding PV, with minor complains of backache, weakness and pain abdomen.

The classification of cervical carcinomas based on Hematoxylin and eosin staining and reclassification with mucin stains is given in Table 1. It shows that around 10.91% mucin secreting neoplasms were falsely classified as squamous cell carcinoma by Hematoxylin and Eosin method.

The histopathological categorization of the 55 cases of carcinoma cervix, before and after mucin histochemistry is shown in Table No. 2. Without the Mucin stain, out of 55 cases, 51 cases were squamous cell carcinoma, 03 cases were adenocarcinoma and 1 case was adenosquamous carcinoma. With the mucin stain, out of 55 cases, 45 cases (81.82%) were classified as squamous cell carcinoma, 03 cases (05.45%) were classified as adenocarcinoma and 07 cases (12.72%) were classified as adenosquamous carcinoma of cervix. There is significant increase in the number of adenosquamous carcinoma with mucin stain.

DISCUSSION

Mucin containing carcinomas are aggressive tumors with high prevalence of lymph node metastasis (9,10), are radioresistant (12,13) and carry poor prognosis. Considering all these factors, it becomes essential to recognize them. This can help in planning the management of patients, as studies have shown improved survival rates when mucin containing tumors are treated with combined radiotherapy and surgery, instead of conventional treatment with radiations only (12).

Buckley et al (1989) stated that mucin secreting cervical, carcinomas occur with greater frequency in women under the age of 40 year (5). In the present study, the mean age of the patients with cervical carcinoma was found to be 49.02 years, and those of mucin secreting cervical carcinomas was 42.84 years.

In the present study, 80% of the cases presented with bleeding (postmenopausal bleeding/post coital bleeding/irregular bleeding) and foul smelling vaginal discharge which is well correlated with the study of Howkins and Boume (1971) (14)

In present study total 55 cases clinically diagnosed and /or suspected of having carcinoma cervix were evaluated histologically and histochemically. The histological case distribution was observed as squamous cell carcinoma - 92.73%, adenocarcinoma - 05.45% and adenosquamous 01.82%. Histochemically they were typed as squamous cell carcinoma - 81.82%, adenocarcinoma - 05.45% and adenosquamous —12.72%

In the present study squamous cell carcinomas form the major proportion of cases number being 51 (92.73%). Out of 55 cases adenocarcinoma was second in the list accounting to 3 in number (05.45%) and adenosquamous was the last common out of these three categories, the number being 1(1.82%). These carcinomas were further sub classified into well, moderate and poorly differentiated categories. Moderately differentiated squamous cell carcinoma were 48 cases (94.12%) which forms the most common category of carcinoma cervix.

100% cases of adenocarcinoma and adenosquamous demonstrated mucin. Only 6 cases of squamous cell carcinoma demonstrated mucin.

As a result of mucin staining, original classification was revised in 6 cases (10.91%) of Squamous cell carcinoma. All the 6 cases were of moderately differentiated squamous cell carcinomas which were reclassified as adenosquamous (mixed) carcinoma.

Frequency of squamous cell carcinoma in this study (94.731/0) was relatively higher than other studies and this could possibly be because of relative low proportion of adenocarcinomas observed in the present study (15).

Recent reports have shown an increase in the proportion of glandular neoplasms, but whether this increase is absolute or relative is undetermined (16).

Benda (1985)⁷ documented maximum percentage (33%) of cases which required reclassification followed by Buckley (15.6%). In present study, reclassification was required in 10.91% cases, which is in close approximation to the percentage reported by Buckley et al (1988) (10).

CONCLUSION

Mucin histochemistry should be carried out routinely in all the cases of carcinoma cervix as Hematoxylin and Eosin staining is not sufficient. This aids in the early detection of previously unrecognized mucin secreting adenocarcinoma and adenosquamous carcinoma, which pursue a more aggressive clinical course, and poorer prognosis than non mucin producing squamous cell carcinoma.

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TABLE NO. 1 Classification by Hematoxylin and Eosin And with Mucin stains.

Diagnosis	Hematoxylin and Eosin	Mucin stain
Squamous cell carcinoma	51 (92.73%)	45 (81.82%)
Adenocarcinoma	3 (05.45%)	3 (05.45%)
Adenosquamous	1 (01.82%)	1 (01.82%)
Squamous cell carcinoma with mucin secretion		6 (10.91%)

TABLE NO. 2: Histopathological categorization before and after mucin histochemistry

Diagnosis	Before mucin stain		After mucin stain	
	No. of cases	Percentage	No. of cases	Percentage
Squamous cell carcinoma	51	92.73%	45	81.82%
Well differentiated	00	00.00%	00	00.00%
Moderately differentiated	48	94.12%	42	93.33%
Poorly differentiated	03	05.88%	03	06.67%
Adenocarcinoma	03	05.45%	03	05.45%
Well differentiated	00	00.00%	00	00.00%
Moderately differentiated	02	66.67%	02	66.67%
Poorly differentiated	01	33.33%	01	33.33%
Adenosquamous	01	01.82%	07	12.72%