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ORIGINAL ARTICLE

Histopathological/immunohistochemical Analysis of Cervical Adenocarcinomas seen in Jos University Teaching Hospital, Jos, Nigeria

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ABSTRACT:
Background: The incidence of adenocarcinoma of the cervix is on the increase in many parts of the world. There is paucity of information regarding this in our setting. **Objective:** To describe the histopathological pattern of cervical adenocarcinomas and to highlight the role of immunohistochemistry in diagnostic dilemmas. **Method:** This is a descriptive analysis of consecutive adenocarcinomas of the cervix as seen in the histopathology department of Jos University Teaching Hospital (JUTH), Jos over a six year period, between January 2005 and December 2010. **Result:** Of the 240 cervical surgical specimens received over the period of study, 44 (18.3%) were cervical malignancies. Of these 13 (30%) were adenocarcinoma and 31(70.5%) squamous cell carcinoma. The percentages for the different histologic subtypes of the adenocarcinomas were, pure adenocarcinoma (53.8%), adenosquamous carcinoma (23.1%) small cell carcinoma (15.4%) and metastatic adenocarcinoma (7.7%). **Conclusion:** Cervical adenocarcinomas constituted 30% of all cervical malignancies in JUTH, second only to squamous cell carcinoma of the cervix. Pure form of adenocarcinoma is the commonest type of adenocarcinoma while metastatic adenocarcinoma is the least common type. Immunohistochemistry to differentiate adenocarcinomas of primary cervical origin from metastases is valuable.

Keywords: Adenocarcinoma, cervix, malignancy, immunohistochemistry.

INTRODUCTION

Cervical cancer is a major public health problem in many developing countries, due largely to limited access to screening and treatment. [1]

In sub-Saharan Africa carcinoma of the cervix is the commonest genital tract malignancy encountered accounting for over 50% of cases. [2]

Squamous cell carcinoma of the cervix is the commonest histological cell type encountered accounting for over 85% of variants followed by adenocarcinoma.[2] The incidence of adenocarcinoma has been on the increase partly due to increasing incidence of human papilloma virus (HPV) infection and due to increase in screening for preinvasive and early invasive lesions of the cervix. [2]

Cervical cancer is preventable because it is a slowly evolving disease that begins as mild dysplasia and progresses over 10 or more years to invasive carcinoma [3]. Among the non-squamous cell carcinoma of the cervix, adenocarcinomas rank the highest in most literatures[3].

It is clear from studies in Canada, Scandinavia and more recently the United Kingdom that routine Pap smear screening has not only reduced the incidence of squamous cell carcinoma of the cervix but indeed in the last 10 – 15 years has halved the mortality rate from this disease. [4] In comparison, however, the incidence rate of adenocarcinoma has at best stabilized and at worst increased by even up to 15% in the last 10 years. [4] It certainly now seems that even well-organized screening programmes have failed to protect women from developing adenocarcinoma of the cervix and that in time, the proportion of glandular to squamous lesions is going to alter remarkably. [4] Data from the United States have clearly shown that invasive adenocarcinoma of the cervix has been increasing in both whites and blacks since the mid-1920s, but that the increase is statistically significant only among whites, reaching 4.2%

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per year for those born since 1935.[5]

Also reports of an increased incidence in younger women are particularly worrying with the suggested link between the development of cervical adenocarcinoma and oral contraceptive use. [5-6] The presence of integrated human papilloma virus (HPV) DNA in squamous neoplasia is now well established but in comparison, data relating to the link between HPV and glandular abnormalities are still controversial. This is true not only for invasive disease but also pre-cancerous abnormalities.

The cause of the increase in cervical adenocarcinoma is unclear but it is of particular concern as studies have shown that glandular disease is often at a more advanced stage when detected. At diagnosis, adenocarcinomas tend to be large and bulky, and local recurrence is more common in such lesions [7].

Adenocarcinomas have been reported to have a higher fatality rate than other cervical cancers, including squamous cell lesions. [8,9] In part the advanced stage of these lesions is related to difficulty associated with detecting them. Precancerous lesions are asymptomatic, and the conventional Pap smear is recognized as having a lower sensitivity for detecting glandular lesions compared with squamous cell carcinoma [9]. Adenocarcinomas arise from endo cervical glands which are less visible than ectocervical squamous cells making detection a challenge. A liquid- based Pap test (the thin prep ® system) has improved the ability to detect glandular disease than the conventional Pap smear [10,11].

It should be noted that the role of HPV in glandular disease has not yet been elucidated and that HPV DNA testing is not included in recommendations for AGC follow-up [12.] Recent publications have cited that up to 57% of glandular cytologic abnormalities found in Pap testing may be HPV negative [12.]

Immunohistochemistry refers to the process of detecting antigens eg proteins in cells of a tissue section by exploiting the principles of antibodies binding specifically to antigens in biological tissues. It is used in diagnosis of abnormal cells such as in cancerous growths and will pin down primary source of metastatic tumours and those with poor differentiation.It is also used in drug development.

In our environment, most reports on patterns of cervical malignancies have focused on the squamous cell carcinomas which is actually the predominant type. No report has been published in our environment on the less radiosensitive non squamous cell carcinoma types which generally have worse prognoses.The role of immunohistochemistry in diagnostic dilemmas cannot be overemphasized as it is the only way some ambiguous morphologic subtypes of adenocarcinomas can be deciphered. This is necessary as management options will vary based on diagnosis.

MATERIALS AND METHODS

Fresh sections of blocks of all previously histologically diagnosed cervical adenocarcinomas by simple Haematoxylin and Eosin(H&E) staining technique during the period of study were made and reported by the lead author and cross checked by another pathologist. Cases that had inconclusive diagnoses like metastatic adenocarcinoma (endometroid type adenocarcinoma) with squamous mataplasia were sent for immunohistochemistry at a private histopathology laboratory in Jos, Plateau State. This was to further confirm primary cervical adenocarcinomas and to detect metastatic adenocarcinomas to the cervix which could not easily be determined by routine H&E microscopy. The patients bio-data were retrieved from their request forms. Diagnosis was done in accordance to the World Health Organisation(WHO) classification of cervical neoplasms.

RESULTS

Out of 240 cases of cervical biopsy specimens received during the six years period of study, 44 cases (18.3%) comprise of cervical malignancies .Of these, 13 consists of the various forms of adenocarcinomas and squamous cell carcinoma accounted for 70.5%.

Of the various histologic subtypes of adenocarcinomas seen, pure form adenocarcinoma was commonest and constituted (53.8%) of the adenocarcinomas and the least form was metastatic adenocarcinoma which accounted for 7.7% of adenocarcinomas of the cervix[table1].This metastatic adenocarcinoma was positive for estrogen and negative for carcinoembryonic

antigen in keeping with immunohistochemistry profile for endometrial adenocarcinoma. The age range for adenocarcinomas was between 30 – 79 years and peak age range was 50-59 years [table2].

Table 1: Frequency of various histologic patterns of cervical adenocarcinomas

Histologic pattern	Frequency	%
Adenocarcinoma (pure type)	7	53.8
Adenosquamous carcinoma	3	23.1
Small cell carcinoma	2	15.4
Metastatic adenocarcinoma	1	7.7
Total	13	100

Table 2: Age distribution of cervical adenocarcinomas

Age Group(years)	Frequency	%
30-49	4	30.8
50-59	6	46.2
60-69	2	15.4
70-79	1	7.6
Total	13	100

DISCUSSION

Adenocarcinoma made up 30% of cervical malignancies seen in JUTH. This value is higher than that reported in a similar study at Zaria because Zaria observed other cervical malignancies like Leiomyosarcomas during their study but only adenocarcinomas was seen as non squamous cancer of the cervix in our setting.[13] In this study, pure form (well differentiated adenocarcinomas) was the commonest histologic pattern of adenocarcinoma observed. This is consistent with other studies in Southern and Northern Nigeria.[12,13] This is closely followed by adenosquamous carcinoma which is also consistent with reports in other centres. [13]

Metastatic adenocarcinoma was the least common type observed in our study but this form was not observed in Zaria's report although the poorly differentiated adenocarcinomas reported in other centres could actually consist of some form of metastatic adenocarcinomas.[13] The metastatic adenocarcinoma observed in this study was actually an endometrial adenocarcinoma by immunohistochemistry as it was positive for estrogen antigen but negative for carcinoembryonic antigen. This is consistent with results of such immunohistochemistry studies in other centers.[15,16]

Age range for adenocarcinomas in this study is also consistent with that seen in most other centres in Africa although peak age observed in this study is higher than reports from western literatures. [11-14]This is attributed to earlier exposure to hormonal contraceptives in the Western world.

Immuno histochemical analysis of all adenocarcinomas suspected not to be of primary cervical origin like endometroid type adenocarcinomas is very helpful in deciding whether it's of primarily cervical origin or metastasis from other structures like endometrium cancer. This is because endometroid carcinomas could be of primarily cervical origin or of endometrial origin.

In conclusion, adenocarcinoma is second to squamous cell carcinoma as a cause of cervical malignancies and tallies with most reports all over the world. It is important to distinguish primary cervical adenocarcinoma from metastatic adenocarcinoma mostly arising from the endometrium since it will influence and inform management options. Thus the role of immunohistochemistry in diagnosis cannot be overemphasized.

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