Histological Pattern of Cervical Malignancies in Southwestern Nigeria

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Abstract

Background: Malignant diseases of the uterine cervix are typically common among women in the developing countries of the world where they cause a lot of reproductive ill-health and mortality at the prime of age.
Objectives: The aim of this study is to present the histological pattern of cervical malignancies as they present at Obafemi Awolowo University Teaching Hospital Complex (OAUTHC) Ile-Ife between 1990 and 1999
Materials and Methods: The data for the study was collected retrospectively from the surgical daybooks of the histopathology department of the OAUTHC Ile-Ife from January 1990 to December 1999. All cervical biopsies and hysterectomy specimens from which a histopathological diagnosis of malignant tumour of the cervix was made form the subject for this study.
Results: The results revealed 192 cases (45.5%) of cervical malignancies out of the 422 cervical surgical biopsies over the period of study. The age range of the patients was 20 to 89 years with a peak age incidence of 40 49 years. Histopathological study revealed squamous cell carcinoma in 85.4% with a preponderance of Large cell non-keratinising squamous cell carcinoma in 41.1%, keratinising squamous cell carcinoma 32.3% while micro invasive carcinoma and small cell non keratinising tumours are seen in 1.0% and 9.9% respectively. Adenocarcinoma, adeno- squamous carcinoma, metastatic carcinoma and sarcomas occur in 8.3%, 3.6%, 1.6% and 1.0% respectively.
Conclusion: Squamous cell carcinoma constitutes the main histological type with a high preponderance of large cell non-keratinising squamous cell carcinoma

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Introduction

The cervix, often referred to as the 'gate way' or entrance to the uterus occupies a strategic place in human sexuality and reproduction, consequently it is prone to insults and associated with many diseases. Malignant diseases of the cervix are typically common among women in the developing countries where they pose a threat to reproductive health and general well being[1]. Malignant tumours of the cervix are predominantly carcinoma in nature. Sarcomas and secondary tumours of the cervix do occur but are rare.

The literature on the malignant tumours of the cervix is almost synonymous with invasive carcinoma of the cervix, which has been the subject of international focus since 1943 when Papanicolaou and Traut described how exfoliative cytology could be used to detect this malignant carcinoma in its pre-malignant stage[2]. However, this is the most common gynecological malignant condition of the cervix uteri [3-6]. Other forms of malignant condition of the cervix arising from the mesenchyme are mainly sarcomas and are not common. These include leiomyosarcoma, endocervical sarcoma, embryonal rhabdomyosarcoma, alveolar soft part sarcoma and mullerian adeno-sarcoma of the cervix. These are slow growing cancers with poor response to radiotherapy and chemo therapy. Metastasis (secondary) to the cervix may arise as a result of local extension of tumours from the uterus and other adjacent organs such as the bladder and the ovary. Choriocarcinoma has a relatively high rate of cervical metastasis. Lymphomas and leukaemia may also secondarily involve the cervix.

In Nigeria and in many other developing countries where the incidence of malignant conditions of the cervix is on the increase,[7] there is paucity of knowledge and information on the pathological identities of the various malignant conditions of the uterine cervix. This work is therefore aimed at describing the histopathological characteristics of malignant tumour of the cervix as they present in our practice at Ile-Ife and to compare our results with those from other parts of the world. The place of health education and information dissemination to increase awareness and knowledge of these conditions that will change the health seeking behaviour of women in developing countries towards early diagnosis and detection of these malignancies in their non-invasive stage is further emphasized.

Materials and Methods

The data for the study was from the surgical daybooks of the histopathology department of the Obafemi Awolowo University Teaching Hospitals Complex,(OAUTHC) Ile-Ife from the period January 1990 to December 1999 (10 years). The original requests cards were retrieved and relevant information extracted.

All cervical biopsies and hysterectomy specimens from which a diagnosis of malignant tumour of the cervix was made were assessed for the study. In our histopathology laboratory at Ile-Ife, cervical surgical

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specimens are routinely formalin fixed, paraffin-embedded, and cut at 2-3m. Sections are routinely stained with haematoxylin and eosin stains. However, special stains such as Alcian blue for mucin and Periodic Acid Schiff (PAS) reagent are used when necessary to reach a definitive diagnosis of adenocarcinoma and adenosquamous carcinoma.

Vital statistical data like age, relevant clinical data, and histopathological diagnosis were noted. All the slides of the patients with cervical tumour were recalled and examined. Where not available, fresh sections were cut and stained with haematoxylin and eosin

The malignant tumours were classified into carcinoma, sarcoma and secondary tumours. Carcinomas were classified according to the modified WHO histological classification of epithelial tumours[8]. Squamous cell carcinoma of the cervix was classified based on the degree of differentiation of the tumour cells. This categorises squamous cell carcinoma into (Well-differentiated) Keratinising, (Moderately differentiated) large cell non- keratinising and (Poorly differentiated) small cell non keratinising variants.

Results

Between the period January 1990 and December 1999, a total of four hundred and twenty-two (422) cervical surgical biopsies were received in the Department of Morbid Anatomy and Forensic Medicine, Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife. 192 cases were malignant tumours while the remaining were benign and non-neoplastic lesions. The malignant tumours represent 45.5% of all cervical lesions. Of the malignant tumours, 190 cases (98.9%) were carcinoma of the cervix. The remaining two cases were sarcomas of the cervix.

Table 1 shows the age distribution of patients with malignant tumours of the cervix. The age range was 20 to 89years.

(Table 1: Age Distribution of Patients with Malignant Tumours of the Cervix.)

Age group	No. Of cases	Percentage
20 -29	4	2.1
30 -39	23	12.0
40 -49	50	26.1
50 -59	45	23.4
60 -69	49	25.5
70 -79	17	8.8
80 -89	4	2.1
TOTAL	**192**	**100**

The peak age incidence for malignant tumours of the cervix was 40-49 years. Carcinoma of the cervix alone showed bimodal peak age incidences of 40 to 49 years and 60 to 69 years with 49 cases (25.8%) each. 85.8% of the cases occurred in patients above 40 years.

Table 2 shows the histological types of malignant tumours of the cervix. Carcinoma of the cervix constituted the bulk of the malignant tumours and accounted for 190 cases (98.9%).

(Table 2: Histological Types of Malignant Tumours of the Cervix.)

Tumour types	*No of cases*	*Percentage of total*
1. **CARCINOMA**	190	98.9
(a)Squamous cell carcinoma(SCC)	164	85.4
Micro-invasive carcinoma	2	1.0
Keratinising SCC	62	32.3
Large cell non-keratinising SCC	79	41.1
Small cell non-keratinising SCC	19	9.9
Papillary (transitional) SCC	2	1.0
(B)Adenocarcinoma	16	8.3
-Endocervical	7	3.6
-Clear Cell Carcinoma	6	3.1
-Papillary	3	1.6
(c) Adenocarcinoma	7	3.6
(d)Metastatic carcinoma	3	1.6
2. SARCOMA	2	1.0
TOTAL	192	99.9

There were only two cases of sarcoma of the cervix (1.0%). Squamous cell carcinoma was the predominant histological type and constituted 164 cases (85.4%). Adenocarcinoma constituted 16 cases (8.3%) and adenosquamous carcinoma 7 cases (3.6%). Of the squamous cell carcinoma, only two (2) cases were micro-invasive carcinoma (1.0%), others were invasive carcinoma (84.4%). There were two cases of papillary (transitional) squamous cell carcinoma. Non-keratinising large cell squamous cell carcinoma was the predominant histological variant (79 cases, 41.1%) keratinising squamous cell carcinoma constituted 62 cases (32.3%) and non-keratinising small cell carcinoma accounted for 19 cases (9.9%). There were sixteen cases (8.3%) of adenocarcinoma of the cervix. Out of these, 7 cases (43.7%) were well-differentiated mucinous adenocarcinoma (endocervical type), clear cell adenocarcinoma, 6 cases (37.5%) and the remaining three (8.8%) were papillary adenocarcinoma. All the cases of clear cell adenocarcinoma occurred in patients' 35 years and above. Three cases (1.5%) of metastatic carcinoma were seen.

Sarcoma of the cervix accounted for only two cases (1.0%). One was a leiomyosarcoma and the other was an endocervical stromal sarcoma presenting as a protruding mass from the external os in a 51-year-old woman.

Table 3 shows the percentage comparison of histological type of invasive cancers from different studies.

Table 3: Percentage Comparison of Histological Types of Invasive Cervical Cancers from Different Studies.

Histologic Types	*Present Study*	*Adelusi et al[4] Ibadan*	*Platzetal[7] (American Blacks)*	*Adeniji[6] (Ilorin)*
Squamous cell carcinoma	85.4	93.9	81.3	92.8
Micro invasive carcinoma	1.0	-	6.8	4.3
Keratinising SCC	32.3	63.2	7.0	60.1
Large cell non-keratinising	41.1	14.9	4.8	5.5
SCC	9.9	15.9	-	22.9
Small cell non- keratinising	-	-	62.7	-
SCC	1.0	-	1.0	-
Other (invasive carcinoma) [a]				
Other specific type				
Adenocarcinoma	8.3	6.1	8.9	2.4
Adenosquamous carcinoma	3.6	-	2.6	4.8
Sarcoma	1.0	-	1.4	-
Unspecified carcinoma (NOS)		-	5.8	-
Metastatic carcinoma	1.6	-	-	-
TOTAL	99.9	100.0	100.0	100.0

Most of the invasive squamous cell carcinomas were not further characterised Transitional (papillary) squamous cell carcinoma.

Discussion

Female genital malignancies are still very common among modern day African women where they constitute a scourge and cause reproductive ill health and mortality in variable proportions. The commonest of these malignancies are those involving the uterus and particularly the uterine cervix. Malignancies of the uterine cervix occur as carcinomas, sarcomas and metastatic tumours as further demonstrated in this study. Variation in the distribution of the histological types of these tumors exists geographically and biologically accounting for different incidences, age distributions and cell types.

In this study, malignancies of the uterine cervix account for 45.5% of all cervical lesions of the four hundred and twenty two cervical surgical biopsies during the 10 years of study. Of these figures, 98.9% of the malignancies were carcinoma of the cervix while the remaining 1.1% was sarcoma of the cervix. This observation further supported the work of earlier authors on the rarity of sarcoma of the cervix in relation to carcinoma of the cervix [6,7]. The ratio of cervical sarcoma to cancer of the cervix is 1:97. This ratio is the same with the findings among American blacks with female genial tract cancers [7]. Of the two cases of sarcoma of the cervix encountered in this study, one was a leiomyosarcoma and the other was an endocervical stromal sarcoma (a very rarer sarcoma) presenting as a protruding mass from the external cervical os in a 51 year old woman. Other forms of sarcoma of the cervix that are known but not documented in this study are embryonal rhabdomyosarcoma (ERMS), which is common in childhood and in the vagina in the second decade of life. Malignant mixed mesodermal tumour whose biologic behaviour can be similar to that of invasive squamous cell carcinoma can also be seen on the cervix. The rarity of these sarcomas have hindered their studies in great details and may perhaps be due to underdiagnosis in this locality where many people dying from these tumours would not consent to post mortem examination for religious and other social reasons.

Most of the histological types of malignancies of the cervix (85.4%) were squamous cell carcinoma. This is comparable with findings of other workers [4,6,7,9]. Large cell nonkeratinising squamous cell carcinoma was the most predominant histological variant in this study accounting for 41.1%. This is very high when compared with figures of 14.9% and 4.8% obtained respectively by Adelusi et al [10] at Ibadan and Platz et al among American Blacks with female genital tract tumours (Table 3). There is a discordance among the histological variant of squamous cell carcinoma as recorded in various places (table 3) [4, 6, 7]. However it is known that the incidence of cancer of the cervix is very low in the developed countries and high regrettably in some poorer countries where the resources to readily diagnose the disease in its early stage are not available [11, 12]. Even in the developed countries such as United States of America the incidence of cancer of the cervix is higher among blacks and other aborigines [7]. This may however, be related to poorer socio economic status of American blacks compared with whites, coupled with reduced awareness of the extent of the problem and relative lack of facility to diagnose and treat the disease in its early form before they become invasive carcinoma. The biologic behaviour of these histological types is similar but little is known whether they affect the prognosis and course of the disease. However it appears that large cell non-keratinising squamous cell carcinoma progress slowly with better five-year survival when compared with other histological types [11].

The proportion of adenocarcinoma (8.3%) and adenosquamous carcinoma (3.6%) in this study compares well with their incidence among the American blacks but a little higher than reports from Ibadan in a study done about 24 years ago in the same region where this study was carried out. Squamous cell carcinoma is now known to have been over-diagnosed in the past. Using PAS/Alcian blue stain, some of the cases diagnosed as pure squamous cell carcinoma are now known to be adenosquamous carcinoma[13] .The high incidence of squamous carcinoma in previous studies from Nigeria may be due to the fact that histopathological diagnosis on cervical biopsies was based purely on H&E stain. Mucinous adenocarcinoma was the most common histological variant. This paralleled report in the literature [14]. Clear cell carcinoma came second with 37.5%. Clear cell carcinoma is common in young women with a history of in-utero exposure to diethystilbesterol (DES). It can also develop in post menopausal women in the absence of exposure to DES. There was no history of DES in all

our patients. Three (1.6%) cases of metastatic carcinoma were seen of which two were from adenocarcinoma of the uterine body and the third from the carcinoma of the sigmoid colon.

Malignant tumours of the cervix occur typically between the ages of 30 69 years in this study (Table 1) reaching the modal peak at 40-49 years, a period where reproduction and socio-economic responsibility to the family, society and nation are in great demand. Only 4 (2.1%) cases are seen below the age of 30 years in this study. The pattern of presentation in early reproductive years (20-29 years) in this study may be one of the reasons for the widely prevalent non-use or under-use of cytological screening programmes among women in this environment. Also most of the cases seen (85.2%) were invasive carcinoma of the cervix with only two cases at the micro invasive stage. From the theoretical prediction that the preinvasive lesion of the cancer of the cervix occurs at least ten years before the development of frank invasive squamous cell cancer of the cervix[15], it may be appropriate to recommend screening programme for the detection of early cervical malignancies in this environment, beginning from about the age of 20 years in all females to diagnose the disease at a stage when cure can be achieved.

Squamous cell carcinoma constitutes the main histological type with a high preponderance of large cell non-keratinising squamous cell carcinoma in this study. The use of special stains to differentiate between squamous cell carcinoma, adenosquamous carcinoma and adenocarcinoma may account for variations in proportions seen in this study.

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