Papillary squamous cell carcinoma of the cervix in Uganda: a report of 20 cases

Michael Odida
Department of Pathology, Faculty of Medicine,Makerere University

Abstract

Background: Non-glandular papillary carcinoma of the cervix are uncommon tumours. In Uganda where cervical carcinoma is very common, no cases of papillary squamous cell carcinoma of the cervix has been reported.
Objectives: To ascertain the occurrence and describe the clinicopathological features of papillary squamous cell carcinoma of the cervix in Uganda.
Study Design: Retrospective review of histologically diagnosed cases of squamous cell carcinoma of cervix with papillary structures.
Methods: Retrospective review of cases of cervical carcinoma diagnosed in the Pathology Department, Makerere University from 1968 to 1973 was done. Cases with features of squamous differentiation and forming papillary pattern were then selected.
Results:Twenty cases were encountered and the ages of the patients ranged from 22 to 70 years (mean 46.6 years). Histologically, the tumours had thin to broad fibrovascular cores covered by multilayered squamous epithelium. In five cases, there were areas with very delicate fibrovascular cores covered by monolayered epithelial cells.
Conclusion: The results of this study show that in Uganda, papillary squamous cell carcinoma of the cervix does occur and is predominantly a disease of older women. The results also confirm that papillary squamous cell carcinoma is a distinct subtype with some variants, and support the hypothesis that squamous cell carcinoma of the cervix is heterogeneous group of tumuors.
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Introduction

Non-glandular papillary carcinoma of the cervix are uncommon tumours with rather sketchy literature [1-7]. In Uganda where cervical carcinoma is very common [8,9], no cases has been reported although a number of neoplastic cell types of squamous cell carcinoma were documented [10]. Since an earlier report from Uganda indicated a large proportion of undifferentiated tumours of the cervix [8], it is worthy to find out if cases of papillary tumours could have been misdiagnosed as they are sometimes difficult to diagnose[6]. In this paper, 20 cases encountered in the Department of Pathology during a period of six years are presented.

Methods

Cases of cervical carcinoma diagnosed in the Department of Pathology, Makerere University from 1968 to 1973 were retrieved. During this period, the Department of Pathology provided free histopathology services for all hospitals and other health units in Uganda [11]. For each case new sections were made and stained with Haematoxylin and eosin (H&E). All cases with poor or small inadequate histological sections were excluded. Each case was then examined by the author without reference to the original diagnosis. Cases with features of squamous differentiation [12] and forming papillary patterns were noted. Clinical information, including patients' particulars were obtained from the histology request forms.

Correspondence author:
Michael Odida
Department of Pathology,
Faculty of Medicine, Makerere University
P.O. Box 7072, Kampala, Uganda
E mail: modida@med.mak.ac.ug

Results

Of the cervical carcinoma cases diagnosed in the Department during this period, histological materials were available for 656 cases. Sixty six cases were excluded, leaving 590 cases for review. Out of the 590 cases reviewed, 20 were papillary squamous cell carcinoma. Ages were indicated in 16 cases and ranged from 22 to 70 years (mean 46.3 years). The main presenting symptom was abnormal vaginal bleeding in most patients. Other symptoms were offensive vaginal discharge and abdominal pain. The duration of symptoms varied from one week to one year with an average of 20 weeks. Grossly, the tumuors were very friable and bled profusely. Microscopically, two variants were recognized:

i) Tumours with thin to broad fibrovascular cores covered by several layers of epithelium showing various degrees of atypia (15 cases). The epithelial cells were basaloid and their long axes were orientated perpendicular to the surface (figure 1a and 1b). In two cases, there were focal areas of keratinisation.

ii) Tumours with broad fibrovascular cores covered by several layers of epithelium in some areas, while in other areas there were very delicate fibrovascular cores covered by mono layered epithelium (five cases). The tumour cells were intermediate cell type and showed various degrees of atypia (figure 2a and 2b). All except one, were aged less than 40 years.

Figure 1: Tumour with thin to broad fibrovascular cores covered by several layers of epithelium. (a) x 100 (b) x400 (H&E)

Figure 1a

Figure 1b

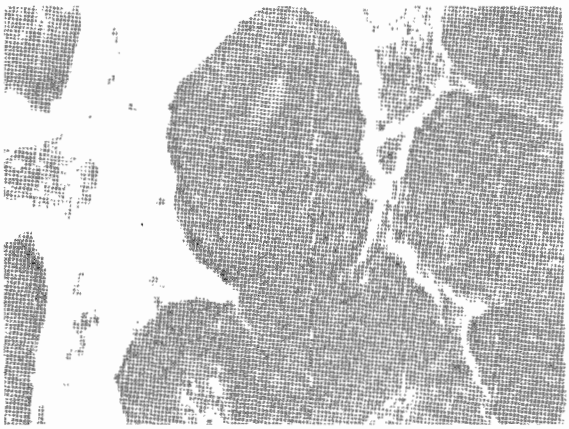


Figure 2: Part of tumour showing thin and delicate fibrovascular cores covered by monolayered epithelium. (a) x 100 (b) x 400 (H&E)

Figure 2a

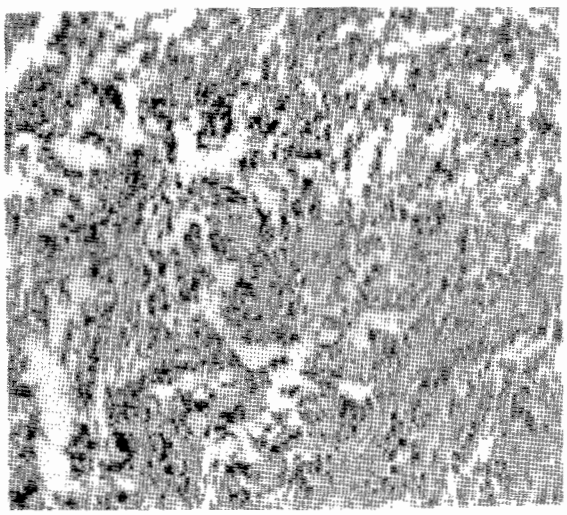
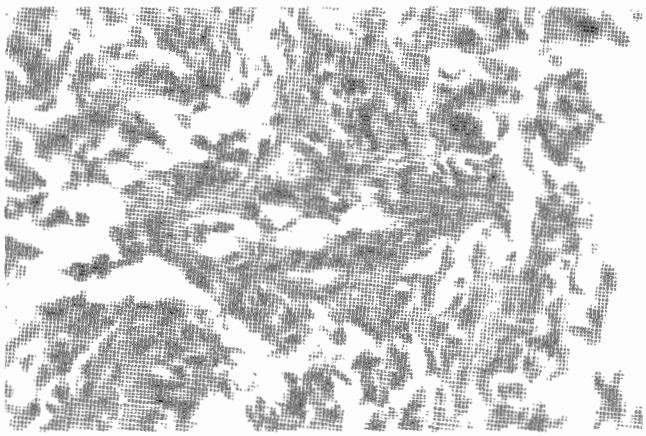


Figure 2b



In the deeper and invasive parts of the tumour, the papillary pattern was still apparent (figure3). Invasion of the stroma was associated with nonspecific chronic inflammatory infiltrate. No invasion of the fibrovascular core was noted in all 20 cases. Cytological changes suggestive of human papillomavirus (HPV) infection was not present in all 20 cases.

Figure 3: Papillary pattern in deeper and invasive part of the tumour. (a) x 100 (b) x 400 (H&E)

Figure 3a

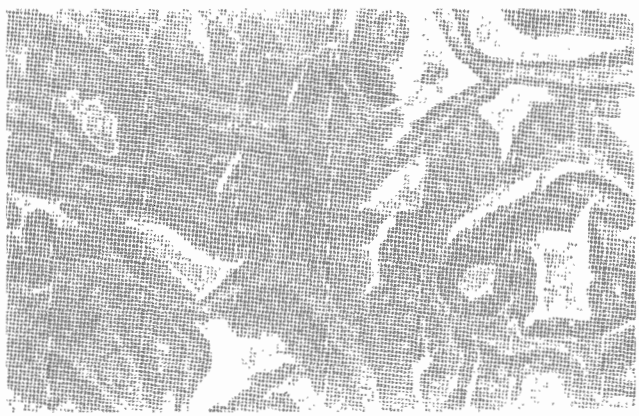
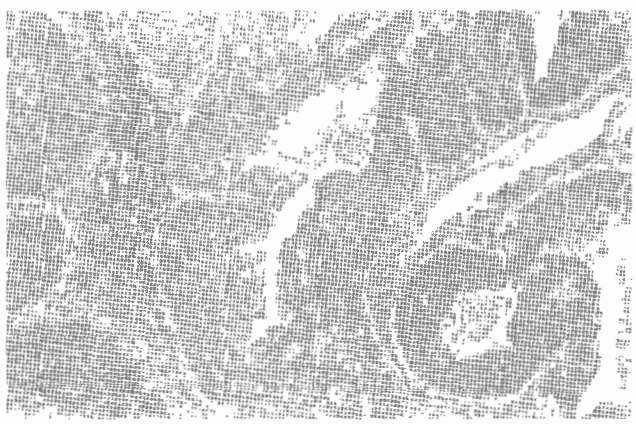


Figure 3b



Discussion

There have been relatively few reports on non-glandular papillary carcinomas of the cervix, with no cases reported from Uganda where cervical cancer is very common [8,9]. The present study is the first to document the occurrence and clinicopathological features of paipillary squamous cell carcinoma of the cervix in Uganda. Clinically most of the cases were older women (mean age 46.3) and a great proportion presented with abnormal vaginal bleeding, similar to cases reported by Randall et al[6]and Koenig et al[7]. The results of the present study suggests that papillary squamous cell carcinoma of the cervix is a distinct clinicopathological entity. This is supported by a previous detailed report of papillary squamous cell carcinoma of the cervix which was given by Randall et al[6], who described nine cases. They suggested that papillary squamous cell carcinoma of the cervix should be considered a distinct clinicopathological entity, separate from verrucous carcinoma. This conclusion was supported by clinical behavior and microscopic appearance of the papillary lesions. Three of the patients had metastases, a phenomenon which usually does not occur with true verrucous carcinoma[5]. Besides, the papillae of papillary squamous cell carcinoma are lined by dysplastic cells, in contrast to verrucous carcinoma which are lined by cytologically benign epithelial cells. They noted that most of the early cases of malignant papillary lesions of the cervix were in fact verrucous carcinomas, with few cases of true papillary squamous cell carcinoma.

The results of this study showed two variants of papillary squamous cell carcinoma of the cervix. One variant was composed of basaloid epithelial cells and the patients were all aged 40 years and above. The other variant was composed of intermediate cell types and all except one patient were aged less than 40 years old. Previous evidence supporting the views that papillary squamous cell carcinoma of the cervix as a distinct entity with variants came from Koenig et al[7]. They reviewed 32 cases and divided them into three groups, viz. predominantly squamous (nine cases), mixed squamous and transitional (16 cases) and predominantly transitional (seven cases). All cases demonstrated a papillary architecture with fibrovascular cores lined by multilayered, atypical epithelium resembling high grade squamous intraepithelial neoplasia of the cervix. In 20 cases with adequate histological materials, stromal invasion occurred in 18. They concluded that papillary squamous cell carcinoma of the cervix is a distinct clinicopathological entity and display a morphologic spectrum.

An interesting observation is that the tumour cells of papillary squamuos cell carcinoma are similar to cells in some conventional non-papillary squamous cell carcinoma of cervix [10,12]. A possible explanation could be that the tumour cells in papillary carcinomas produce some factors which induces papillary desmoplasmic reaction. The findings of Randall et al[6], that some of their cases showed papillary structures only in the superficial parts of the tumours suggest that some of these factors may sometimes be operating only in the tumour surfaces.

Papillary carcinomas exhibit peculiar morphologic variants in differentiation. In the present series, the tumour cells showed features of squamous differentiation. Some of the cases were composed of basaloid like cells while others were of intermediate cell type. The findings of the present study lent further support that these papillary tumours of the cervix are actually variants of squamous cell carcinomas. All the cases reported by Randall et al. [6], had squamous differentiation. Cases with transitional morphology have also been reported by Koenig et al.[7] and Ng [18]. Although some of the cases of Koenig et al. [7] showed features of transitional epithelium, application of immunohistochemical staining showed the vast majority of these tumours displayed the cytokeratin profile of squamous cell carcinoma of cervix. These findings support the hypothesis that squamous cell carcinoma of the cervix are heterogenous group of tumours like the non Hodgkin's lymphomas[10].

Papillary squamous cell carcinoma of the cervix may be difficult to diagnose. None of the cases reported in these series had been diagnosed as papillary squamous cell carcinoma. This difficulty had been reported by Randall et al [6]. In addition, it was observed that invasion may be difficult to demonstrate histologically unless deep biopsies are obtained. A high index of suspicion on the part of the clinician and an awareness of papillary squamous cell carcinoma by the pathologist are required to make an accurate diagnosis. Presently there is no precise definition of papillary squamous carcinomas. Ng [18] suggested that papillary tumours should be diagnosed only if papillary or anastomosing frond-like architectural pattern was seen in >70% of the tumour tissue. Although the suggestion is good, it would be better it was based on many cases with well defined criteria.

Data on the behavior of papillary squamous carcinoma of the cervix are few. In the present series, no follow-up data were available because of lack of a system for tracing patients [11]. Two studies from U.S.A [6,7] showed that these tumours probably have the propensity of late recurrences and possibly late metastases. In the cases reviewed by Koenig et al. [7], of the three patients who presented with advanced disease, the one who received chemotherapy survived for 33 months, compared to three and four months respectively for the other two patients. They thought that there may be a role for chemotherapy in treating these tumours.

The role of human papillomavirus (HPV) in squamous cell carcinoma of the cervix have come from many studies [13-17]. Whether papillary squamous carcinoma of the cervix is associated with HPV is not clear. In the present series, none of the cases had features of HPV infection. Randall et al [6] found no cytologic changes associated with viral replication that is koilocytosis. Koenig et al [7] found changes suggestive of HPV infection in six cases.

In summary, the results of this study show that in Uganda, papillary squamous cell carcinoma of the cervix does occur with morphologic variants. It is suggested that additional studies to further characterize the clinicopathologic features of these tumours and their response to different therapeutic agents be carried out.

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