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A Histo patho logical and immuno histochemical study of papillary squamotransitional carcinoma of cervix - Case series of 10 cases

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Abstract

Background: Papillary Squamotransitional cell carcinoma of cervix is the distinctive tumor of cervix and is known for its aggressive behaviour, late recurrences and metastasis. Morphologically it is similar to other lesions of cervix like verrucous carcinoma, condyloma, CIN III with papillary configuration.

Material and Methods: Ten cases included in the study which were diagnosed Histo pathologically as papillary squamotransitional carcinoma of cervix. Further evaluation was done by immunohistochemistry.

Observation: Age of the patients ranged from 30-70 years. Common presenting features were postcoital and post-menopausal bleeding. Histopathological examination revealed papillary architecture with fibrovascular core in all the cases. Eight cases were CK7+, CK20- whereas two cases were negative for both cytokeratin. p53 was positive in all the cases. Ki 67 shows moderate to high proliferative activity.

Conclusion: Due to its aggressive behaviour papillary squamotransitional carcinoma of cervix should be distinguished from other lesions. IHC will help in the diagnosis.

Keywords: menopausal bleeding, cytokeratin, histopathology

Introduction

Carcinoma cervix is the fourth most common cancer in women. Papillary squamotransitional cell carcinoma (PSCC) is one of the uncommon variants of squamous cell carcinoma of cervix. [1, 2] It differs from Conventional squamous cell carcinoma by its histomorphology and clinical behaviour. It is also seen at other sites like ovary, uterus and vagina, where initially they were known as transitional cell carcinoma and now termed as PSCC. [2, 3, 4] PSCC has varied spectrum of morphology, it can appear as pure squamous, pure transitional and mixture of both squamous and transitional. [5,6,7] It has a peculiar papillary growth architecture, aggressive biologic behaviour and have a tendency of locoregional recurrence and metastasis. Therefore, it should be insulated from other benign, premalignant and malignant lesions of cervix like Condyloma, squamous papilloma, verrucous carcinoma, CIN grade III with papillary configuration. [8,9]

Herein we analyse histopathological and immunohistochemical features of ten cases of PSCC.

Materials and Methods

Specimens received in histopathology section of Department of Pathology over a period of two years, were processed routinely and were stained by hematoxylin and eosin stain. Out of 40 Cervical biopsies, 10 were diagnosed as PSCC on microscopy.

All the biopsies undergo immunohistochemistry. The antibodies which were used are CK7, CK20, p53 and Ki 67. Assessment of immunoreactivity for CK7 and CK 20 was done quantitatively. Percentage of cells with membrane staining estimated and intensity of staining was scored as 0, 1+, 2+, 3+. The case was considered positive if at least 5% of cells shows 1+ intensity. Immunoreactivity for p53 was estimated as positive or negative. Ki 67 immunoreactivity was assessed by its nuclear staining and graded as minimal, moderate and high depending on percentage of cells showing nuclear reactivity (minimal if 10% of cells shows nuclear reactivity, moderate if 10-50% and high if > 50% of cells shows nuclear staining.

Observation

Cases of PSCC included in the study presented in the Gynaecology OPD with varied symptoms like 3 out of 10 cases presented with postcoital bleeding and discharge. 5 cases presented with post-menopausal bleeding. 2 cases came with abnormal pap smears findings on cytopathology. 4 cases also complaints of weight loss, fever and pain in pelvic area. Local examination revealed ulcerated growth or friable polypoidal masses involving cervix. Age ranges from 30 to 70 years with the mean age of 45 years.Six of the patients underwent MRI, which shows cervical mass. One of them shows extension into lower uterine segment. One case shows evidence of parametrial invasion and two cases shows bilateral pelvic lymphadenopathy. All the cases were subjected to cervical biopsy and histopathological examination shows presence of papillae in all the cases. Papillae showsfibrovascular cores and are lined by multi-layered epithelial cells showing atypia in the form of pleomorphism, anisocytosis, hyperchromasia and high N/C ratio. Multi layered papillae with fibrovascular core resembles transitional epithelium. 6 cases show mitotic activity ranged from 1 to 7/HPF. Abnormal mitotic activity noticed in 2 cases. 4 cases shows intracellular keratinisation and 2 among those shows keratin pearls. Stromal invasion is seen in 5 cases in the form of nests and projections.2 biopsy were superficial and invasion cannot be assessed in them. Other features were presence

of chronic inflammatory infiltrate, necrosis, micro papillae and koilocytes. Immunohistochemical profile shows positive CK7 and negative CK 20 in 8 cases whereas 2 cases shows negative staining for both CK7 and CK 20. All the cases shows immunoreactivity with p53 and Ki 67 immunostaining shows moderate to high proliferative activity in all the cases. All the patients underwent hysterectomy.

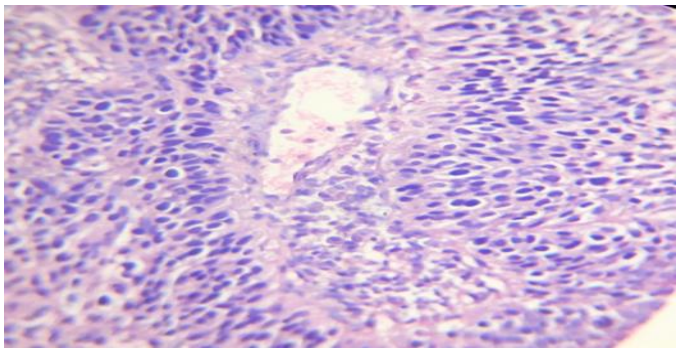

Figure 1: Tumor showing high N/C ratio with hyperchromatic nuclei.

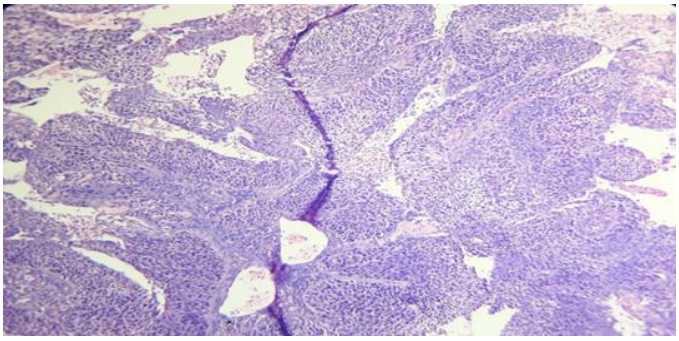

Figure 2: Tumor showing papillary configuration with multi-layering of cells.

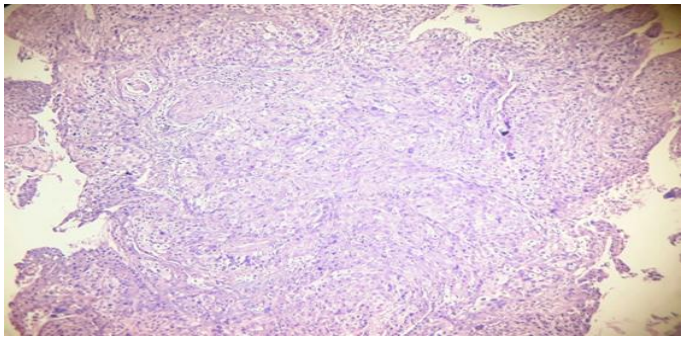

Figure 3: Tumor showing malignant Squamous epithelium. (10x)

Discussion

Marsh MR in 1952 identified papillary tumors.[10] These tumors are rare and resemble Transitional cell carcinoma of urinary tract. He did a study on 31 papillary tumors of cervix, out of 31, 3 cases were malignant. Similarly, Kazal et al in 1958 did a study on 20 papillary tumors of cervix, 2 out of 20 shows turned to be malignant.[11] Randall et al in 1986 termed these tumors as PSCC. [12] Koeing et al in 1997 shows that PSCC can be divided into 3 subtypes.

They are predominantly squamous, predominantly transitional and mixed showing features of both squamous and transitional.[6]

Several reports shows that PSCC can also be seen in vagina and endometrium. [1, 2, 3, 4] They also shows association with HPV and histomorphological features were same as that of the PSCC. [3, 4] Mostly the tumors occurs in post-menopausal age and were presented clinically with post-menopausal bleeding or abnormal pap smear. Our study evidenced 3 cases belonged to younger age group and presented with postcoital bleeding. [2, 4, 5, 6]

Due to complex architecture of PSCC, most of the biopsies are superficial and therefore it is difficult to interpret on stromal invasion. Diagnosis are routinely made on architecture and atypia. Our study shows papillae with fibrovascular cores in all cases on histopathology. Other authors have similar findings. [2, 3, 6] Due to complex architecture of PSCC, assessment of tumor depth in given biopsy were difficult which leads to incorrect staging and treatment. Our study shows stromal invasion in 50% of cases. Study did by Anand et al, Koeing et al and Kokka et al shows similar findings with 55%, 56% and 66% respectively. [3, 6, 9] In our study 80% of cases shows immunoreactivity with CK 7 and all

of the cases were negative with CK 20. Similarly, Koeing et al and Lininger et al reported that majority of cases display CK7+/CK20- cytokeratin profile. [6, 13] Moll et al found that CK20 immunoreactivity parallels with squamous cell differentiation of transitional cells. In our study all cases show immunoreactivity with p53 with suggest its strong association with HPV infection. [6,] Anand et al reported p 53 immunoreactivity in all 9 cases. [3] Whereas Mir Hashemi et al reported 3 out of 12 cases stained positive for p53.[8]

Growth fraction of the tumor was assessed using Ki-67. It is a proliferative marker and reflects the growth fraction of a tumor. Study did by Anand et al shows two cases with moderate and 7 with high proliferative activity.[3] Similarly study carried by Mir Hashemi et al shows high proliferative activity in 8 out of 12 cases.[8] There are various lesions in cervix which can be mistaken for PSCC like condyloma, squamous papilloma, CIN 3 with papillary configuration, Transitional cell carcinoma and well differentiated villoglandular Adenocarcinoma. PSCC is aggressive and is known for late recurrences and metastasis. Therefore, it is very important to differentiate it from other known lesions of cervix. [2 ,3]

Conclusion

PSCC is a distinctive tumor of cervix both clinically and morphologically. They are biologically aggressive and should be diagnosed carefully using IHC markers particularly Ki – 67 and p53.

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