Primary Papillary Serous Carcinoma of Cervix: A Rare Variant of Cervical Malignancy
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ABSTRACT
Papillary serous carcinoma of the uterine cervix is a very rare tumour, and is a recently described variant of cervical adenocarcinoma. It is an aggressive tumour with unpredictable course and poor prognosis. The incidence of cervical adenocarcinoma is 5–15%. This variant accounts for less than 50 cases in literature, has bimodal age distribution with one peak occurring less than 40 years and other occurring greater than 65 years age groups. Here, we present a 53-year-old woman presented with severe low backache and lump abdomen of 4 months duration. Per vaginal examination showed endophytic growth high up in the cervix. Pap smear and cervical biopsy done. Histopathological examination of cervical biopsy revealed papillary serous adenocarcinoma. Later, we received hysterectomy specimen with regional lymph nodes, which showed tumour limited to endocervix.

Keywords: Uterine cervix, Squamous cell carcinoma, Adenocarcinoma of endocervix, Immunohistochemistry, HPV

INTRODUCTION
Cervix is the lower part of uterus, also called uterine cervix. The most common cervical cancer is squamous cell carcinoma (SCC) from ectocervix accounting for 85% of cases. Adenocarcinoma of endocervix accounting for 5–15% is more difficult to diagnosis because it starts high in the cervix. Risk factors and symptoms are almost common for both histological types of malignancy. Risk factors are persistent infection with high risk types of human papilloma virus (HPV 16, 18 is seen in people who smoke women exposed to diethylstilbestrol and long-term use of oral contraceptive pills. As they arise high in the cervix, their detection by routine Pap test may not be as effective as ectocervical SCC; and, hence, endocervical adenocarcinoma is slowly increasing due to delay in early detection. Primary papillary serous adenocarcinoma is also common in the ovaries, fallopian tube, endometrium and peritoneum. Hence, metastatic deposit to cervix from these primary sites should be excluded. Common clinical symptoms with which the patients present are post-menopausal bleeding, inter-menstrual bleeding, menorrhagia, post-coital bleeding, dyspareunia, low backache, radiating pain to lower legs and very rarely lump abdomen. Other histological variants of cervical adenocarcinoma of endocervix are adenocarcinoma NOS (Not otherwise specified), mucinous adenocarcinoma, endocervical carcinoma with intestinal differentiation, villoglandular and mesonephric adenocarcinoma. Before the diagnosis of serous adenocarcinoma of cervix is made, metastatic deposits from other sites should be excluded particularly from the endometrium.

CASE HISTORY
A 53-year-old female patient presented to gynaecology outpatient department, with chief complaints of severe lower backache and heaviness in abdomen from four

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months. The patient was apparently asymptomatic 4 months back; later, she developed pain in abdomen, loss of appetite and loss of weight. She got married at an age of 14 and attained menopause 1 year back. On physical examination, the patient is ill built, ill nourished with pallor and inguinal lymphadenopathy noted. Vital parameters are normal. Per vaginal examination shows normal external genitalia, and pale, hard and indurated vagina with hard and keratinised cervix. After per vaginal examination, bleeding with mucus stain was noted. Papanicoloau stained smear showed sheets of atypical endocervical cells. Some of the cells were arranged in glandular pattern against haemorrhagic background. With this cytological findings, report of suspicious of malignancy was given with advice of cervix biopsy.

Colposcopy showed endophytic growth in the endocervix. Histopathological examination of the lesion showed keratinised stratified squamous epithelium of ectocervix with koilocytic change in full thickness of epithelium.

At transition zone, tumour is seen arising from endocervical glands arranged in papillary pattern, tubulopapillary and glandular pattern, lined by cells with stratification, moderate eosinophilic cytoplasm and
hyperchromatic pleomorphic nucleus. Mitotic activity of 2–3 per hpf high power field was noted. Psammoma bodies are seen focally in papillae. Histological features were in favour of papillary serous adenocarcinoma of cervix.

Immunohistochemistry revealed P16 positivity (nuclear and cytoplasmic). Estrogen receptor, progesterone receptor, Her-2 neu showed weak expression, Vimentin showed negativity. Later, the patient underwent hysterectomy with bilateral salpingo-oophorectomy and regional lymph node resection. Histopathological examination showed tumour with depth of 5 mm and maximum length of 7 mm (stage Ib) limited to endocervix, endomyometrium. Both ovaries were unremarkable. No vascular emboli noted. Lymph nodes show reactive changes. Postoperative period was uneventful.

DISCUSSION

Papillary serous adenocarcinoma of cervix has bimodal age distribution with two peaks occurring less than 40 years and above 65 years with average age of 45–55 years. Now, the incidence is on the rise in the general population particularly in young women. Because of their location high up in the cervix, sometimes, it is not picked up as effectively as SCC in routine Pap test. Any a typical endocervical cells in Pap smear should be followed by cervical biopsy. Per vaginal and gross examination of all histological types may look alike only.

Histopathological examination will help us to differentiate the sub-type as prognosis varies between different types. The most common growth pattern is exophytic. The most common presentation is with abnormal vaginal bleeding. Microscopy shows the tumour arranged in a papillary pattern, glandular pattern and variable amount of solid sheets. The tumour cells are low columnar with hyperchromatic nuclei. Nucleoli may be present. Brisk mitotic activity is seen. Psammoma bodies may be present. Lymphovascular invasion is frequently identified. Serous carcinoma can occur as a pure type or a second type of cervical adenocarcinoma can be mixed frequently with villoglandular component in young patients. Since papillary serous adenocarcinoma is seen in other sites, spread of tumour from the common primary sites to cervix must be excluded, especially from endometrium.

Immunohistochemistry, sometimes, helps to differentiate from other primary sites. p53 is positive in all serous type. CEA carcino embryonic antigen is negative in papillary serous adenocarcinoma cervix compared to other variants of endocervical cancer. p16 is positive only in cervical adenocarcinomas. Histological features that favour primary cervical origin are foci of adenocarcinoma in situ, vimentin negativity. PR, ER Progesterone Receptor, Estrogen Receptor and Her-2 receptor negativity or weak positive. Detection of human papilloma virus by flourescent in situ hybridisation (FISH).

CONCLUSION

Primary papillary serous adenocarcinoma of cervix is a rare and recently described variant of cervical adenocarcinoma that is histologically similar to papillary serous adenocarcinoma arising from the ovary, uterine endometrium, fallopian tube and peritoneum. IHC Immuno histochemistry will help in differentiating primary from the metastatic origin. This helps the clinician in deciding the appropriate management. In general, adenocarcinomas of the uterine cervix have poor chemosensitivity and radiosensitivity. Recent studies reveal that papillary serous adenocarcinoma shows response to paclitaxel and carboplatin combination chemotherapy.

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