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PAPILLARY SEROUS ADENOCARCINOMA OF CERVIX- REPORT OF THREE CASES

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ABSTRACT
Papillary serous carcinoma of uterine cervix(PSCC) is a rare histological variant of cervical adenocarcinoma with very few cases being reported in literatures. Extensive study of world literatures revealed only around 50 cases documented by the end of 2015. It is known for its aggressiveness, and usually diagnosed at advanced stage. So its often considered as tumour with unpredictable course and poor prognosis. We hereby report three cases of PSCC with complete IHC work up found coincidentally in 2 consecutive months in our dept.

KEYWORDS: Papillary serous carcinoma of cervix, Adenocarcinoma of endocervix.

INTRODUCTION
Papillary serous carcinoma of cervix is a rare and recently described variant of cervical adenocarcinoma that is histologically similar to papillary serous carcinoma arising from ovary, uterine endometrium, fallopian tube and peritoneum.[1] Hence metastatic deposit to cervix from these primary sites (especially endometrium) should be excluded before making an accurate diagnosis of PSCC. It has bimodal age distribution with two peaks, one occurring at the age of 40 year and other at the age of 65 year. Cervical adenocarcinoma accounts for 10-20% of invasive cervical cancer having poor radiosensitivity and chemosensitivity.[2] Incidence of cervical adenocarcinoma is gradually on rise due to delay in early detection. As it arises high up in cervix in comparison to Squamous cell carcinoma (that arises in ectocervix) it is usually missed out in pap smears.

CASE REPORT
CASE 1
A 41 yr old female presented with bleeding PV of 1 year duration and white discharge since 4 months. Her menstrual history revealed that she had attained menarche at the age of 12 yrs with a flow of 4-5 days in 28-30 days cycle. Her local pelvic examination was normal with healthy vulva. Per speculum showed a cauliflower like growth of size 3x2 cm arising from anterior lip of cervix. Bimanual Examination confirmed the mass arising from the endocervical canal. Routine haematological examinations were normal other than anemia (Hb 7g%). USG was done which showed normal myometrial echo with hypoechoic SOL measuring 35x25mm in endocervix. No evidence of invasion of contiguous structure was noted. Uterus was normal in size and endometrial thickness was normal. Pap smear was done which showed atypical endocervical cells arranged in papillary to glandular pattern against a haemorragic background [Fig 1 (a, b)]. So a final pap report of suspicion of malignancy with an advice to go for biopsy was finally despatched. Wertheims hysterectomy was planned and the specimen was sent for histopathological examination. Gross examination showed uterus, Cervix with b/l adnexa measuring 8x5x3. An exophytic growth measuring 3. 5x2 cms in endocervical canal [Fig 1(c)]. Both ovaries grossly appeared normal. Sections from Endomyo showed features of Non secretory endometrium over normal myometrium. Ovary from one side showed normal ovarian structure while other side showed a persistent corpus luteum. Section from the cervix (tumour proper) showed tumor cells arranged in complex branching papillae lined by moderate to severe pleomorphic cells with cellular tufting and micropapillae [Fig 1 (d, e)]. Numerous mitotic activity present. Thus diagnosis of papillary serous carcinoma of cervix was given that was further confirmed by IHC P53 which was strongly positive [Fig 1 (f)], ER and PR nuclear stains were negative [Fig 1(g), (h)]. Sections from vaginal flap and both the parametriums were free from tumour infiltrates. All the pelvic lymphnodes supplied were also free, without tumour infiltration.

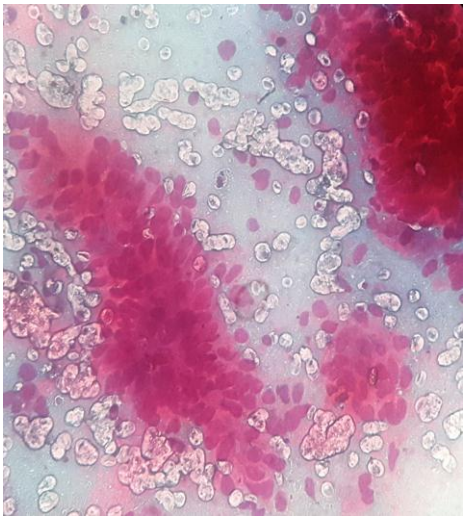

Fig-1(a).

Fig-1(b).

PAP SMEARS:- Atypical endocervical cells arranged in papillary to glandular clusters.

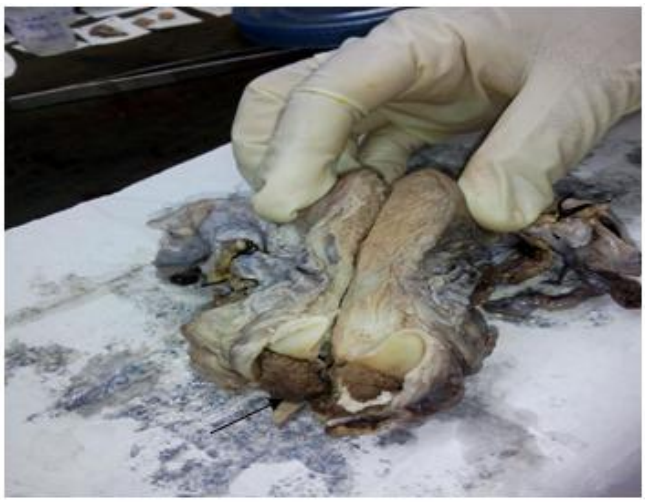

Fig 1(c): Gross- Uterus Cx with b/l adnexa measuring 8x5x3, Cervix –shows exophytic growth of 2x2x1 cm(arrow).

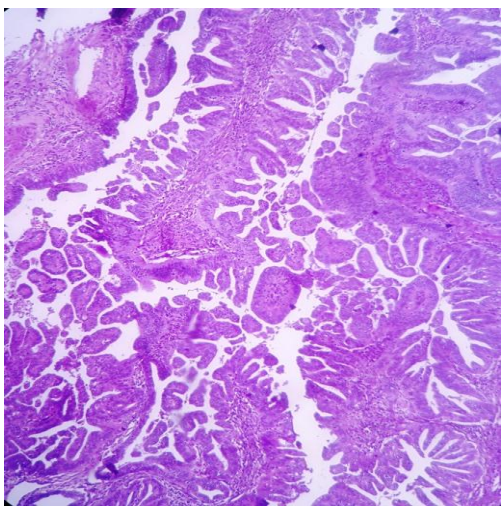

Fig 1(d): Scanner view 40x.

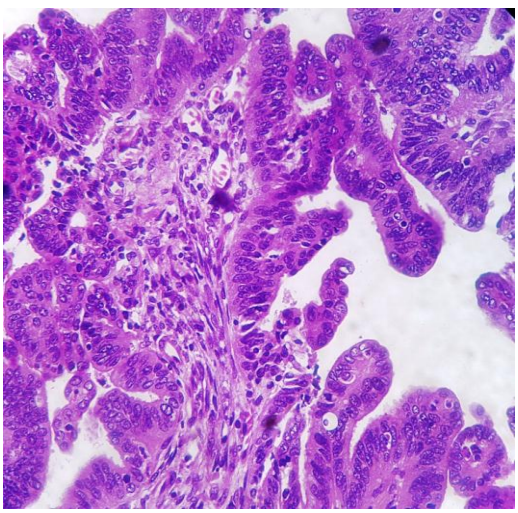

Fig 1(e): LP 100 x.

Histopath 1 (d, e)- Tumor cells in complex branching papillae lined by moderate to severe pleomorphic cells, cellular tufting and micropapillae present.

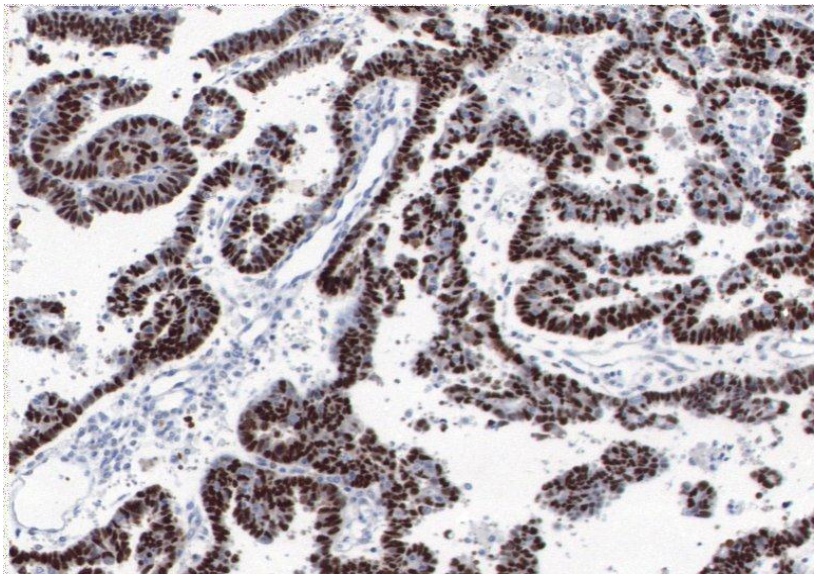

Fig 1(f): IHC LP (100x) - P53 Strongly positive.

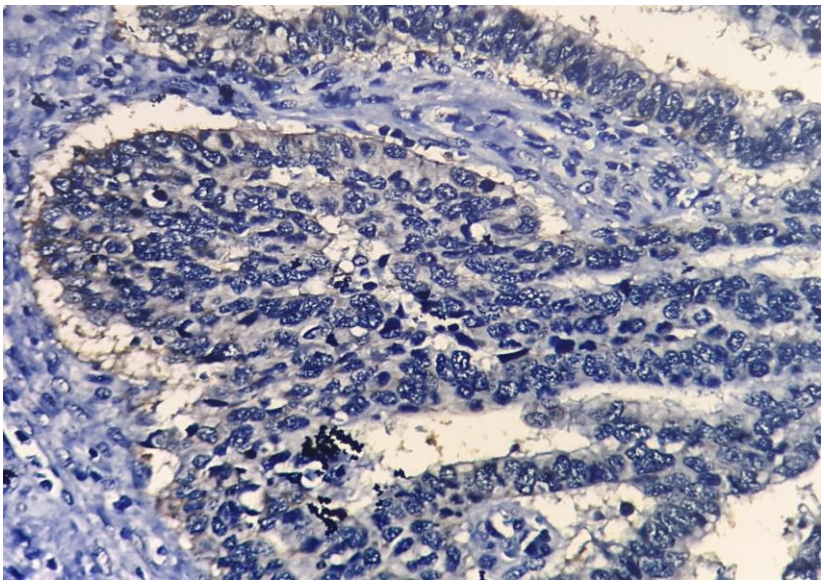

Fig 1(g): IHC LP 100x -ER Negative.

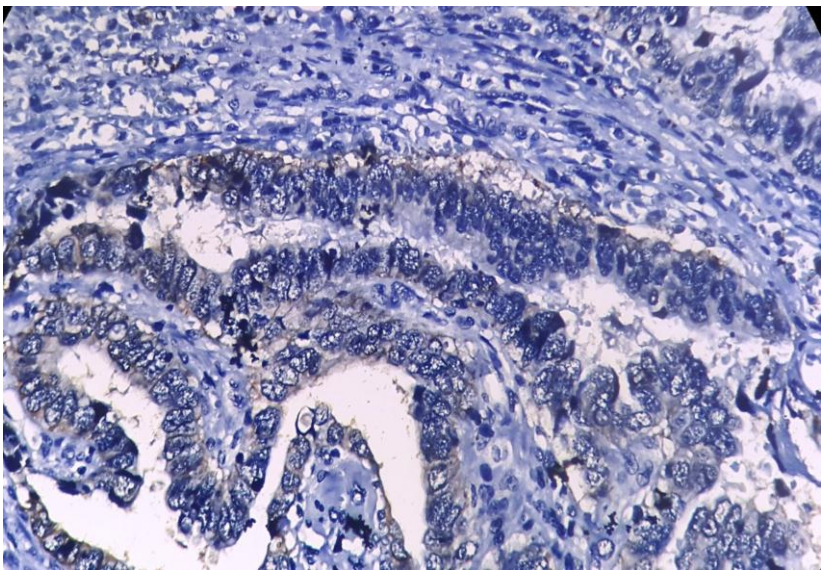

Fig 1(h): IHC LP 100x–PR Negative.

CASE 2

A 38 yr female presented with menorrhagia since 8 months. Her menstrual history was normal with 4-5 days flow in a 28-30 day cycle. Per speculum showed a warty growth of 2 x2 cms in the endocervical canal. USG diagnosis was endocervical polyp. Pap smear done revealed an inflammatory smear. Wertheim's hysterectomy was planned with a provisional diagnosis of carcinoma cervix. Gross examination revealed uterus, cervix with b/l appendages measuring 9x5x3 cm. Cervix showed a warty growth measuring 2x2x0. 5 cm. Section from the cervix (tumour proper) showed tumor cells in complex branching papillae lined by moderate to severe pleomorphic cells, high grade nuclei and hobnail appearance with clear to eosinophilic cytoplasm [Fig 2 (a)]. Diagnosis of primary papillary serous adenocarcinoma of cervix was made. Histosections from endometrium. vaginal flaps, both the parametriums and ovaries and all the pelvic lymphnodes that were supplied were normal without any tumour infiltrate. IHC of P53 was positive in tumour cells [Fig 2(b)].

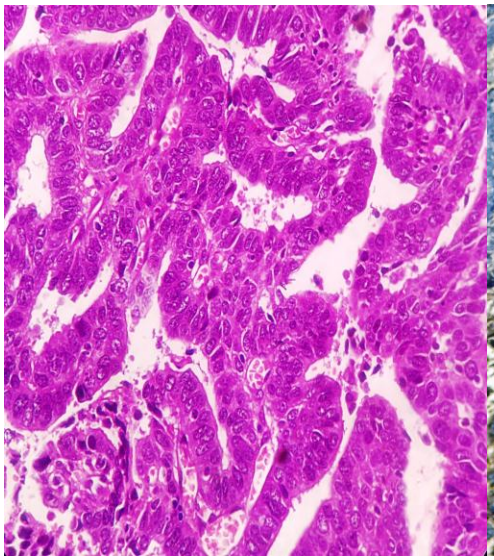

Fig-2(a).

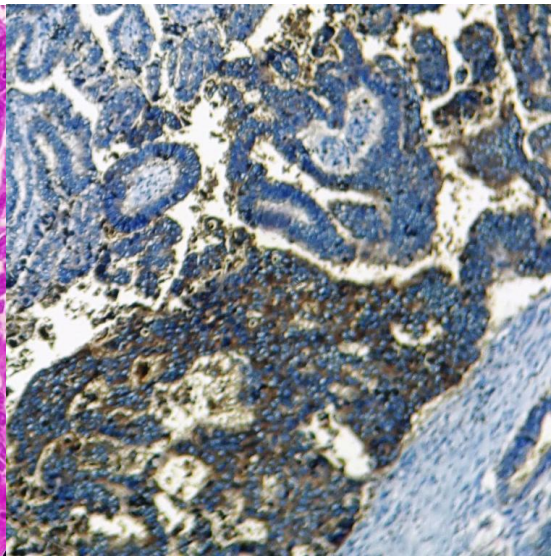

Fig-2(b).

Histopath- Fig 2 (a) - Tumor cells in complex branching papillae lined by moderate to severe pleomorphic cells, high grade nuclei. 2 (b)-IHC p53 positive.

CASE 3

A 55 yr female presented with post menopausal bleeding since 4 months. She attained menarche at age of 13 and menopause 2 yrs back. Per speculum revealed warty growth of 1 x0. 5 cm at the internal os. Pap smear was suspicious for malignancy. Incisional biopsy was send to our department from minor OT. Histosections showed complex papillary pattern lined with pleomorphic cells and high mitotic activity [Fig 3]. Thus a diagnosis of papillary serous adenocarcinoma of cervix was made and confirmed by P 53 positivity.

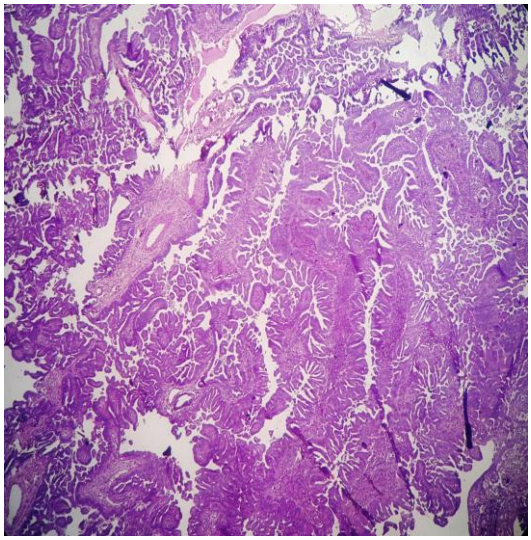

Fig-3(a).

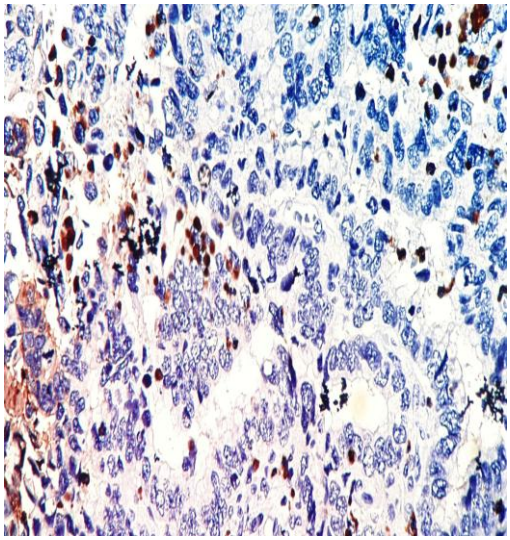

Fig-3(b).

Fig 3(a) Scanner view 40x - Tumor cells in complex branching papillae lined by moderate to severe pleomorphic cells, high grade nuclei. Fig 3 (b)- IHC LP 100x- P53 positive.

DISCUSSION

Adenocarcinomas of uterine cervix represents 10-20% of invasive cervical carcinomas with increased incidence in recent years, especially in young women.[3] 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.

Common clinical symptoms with which the patients usually presents are post-menopausal bleeding, inter-menstrual bleeding, menorrhagia, post-coital bleeding, dyspareunia, low backache, radiating pain to lower legs and very rarely lump abdomen. Most common growth pattern is exophytic and most common presentation is abnormal vaginal bleeding.

Histopathological examination is vital as it will help us to differentiate the different sub-types of cervical adenocarcinoma and moreover the prognosis also varies between different types of carcinomas. Characteristic microscopy findings that clinches the diagnosis includes the tumour cells being arranged in a papillary pattern, glandular pattern and variable amount of solid sheets. The tumour cells are usually low columnar with hyperchromatic nuclei. Presence of Nucleoli along with brisk mitotic activity. Psammoma bodies may be present. Lymphovascular invasion is frequently identified.

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. As its an aggressive neoplasm, it needs to be distuinguished histologically from other papillary carcinomas of the cervix that are associated with better prognosis, such as villoglandular papillary adenocarcinoma.[4] Few studies have reported mixed papillary serous carcinomas containing endometroid adenocarcinoma, clear cell adenocarcinoma or well differentiated villoglanular adenocarcinoma.[1]

Role of Immunohistochemistry in diagnosis of PSCC is to differentiate PSCC from other primary sites. p53 is generally positive in all serous type where as p16 is positive only in cervical adenocarcinomas. CEA (carcino embryonic antigen) is negative in papillary serous adenocarcinoma cervix compared to other variants of endocervical cancer. Negativity to ER, PR, Her 2 favours a primary cervical origin. Both our cases were strongly positive for P53 and negative for CEA, ER, PR and HER-2 thus proving that all the cases were primary papillary serous adenocarcinoma of cervix.

CONCLUSION

Papillary serous carcinoma of cervix is extremely rare and very specific type of cervical adenocarcinoma. They are aggressive tumours with unpredictable course and poor prognosis. It is usually found with lymph node metastasis and occasionally staged III or IV.[5] Role of IHC is crucial in differentiating a primary from a metastatic origin as it helps clinicians in deciding appropriate therapy for the patients. As per the recent literatures combined use of paclitaxel and carboplatin chemotherapy in PSCC seems promising.

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