



Primary Signet Ring Cell Carcinoma of Cervix - A Rare Case Report

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ABSTRACT

Introduction

Mucinous adenocarcinoma of the cervix has the subtypes of mucinous NOS, intestinal, signet ring cell and stratified mucin-producing carcinoma. Primary cervical signet ring cell carcinoma is extremely rare, and it is mostly a metastasis of cancers originating in other organs such as the stomach, breast, colon/rectum, or ovaries. To date, 31 cases of primary signet-ring cell carcinoma of the uterine cervix have been reported.

Case history

35-year-old multigravida presented with one-month history of dyspareunia. Pervaginal examination revealed polypoid 6x3 cm growth from the cervical os. Patient initially had biopsy, later underwent radical hysterectomy. **Gross:** Received radical hysterectomy and right and left PLND. Hysterectomy specimen

measuring 80x50x35mm. External surface of cervix showed an exophytic growth. Cut section showed grey tan lesion involving endocervix and both lips measuring 40x25x25 mm. Isthmus and endometrial cavity appear free of tumor.

Microscopy

Multiple sections from the lesion showed tumor in the endocervical region consisting of pleomorphic endocervical glands showing signet ring cell type of cells in single and multi-layers. Cells are arranged in diffuse discohesive sheets. PAS stain was positive in the signet ring cells.

Discussion

P16 diffuse positivity for HPV, CEA positive indicating the origin of tumor is from cervix. CK7 was positive, ER, PR and SATB2 were negative.

Mammogram, upper GI endoscopy and MRI of abdomen excluded metastatic deposits from breast, stomach and colon.

Keywords

Primary signet ring cell carcinoma of cervix, Adenocarcinoma cervix, HPV dependent adenocarcinoma, p16 in cervical carcinoma, signet ring cell carcinoma cervix.

INTRODUCTION

Primary signet ring cell adenocarcinoma cervix is extremely rare and most cases of signet ring carcinoma in the cervix are metastatic³deposits. Signet ring cell carcinoma is more commonly primary in the stomach or breast, can also arise in the colon and metastatic disease to the cervix from one of these¹ or less common sites needs to be ruled out.

Cervical cancer was the 4th most common cancer in women worldwide in 2018, with over 5,60,000 new cases per year⁴. It was also the 4th leading cause of cancer death in women, accounting for over 310000 deaths per year⁴. The incidence of cervical cancer declined in the early 2000s in developed countries due to introduction of screening, improved lifestyle change⁴. The classification of cervical adenocarcinoma was redefined by the WHO in the year 2020.

Adenocarcinoma cervix accounts for approximately 5% of all cervical carcinomas. Most endocervical adenocarcinoma are usual type and <10% are mucinous type (WHO). Of

these signet ring cell carcinomas are exceedingly rare type. A metastasis may originate more commonly from stomach followed by colon, lung, breast, appendix, gall bladder and ovaries⁶. A full metastatic workup and HPV testing is required to distinguish primary cervical signet ring cell carcinoma from metastatic deposit⁶.

To date only 31 cases of PRSCC have been reported². we report one of the rare cases presented with dyspareunia in OBG.

CASEPRESENTATION

The patient was 35-year-old woman, para 3, living 3 and had all 3 normal vaginal deliveries, presented with history of dyspareunia since one month with no other significant past history. On per speculum bimanual and rectovaginal examination uterus was normal and a bulky polypoidal growth of size measuring 6x3 cm on cervical os was noted extending into the vaginal cavity. The rectum was smooth and there was no palpable rectal extension.

MRI pelvis revealed a mildly enhancing T2 hyper intense, T1 isointense thickening measuring 57x30 x 52 mm n extent involving the distal uterine cervix, protruding into the anterior and posterior vaginal fornix. Fat planes within the urinary bladder and rectum are maintained.

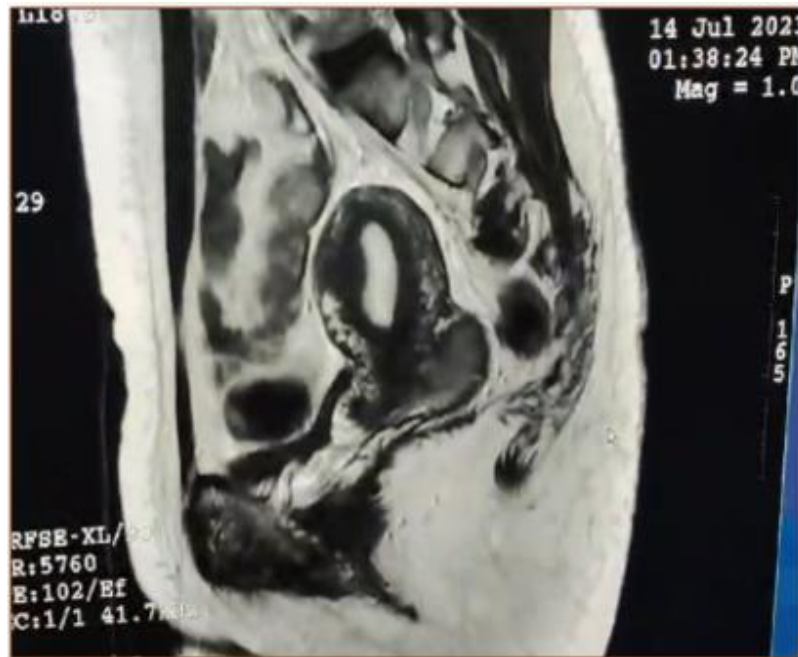


Fig. 1: MRI T2 weighted sagittal image shows 5.7 cm sized mass in cervical canal

Initially a biopsy was performed and later a radical hysterectomy was done. We received radical hysterectomy and right and left PLND. Hysterectomy specimen measuring 80x50x35mm. External surface of cervix showed an exophytic growth. Cut section showed grey tan lesion involving endocervix and both lips measuring 40x25x25 mm. Isthmus and endometrial cavity appear free of tumor.

On microscopic examination from multiple sections of the lesion showed tumor in the endocervical region consisting of pleomorphic endocervical glands showing signet ring cell type of cells in single and multi-layers. Cells are arranged in diffuse discohesive sheets. The signet ring cell dominance was >50%. Stromal invasion was noted. Tumor is extending upto ectocervix. PAS stain was positive in the signet ring cells. IHC stain for p16,

marker for high-risk HPV, showed diffuse and strong positivity. IHC expression of the estrogen receptor and progesterone receptor was negative. Also CK7 and CEA IHC markers were positive. SATB2 IHC was negative.

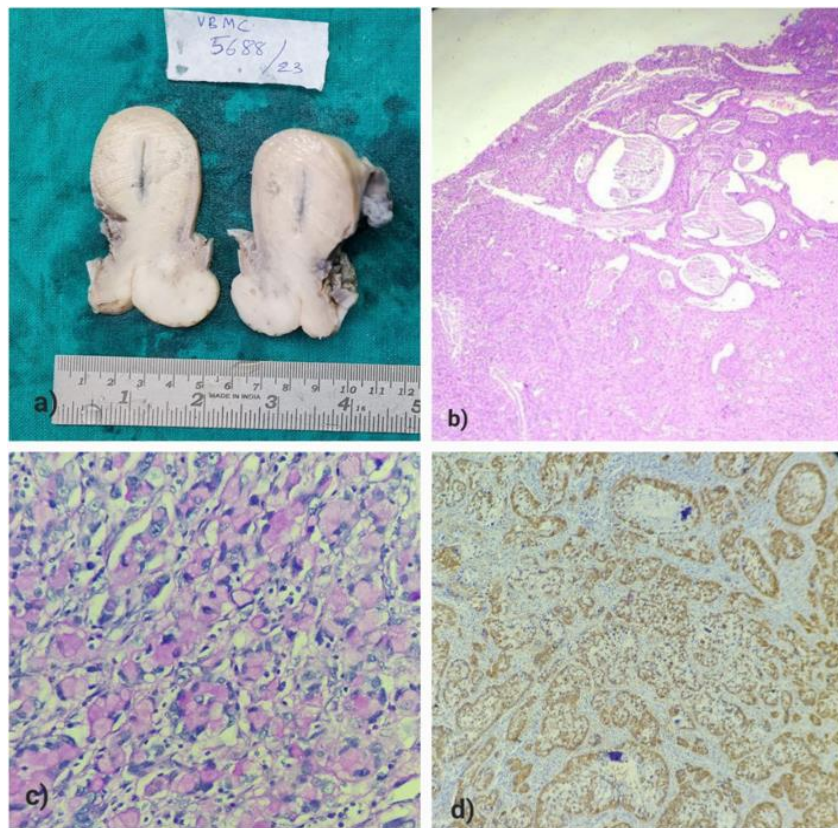


Fig. 2: a) gross specimen showing tan white lesion in the cervix. Fig b) photomicrography in H&E stain at 40 X Showing diffuse sheets of tumor cells in the ecto cervix. Fig: c) PAS stain positive discohesive cells with signet ring cells morphology. Fig: d) p16 IHC showing diffuse nuclear and cytoplasmic positivity

DISCUSSION

The most common type of cervical carcinoma is squamous cell carcinoma⁵. Adenocarcinoma represents only 10 to 25 % of cervical carcinomas. According to WHO 5th edition, adenocarcinomas are divided as HPV associated and HPV independent types. HPV associated adenocarcinomas are again divided into usual type and mucinous type. In mucinous type there are a mucinous NOS, intestinal, signet ring cell, stratified mucin producing types. Signet ring cell adeno carcinoma is defined as loose non cohesive round cells with a mucinous vacuole displacing the nucleus, representing >50 % of the tumor cells.

The rarity of this disease makes its diagnosis difficult. PSRCCC in a pure or predominant form is extremely rare, and PSRCCC usually coexists with the usual endocervical type or intestinal type⁹. In our case the signet ring cells were more than 50% and few mucinous cells in groups were noted. Special stain like PAS also demonstrated the signet ring cell morphology.

Carcinoma with signet ring cell morphology arises more commonly in the gastrointestinal tract or breast. Therefore, metastasis from these organs should be carefully ruled out. In our cases, both PET/CT and MRI abdomen and pelvis showed no evidence of

possible primary sites other than the cervix. Also, an upper GI endoscopy and mammogram showed no evidence of tumor in the respective locations. Other than the metastatic workup IHC was also proven useful to establish the origin of the tumor. IHC expression for estrogen receptor and progesterone receptor were negative. The primary cervical origin could be supported by the presence of HPV DNA. HPV infection contributes to the onset and progression of cervical cancer⁸. Our case was block-positive for p16 immunostaining. Paquette et al. reported that a positive cervical cytokeratin 7 (CK7) result is associated with high-grade cervical lesions. To date, nearly one-third of cases were positive for CK7. Therefore, CK7 may be a significant indicator. In our case also the tumor cells expressed CK7 positivity. Various studies showed that CEA was positive in adenocarcinoma of cervix³.

In our case IHC for CEA was positive and SATB2 was negative. All these IHC markers also indicated that the tumor is primary cervical neoplasm.

Cervical adenocarcinomas can present markers common to gastric, intestinal, and pancreatobiliary epithelial cells.

Prognosis of mucinous adenocarcinomas and its variants is usually less favourable¹⁰. The presence of nodal metastasis is an ominous prognostic sign. Our patient had a single pelvic lymph node metastasis. She was staged as stage IIIC1 and now on combination of adjuvant radiotherapy and chemotherapy.

CONCLUSION

A complete tumor survey should be performed to exclude the possibility of metastasis from another organ. A combination of patient history, clinical presentation, physical examination, imaging, endoscopic findings, and pathology and IHC are essential to distinguish PCSRCC from other primary sites.

ABBREVIATIONS

CK7 -	Cytokeratin 7
HPV -	Human papilloma virus
ER -	Estrogen receptor
PR -	Progesterone Receptor
CEA -	Carcinoembryonic antigen
SATB 2 -	Special AT rich sequence binding protein
MRI -	Magnetic Resonance Imaging
PET -	Positron Emission Tomography

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