

## Primary Vaginal Clear Cell Adenocarcinoma: Case Report with Literature Review

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### Abstract

### Case Report

Very few cases of Primary Vaginal Clear cell Adenocarcinoma (PVCAA) have been reported in literature. A multiparous lady aged 52 years presented with bleeding per vaginum for 1 week. On examination 3x3 cm ulceroproliferative growth involving lower third with subvaginal extension seen. On colposcopy cervix was normal. The uterus and ovaries were normal on imaging. Biopsy from the mass revealed Clear Cell carcinoma. She underwent radical vaginectomy, distal urethral resection (approx 3cm), bilateral groin node dissection and lotus flap reconstruction of defect. Histopathology showed Clear Cell Carcinoma of vagina, Stage III. Adjuvant chemotherapy with cisplatin and paclitaxel 3 weekly for 6 cycles was followed by adjuvant External Beam Radiotherapy. Patient had presented with occasional involuntary dribbling of urine following the surgery which was managed with foleys catheterisation. The incontinence resolved without any intervention one month following radiotherapy. The patient has been recurrence free for past 3 years. The tumour board faced difficulty in taking decisions due to dearth of reported cases and consensus guidelines, prompting the authors to report the case.

**Keywords:** Vaginal cancer, vulvectomy, radiotherapy, chemotherapy, clear cell adenocarcinoma.

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## INTRODUCTION

Primary Vaginal Clear Cell Adenocarcinoma (PVCCA), also known as mesonephroid cancer, has been historically linked to Diethylstilbesterol (DES). It accounts for 5-10% of primary vaginal cancers. It has a bimodal age distribution: 22yrs in those associated with DES, but also seen in 55year old with no such history. There are cases reported in the literature where PVCAA has been associated with pelvic endometriosis [1]. PVCCA most commonly involves the anterior wall of the upper third of vagina, corresponding to the most frequent site of adenosis, with which it has been associated [2].

## CASE REPORT/CASE PRESENTATION

A 52-year-old multiparous (P<sub>2+0+0+2</sub>) lady presented with burning micturition and vaginal bleeding for a week. She had no history of menstrual irregularities, dysmenorrhoea, previous bad obstetric history or miscarriages. She had moderate pallor, Eastern Cooperative Oncology Group (ECOG) Performance Status of 1, with no comorbidities. No

clinical supraclavicular, axillary or inguinal lymph nodes were noted. There was no calf tenderness.

Genital examination revealed a 3x3 cm ulceroproliferative growth involving lower 1/3<sup>rd</sup> of anterior vagina, clitoris with clinical involvement of the subvaginal tissue. Clitoris was also involved (Figure-1). No palpable inguinal lymph nodes were noted. No mass was palpable abdominally. On per speculum examination, cervix was healthy. Bimanual examination revealed a normal sized uterus with no adnexal mass. Per rectal examination was normal. Colposcopy examination of the cervix was adequate and swede score of 2 with no acetowhite changes. Biopsy from the mass showed clear cell adenocarcinoma.

Contrast enhanced MRI pelvis revealed a lobulated heterogeneous mass lesion involving the distal vagina. The lesion, measuring 3.4x2.4 cm, appeared hypointense on T1 and hyperintense on T2weighted images. It involved the distal urethral orifice with approximate 2cm distance from the bladder neck or the interna. Enlarged inguinal lymph nodes were seen on the left side, the largest measuring 1.5cm. No pelvic lymphadenopathy. Uterus, ovaries, and

urinary bladder were normal. A contrast-enhanced computed tomography thorax and whole abdomen was normal. Cystoscopy revealed that the urethral meatus was involved but the urinary bladder and rest of the urethra was uninvolved. Ultrasound guided Fine Needle Aspiration Cytology (FNAC) from the inguinal nodes was inconclusive.

The case was presented to the tumour board and decision for radical vulvectomy with excision of distal vagina with inguinal lymphadenectomy was taken. In case the patient has urinary incontinence after excision of distal urethra, a second procedure for urinary diversion would be planned.

She underwent radical vulvectomy, distal vaginectomy, resection of distal urethra (~3cm) with bilateral inguinal lymphadenectomy and lotus flap reconstruction of the defect (Figure-2). Intraoperative and postoperative period was uneventful (Figure-3). However, she developed continuous urinary incontinence which was assumed to be due to intrinsic sphincter deficiency following distal urethral resection. On urology consultation, it was planned that a second surgery may be needed after completion of adjuvant treatment.

Histopathological examination revealed invasive moderately differentiated adenocarcinoma with clear cell changes. Tubular and glandular architectural pattern, with cells having abundant clear cytoplasm, vesicular chromatin, hob-nailing seen. Tumour free margin was 2mm. Lympho-vascular emboli seen but no perineural invasion seen. Right sided inguinal node (0/13) showed reactive hyperplasia and one left sided inguinal lymph node showed metastatic adenocarcinoma (1/9). The staging was ascertained as stage III. Immunohistochemistry was not done due to logistic issues.

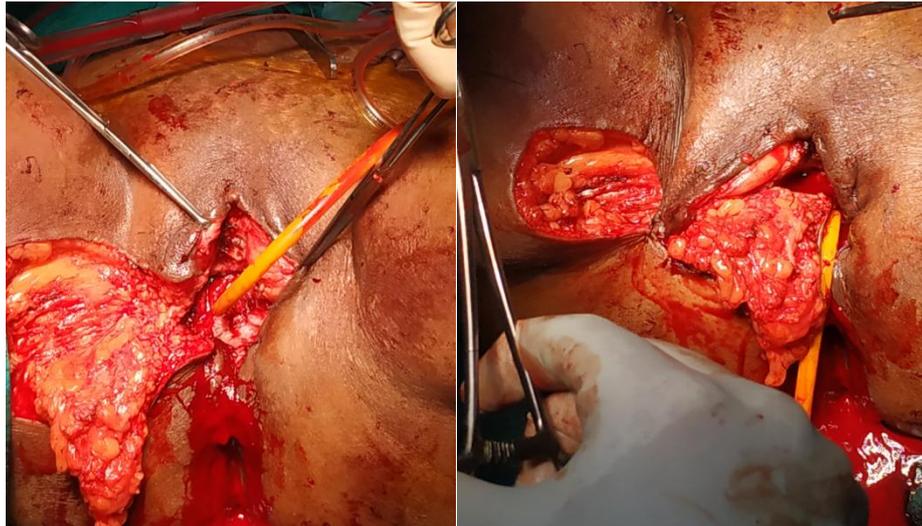
Tumour board decision was adjuvant chemotherapy with radiotherapy. She received adjuvant chemotherapy regimen with cisplatin with paclitaxel

every 3 weeks for 6 cycles. Post chemotherapy, removal of the catheter was tried, but she still remained incontinent. Decision was taken to retain the catheter. She then received adjuvant External Beam Radiotherapy (EBRT) of 50Gy in 25 fractions to pelvis in Linear Accelerator 6MV by conformal planning with Intensity-Modulated Radiation Therapy (IMRT). After the radiotherapy was completed, on removing the catheter she became continent again with no surgical intervention. She has been disease free till date and survival period of 36 months since the time of diagnosis.

Incidentally her 35-year-old daughter, was diagnosed with a complex ovarian mass while her mother was undergoing treatment at our institute. Her CA125 was 1931 IU/ml. She underwent laparotomy followed by total abdominal hysterectomy and bilateral salpingo-oophorectomy and Infra-colic Omentectomy. Intraoperatively, the mass was diagnosed as a 10cm x 10cm endometrioma. Histopathology revealed Ovarian Endometriotic cyst with focal areas of dysplasia (Immunohistochemistry - benign). She is under follow-up at present.



**Fig-1: Clinical presentation**



**Fig-2: Intraoperative pictures: Vulvectomy followed by lotus flap reconstruction**



**Fig-3: Postoperative day 21**

**Table-1: Literature review of previously reported cases of PVCAA**

	Reported by	Age	Vaginal adenosis	Mullerian anomalies	DES	Surgery	Radiotherapy	Chemotherapy	Stage	Disease free Survival
1	Uehara T <i>et al.</i> , 2010	54	No	Yes	No	Anterior pelvic exenteration	No	No	I	43 months
2	Zeesan-uddin <i>et al.</i> , 2009	27	No	Yes	No	Wertheim's hysterectomy+ partial vaginectomy + pelvic lymph node dissection	Not Mentioned	Not Mentioned	III	Not reported
3	Bhattacharya <i>et al.</i> , 2016	45	No	Yes	No	Hysterectomy + removal of pelvic lymph nodes.	None	None	I	2 months
4	Sachan <i>et al.</i> , 2013	27	No	No	No	Radical hysterectomy + vaginectomy + lymph node dissection	No	No	I	Not reported

	Reported by	Age	Vaginal adenosis	Mullerian anomalies	DES	Surgery	Radiotherapy	Chemotherapy	Stage	Disease free Survival
5	Mufti <i>et al</i> 2014	9	No	No	No	Surgical resection	No	No	IVB	Died shortly after surgery
6	Mufti <i>et al</i> 2014	27	No	No	No	Neoadjuvant radiotherapy followed by hysterectomy	Neoadjuvant	No	III	24 months
7	Hasanzadeh <i>et al.</i> , 2019	49	No	No	No	Radical hysterectomy with excision of ~ 4 cm of the vaginal wall + bilateral oophorectomy +pelvic and paraaortic lymph node dissection	Concurrent Chemoradiotherapy	No	III	10 months
8	Pang <i>et al.</i> , 2019	45	Yes	No	No	wide local resection	No	No	I	20 months
9	Mei <i>et al.</i> , 2020	41	No	Yes	No	Radical hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy	No	No	I	17 months
10	Güzin <i>et al.</i> , 2006	23	No	No	No	No	Yes	Yes	II	14 months
11	Cello <i>et al.</i> , 2019	28	No	Yes	No	Oocyte cryopreservation > laparoscopic pelvic lymphadenectomy. Uterus, tubes, and ovaries preserved. Wide local excision of vagina with resection of septum	Yes	No	I	60 months
12.	Watanabe <i>et al.</i> , 2000	63	No	No	No	No	No	No	IV B	1 month

## DISCUSSION/ CONCLUSION

The tumour board faced difficulty in coming to an agreement regarding the extent of surgery and requirement of adjuvant chemotherapy, however the decision for adjuvant radiotherapy was unanimous. Review of literature shows that surgery is the mainstay of treatment for early localised disease however there is disparity in the type of surgery performed, ranging from anterior exenteration, radical hysterectomy to wide local excision (Table-1). There was no consensus regarding pelvic or inguinal lymph node dissections. Adjuvant radiotherapy is recommended for the cases which more than stage I at the time of diagnosis. Adjuvant chemotherapy was used in only one of the patients out of the 12 analysed case reports [1-12].

Vaginal adenosis is associated with PVCCA in 90% cases, suggesting adenosis to be a precursor lesion [3]. In retrospective study, it was found that 69.4% of the analysed patients with genitourinary tract malformations had adenocarcinoma of the lower genital tract [13]. This suggested that genitourinary anomalies were associated with an increased risk of adenocarcinoma, but the mechanism was not clear. There is no definite history of DES exposure in this

patient. There was no evidence of vaginal adenosis or any Mullerian anomalies in this case.

Frank *et al* assessed the outcomes of 26 patients with Primary non-DES-associated adenocarcinoma of the vagina (NDAV) and compared with it with patients with squamous cell carcinoma (SCC) of the vagina treated similarly over the same period. At 5 years, the overall survival rates of patients with NDAV and SCC were 34% and 58%, respectively ( $p < 0.01$ ). Patients with NDAV had a significantly worse pelvic disease control rate than patients with SCC (31% vs. 81%;  $p < 0.01$ ). At 5 years, 39% of patients with NDAV and 15% with SCC had developed distant metastasis ( $p < 0.01$ ) [14]. Tanaka *et al.*, concluded that the 5-year survival rates were 91%, 80%, 37%, and 0% for stages 1, 2, 3, and 4 tumours in PVCCA respectively [15].

**Conflict of Interest Statement:** None

**Funding Sources:** None

**Compliance with Ethical Standards**

- Disclosure of potential conflicts of interest- None

- Research involving Human Participants and/or Animals- The patient received standard of care treatment
- Informed consent- Informed consent from the patient was obtained before preparing the manuscript.

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