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CASE REPORT

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Human papilloma virus associated primary vaginal adenocarcinoma

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Abstract

Primary vaginal adenocarcinoma associated with human papillomavirus (HPV) infection is extremely rare. We report a case of primary adenocarcinoma of the vagina associated with human papilloma virus successfully treated with anterior pelvic exenteration and adjuvant concurrent chemoradiation therapy. A 51-year-old postmenopausal woman (gravida 1, para 1) presented with intermittent vaginal bleeding and pelvic pain. She was found to have a 5 $\times$ 5 cm necrotic tumor took up the vaginal. She had no previous history of antenatal exposure to diethylstilbestrol (DES). Pelvic magnetic resonance imaging (MRI) demonstrated a 4.8 $\times$ 6.0 cm mass in the vaginal canal, an 1.1 $\times$ 2.6 cm mass at the urinary bladder dome and a 1.1 cm irregular lymph node at the right external iliac chain with increased fluorodeoxyglucose (FDG) uptake from Fused whole-body positron emission tomography-computed tomography (PET-CT). Based on clinical investigations, the patient was diagnosed with a primary adenocarcinoma of vagina, staged International Fedestration of Gynecology and Obstetrics (FIGO) IVa. Anterior pelvic exenteration, simple vulvectomy, total vaginectomy, both pelvic lymph node dissection, and para-aortic lymph node dissection with ileal conduit urinary diversion (Bricker's operation) was done. Histologically primary vaginal HPV type 16-associated adenocarcinoma was confirmed. Both obturator lymph node was positive for metastasis. Postoperatively, the patient received weekly cisplatin regimen administered with a dose of 40 mg/m^2 on day 1 of external radiation therapy (RT), 1 to 4 hours before RT initiation. External beam pelvic RT dose prescription to the whole pelvis was 59.4 Gy in 33 fractions at the isocenter. But, after total dose of 43.2 Gy, patient complained severe bowel habit change and discontinued further treatment. The patient remains free from recurrence 8 months after initial surgery. In the lack of information and comparative analysis of management options for the more unusual and rare varieties of primary vaginal neoplasms in the literature, this suggests the possibility that surgical treatment may be preferentially selected on a case-by-case basis.

Keywords

Primary vaginal cancer; Primary vaginal adenocarcinoma; Anterior pelvic exenteration; Adjuvant concurrent chemoradiation therapy

1. Introduction

Primary vaginal cancer is a rare tumor, representing only 1% to 2% of all gynecologic malignancies [1]. Adenocarcinoma compromise approximately 8% to 10% of primary vaginal cancer [2]. Most vaginal cancer, 80% to 90%, represents metastasis from other primary gynecologic and non-gynecologic sites. Thus, vaginal adenocarcinoma must be differentiated from metastatic adenocarcinomas.

Primary vaginal adenocarcinoma associated with HPV infection is extremely rare. To our knowledge, only four cases were reported [3]. We report a case of primary adenocarcinoma of the vagina associated with HPV successfully treated with anterior pelvic exenteration and adjuvant concurrent chemoradiation therapy (CCRT). Because of the diagnostic and management problems, the case is reported.

2. Case report

A 51-year-old postmenopausal woman (gravida 1, para 1) presented to a local hospital with intermittent vaginal bleeding and pelvic pain. She was found to have a necrotic tumor in the upper one third of the vagina and was referred to the gynecologic department of Saint Vincent's Hospital in April 2020. She experienced menopause at 50 years of age, and had no previous history of antenatal exposure to DES.

The external genitalia were normal and there was no suspicious inguinal lymphadenopathy. Vaginal examination re-

vealed a necrotic, nontender tumor measuring 5 × 5 cm in the posterior vaginal wall. Because the tumor took up the entire vaginal canal, the uterine cervix was not detected and transvaginal ultrasonography could not be performed. Recto-vaginal examination suggested that rectum was free from the lesion.

Pelvic MRI demonstrated a 3.4 × 4.8 × 6.0 cm mass in the vaginal canal with the paravaginal infiltration at the left side of the mass arising from the anterior wall of the vagina with encasement of the entire urethra (Fig. 1A). An 1.1 × 2.6 cm mass is identified at the urinary bladder dome (Fig. 1B). An 1.1 cm irregular lymph node is noted at the right external iliac chain (not shown). Fused whole-body PET/CT shows increased FDG uptake along the vaginal canal and focal FDG activity at the right external iliac chain regarded as FDG-aid malignant tumor and suspicious metastatic lymph node (Fig. 1C).

Mammography, gastroscopy, colonoscopy and PET-CT demonstrated no metastases, other than the tumor within the vagina. The laboratory data did not demonstrate anemia, and liver function tests, renal function tests were normal. Serum Carcinoembryonic Antigen (CEA) level was 0.88 ng/mL (normal <1~5), and serum Squamous Cell Carcinoma (SCC) Ag level was 1.5 ng/mL (normal 0~1.5) within normal range.

Based on clinical findings and investigations, patient was diagnosed with a primary adenocarcinoma of vagina, staged FIGO IVa. After a multidisciplinary team meeting, the primary surgery was decided upon because the disease was highly advanced but localized and ultimately performed was anterior pelvic exenteration, simple vulvectomy, total vaginectomy, both pelvic lymph node dissection, and para-aortic lymph node dissection with ileal conduit urinary diversion (Bricker's operation) in consultation with the urology surgeons.

On gross examination, a 4.9 × 4.1 cm sized main mass at the anterior vagina was directly invaded into the urinary bladder wall. A secondary mass measured 2.3 × 1.6 cm noted at the bladder dome. The uterine cervix was intact. Microscopically, both masses had identical histologic features as adenocarcinoma. On immunohistochemistry, the tumor cells were positive for Cytokeratin 7 (CK7) and cyclin-dependent kinase inhibitor 2A (p16), and negative for CK20 and Caudal Type Homeobox 2 (CDX-2) (Fig. 1D–F). HPV type 16 was detected on real-time Polymerase Chain Reaction (PCR), confirming the diagnosis of primary vaginal HPV-associated

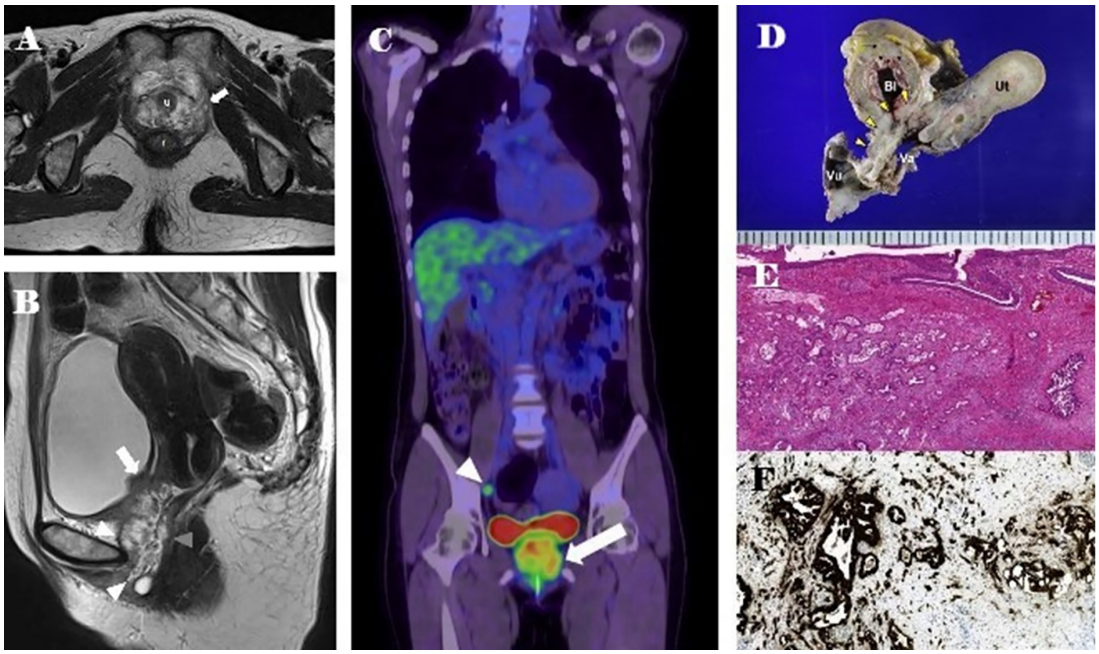

FIGURE 1. Imaging tests and Pathology. (A) Axial T2-weighted magnetic resonance (MR) image demonstrates a heterogeneous, 3.4 × 4.8 × 6.0 cm, high-signal-intensity mass at the vagina and posterior aspect of urethra (u). This mass shows the paravaginal infiltration at left side of the mass (arrow). (B) Sagittal T2-weighted MR image shows a heterogeneous high-signal-intensity mass (white arrow heads) arising from the anterior wall of the vagina with invasion of the urethra and posterior vaginal wall (grey arrow head). Direct tumor invasion of the urinary bladder is suspected (arrow). (C) Coronal fused fluorodeoxyglucose (FDG) positron emission tomography (PET)/computed tomography (CT) image shows heterogeneous increased tracer uptake along the vaginal canal, below the bladder base (arrow) and focal FDG uptake in the right external iliac chain (arrow head). (D–F) Pathologic features. (D) Gross findings of the anterior pelvic exenteration specimen consisted with the uterus (Ut), vagina (Va), vulva (Vu) and urinary bladder (Bl). A 4.9 × 4.1 cm sized white colored ill-defined main mass (arrowhead) is located at the anterior vagina showing direct invasion into the urinary bladder. The uterine cervix is intact and has a smooth surface. A secondary white colored nodular solid mass (arrow) is noted at the bladder dome. (E) Histologic findings of the main mass infiltrating the urethra. Glandular differentiation is predominant on the left with focal papillary features on the right (hematoxylin & eosin, ×40). (F) Immunohistochemistry for p16 revealed a diffuse block positive pattern, confirming human papillomavirus (HPV) association (×100).

adenocarcinoma. Out of the retrieved 27 pelvic lymph nodes, both obturator lymph nodes were positive for metastasis.

Postoperatively, the patient received weekly CCRT. Weekly cisplatin regimen administered with a dose of 40 mg/m^2 on day 1 of external RT, 1 to 4 hours before RT. Initiation, External beam pelvic RT dose prescription to the whole pelvis was 59.4 Gy in 33 fractions at the isocenter. But, after total dose of 43.2 Gy, patient complained severe bowel habit change and discontinued further treatment. The patient remains free from recurrence 8 months after initial surgery although fell once into an AKI (acute kidney injury) state due to urostomy site infection, she recovered through conservative care.

3. Discussion

The malignant histologies of the vagina are so rare that randomized clinical trials have not been undertaken and there are no National Comprehensive Cancer Network (NCCN) guidelines for vaginal cancer. Instead, some retrospective studies and case reports can be found. Treatment differs from case to case. Thus, standard treatment for vaginal cancer is not well established [4].

In most cases, especially in the advanced stages, radiation is the cornerstone of treatment for this disease and consists of a combination of external beam radiation (EBRT) and intracavity radiation therapy (ICRT) or brachytherapy. The main advantage of radiation is organ preservation. Modern management of vaginal cancer often combines concurrent chemotherapy such as cisplatin or 5 FU. The combination of EBRT and brachytherapy to a total dose of 70–80 Gy with concomitant weekly cisplatin-based chemotherapy is the current standard of care for locally advanced vaginal cancer.

Surgery may be possible for localized lesions and pelvic exenteration may play a role in patients with stage IV disease with recto-vaginal or vesico-vaginal fistula. In this case, the surgery may be done with pelvic node dissection. Another scenario where pelvic exenteration may play a role is when a patient has a central recurrence after radiation therapy [1].

In summary, we encountered an extremely rare case of primary vaginal adenocarcinoma without any evidence of cervical cancer. A successful anterior pelvic exenteration, total vaginectomy and simple vulvectomy was performed without any serious perioperative complication. In the lack of information and comparative analysis of management options for the more unusual and rare varieties of primary vaginal neoplasms in the literature, this suggests the possibility that surgical treatment may be preferentially selected on a case-by-case basis.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

JoY—the design of study and Responsible Surgeon; AL, JiY, CY and SK—the reference collection and manuscript preparation was done; SI—description on pathological findings was prepared; HAK—radiological findings and significance were described by.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This is a report by using already existing data which does not reveal the subjects' identification from the result and a case report for single case. In accordance with the CHRPP106-109 (Catholic Central Medical Center Human Research Protection Program) review exemption regulation, the IRB (St. Vincent's Hospital Institutional Review Board) administrator reviewed the checklist and confirmed that this case report is exempted the review under the approval of the IRB chairperson. Patient consent form has already been waived by IRB.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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