Primary endometrioid adenocarcinoma of the vagina after total hysterectomy for adenomyosis: A case report

TINGTING WANG[1], XIN LI[1], LIPING CHEN[1], JING ZHANG[1], LINA PENG[2] and HAITAO YANG[3]

[1]Department of Gynecology, Women and Children's Hospital Affiliated to Ningbo University, Ningbo, Zhejiang 315000, P.R. China;
[2]Department of Imaging, Women and Children's Hospital Affiliated to Ningbo University, Ningbo, Zhejiang 315000, P.R. China;
[3]Department of Histopathology, Ningbo Clinical Pathology Diagnosis Center, Ningbo, Zhejiang 315000, P.R. China

Received February 25, 2026; Accepted April 16, 2026

DOI: 10.3892/ol.2026.15650

Abstract. Primary vaginal cancer is a rare malignant tumor; its pathogenesis remains unclear and only a limited number of cases have been documented in the literature. The present report outlines a rare case of primary vaginal endometrioid adenocarcinoma that occurred in a patient 3 years after a total hysterectomy for uterine adenomyosis. Pathogenesis, clinical features, diagnosis, treatment and prognosis are discussed to improve clinical recognition and management of this rare condition. A 49-year-old female patient who had undergone a total hysterectomy for uterine adenomyosis 3 years earlier presented with postcoital vaginal bleeding. Gynecological examination identified a mass in the vaginal stump. A biopsy revealed low-grade vaginal adenocarcinoma. The patient underwent an extensive laparoscopic parametric resection, partial upper vaginectomy, pelvic lymph node dissection and bilateral oophorectomy. The postoperative pathology determined a diagnosis of primary vaginal endometrioid adenocarcinoma. Concurrent chemoradiotherapy was initiated 6 weeks after surgery. At the last follow-up (15 months postoperatively), the patient was in good general condition with no evidence of recurrence. The present case indicates that long-term surveillance of the vaginal stump is valuable for patients who have undergone total hysterectomy for benign uterine diseases, as it allows early detection of vaginal stump lesions. In particular, for patients with a history of other malignant tumors, specific attention should be paid to the genetic susceptibility of the underlying tumor.

Correspondence to: Dr Jing Zhang, Department of Gynecology, Women and Children's Hospital Affiliated to Ningbo University, 339 Liuting Street, Haishu, Ningbo, Zhejiang 315000, P.R. China
E-mail: zhangjyy1978@163.com

Abbreviations: PVC, primary vaginal cancer; HPV, human papillomavirus; DES, diethylstilbestrol; TCT, ThinPrep cytology test; CA125, cancer antigen 125

Key words: adenomyosis, hysterectomy, primary vaginal cancer, endometrioid adenocarcinoma, case report

Introduction

Primary vaginal cancer (PVC) is a rare malignancy, accounting for 1-2% of all gynecological malignancies and 10% of vaginal malignancies (1). Furthermore, ~90% of primary vaginal malignancies are squamous cell carcinomas, primarily associated with persistent high-risk human papillomavirus (HPV) infection, particularly HPV16 and HPV18 (2). Vaginal adenocarcinoma accounts for 8-10% of cases and is not considered to be associated with HPV infection (3). Additional rare pathological types include melanoma, lymphoma and sarcoma. Previous epidemiological cohort studies and population-based surveillance studies have consistently shown that intrauterine exposure to diethylstilbestrol (DES) during early pregnancy (within 16 weeks of gestation) is associated with the development of cervical or vaginal clear cell adenocarcinoma in female offspring (4-6). Since the discontinuation of DES use during pregnancy, the incidence of DES-related clear cell adenocarcinoma has decreased markedly (7). However, non-DES-associated vaginal adenocarcinoma, including endometrioid or mucinous subtypes arising from endometriosis, remains rare and occurs more frequently in postmenopausal women, with a median age at diagnosis of 60-68 years, as documented in recent epidemiologic reviews (8). Total hysterectomy is an important risk factor for PVC, with 20-30% of such procedures being performed for cervical precancerous lesions (9). Therefore, regular gynecological follow-up is still recommended, even after hysterectomy, for benign uterine diseases. The present report outlines a case of vaginal endometrioid adenocarcinoma occurring after a total hysterectomy for uterine adenomyosis, which represents a rare clinical event. The previous treatment history, clinical manifestations, diagnosis, treatment and prognosis of the patient are described in detail (Fig. 1). Based on the history and clinical course of the patient, the aim of the present report was to improve the clinical understanding of this condition and provide a reference for further exploration of the molecular mechanisms underlying PVC.

Case report

A 49-year-old woman presented to the Department of Gynecology at the Women and Children's Hospital Affiliated

to Ningbo University (Ningbo, China) in April 2020 with a 1-year history of menorrhagia and dysmenorrhea. Ultrasonography revealed an anteflexed uterus measuring ~87x89x87 mm. The posterior uterine wall was diffusely thickened, with a hypoechoic lesion of 37x28x39 mm showing heterogeneous echotexture and poorly defined borders in the posterior myometrium. Color Doppler flow imaging demonstrated a semi-ring blood flow signal around the lesion. The remaining myometrium exhibited coarse and uneven echoes. The double-layer endometrial thickness was 6 mm, with a three-dimensional ultrasound revealing a normal inverted triangular uterine cavity (Fig. S1).

Gynecological examination identified the presence of a cervical mass. Cervical cancer screening, including gynecological cervical cytology was performed using Papanicolaou-stained ThinPrep cytology test (TCT), showing no malignant cells, and HPV testing was negative. The patient was therefore diagnosed with uterine adenomyosis and a cervical neoplasm. After excluding contraindications, cervical mass resection, diagnostic curettage and placement of a Mirena® (Bayer) levonorgestrel-releasing intrauterine system (LNG-IUS), were determined to be the most appropriate therapeutic plan and were subsequently performed in May 2020. Pathological examination of the cervical mass exhibited features consistent with a cervical polyp with squamous metaplasia, and pathological analysis of the endometrial curettage specimen revealed a small amount of endometrium with proliferative changes (Fig. 2). For this analysis, tissue specimens were fixed in 4% paraformaldehyde at room temperature for 24 h, embedded in paraffin, sectioned at a 4-μm thickness and stained with H&E according to standard histological protocols (10). Sections were deparaffinized, rehydrated, stained with hematoxylin, differentiated, blued and counterstained with eosin. The H&E-stained sections showed characteristic morphology, including fibrovascular stroma with cystically dilated glands and chronic inflammatory cell infiltration. The surface epithelium exhibited columnar epithelium with focal squamous metaplasia. Morphological features were observed and captured using a light microscope (BX53; Olympus Corp.). Postoperatively, goserelin (3.75 mg) was injected subcutaneously once and dienogest (2 mg) was administered orally once daily for 28 days. Following this 28-day course, dienogest was continued orally without interruption until a follow-up ultrasound examination was conducted in July 2021. After treatment, menstrual flow decreased notably. No other major adverse events or additional surgical interventions occurred during this period.

Owing to the patient's good clinical tolerance, absence of severe symptoms, and stable general condition during treatment, regular follow-up ultrasound evaluation was not performed until July 2021. Subsequent ultrasonography showed that the uterus had enlarged to 90x124x98 mm and the hypoechoic lesion in the posterior myometrium had increased to 65x47x65 mm with slightly ill-defined borders, suggesting progression of the adenomyosis (Fig. S2). Goserelin (3.75 mg) was administered subcutaneously every 28 days for three consecutive courses before surgery. Subsequently, a laparoscopic total hysterectomy, bilateral salpingectomy and pelvic adhesiolysis were performed in November 2021. Postoperative pathological findings were as follows: i) Uterine adenomyosis and leiomyoma; ii) chronic cervicitis; iii) senile atrophic endometrium; and iv) normal left and right fallopian tubes (Fig. 3). Between November 2021 and June 2024, no further treatments, imaging examinations or routine clinical follow-ups were conducted for the present patient, primarily due to the patient's personal reasons and loss to clinical follow-up during this period.

In June 2024, the patient experienced postcoital vaginal bleeding characterized by small volumes of bright red blood with no abdominal pain. The patient once again presented to the Women and Children's Hospital Affiliated to Ningbo University (Ningbo, China) and a gynecological examination revealed a hard nodule at the vaginal apex. HPV testing was negative. TCT showed atypical glandular cells favoring neoplasia and the diagnosis was reported in accordance with the 2014 Bethesda System for Reporting Cervical Cytology (11) (Fig. S3). A vaginal biopsy was performed under colposcopy. Pathological examination revealed poorly differentiated adenocarcinoma on both the left and right vaginal walls (Fig. 4). The patient was then diagnosed with low-grade vaginal adenocarcinoma and was advised to undergo further surgical treatment, for which the patient was admitted in July 2024. Physical examination showed a patent vagina with an erosion-like mass at the vaginal apex, ~2.0 cm in diameter and firm in consistency. No pelvic tenderness was observed. A combined rectovaginal-abdominal examination further determined smooth rectal mucosa and soft bilateral parametrial tissues. Preoperative evaluation revealed no notable abnormalities in serum levels of cancer antigen 125 (CA125), squamous cell carcinoma antigen, α-fetoprotein, carcinoembryonic antigen or CA19-9, all of which were measured in peripheral venous blood samples.

Computed tomography of the urinary tract showed postoperative pelvic changes, including a cyst in the left pelvic wall (interpreted as a lymphatic retention cyst) and thickening of the vaginal stump (Fig. 5). Contrast-enhanced MRI revealed a punctate soft-tissue shadow on the left posterior vaginal wall, with a slightly high signal intensity on T1-weighted imaging, a moderately high signal on T2-weighted imaging and a notably high signal on diffusion-weighted imaging. The lesion showed obvious enhancement after contrast administration, with unclear boundaries to the vaginal wall and a slight irregularity of the outer vaginal wall, highly suggestive of a malignant tumor of the vaginal stump (Fig. 6). The patient had no family history of malignant tumors but had undergone a unilateral thyroidectomy for thyroid cancer in 2019.

In July 2024, the patient underwent an extensive laparoscopic parametric resection, upper vaginectomy, pelvic lymph node dissection and bilateral oophorectomy. Surgical specimens were fixed in 10% neutral buffered formalin at room temperature (20-30˚C) for 24 h, followed by dehydration through a graded ethanol series, clearing in xylene and embedding in paraffin. Tissue sections at a 4- to 5-μm thickness were cut, deparaffinized in xylene, rehydrated through a graded ethanol series and stained with H&E. Sections were stained with hematoxylin at room temperature for 5 min, followed by counterstaining with eosin at room temperature for 1 min. No additional blocking reagent was used for H&E staining. Finally, the sections were mounted with neutral resin and examined under a light microscope. Pathological analysis

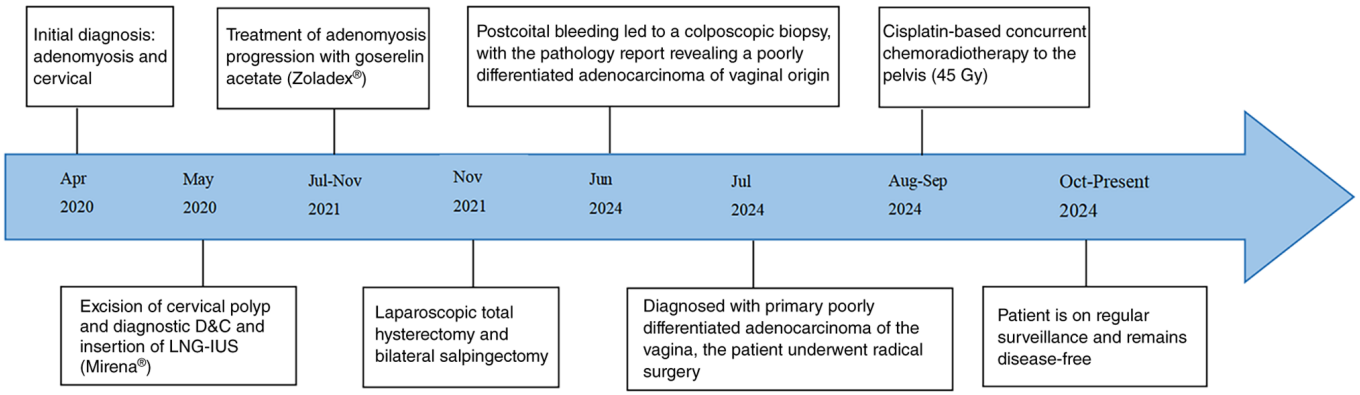

Figure 1. Clinical timeline summarizing the disease course. Schematic illustrating the entire process from the initial diagnosis, progression of the disease and discovery of vaginal stump lesions, through to surgery, radiotherapy and chemotherapy. D&C, dilation and curettage; LNG-IUS, levonorgestrel-releasing intrauterine system.

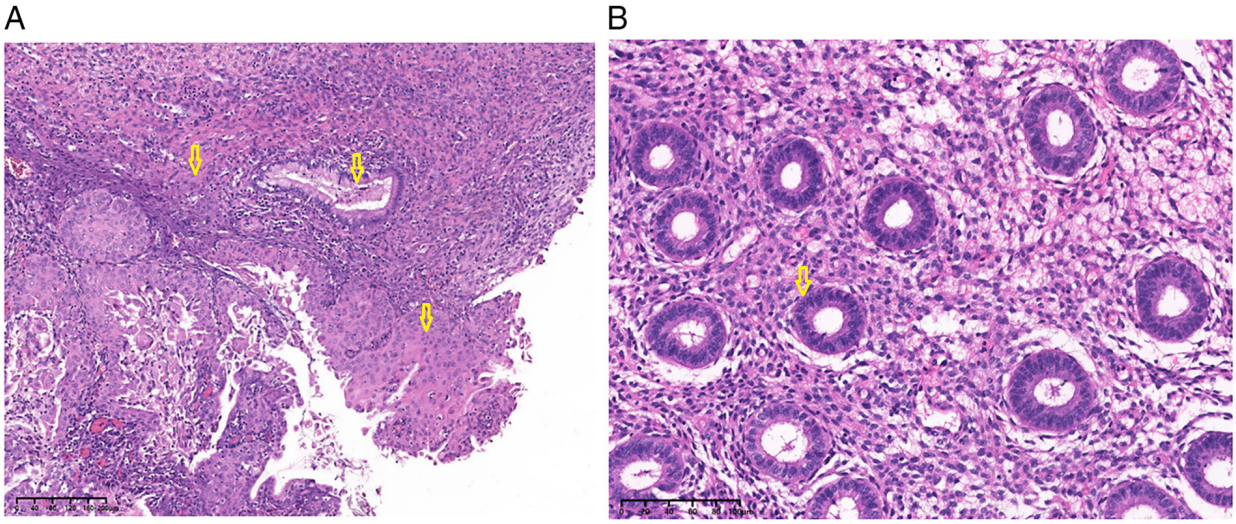

Figure 2. Histopathological features of a cervical polyp. (A) H&E-stained section showing characteristic morphology. In the upper left quadrant (arrow) fibrovascular stroma shows dense chronic inflammatory cell infiltration. The mid-upper field contains cystically dilated glands (arrow). The lower right area (arrow) shows the surface epithelium with focal squamous metaplasia overlying columnar epithelium (magnification, x10; scale bar, 200 μm). (B) H&E-stained section of an endometrial curettage specimen. Pathological analysis revealed a small amount of endometrium with proliferative changes (arrows) (magnification, x20; scale bar, 100 μm).

revealed that the vaginal tumor was 2.5x2.0x1.5 cm in size and was diagnosed histologically as a poorly differentiated adenocarcinoma. The tumor infiltrated the full thickness of the vaginal wall into the surrounding fibrous and adipose tissue, with the following analysis results: Vascular invasion, positive; perineural invasion, positive (Fig. 7); left parametrium, negative; right parametrium, negative; and vaginal resection margin, negative; bilaterial ovaries, follicular cyst of the left ovary and right ovary unremarkable; lymph node metastasis, right obturator + internal iliac (0/3), right external iliac (0/1), right common iliac (0/1), right inguinal (0/6), left obturator + internal iliac (0/3), left external iliac (0/1), left common iliac (0/3) and left inguinal (0/10). Based on clinical, imaging and histopathological findings, the tumor was classified as a FIGO 2009 stage I PVC (12), with a final diagnosis of cT1N0M0 poorly differentiated primary vaginal adenocarcinoma according to the AJCC 8th edition staging system (13).

Postoperative radiotherapy was then recommended for the patient. Concurrent chemoradiotherapy was initiated 6 weeks after surgery and consisted of 60 mg of cisplatin once a week for 4 weeks with intensity-modulated radiotherapy totaling 45 Gy in 25 fractions (completed in September 2024). At 3, 5, 9, 13 and 15 months after surgery, follow-up examinations, including tumor markers (such as CA125), pelvic ultrasound and TCT, were all unremarkable (Table I; Fig. 8). The patient has since remained in good condition with no evidence of recurrence.

Discussion

PVC is defined as a strictly confined malignant lesion in the vagina with no clinical or histological evidence of cervical or vulvar cancer or such history within the preceding 5 years (14). Common clinical manifestations include increased vaginal discharge, irregular vaginal bleeding or postcoital bleeding. The present report outlined a case of non-DES-associated vaginal endometrioid adenocarcinoma following a hysterectomy for a benign uterine condition, which is a rare occurrence

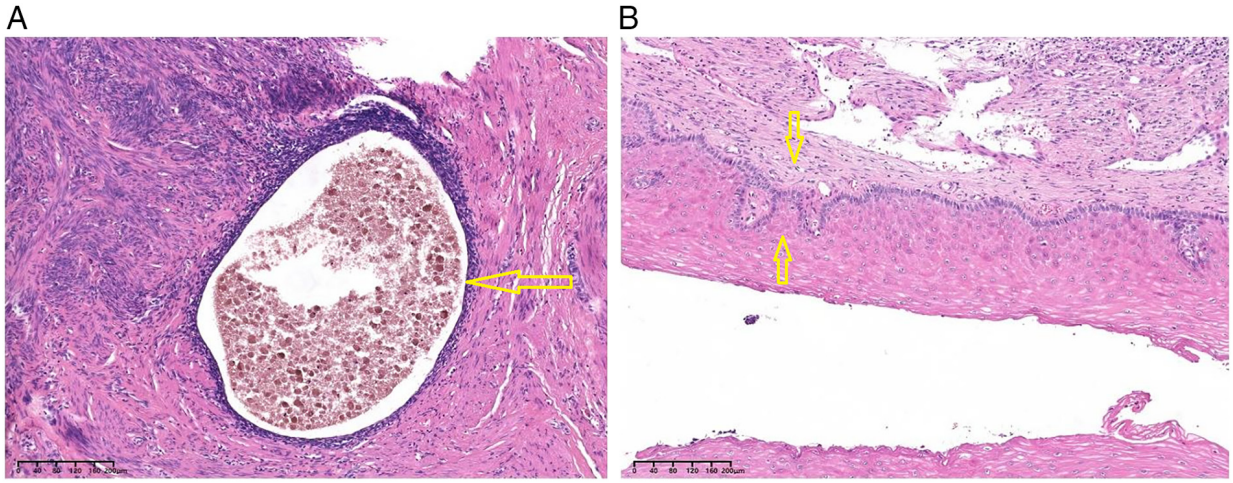

Figure 3. Histopathological findings in a hysterectomy specimen for adenomyosis. (A) H&E staining of the uterine corpus demonstrating typical features of adenomyosis. Ectopic endometrial glands and stroma (arrow) are present within the hypertrophic myometrium, extending beyond the normal endometrial-myometrial junction. The ectopic glands appear irregular and dilated, accompanied by surrounding stromal proliferation (magnification, x10; scale bar, 200 μm). (B) H&E staining of normal cervical tissue from the same specimen. The ectocervix is covered by intact, orderly stratified squamous epithelium (arrow), with underlying fibrous stroma containing scattered stromal cells (arrow) (magnification, x10; scale bar, 200 μm).

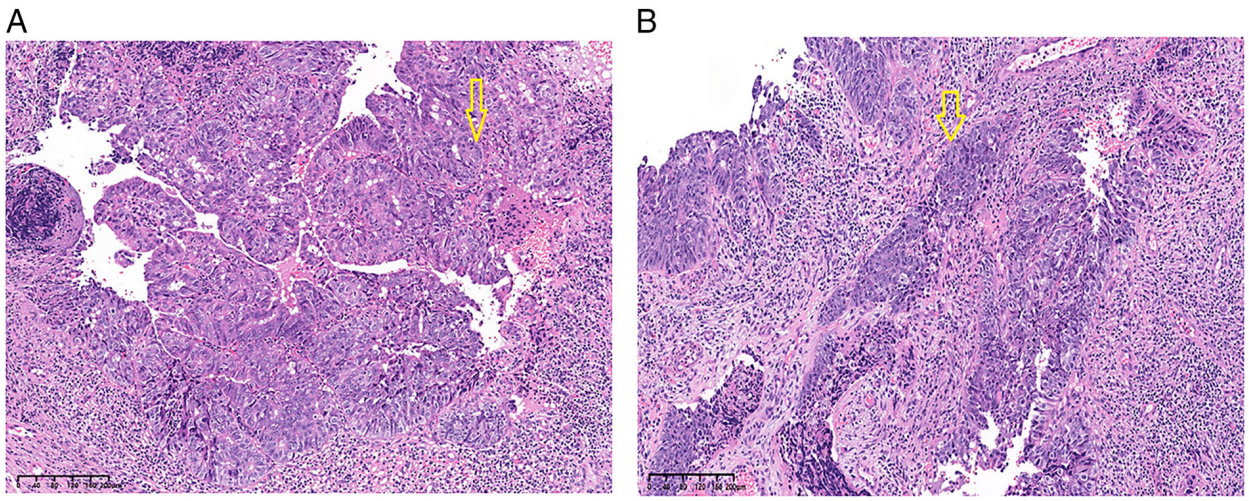

Figure 4. Histopathological features of poorly differentiated adenocarcinoma of the vagina. H&E-stained sections showing an infiltrative adenocarcinoma characterized by markedly atypical glands and pleomorphic cells with hyperchromatic nuclei. Lymphocytic infiltration is evident in the adjacent stroma of (A) the left vaginal wall (arrow) (magnification, x10; scale bar, 200 μm) and (B) the right vaginal wall (arrow) (magnification, x10; scale bar, 200 μm).

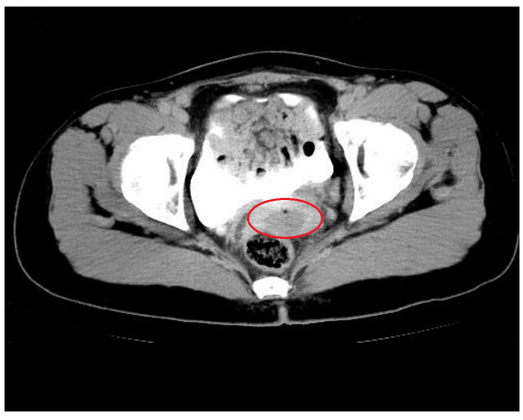

Figure 5. Computed tomography of the urinary tract demonstrating postoperative changes in the pelvis, including a left pelvic sidewall cyst, consistent with a lymphocele and prominence of the vaginal cuff (highlighted by the red circle).

in clinical practice. Previous studies have reported vaginal endometrioid adenocarcinoma detected >10 years after hysterectomy for benign diseases (15,16), similar to that described in the present case. This suggests that further investigation of the development of rare malignant tumors after hysterectomy for benign conditions is warranted.

The pathogenesis of vaginal endometrioid adenocarcinoma remains in need of full elucidation. Depending on the location of the tumor and the pathological type, this condition may be associated with the theory of malignant transformation of endometriosis. The literature states that endometriotic lesions carry a risk of malignancy and can develop into endometrioid adenocarcinoma and clear cell carcinoma (17,18). In the present case, although hemostasis was achieved after curettage due to menorrhagia, the patient still exhibited marked adenomyosis with a notably enlarged uterine volume. To rapidly reduce uterine size, relieve severe symptoms and create favorable

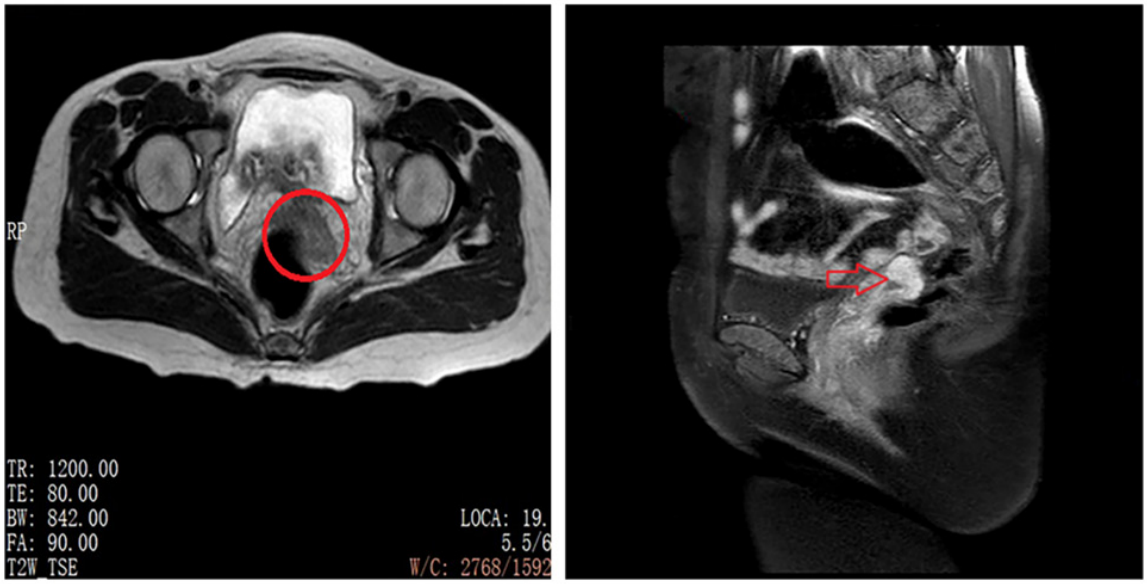

Figure 6. Post-contrast MRI demonstrating a punctate soft-tissue nodule along the left posterolateral aspect of the vaginal cuff. (A) The nodule exhibits mildly high signal intensity on axial T2-weighted imaging (red circle). (B) Marked enhancement on sagittal contrast-enhanced T1-weighted imaging is shown (red arrow). The lesion shows ill-defined margins with the vaginal wall, with slight irregularity of the outer vaginal contour. These imaging features are highly suggestive of a vaginal cuff malignancy.

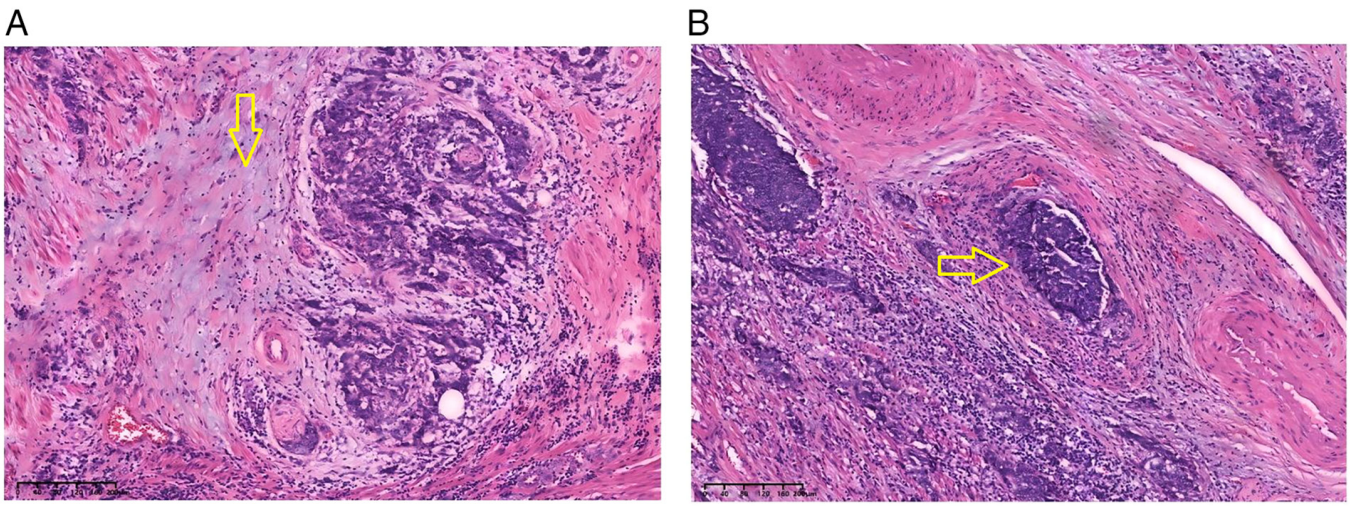

Figure 7. Histopathological evidence of aggressive local invasion. (A) Perineural invasion (arrow). H&E-stained section of the parametrial and upper vaginal resection specimen showing a nerve bundle encircled and invaded by nests of adenocarcinoma cells (magnification, x10; scale bar, 200 μm). (B) Lymphovascular invasion (arrow). H&E-stained section from the same specimen demonstrating tumor cell emboli within a vascular channel, demonstrating lymphovascular invasion (magnification, x10; scale bar, 200 μm).

anatomical conditions for subsequent long-term management, a combination of a gonadotropin-releasing hormone agonist, an LNG-IUS and dienogest were administered. This triple regimen was used in combination to achieve rapid symptom control and quick uterine volume reduction, which is difficult to obtain with single-agent therapy in severe adenomyosis (19). The treatment was limited to 1 month as the goal was not long-term maintenance, but rather to achieve sufficient uterine shrinkage in a short period to facilitate successful retention and effective function of the LNG-IUS; once this objective was met, the short-term intensive combination therapy was discontinued. After 1 month of treatment, clinical symptoms were rapidly controlled, uterine volume was markedly reduced and favorable anatomical conditions for safe and sustained long-term retention of the LNG-IUS were achieved. However, 1 year after LNG-IUS insertion, the uterine volume increased by ~62%. According to clinical evidence, LNG-IUS typically stabilizes or reduces uterine volume in adenomyosis within 12 months (20); a 62% increase was markedly outside the expected therapeutic response range and thus indicated treatment failure (21). This marked volume expansion demonstrated an inadequate response to hormonal therapy and progressive adenomyosis. For these reasons, the patient underwent a total hysterectomy with vaginal extraction. Residual microscopic endometriotic tissue at the vaginal stump could theoretically undergo malignant transformation under long-term estrogenic

Table I. Changes in tumor marker, TCT and HPV status before and after surgery.

Incident	Time	TCT	HPV	CA125 (normal range, 0-35 U/ml)	AFP (normal range, 0-9 ng/ml)	CA19-9 (normal range, 0-35 U/ml)	CEA (normal range, 0-5 ng/ml)	SCC (normal range, 0-1.5 ng/ml)
Early diagnosis	April 2020	Negative	Negative	52.60[a]	1.42	21.6	1.34	-
5-month follow-up for Mirena IUS placement	October 2020	-	-	31.20	1.72	13.9	1.13	-
1-year follow-up for Mirena IUS	April 2021	-	-	50.90[a]	1.85	16.0	1.25	0.70
Total laparoscopic hysterectomy	November 2021	-	-	17.70	1.83	17.4	1.61	-
No routine health screening	Throughout 2022	-	-	-	-	-	-	-
No routine health screening	Throughout 2023	-	-	-	-	-	-	-
Vaginal bleeding after intercourse	June 2024	AGC-FN	Negative	-	-	-	-	-
Lesion identified at the vaginal cuff	July 2024	-	-	9.81	2.77	11.57	1.03	0.70
3-month postoperative follow-up	October 2024	-	-	5.16	2.11	8.94	1.10	-
5-month postoperative follow-up	December 2024	Negative	-	7.08	1.99	9.79	1.17	-
	April 2025	Negative	-	-	-	-	-	-
	August 2025	Negative	-	-	-	-	-	-
15-month postoperative follow-up	October 2025	-	-	9.62	1.82	9.08	1.29	-

[a]Value that exceeded the reference range. HPV, human papilloma virus; TCT, ThinPrep cytology test; AFP, α-fetoprotein; CEA, carcinoembryonic antigen; AGC-FN, atypical glandular cells favor neoplasia; CA125, cancer antigen 125; SCC, squamous cell carcinoma antigen; IUS, intrauterine system.

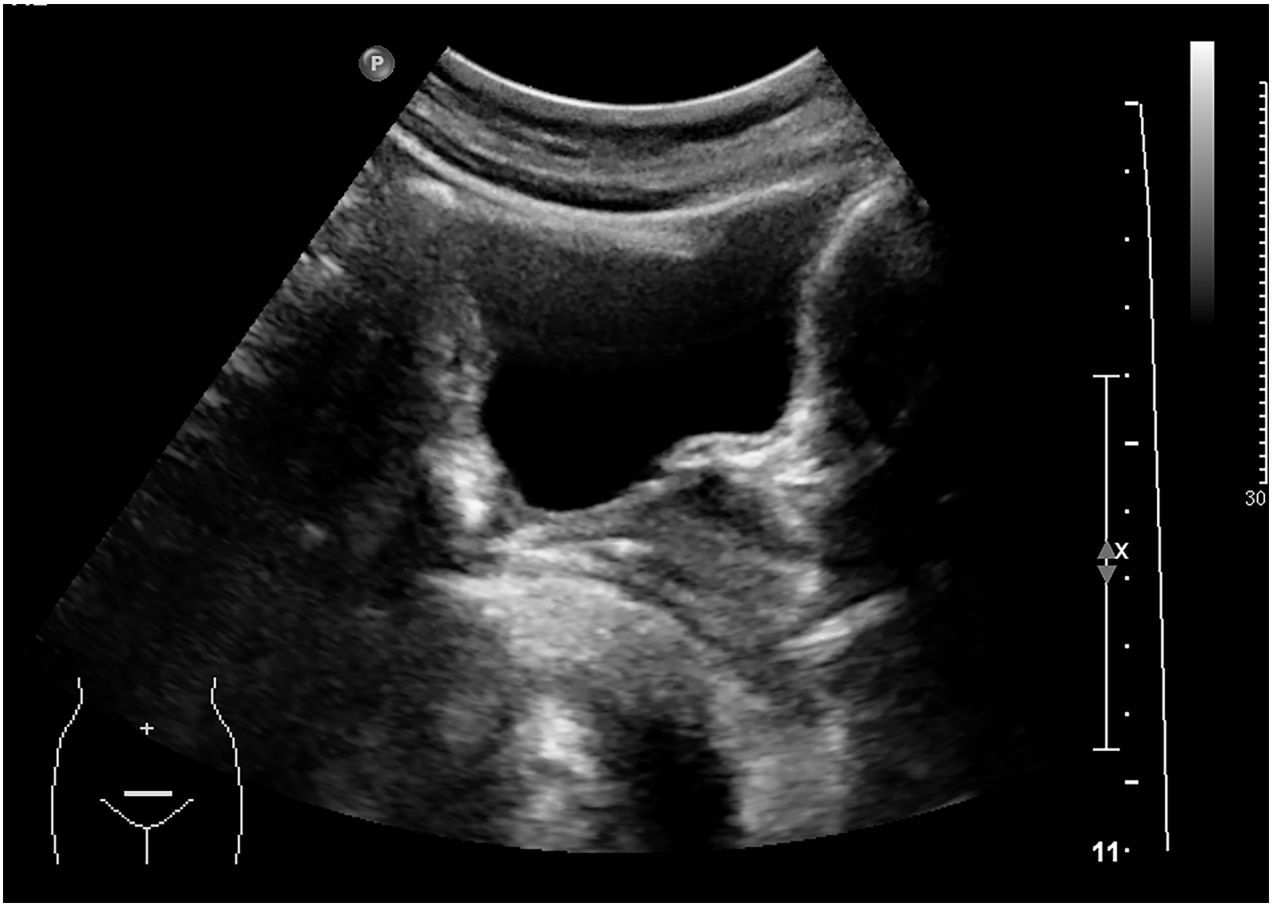

Figure 8. Findings from the 15-month postoperative surveillance pelvic ultrasound appear unremarkable, with no identifiable mass or suspicious soft tissue lesion.

stimulation. However, in the present case, only 3 years had elapsed between hysterectomy and the diagnosis of vaginal cancer, and the original surgical pathology was benign. Thus, this mechanism alone could not fully explain the clinical course. However, an alternative mechanism may involve the Müllerian tissue. As the upper vagina is derived from the Müllerian duct, residual Müllerian tissue may retain the potential to differentiate into endometrial-like glands during embryonic development (22). Abnormal development of the Müllerian duct is not only associated with endometriosis, but the abnormal cell differentiation involved may also induce tumors of the reproductive system (23). Therefore, the lesion at the vaginal stump observed in the present case may be associated with residual endometriotic tissue, although an abnormal proliferation or malignant transformation tendency of the residual Müllerian duct tissue may not be excluded. Uterine adenomyosis and primary vaginal adenocarcinoma may represent manifestations of the same pathological process but at different sites and at different time points.

The present patient had a history of thyroid cancer. In the context of combining a rare PVC with another relatively common malignant tumor, it is evident that contemplations beyond a single lesion should be made and patient tumor susceptibility evaluated as a whole. This would therefore lead to a clinical issue worthy of in-depth discussion, thus suggesting that the two tumors may have been associated. Previous studies have shown that the PI3K/AKT signaling pathway is a key oncogenic driver for a number of thyroid cancers, including follicular thyroid carcinoma, papillary thyroid carcinoma and anaplastic thyroid carcinoma, and can be regulated by the co-expression of PTEN (24,25). Activated variants in the PTEN/PI3K/Akt/mTOR pathway are frequent in thyroid cancer (especially the follicular subtype) and contribute to tumor cell proliferation, survival, invasion and metastatic progression during thyroid carcinogenesis and disease progression (26). Abnormalities in this pathway represent a classical molecular mechanism underlying endometrioid adenocarcinoma, and variants that can inactivate the PTEN gene are important molecular markers (27). Germline variants of the PTEN gene can cause autosomal dominant genetic disease, known as PTEN hamartoma tumor syndrome (PHTS), and patients with this syndrome exhibit a notably higher risk of breast cancer (67-78% among those aged ≥60 years), endometrial cancer (19-28%) and thyroid cancer (6-38%) (28). Although the uterine pathology in the present case was benign, the endometrioid adenocarcinoma in the upper part of the vagina originated from the Müllerian duct, which is homologous to the endometrium. Therefore, in the context of PHTS, the occurrence of endometrioid adenocarcinoma in a derivative of the Müllerian duct (the upper part of the vagina) is biologically plausible and theoretically possible, although direct clinical evidence for this specific association remains limited.

The present case was diagnosed as a primary vaginal adenocarcinoma by vaginal biopsy. Research regarding this disease is currently limited to case reports and retrospective analyses with small sample sizes (29,30). Furthermore, the relatively short 15-month follow-up period represented a limitation of the present case report and a longer follow-up is thus required to further evaluate long-term prognosis and recurrence. Furthermore, to the best of our knowledge, no standard screening or treatment strategies have been established. Clinically, mention of this disease predominantly refers to cervical squamous cell carcinoma and management includes surgery, radiotherapy and chemotherapy, immunotherapy, targeted therapy and molecular testing (31). The present patient underwent surgery and concurrent radiotherapy and chemotherapy. During the 15-month follow-up period, no recurrence was observed and the prognosis was good. However, a notable limitation was that the present patient did not undergo relevant genetic testing, mainly owing to the patient's personal refusal and financial constraints.

In the future, for similar cases, genetic counseling and testing should be considered, with a focus on germline variants associated with numerous primary malignancies such as PTEN and PIK3CA. Performing next-generation sequencing in both thyroid cancer and vaginal adenocarcinoma to identify shared driver variants could advance this from a simple clinical description to a condition with a deeper mechanistic understanding of its pathophysiology, which would support risk assessment and cancer prevention for first-degree relatives of the patient.

In summary, although the American College of Obstetricians and Gynecologists recommends that routine cytological screening be discontinued in women with benign uterine diseases and no history of high-grade cervical intraepithelial neoplasia (32), the present case highlights the need for regular surveillance of the vaginal stump after hysterectomy. For rare multiple primary cancers, especially those with potentially associated histological types, clinicians should adopt a 'molecular detective' approach and investigate possible shared genetic susceptibility. The present report recommends multi-institutional registration and long-term follow-up of such rare cases to accumulate evidence, clarify optimal treatment strategies and identify prognostic factors, with the aim of advancing research regarding underlying molecular mechanisms.

In conclusion, PVC, particularly when occurring after hysterectomy, is rare. The present case suggested that PVC may be associated with the malignant transformation of residual endometriotic (adenomyotic) lesions. Regular monitoring of the vaginal stump is necessary in patients with a history of hysterectomy for benign diseases. Furthermore, given the previous history of thyroid cancer in the present patient, possible underlying genetic susceptibility to tumors should also be considered in such rare tumor cases. Further elucidation of the molecular mechanisms involved in the pathogenesis of this disease is warranted.

Acknowledgements

Not applicable.

Funding

The present study was funded by the Ningbo Clinical Medical Research Center for Gynecological Diseases (grant no. 2024L002) and the Ningbo Major Breakthrough Project for High-End Medical and Health Teams (grant no. 2024021020).

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

TW and LC conceptualized and designed the present case report and provided overall supervision of the research. TW performed a comprehensive literature search, conducted analysis and interpretation of the clinical course and drafted the initial manuscript. JZ provided clinical care for the patient, contributed to the diagnosis and management of the case and critically revised the manuscript. XL and LP collected and assembled all clinical data, including imaging studies and laboratory results, performed data curation and verification and contributed to the description of clinical findings. HY contributed to data analysis, organized all graphical presentations, prepared and edited the figures, and revised the manuscript critically. LC critically reviewed and revised the manuscript for important intellectual content. TW and JZ confirm the authenticity of all the raw data. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of the present case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

References

1. Adams TS, Maluleke JC and Cuello MA: Cancer of the vagina: 2025 update. Int J Gynaecol Obstet 171 (Suppl 1): S48-S59, 2025.
2. Rajaram S, Maheshwari A and Srivastava A: Staging for vaginal cancer. Best Pract Res Clin Obstet Gynaecol 29: 822-832, 2015.
3. Kulkarni A, Dogra N and Zigras T: Innovations in the management of vaginal cancer. Curr Oncol 29: 3082-3092, 2022.
4. Frank SJ, Deavers MT, Jhingran A, Bodurka DC and Eifel PJ: Primary adenocarcinoma of the vagina not associated with diethylstilbestrol (DES) exposure. Gynecol Oncol 105: 470-474, 2007.
5. White MC, Weir HK, Soman AV, Peipins LA and Thompson TD: Risk of clear-cell adenocarcinoma of the vagina and cervix among US women with potential exposure to diethylstilbestrol in utero. Cancer Causes Control 33: 1121-1124, 2022.
6. National Cancer Institute (NCI): Diethylstilbestrol (DES) exposure and cancer. National Institutes of Health, Bethesda, MD, 2025.

7. Smith EK, White MC, Weir HK, Peipins LA and Thompson TD: Higher incidence of clear cell adenocarcinoma of the cervix and vagina among women born between 1947 and 1971 in the United States. Cancer Causes Control 23: 207-211, 2012.
8. Hong MK and Ding DC: Vaginal adenocarcinoma: A review of a rare gynecologic cancer. Cancers (Basel) 17: 2130, 2025.
9. Van der Aa MA, Helmerhorst TJM, Siesling S, Riemersma S and Coebergh JW: Vaginal and (uncommon) cervical cancers in the Netherlands, 1989-2003. Int J Gynecol Cancer 20: 638-645, 2010.
10. Chan JKC: The wonderful colors of the hematoxylin-eosin stain in diagnostic surgical pathology. Int J Surg Pathol 22: 12-32, 2014.
11. Nayar R and Wilbur DC: The Pap test and Bethesda 2014. Cancer Cytopathol 123: 271-281, 2015.
12. FIGO Committee on Gynecologic Oncology: Current FIGO staging for cancer of the vagina, fallopian tube, ovary, and gestational trophoblastic neoplasia. Int J Gynaecol Obstet 105: 3-4, 2009.
13. Amin MB, Greene FL, Edge SB, Compton CC, Gershenwald JE, Brookland RK, Meyer L, Gress DM, Byrd DR and Winchester DP: The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA Cancer J Clin 67: 93-99, 2017.
14. Yang J, Delara R, Magrina J, Magtibay P, Langstraat C, Dinh T, Karlin N, Vora SA and Butler K: Management and outcomes of primary vaginal cancer. Gynecol Oncol 159: 456-463, 2020.
15. Alfonzo E, Holmberg ECV, Sparén P, Milsom I and Strander B: Risk of vaginal cancer among hysterectomised women with cervical intraepithelial neoplasia: A population-based national cohort study. BJOG 127: 448-454, 2020.
16. Qian J, Gracious K, Chen L and Xu S: Primary vaginal cancer after hysterectomy for benign conditions: A systematic review of the literature. Front Oncol 14: 1334778, 2024.
17. Barnard ME, Farland LV, Yan B, Wang J, Trabert B, Doherty JA, Meeks HD, Madsen M, Guinto E, Collin LJ, *et al*: Endometriosis typology and ovarian cancer risk. JAMA 332: 482-489, 2024.
18. Kim H, Kim HJ and Ahn HS: Does endometriosis increase the risks of endometrial hyperplasia and endometrial cancer? Gynecol Oncol 169: 147-153, 2023.
19. Etrusco A, Barra F, Chiantera F, Ferrero S, Bogliolo S, Evangelisti G, Oral E, Pastore M, Izzotti A, Venezia R, *et al*: Current medical therapy for adenomyosis: From bench to bedside. Drugs 83: 1595-1611, 2023.
20. Zhang P, Song K, Li L, Yukuwa K and Kong B: Efficacy of combined levonorgestrel-releasing intrauterine system with gonadotropin-releasing hormone analog for the treatment of adenomyosis. Med Princ Pract 22: 480-483, 2013.
21. Lee KH, Kim JK, Lee MA, Ko YB, Yang JB, Kang BH and Yoo HJ: Relationship between uterine volume and discontinuation of treatment with levonorgestrel-releasing intrauterine devices in patients with adenomyosis. Arch Gynecol Obstet 294: 561-566, 2016.
22. Kyei-Barffour I, Margetts M, Vash-Margita A and Pelosi E: The embryological landscape of Mayer-Rokitansky-Kuster-Hauser Syndrome: Genetics and environmental factors. Yale J Biol Med 94: 657-672, 2021.
23. Bhamidipaty-Pelosi S, Kyei-Barffour I, Volpert M, O'Neill N, Grimshaw A, Eriksson L, Vash-Margita A and Pelosi E: Müllerian anomalies and endometriosis: Associations and phenotypic variations. Reprod Biol Endocrinol 22: 157, 2024.
24. Manfredi GI, Dicitore A, Gaudenzi G, Caraglia M, Persani L and Vitale G: PI3K/Akt/mTOR signaling in medullary thyroid cancer: A promising molecular target for cancer therapy. Endocrine 48: 363-370, 2015.
25. Hendricks LAJ, Verbeek KCJ, Schuurs-Hoeijmakers JHM, Jong MM, Links TP, Brems H, Aerden M, Brunet J, Lleuger-Pujol R, Hüneburg R, *et al*: The risk of a second primary cancer in PTEN hamartoma tumor syndrome (PHTS). Genet Med 27: 101467, 2025.
26. Ramírez-Moya J, Wert-Lamas L and Santisteban P: MicroRNA-146b promotes PI3K/AKT pathway hyperactivation and thyroid cancer progression by targeting PTEN. Oncogene 37: 3369-3383, 2018.
27. Nero C, Ciccarone F, Pietragalla A and Scambia G: PTEN and gynecological cancers. Cancers (Basel) 11: 1458, 2019.
28. Hendricks LJ, Hoogerbrugge N, Mensenkamp AR, Brunet J, Lleuger-Pujol R, Høberg-Vetti H, Tveit Haavind M, Innella G, Turchetti D, Aretz S, *et al*: Cancer risks by sex and variant type in PTEN hamartoma tumor syndrome. J Natl Cancer Inst 115: 93-103, 2023.
29. Staats PN, Clement PB and Young RH: Primary endometrioid adenocarcinoma of the vagina: A clinicopathologic study of 18 cases. Am J Surg Pathol 31: 1490-1501, 2007.
30. Ugwu AO, Haruna M, Okunade KS, Ohazurike E, Anorlu RI and Banjo AAF: Primary vaginal adenocarcinoma of intestinal-type: Case report of a rare gynaecological tumour. Oxf Med Case Reports 2019: omz088, 2019.
31. Westerveld H, Nesvacil N, Fokdal L, Chargari C, Schmid MP, Milosevic M, Mahantshetty UM and Nout RA: Definitive radiotherapy with image-guided adaptive brachytherapy for primary vaginal cancer. Lancet Oncol 21: e157-e167, 2020.
32. ACOG practice bulletin No 109: Cervical cytology screening. Obstet Gynecol 114: 1409-1420, 2009.