



Case report

Recurrent cervical cancer after trachelectomy diagnosed by hysteroscopy: A case report

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ARTICLE INFO

Keywords:

Trachelectomy
Cervical cancer recurrence
Cervical cancer screening
Hysteroscopy
Case report

ABSTRACT

Surveillance for cervical cancer recurrence after radical trachelectomy is challenging and warrants additional research to establish evidence-based screening guidelines. Papanicolaou (Pap smear) with HPV testing, physical exam, and symptom reporting remain the standard of care despite high false positive rates. In this patient with a history of early-stage cervical adenocarcinoma status post radical trachelectomy, a diagnosis of recurrence was made hysteroscopically, prompting evaluation of the utility of this technique for screening and management of patients with suspected recurrent cervical cancer after trachelectomy.

1. Introduction

A large proportion of women diagnosed with early-stage cervical cancer are young and desire to maintain their fertility, making radical trachelectomy a reasonable treatment option (Zaccarini et al., 2021). In these women, surveillance for recurrence poses a challenge as post-operative changes at the newly established immature squamocolumnar junction make the interpretation of pap smears difficult (Zaccarini et al., 2021; Feratovic et al., 2008; Sonoda et al., 2017). Traditionally, annual symptom review, physical exam, and pap smear have been recommended by the National Comprehensive Cancer Network (NCCN) and the Society of Gynecologic Oncology (SGO) but with a disclaimer that the use of pap tests in screening for recurrence is not well supported by published data (Brown et al., 2016; Koh et al., 2015; Salani et al., 2011). False positive rates for pap test screening remain high and can lead to increased office visits and anxiety (Brown et al., 2016). Additional studies have suggested that colposcopy alone and in association with HPV positivity showed the best sensitivity to predict recurrence (Slama et al., 2017) and that up to 96% of abnormal pap smear results normalize within 12–24 months postoperatively. (Sonoda et al., 2017).

Though diagnosis of cervical cancer recurrence remains challenging, in-office hysteroscopy is growing in popularity given its ease of use, safety, and versatility (Slama et al., 2017). This case demonstrates the potential utility of hysteroscopic diagnosis of cervical cancer recurrence after radical trachelectomy.

2. Patient information

A 34Y G1P0010 woman with a past medical history significant for obesity (BMI 37) and polycystic ovarian syndrome initially presented to gynecologic oncology after a pap smear demonstrating atypical squamous cells of undetermined significance (ASCUS) cannot rule out high grade lesion, atypical glandular cells, and HPV 16 positivity. Colposcopy was significant for an endocervical curettage (ECC) with endocervical adenocarcinoma in situ. Endometrial biopsy was benign.

The patient underwent a cold knife conization (CKC) demonstrating CIN III (cervical intraepithelial neoplasia III) at the transformation zone with positive endocervical margins. Endocervical curettage was also significant for rare fragments of CIN III. The patient was then lost to follow up for the following 10 months.

Upon representation, a pap smear was collected and negative for intraepithelial lesion or malignancy. Follow up pap smear collected eight months later was significant for ASCUS. Colposcopy was performed demonstrating negative biopsies with ECC significant for endocervical adenocarcinoma. The patient underwent an additional cone biopsy and endocervical curettage significant for fragments of endocervical adenocarcinoma which were also present in the cone margin and endocervical curettage. Endometrial biopsy demonstrated separate fragments of proliferative endometrium and benign squamous epithelium. At this time, the patient was diagnosed with stage 1A1 cervical adenocarcinoma.

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Approximately one month later, the patient underwent her third cervical cold knife cone demonstrating residual endocervical adenocarcinoma at the endocervical margin, CIN III at the endocervical margin at 3–6o'clock and ECC significant for fragments of endocervical adenocarcinoma. Preoperative MRI demonstrated no visible cervical cancer with borderline ovarian enlargement with multiple prominent peripheral follicles consistent with polycystic ovaries. As the patient desired future fertility, the decision was made to proceed with radical abdominal trachelectomy.

Exploratory laparotomy, radical abdominal trachelectomy, reconstruction of the uterus, pelvic lymph node dissection and removal of a right adnexal lesion was performed. Pathology demonstrated a cervix with residual endocervical adenocarcinoma in situ with CIN III. Surgical margins (anterior and posterior lower uterine segment and ECC), lymph nodes, parametria and right paratubal cyst were all negative for malignancy.

At the 3-month follow-up visit, pap smear was negative for intra-epithelial lesion or malignancy (NILM) and at 15 months, it was NILM, HPV 16+. Colposcopy was performed demonstrating one acetowhite lesion and no punctations, mosaic patterns or atypical vessels; the resulting pathology was negative. At 19 months, her Pap smear resulted as ASCUS and HPV 16 positivity and the following colposcopy and ECC were negative.

She continued to report oligomenorrhea and returned to her reproductive endocrinology team for infertility evaluation (see Table 1).

3. Clinical findings

Twenty-two months after her exploratory laparotomy she underwent an operative hysteroscopy for suspected endometrial adhesions and polyps. The lower uterine segment was noted to have small white adhesions easily lysed with graspers and papillary tissue excrescences which were white-gray in appearance (Fig. 1). A curettage was done and sent to pathology.

4. Diagnostic assessment

Pathology from the hysteroscopy with curettage was significant for

Table 1
Timeline of patient events.

Time (months)	Event
0	Pap: ASCUS HPV 16, cannot rule out high grade/AGUS
1	Colpo: Biopsy neg ECC: endocervical adenocarcinoma in situ EMB: benign
1.5	CKC #1: CIN III at T zone
12	Pap: NILM
20	Pap: ASCUS Colpo: Neg biopsies ECC with endocervical adenocarcinoma
21	CKC #2: Fragments of endocervical adenocarcinoma → Stage 1A1 cervical adenocarcinoma (greatest size 6 mm) EMB: proliferative endometrium and benign squamous epithelium
22	CKC #3: Residual endocervical adenocarcinoma at endocervical margin at 3–6o'clock (greatest size 3 mm) ECC significant for fragments of endocervical adenocarcinoma
24	Abdominal trachelectomy: Cervix with residual adenocarcinoma in situ with CINIII, surgical margins negative
27	Pap: NILM, Amenorrhea x5m
39	Pap: NILM, HPV16, Colpo: Path negative
41	Continued amenorrhea, started oral contraceptives
58	Hysteroscopy with lower uterine segment gray-white in appearance: moderately differentiated adenocarcinoma consistent with recurrence
60	Hysterectomy, bilateral salpingo-oophorectomy, peritoneal biopsy from the anterior abdominal wall, lysis of adhesions and cystoscopy

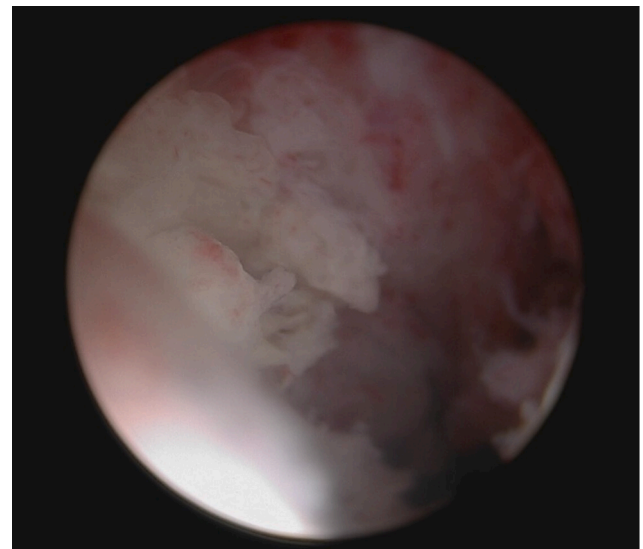


Fig. 1. Hysteroscopic appearance of lower uterine segment.

multiple foci of moderately differentiated adenocarcinoma compatible with endocervical primary involving the endometrium. Morphological features were similar to the tumor previously identified at time of trachelectomy.

5. Therapeutic intervention

The patient underwent an MRI demonstrating polycystic ovaries and a ventral hernia; cervical cancer was not able to be appreciated. PET CT at this time also demonstrated focal areas of increased activity in the lateral aspect of the left and right ovary likely represent areas of metabolically active follicular cysts, punctate areas of increased activity in the anterior abdominal wall, no evidence of nodal activity in the chest, and no intraperitoneal activity.

Two months after the hysteroscopy (five years after initial abnormal pap smear) the patient underwent an exam under anesthesia, hysterectomy, bilateral salpingo-oophorectomy, peritoneal biopsy from the anterior abdominal wall, lysis of adhesions and cystoscopy.

Pathology demonstrated a uterus with multiple foci of moderately differentiated adenocarcinoma with immunohistochemistry compatible with recurrence of endocervical primary involving the endometrium (Fig. 2). In addition, the abdominal wall lesion was positive for metastatic adenocarcinoma with associated lymphovascular invasion and



Fig. 2. Uterus with residual endocervical adenocarcinoma involving lower uterine segment.

microcalcifications, consistent with known endocervical primary.

6. Follow-up and outcomes

Pathology was significant for an abdominal wall nodule demonstrating metastatic carcinoma, residual endocervical adenocarcinoma involving the lower uterine segment with a 2 mm depth of stromal invasion and 5 mm horizontal extent of stromal invasion at the surgical margins of the uterus as well as the bilateral adnexa negative for carcinoma. The patient is currently undergoing chemotherapy with paclitaxel, carboplatin and bevacizumab. PD-L1 testing was positive and pembrolizumab was started.

7. Discussion

Screening for recurrence of cervical cancer after trachelectomy is critical yet remains a challenge. Patients are often followed by isthmic-vaginal smear cytology using the conventional Papanicolaou method, but this method has a high false positive rate, especially in the first few years postoperatively. Patients who have follow-up smears showing abnormal cytology often undergo colposcopic examination and biopsy. In one study, 73% of patients with abnormal cytology results were within 12 months of surgery, (Lanowska et al., 2014) likely attributable to the immature squamocolumnar junction. Further, the permanent cervical sutures can cause local inflammation and alter cytological specimens. (Feratovic et al., 2008; Lanowska et al., 2014) In addition, false negative results can occur, such as in this case report. Cervical adenocarcinoma lesions can be retracted into the uterine cavity and therefore be missed with pap screening alone.

Pap smears are known to be imperfect postoperative screening in patients who have received a trachelectomy but are still widely utilized. The patient described here had normal pap smears until approximately 22 months after her radical trachelectomy. She had conflicting screening results with a pap showing ASCUS HPV16+, but a negative colposcopy and curettage, emphasizing the variability in interpreting cytology results that is typical of post-trachelectomy pap smears.

There have been few reports demonstrating the best means for postoperative follow-up in patients after a trachelectomy. Most traditional screening methodologies have a high false positive rate; however, this case demonstrates the utility of visualization and directed biopsy of the lower uterine segment in patients who have undergone trachelectomy.

Hysteroscopic surveillance may be a more specific means for screening after a trachelectomy but no prior case reports using hysteroscopy for follow up have been published. More recently, many practitioners have been using these scopes in the office setting (Vitale et al., 2021a,b) and availability is increasing. Hysteroscopy provides adequate visualization of the endocervical and lower uterine segments and permits visual evaluation of the remaining tissues in a manner that pap smears alone do not. In addition, operative hysteroscopy can be done in the office under minimal to no anesthesia, prompting consideration for hysteroscopy rather than excisional biopsy in cases of abnormal pap results or abnormal cervical appearance after trachelectomy.

Overall, there is no consensus and minimal data to guide cervical cancer recurrence surveillance after trachelectomy, but this case suggests the potential utility of hysteroscopy as an adjunct to screening and diagnosis of recurrent disease. Additional studies of larger populations are needed to define the sensitivity and specificity of hysteroscopy in this setting. Given the rarity of cervical cancer recurrence after trachelectomy and limitations of hysteroscopy, further study regarding the role of hysteroscopy in this patient population would be challenging but may promote utilization of this technique in select patients.

8. Patient perspective

Patient declined to provide a written perspective on her experience but desires that her case be published so that others may learn from it. Informed consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author Contributions

AF, AL, and AY were responsible for literature review, chart review, drafting, proofreading, and editing this manuscript under the guidance of LC and JH. LC was the primary surgeon who conceived the main concept of this case report. JH performed the hysteroscopy and diagnosed the recurrence. Both LC and JH provided experience, patient information, and manuscript editing prior to publication.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

No financial assistance was provided in creation of this case report.

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