Rectal Adenocarcinoma Presenting as a Cervical Mass: A Case Report

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Patient: Female, 68-year-old
Final Diagnosis: Mucinous rectal adenocarcinoma
Symptoms: Vaginal bleeding
Clinical Procedure: Abdominoperineal resection • bilateral salpingo-oophorectomy • en-bloc hysterectomy • posterior vaginectomy
Specialty: Gastroenterology and Hepatology • Obstetrics and Gynecology • Oncology • Pathology • Radiology • Surgery

Objective: Challenging differential diagnosis
Background: Invasive cervical tumors are often seen in clinical practice. However, there are multiple structures within the pelvis, and invasion of the cervix from another site must be included in the differential diagnosis. In such cases, a multidisciplinary approach is needed to define the organ of tumor origin. Ensuring proper staging and histologic analysis are critical for optimal management.

Case Report: We present a case of a 68-year-old woman who presented to her gynecologist with painless post-menopausal vaginal bleeding. She was diagnosed with a locally aggressive cervical adenocarcinoma, which was histologically confirmed by an in-office biopsy. She was referred to the gynecologic oncology service at a tertiary care hospital for definitive management, where a thorough clinical workup was performed. Physical exam revealed that the mass had invaded the anterior rectal wall. Through a multidisciplinary approach and a repeat biopsy, she was correctly diagnosed with an invasive rectal adenocarcinoma. She was treated with neoadjuvant chemoradiation therapy and underwent curative surgery. Had she been incorrectly treated as having a primary cervical adenocarcinoma, there would have been no role for surgery. The change in the organ of primary drastically altered the patient’s management and outcome. She is currently undergoing surveillance with cross-sectional imaging.

Conclusions: Cervical masses originating from non-gynecologic organs can be difficult to differentiate on physical exam and histologic analysis. When a mass involves the rectum, an invasive primary rectal adenocarcinoma must be included in the differential. This will have a significant impact on patient management and ultimately on patient survival.

Keywords: Colorectal Neoplasms • Diagnostic Errors • Uterine Cervical Neoplasms

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Background

Cervical adenocarcinoma is the third most common type of gynecologic malignancy in the United States, and approximately 20-30% are adenocarcinomas [1,2]. In late-stage disease, it can be difficult to determine whether the cervix is primarily or secondarily involved. This distinction can also be difficult to make on histologic analysis [3] but is critically important, as it carries prognostic and therapeutic implications. Rarely, other pelvic malignancies invading into the uterus are misdiagnosed as a primary cervical carcinoma. Rectal carcinoma is one such cancer where the staging system and treatment are very different from cervical carcinoma for otherwise grossly similar-appearing masses. Comprehensive physical exam, diagnostic imaging, and histopathologic and serologic correlation are essential in determining the organ of primary origin.

Case Report

A 68-year-old woman with a history of beta thalassemia and an incidental biopsy-proven 8-mm low-grade neuroendocrine tumor of the lung presented to her community gynecologist with new-onset post-menopausal bleeding and microcytic anemia (hemoglobin=11.1 g/dL). She had not had routine colorectal cancer screening. The physical exam was notable for “a mass with a large, firm and indurated barrel-shaped cervix that is very suspicious of cervical cancer.” Transvaginal ultrasound revealed an irregular, heterogeneous mass in the posterior cul-de-sac measuring 6.5x6.9x6.7 cm. Despite the presence of a large mass, she was surprisingly asymptomatic apart from vaginal bleeding and some yellowish/bloody discharge. She denied weight loss or a change in appetite. There were no bowel habit changes, with regular bowel movements every second day.

A pap smear and ultimately an in-office cervical biopsy were performed, revealing an adenocarcinoma originating from the cervix. A PET/CT was ordered by her gynecologist as the next step of the workup, disclosing an intensely hypermetabolic 9.7-cm pelvic mass intimately associated with the cervix and rectum, and a tortuous sigmoid colon (Figure 1). No distant metastatic disease was seen.

The patient was then referred to the gynecologic oncology service at a tertiary care hospital and the initial biopsy specimen was reviewed. This revealed an adenocarcinoma with carcinoma and mucin-infiltrating stromal tissue, patchy staining for CEA, and ≤5% nuclear staining for estrogen and progesterone receptors. The findings were interpreted as indeterminate for the organ of primary origin, but favored secondary cervical involvement. A repeat biopsy was recommended. Her CEA was elevated at 76.2 ng/mL (reference range <3.8 ng/mL).

On speculum exam, the cervix demonstrated a friable 9-cm tumor involving the posterior lip, closely abutting or invading the rectal wall. On bimanual exam, a large mass involving the posterior aspect of the cervix and the vagina was noted and confirmed on rectovaginal exam. She underwent a colonoscopy, showing a 4-cm non-obstructing rectal mass with a secondary lesion in the sigmoid colon (Figure 2). Repeat biopsies were performed.

The specimens were then re-evaluated by a pathologist in the Section of Gynecologic Pathology at our institution. The tumor showed large incomplete glands with luminal mucin (Figure 3A). Additional areas of inflamed mucin pools were seen. The tumor infiltrated a fibrotic stroma with inflammation and granulation tissue. The cells showed enteric features (columnar tumor cells with pseudostratified hyperchromatic nuclei and occasional goblet cells) (Figure 3B). Additional immunohistochemical stains were performed, showing expression of cytokeratin 20, CDX2, and SATB2 in the neoplastic cells (Figure 3C, 3D). The tumor cells were negative for monoclonal PAX8 and cytokeratin 7. Expression of DPC4 was retained in the tumor cells. In light of these findings (enteric morphology and immunophenotype), secondary cervical involvement was favored. The rectal biopsy revealed an invasive moderately-differentiated microsatellite-stable adenocarcinoma with mucinous features, morphologically identical to the features seen in the cervical biopsy.

Given these pathologic findings and the demonstratable rectal mass, a rectal primary cancer with secondary involvement of the cervix was diagnosed. A rectal MRI revealed a locally advanced carcinoma with mucinous features measuring 9.7 cm in length, Nx, and T4b, with invasion into the posterior cervix and vagina, an adjacent loop of sigmoid colon, and a mucin...
Figure 2. (A, B) Images from a colonoscopy demonstrating an oozying, fungating, and infiltrative non-obstructing mass 7 cm from the anus. The mass involved one-third of the luminal circumference.

Figure 3. Cervical biopsy findings: (A) One fragment of the tumor is shown here (hematoxylin and eosin; magnification 2× on Aperio Imagescope). Irregularly-sized glands with haphazard arrangement are seen in a fibrotic and inflamed stroma. Granulation tissue is seen in the left corner of the tissue. Many of the large glands are incomplete and contain inflamed mucin spilling into the tissue. (B) The tumor is composed of columnar cells with hyperchromatic pseudostratified nuclei. Occasional goblet cells (cells with increased ovoid collections of cytoplasmic basophilic mucin, often at the luminal aspect of the cell) are seen (arrowheads). These features are often seen in tumors with intestinal (enteric) differentiation. (Hematoxylin and eosin; magnification 10× on Aperio Imagescope). (C) An immunostain for CDX2 shows diffuse and strong nuclear staining in the tumor cells (anti-CDX2, clone EP25, Leica Biosystems; magnification 10× on Aperio Imagescope). (D) An immunostain for SATB2 shows diffuse nuclear staining of moderate intensity in the tumor cells (anti-SATB2, clone CL0276, Sigma Life Science; magnification 10× on Aperio Imagescope).
deposit in the internal anal sphincter. A large vaginal fistula was present, with a bulky tumor infiltrating along the fistula. There was no extramural vascular invasion (Figure 4).

The option of a diverting colostomy prior to radiation therapy was discussed with the patient, but she declined as she was having normal bowel function and no abdominal pain. She was treated with induction chemotherapy consisting of modified FOLFOX-6 for 8 cycles. Her tumor progressed (Figure 5). She then received 25 Gray of pelvic radiation therapy in 5 fractions followed by modified FOLFIRI for 4 cycles. She had an excellent biochemical response, with her CEA level declining from 87 to 10. An abdominoperineal resection with en-bloc hysterectomy, bilateral salpingo-oophorectomy, and posterior

Figure 4. T2-weighted MRI sagital (A) and axial (B) images demonstrate a mucinous rectal carcinoma invading a loop of adjacent sigmoid colon (white arrow), the posterior vagina, and cervix (black arrow).

Figure 5. T2 weighted MRI sagital (A) and axial (B) images demonstrate progression of disease after modified FOLFOX-6 therapy. The rectum (white arrow), adjacent loop of sigmoid colon (black arrow), and cervix (star) are indicated.
vaginectomy was performed (Figure 6). The surgery lasted 12 h, with an estimated blood loss of 1850 mL. Her postoperative recovery included an 18-day hospital stay. Her hospital stay was complicated by ileus and urinary retention, which resolved prior to discharge.

Final pathology demonstrated an invasive moderately-to-poorly differentiated adenocarcinoma with a stage of ypT4ypN1a, with 1 out of 32 lymph nodes positive. There was 80% tumor viability after total neoadjuvant therapy. Final surgical margins were negative (1.3 cm). She recovered well and no adjuvant chemotherapy was administered. She has transitioned to surveillance with cross-sectional imaging. Her last follow up was at 7 months after her surgical resection, at which time CT scans of the chest, abdomen, and pelvis showed no visible metastatic disease. She did develop scarring in the pelvis, resulting in partial ureteral obstruction. Physical exam at that time identified a small polypoid recurrence on the vaginal mucosa, which was excised.

Discussion

Non-gynecologic primaries account for <2% of cervical masses and can be difficult to differentiate on physical exam and histologic analysis [3]. A comprehensive team approach is needed, as the histologic findings and tumor markers may not be definitive. When these tumors are locally advanced, the symptoms can be misleading. A complete work up to include gynecologic evaluation and colonoscopic assessment together with a high-quality pelvic MRI can aid in making the correct diagnosis. The findings on colonoscopy can suggest a primary mucosal-based process versus an extraluminal source of invasion. In our case, despite the symptoms suggesting a cervical or uterine primary, the rectum was the site of origin. The reverse can be true as well. Sweetser and Ahlquist described a case in which a recurrent cervical carcinoma mimicked a rectal carcinoma [4]. Multidisciplinary assessment revealed the cervix to be the organ of primary origin, despite the clinical and morphologic presentation.

This distinction is not simply an academic one, but carries tremendous prognostic and therapeutic implications. The survival of women with locally advanced stage IVA cervical cancer is variable, with the 5-year survival ranging from as low as 5.1% to as high as 52% [5-8]. Modern therapies have been instrumental in improving outcomes and are largely responsible for the higher end of this survival range. If patients undergo suboptimal treatment, survival is greatly impacted. Conversely, with appropriate therapy, the 5-year survival for patients with stage IIC rectal cancer is approximately 46% [9]. If our patient had been diagnosed with a cervical carcinoma, the treatment would have been very different. For locally advanced cervical cancer, even with rectal involvement, the treatment is normally definitive pelvic radiation with chemosensitization with cisplatin [10,11]. Usually, there is no role for surgery.

Mucinous rectal adenocarcinoma (MRC) has a propensity to be locally aggressive at a higher rate than other rectal carcinomas [12]. Our patient presented with what was initially felt to be a locally invasive cervical carcinoma infiltrating into the rectum. However, the pathologic and endoscopic findings ultimately determined the tumor to be of rectal primary origin. Certainly, occasional primary cervical tumors can show mucinous or intestinal histologic features; however, immunostains typically expressed in the lower gastrointestinal tract primaries (CDX2, SATB2, and cytokeratin 20) often show patchy expression with weaker intensities and they often show some expression of cytokeratin 7 [13]. An elevated CEA, as in this case, can be seen in many tumors. It is most often elevated in colorectal cancer but also commonly in advanced cervical adenocarcinoma [14]. As such, careful detailed evaluation of the immunostains, clinical (endoscopic and tumor marker studies) and imaging findings assist in making the correct diagnosis.

Conclusions

Locally invasive rectal adenocarcinomas invading the cervix can be misinterpreted as primary cervical adenocarcinomas.
Immunohistochemical staining of the biopsy specimen and through imaging and diagnostic workup are important in establishing a colorectal origin. Patients can then be appropriately treated, greatly benefiting survival.

**Institution Where Work Was Done**

This research was performed at the University of Texas MD Anderson Cancer Center, Houston, TX, USA.

**References:**


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