Case Report

Kurume Medical Journal, 71, 163-166, 2024

Rectal Metastasis from Early-Stage Endometrial Carcinoma Not Associated with Endometriosis: A Case Report and Literature Review

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Received 26 March 2024, accepted 25 July 2024
J-STAGE advance publication 13 June 2025

Edited by NAOTAKE TSUDA

Summary: ***Objective*:** Endometrial cancer (EC) is the third most common malignancy in woman with excellent prognosis when diagnosed in early-stage. Recurrences are extremely rare in Stage I EC especially in rectum when not associated with endometriosis. We present a case of rectal metastasis from endometrial carcinoma after 8 years of primary diagnosis. A review of the literature showed only 6 published cases.
***Case presentation*:** Herein we present a 59-year-old woman with a rectal tumor mass. The patient before 8 years was surgically treated for EC Stage IA with bilateral salpingo-oophorectomy and hysterectomy. After ultra-low anterior resection rectum was removed with the tumor. Histology revealed adenocarcinoma with positive immunohistochemistry for CK7, ER, PAX8, Vimentin which confirmed endometrial origin. Endometriosis was not found.
***Conclusion*:** Although rectum is a rare site of recurrence from endometrial cancer, rectal tumors should be sampled carefully. Previous patient history and positive immunohistochemistry for EC are in favor of recurrent disease. Screening of colorectal carcinoma should be performed in patients with previous gynecologic diagnosis. Further genetic analysis in bigger case series is needed in order to explain the time and the site of recurrence of early-stage endometrial carcinoma.

Keywords secondary carcinoma, rectum, endometrial carcinoma, recurrence, rectal metastasis

INTRODUCTION

Endometrial cancer (EC) is the third most common malignant neoplasm among woman in North Macedonia after breast cancer and colorectal cancer, with 298 new cases reported in 2022 [1]. Most of the cases are diagnosed as low grade and International Federation of Gynecology and Obstetrics (FIGO) Stage I, with a recurrence risk cited as less than 9 % in the first 2–3 years post-treatment. EC metastasis typically recurs in the pelvis, paraaortic lymph nodes, vagina, peritoneum and lungs, whereas atypical metastatic sites are extra-abdominal lymph nodes, liver, adrenal glands, spleen, brain, soft tissue and bone. Metastases to small intestine, large intestine and rectum are extremely rare [2-4]. Moreover, rectal metastasis (RM) typically originates from urogenital cancer, breast cancers, melanoma, pancreas and liver cancers, gastrointestinal cancers, lungs and other [5]. We report a rare case of rectal metastasis of stage I endometrial carcinoma not associated with endometriosis, and review the literature.

CASE PRESENTATION

A 59-year-old female patient was admitted to the

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Abbreviations: CDX2, caudal-type homeobox transcription factor 2; CK20, cytokeratin 20; CK7, cytokeratin 7; CT, computed tomography; EC, endometrial carcinoma; ER, estrogen receptor; FIGO, International Federation of Gynecology and Obstetrics; MRI, magnetic resonance imaging; PR, progesterone receptor; PAX8, Paired box gene 8; RM, rectal metastasis.

University Clinic for digestive surgery in Skopje with the complaints of weight loss of 6 kg in the previous 2 months, abdominal pain and changes in bowel habits without blood in the stool. Blood work revealed parameters within normal limits. A computed tomography (CT) scan of the abdomen and small pelvis was performed, which revealed a cystic mass with the largest diameter of 94 mm, filled with dense contents. It had a septate structure and a thickened wall, localized in front of the sacrum, posterior to and in intimate contact with the rectum. Magnetic resonance imaging (MRI) of the abdomen and small pelvis revealed a large tumor mass with dimension of 86 × 63 mm, localized posterior to the rectum, which was clearly limited and compressed and displaced the rectum, which suggests a secondary MS deposit. Colonoscopy revealed a submucosal spherical protrusion of the mucosa that was neat and was not separated from the surrounding mucosa, 20 cm in length, located in the rectum. The patient was hospitalized for further surgical treatment.

The patient's medical history showed that 8 years earlier she had undergone a total hysterectomy with bilateral adnexectomy due to endometrial adenocarcinoma of the endometrioid type. The endometrial tumor measured 3 × 2 × 1 cm and was found in the fundus of the uterus. The histology showed low grade endometrial adenocarcinoma, endometrioid type, with the following postoperative features, according to FIGO-2010: stage IA disease (pT1a; G2/NG2 pL0; pV0) that invaded less than half of the myometrial thickness. The patient didn't receive chemotherapy after the hysterectomy.

As a result of the current illness, the patient underwent surgical treatment during which the rectum was removed together with the tumor mass, and low anterior rectal resection was made with ileostomy (Figure 1). Histological examination of the tissue sections revealed adenocarcinoma composed of atypical adenoid formations and cribriform structures, infiltrating the subserosal adipose tissue and muscularis propria,

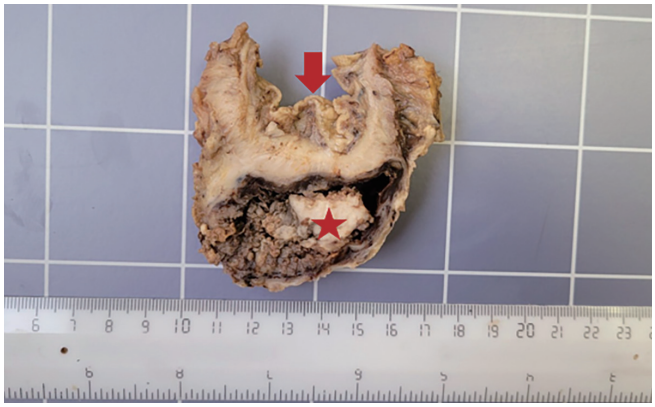

Fig. 1. Gross findings of the resected specimen. Intact mucosa (arrow) with cystic and solid tumor in the perirectal fat and muscularis propria (star).

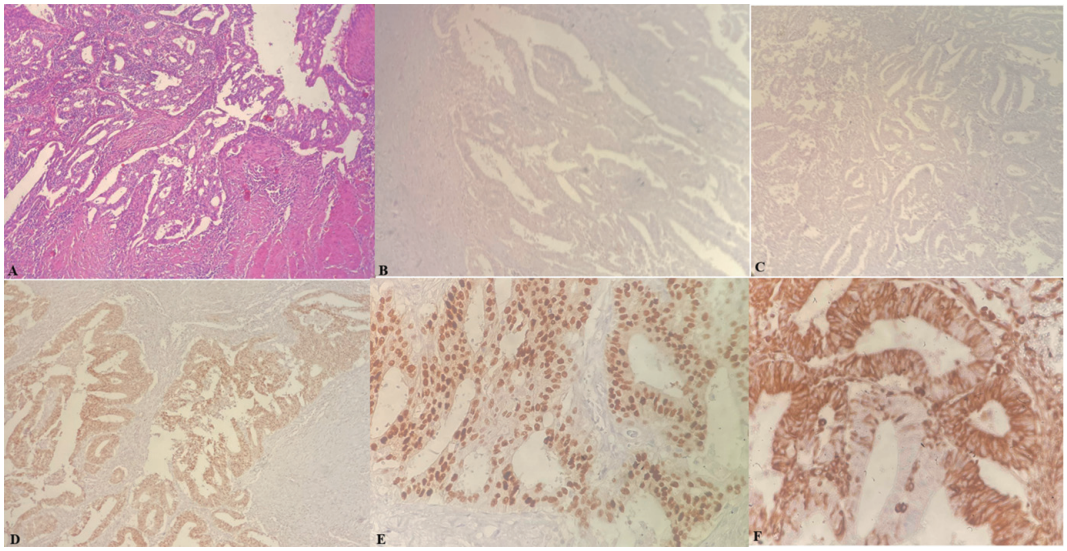

Fig. 2. Histology and immunohistochemistry of rectal tumor.
A. Adenocarcinoma infiltrating muscularis propria of rectal wall (HE×100)
B. CDX2 negative (×100)
C. CK20 negative (×100)
D. PAX8 positive (×100)
E. ER positive (×400)
F. Vimentin positive (×400)

without ulceration and mucosal infiltration (Figure 2A). Abnormal mitosis and tumor necrosis were frequently seen. Lymph node samples showed reactive changes without metastatic deposits. The results of immunohistochemistry showed that the tumor cells were positive for Cytokeratin 7 (CK7), estrogen receptor (ER), progesterone receptor (PR), Paired box gene 8 (PAX8) and Vimentin, and were negative for CK20 and CDX2 (Figure 2B-F). This immunophenotype suggested the endometrial origin of the tumor.

Considering the findings of the described histomorphology, immunoprofile, and previous findings, we made a diagnosis of metastatic endometrial adenocarcinoma, endometrioid type in rectum. The patient started an oncological treatment with first line chemotherapy.

DISCUSSION

Endometrial carcinoma sites of recurrence

The incidence of EC is increasing in recent decades due to increased obesity, hormonal changes and lifestyle habits. The overall prognosis is good if diagnosed at an early stage with primary treatment that involves total hysterectomy and bilateral salpingo-oophorectomy as a must, with lymph node assessment based on uterine factors. The risk of recurrence for low-risk disease has been found to be less than 5% [6]. The most frequent sites of recurrence in the study of Hodge T. et al. were pelvic space, vaginal vault and intraabdominal organs [6].

Rectal metastasis

We report here an extremely rare case of metastasis of endometrial cancer to the rectum, and a literature review is made of published cases (Table 1). As endometriosis is an estrogen-related disease with an increased risk for development of endometrial cancer, we looked for ectopic endometrial tissue in the resected specimen in our case but didn't find any. We found only 6 published cases of rectal metastasis from endometrial cancer that showed no signs of endometriosis [7-11]. If lymphovascular spread is a rare event in early-stage EC, then the pathogenesis of recurrence in the rectum remains unknown after period more than 6 months. Sakata et al. suggest that surgical implantation might be the reason of rectal recurrence after 7 years of Stage I endometrial cancer [7]. Bailey and Gilbert present six cases of rectal metastasis of which 3 were prostatic cancers, 1 breast cancer and two of them were endometrial as in our case [8]. Franchello et al. report recurrence of endometrial carcinoma in rectum after 28 years which is the longest period recorded in the literature [9]. Palla et al. reported endomerioid adenocarcinoma arising from colon endometriosis and these cases of endometriosis-associated adenocarcinoma were not included in this review [12]. RM from endometrial carcinoma may clinically present with diarrhea, rectal bleeding, abdominal cramps and change in bowel habits.

Final diagnosis

Secondary malignancies in rectum may be mistaken for primary rectal origin tumors, especially when the whole wall thickness is infiltrated or/and there is a bulky intraluminal mass with ulceration. Our

TABLE 1.
Case reports in literature of rectal metastasis from endometrial carcinoma not associated with endometriosis

Reference number	Author/Year	Patients age	Stage of endometrial carcinoma	Time between primary and RM	Clinical presentation	Prognosis
7	Sakata et al./2013	65	IA	7 years	/	Good postoperative progress
8	Bailey and Gilbert/2002	62, 63	Not specified	5years, 7years	Change in bowel habits, rectal bleeding	Median survival 7, 5 months
9	Franchello et al./2015	72	IB	28	Rectal mass	After 23 months disease-free
10	Wou et al./2014	59	IB	6 years	Abdominal cramps, rectal bleeding, diarrhea	Unremarkable postoperative recovery
11	Li and Zheng/2023	68	IA	5 years	Diarrhea, hematochezia	After chemotherapy, 6 months no recurrence
Current case	Krsteska et al./2024	59	IA	8 years	Weight loss, change in bowel habits	Ongoing chemotherapy

case had intact rectal mucosa and an intraluminal bulk which may suggest secondary or submucosal lesion on colonoscopy. Two of the presented cases in the table showed normal mucosa on colonoscopy as in our case [7,9]. Previous diagnosis of endometrial carcinoma should suggest recurrent tumor over a primary one. Immunohistochemical analysis of primary rectal carcinoma shows positivity for CDX2, CK20, and EC shows positivity for CK7, PAX8, ER, PR, and Vimentin. Our case was positive for CK7, PAX8, ER, Vimentin and was negative for CDX2 and CK20. All published cases with rectal metastasis from early-stage endometrial cancer showed good postoperative recovery; two of them had a median survival of 7.5 months, while our patient is currently on chemotherapy.

CONCLUSION

Although some sites of recurrent endometrial carcinoma, such as vagina, nodes, peritoneal and lung metastases, are well known, other sites such as liver, adrenals, spleen, brain, osseous and soft tissue metastases, small intestine, rectum are extremely rare. Screening of colorectal carcinoma with colonoscopy should be performed in patients with previous gynecologic history to exclude recurrence. Previous patient history and positive immunohistochemistry for EC may suggest recurrent disease. Further genetic analysis in a larger case series is needed in order to better understand the period and the site of recurrence of early-stage endometrial carcinoma.

AUTHOR CONTRIBUTIONS: BK, VR and AJ performed the histologic and immunohistochemical examination and analyzed the data. SA performed the surgical intervention and obtained the clinical data. All authors made the major contributions to the design, concept and writing of the manuscript. All authors have read and approved the final manuscript.

CONFLICT OF INTEREST: The authors declare that they have no conflict of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE: Written consent was obtained from the patient and the report follows the recommendations of Ethics Board of Faculty of Medicine in Skopje.

CONSENT FOR PUBLICATION: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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