

Uterine Cervix Metastasis from Primary Colorectal Carcinoma: a Report of Two Cases with Review of Literature

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Introduction

Metastatic spread from colorectal carcinoma is quite predictable, initially through lymphatic vessels followed by the hematogenous route. Common metastatic sites of colorectal cancer are the liver, lung, lymph nodes, and peritoneum and metastasis to the uterine cervix is an uncommon event. Herein we report two cases of cervical metastasis from colorectal carcinoma.

Case Presentation

Case 1

A 26-year-old female presented with complaints of bleeding per rectum for 6 months. Per rectal examination revealed growth in lower third of rectum. Complete gynecological examination was performed followed by cytological analysis of uterine cervix cell smear and all findings were normal. Lower gastrointestinal endoscopy (LGIE) was suggestive of 5 cm ulcerative

growth in the rectal area. Contrast-enhanced computed tomography (CECT) showed circumferential thickening of rectal wall with a length of 5 cm with an eccentric growth on right rectal wall with maximum wall thickness of 10 mm. Biopsy was suggestive of moderately differentiated mucin-secreting adenocarcinoma. Hence, patient was diagnosed with rectal cancer. She was treated with neoadjuvant chemoradiation with 45 Gy in 25 fractions and weekly chemotherapy with 5-FU and leucovorin. The patient then underwent low anterior resection with total mesorectal excision. Pathological examination found a moderately differentiated adenocarcinoma with serosal involvement. Perineural spread and lymphovascular emboli were present; however, lymph nodes dissected were free of tumor. She was pathologically staged as pT4aN0M0. She was then treated with six cycles of adjuvant chemotherapy with FOLFOX. CECT at 1-month post-completion of chemotherapy and at 4 months did not reveal any abnormality. Eight months later, she came with complaints of postcoital bleeding and leucorrhea. On pelvic examination, an ulceroproliferative growth was found at cervix which was involving all fornices and upper half of all vaginal walls. Biopsy was suggestive of metastatic adenocarcinoma with mucin-secreting features. Immunohistochemistry (IHC) performed showed positivity of tumor cells for CK20 and negative for CK7, confirming metastasis from colorectal primary (Fig. 1a). PET-CT showed a lesion in the cervix with parametrial infiltration and loss of fat planes between lesion and bladder. As the patient was not a candidate for surgery in view of the involvement of vaginal walls, so she was started on second-line chemotherapy with FOLFIRI regimen. Chemotherapy was stopped after three cycles due to progression of disease and intolerance. The patient died of progressive disease.

Case 2

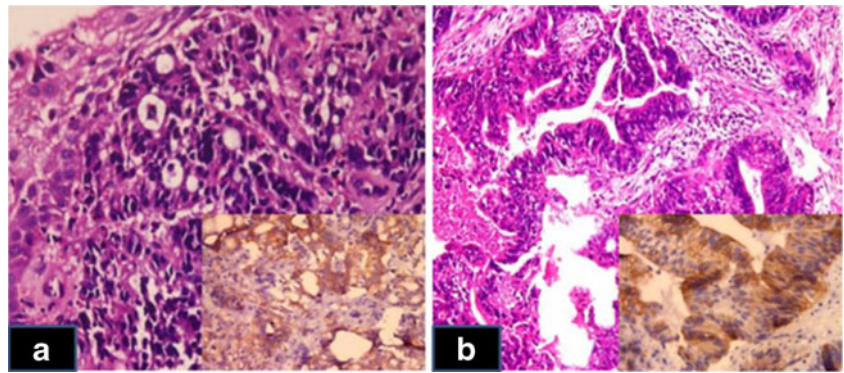
A 21-year-old female presented with complaints of bleeding per rectum for 8 months. Per rectal examination revealed

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Fig. 1 Cervical biopsies of the two cases showing metastatic tumors from the colon. (a) Moderately differentiated metastatic adenocarcinoma and (b) well-differentiated metastatic adenocarcinoma with insets showing positivity for cytokeratin 20 in the tumor. [a, b Hematoxylin–eosin stain, $\times 400$; insets, immunoperoxidase stain $\times 400$]



growth at 8 cm from anal verge. Complete gynecological examination (including bimanual pelvic examination and cytological analysis of uterine cervix cell smear) was normal. LGIE and CECT were suggestive of growth in rectosigmoid area. Biopsy from growth was suggestive of well-differentiated adenocarcinoma. The patient then underwent anterior resection with total mesorectal excision and colocolic anastomosis for rectosigmoid cancer. Histopathological examination revealed a well-differentiated adenocarcinoma with tumor reaching up to serosa with lymph nodal involvement and presence of lymphovascular emboli. Circumferential resection limit was involved by tumor. The patient was staged as pT4aN2M0. Postoperatively, she received adjuvant radiotherapy of 50 Gy in 25 fractions over 5 weeks followed by 12 cycles of chemotherapy with 5-FU and leucovorin. CECT done 1 month after completion of chemotherapy and at 6 months did not reveal any abnormality. One year later, patient presented with complaints of leucorrhea. On pelvic examination, an ulceroproliferative growth was found at the cervix which was involving all fornices and filling the vagina. Biopsy was suggestive of well-differentiated metastatic adenocarcinoma and IHC showed positivity of tumor cells for CK20 and negative for CK7, confirming metastasis from colorectal primary (Fig. 1b). CECT showed a 6 \times 7-cm lesion in the region of cervix with extension to vagina with loss of fat planes between lesion and bladder with parametrial stranding. The patient was given the option of palliative chemotherapy but refused and opted for palliative care. The patient ultimately died of disease 4 months later.

Discussion

Development of metastasis to the feminine genital tract is an infrequent condition and represents a diagnostic challenge for clinicians and pathologists. The uterus, and especially the uterine cervix, is a rare location of colorectal metastasis: involvement of the uterus represents less than 10 % of all cases of metastases to the female genital tract from extragenital cancers (3.4 % for the uterine cervix alone) [1]. Extragenital tumors most often metastasizing to the uterine

cervix or corpus generate from the breast (42.2 %), stomach (18.5 %), pancreas (5.2 %), lung (4.6 %), urinary bladder and kidney (4.6 %), gallbladder (2.3 %), and cutaneous melanoma (1.7 %) [1]. Involvement of the uterine cervix is usually by direct extension of extragenital neoplasias and this is relatively frequent. The reason why metastatic carcinoma to the cervix alone through hematogenous or lymphatic spread is so rare is because of its small size, relatively limited blood flow, distal circulation, as well as organ's abundant content of fibrous tissue, which makes the uterine cervix a medium that is scarcely favorable for the propagation of malignant cells. Moreover, the lymphatic vessels of the pelvis all drain away from the cervix [2].

Exhaustively reviewing all metastatic rectal carcinomas to the uterine cervix from the pertinent literature [2–7] is difficult because some cases are poorly documented; some series mixed uterine metastases to the corpus/to the cervix, direct invasion/distant spread, or colon/rectal primaries. Nakagami et al. [4] reported a case of uterus cervix metastasis from rectal cancer and reviewed 27 cases of cervical metastases from colorectal carcinomas which constitute the largest review to date. Two other case reports were published by Trastour et al. [6] and Chereau et al. [7]. The interval between primary carcinoma and the uterine cervix metastatic disease diagnosis was 17 months with a range from 0 to 60 months. Gynecological symptoms were vaginal bleeding, pelvic pain, mass, and vaginal discharge. In our study, vaginal discharge was present in both patients and bleeding per vaginum in one. Gynecological symptoms following medical history of colorectal carcinoma should call to mind metastases in order to refer rapidly patients for appropriate treatment. Mazur et al. [1] reported that up to 42 % of metastatic cervical lesions are mistaken for primary tumors. The survival period after the diagnosis of the secondary deposit was 11 months, ranging from 1 to 60 months [4].

The present case report addresses several issues. First, both the patients in our study were young and had advanced disease at presentation. Second, in patients with prior colorectal carcinoma, the practitioner should be aware of a

possible metastasis to the uterine cervix on detection of adenocarcinoma. Uterine cervical metastasis from colorectal cancer is a diagnostic challenge both clinically as well as pathologically. In this specific setting, the contribution of IHC is crucial to differentiate a genital from extragenital origin of the uterine cervix tumor. IHC profile which is CK20 positive and CK7 negative reveals metastasis from colorectal cancer primary. Third, the spread of the tumor to the uterine cervix in both cases might have been due to lymphatic and/or hematogenous pathways because lesions by direct extension from the rectum or by peritoneal implantation had been excluded and lymphovascular emboli were present in both previously resected specimens.

Treatment of metastatic adenocarcinoma of the cervix does not differ from one of recurrent cervical cancer. The salvage therapy with chemotherapy is used mainly when the disease is unresectable. In conclusion, metastatic cancer to the uterine cervix should always be considered when patient experiences abnormal vaginal bleeding or discharge with a history of primary gastrointestinal tract carcinoma.

Conflict of Interest The authors declare no conflicts of interest in the preparation of the manuscript or during the study.

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