

Cutaneous Metastasis of Rectal Cancer: A Case Report and Literature Review

Ahmed Dehal, MD; Sunal Patel, MD; Sean Kim, MD; Emanuel Shapera, MD; Farabi Hussain, MD

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ABSTRACT

Cutaneous metastasis of rectal cancer is rare. It typically indicates widespread disease and poor prognosis. We report an exceedingly rare case of rectal cancer with metastasis to the skin and review the literature on cutaneous metastasis of rectal cancer. A 47-year-old man presented with stage IV unresectable adenocarcinoma of the rectum and received palliative chemoradiation for local pain control. About a year later he developed extensive skin lesions involving the genital area, bilateral groin, and perineum. Biopsy specimen showed mucinous adenocarcinoma compatible with rectal origin. Palliative treatment with radiation therapy was initiated. The patient responded well to treatment and is still alive more than a year after diagnosis of cutaneous metastasis. Surgeons should maintain strong suspicion of cutaneous metastases when patients with rectal cancer have new or evolving skin lesions.

INTRODUCTION

Cutaneous metastasis of internal malignancies is rare, occurring in 0.7%-9.0% of all malignancies.^{1,2} It usually indicates intralymphatic and/or intravascular tumor dissemination with a poor prognosis. The neoplasms that most often metastasize to the skin are the most frequently occurring human cancers, such as breast cancer in women and lung cancer in men. Other tumors with a high cutaneous metastatic potential include gastrointestinal tract carcinomas.^{1,2}

Similarly rare, cutaneous metastases from abdominal malignancies occur in less than 4% of patients.^{2,3} Those arising from adenocarcinomas of the colon and rectum are even more rare and typically signify widespread disease with a poor prognosis.^{2,3} Cutaneous metastases of rectal cancer usually occur within the first 3 years of follow-up.^{3,4} Most cases occur late in the course of the disease, but cutaneous metastases may be the initial presentation of the internal malignancy. Rectal carcinoma metastases to the skin have no distinctive features, presenting most often as small subcutaneous or intradermal nodules that measure 1 cm to 2 cm in diameter and tend to coalesce. These nodules tend to be asymptomatic, firm, rubbery, and painless.^{4,5} Surgical intervention is not feasible, but systemic chemotherapy and radiotherapy may help control

symptoms. Prognosis is poor and median survival of patients after the appearance of cutaneous metastatic lesions is reported to be approximately 3 to 18 months.⁵

We present a case of metachronous skin metastasis during chemoradiation treatment in a patient with advanced rectal cancer. This case is different from others previously reported because it is an exaggerated and uncommon form of metastatic dissemination to the skin, with massive soft tissue infiltration of the perineum. We also present a comprehensive review of all reported cases of cutaneous metastasis from rectal cancer and summarize the clinical characteristics of these patients, the treatments they received, and their outcomes.

CASE REPORT

A 47-year-old man presented in December 2012 with a 10-month history of an approximately 10 cm × 15 cm mass bulging from his anus and associated severe rectal pain, weight loss of 23 kg (50 lbs), and change in bowel habits. A biopsy of the mass revealed invasive mucinous adenocarcinoma. Colonoscopy could not be performed because of the size of the rectal mass. Computed tomography scan of the chest/abdomen and pelvis demonstrated a locally invasive rectal mass, significant aortocaval and left inguinal lymphadenopathy (Figures 1 and 2), and bibasilar tiny nodules consistent with metastatic disease. Biopsy findings of the left inguinal lymph nodes were consistent with metastatic mucinous adenocarcinoma. Given that the disease was, on the basis of the American Joint Commission on Cancer tumor-node metastasis staging system, stage IV (T4N2M1b), surgery was not feasible. The patient was referred to medical and radiation oncology for palliative chemoradiation because of his severe rectal pain.

In January 2013, a total dose of 5040 cGy was given, delivered in 28 fractions concomitant with XELOX (capecitabine plus oxaliplatin). However, intravenous chemotherapy was stopped because of significant neuropathy as well as poor patient adherence. The patient refused any further chemotherapy. Given that his *K-ras* gene was not mutated, cetuximab was not administered. In September 2013, the patient was reevaluated in the surgery clinic for possible palliative resection. Repeat computed tomography scans showed minimal improvement in the size of the tumor and the

Ahmed Dehal, MD, is a Surgery Resident at the Fontana Medical Center in CA. E-mail: ahmed.dehal@gmail.com. Sunal Patel, MD, is a Surgery Resident at the Fontana Medical Center in CA. E-mail: sunal17@gmail.com. Sean Kim, MD, is a Surgery Resident at the Fontana Medical Center in CA. E-mail: y32kim@gmail.com. Emanuel Shapera, MD, is a Surgery Resident at the Fontana Medical Center in CA. E-mail: emanuelshapera@gmail.com. Farabi Hussain, MD, is a Surgeon at the Arrowhead Regional Medical Center in Colton, CA. E-mail: hussainf@armc.sbcounty.gov.



Figure 1. Computed tomography image of the rectal tumor and the left inguinal lymphadenopathy (86 mm × 49 mm).



Figure 2. Computed tomography image of the aortocaval lymphadenopathy (87 mm × 48 mm).

retroperitoneal lymphadenopathy. However, in the absence of tumor-related complications, we thought that palliative surgery would be of no benefit to the patient in terms of survival and quality of life. In April 2014, the patient returned to the surgery clinic and was found to have extensive new skin lesions involving the genital area, bilateral groin, and perineum (Figure 3). A biopsy of the skin lesion found metastatic moderately differentiated adenocarcinoma, most likely of rectal origin, infiltrating the skin and subcutaneous tissue. Palliative radiation therapy was initiated. The patient tolerated the additional radiation dose, and he had excellent local response to it. He is still alive more than a year after the diagnosis of skin metastasis and has not shown any disease progression.

DISCUSSION

Metastases to the skin occur in the course of malignancy, especially in extensive metastatic disease. They may represent failure of ongoing therapy or recurrence of a neoplasm thought to have been eradicated; or, they may be the first manifestation of asymptomatic, unsuspected occult malignancy. We present a case of extensive skin metastasis to the perineum in a patient with unresectable rectal cancer receiving palliative chemoradiation. To date, there has been no solid data about the incidence of cutaneous metastasis from rectal carcinoma because most of the data have been obtained

from autopsy series. Reingold reviewed the autopsy findings of 32 patients with cutaneous metastasis from internal carcinoma, excluding breast cancer.⁴ He found that the prevalence of cutaneous metastasis was 32 cases out of 2300 internal carcinomas studied. The most common primary site was the lung (16 cases). The rectum was the site of the primary tumor in only 1 case. The most common sites of metastasis were chest skin and abdominal skin, with rectal carcinoma cutis occurring in the right first toe, chest, and abdomen.

Lookingbill et al^{2,6} conducted two large retrospective studies at Hershey Medical Center in Pennsylvania to analyze the relative frequencies of skin metastases according to the type and location of the primary tumor and the site of the cutaneous metastases. The first study,⁶ performed in 1990, reported on 7316 cancer patients, including 772 with colorectal cancer. Cutaneous involvement was present at the time of diagnosis in 4 patients (0.05% of patients with colorectal cancer); clinical information was not available for those patients, and it is not clear whether the primary cancers were rectal or colonic. The second study,² conducted in 1993, examined the records of 4020 patients with metastatic disease, including 420 (10%) with skin metastases. In the cohort of 413 patients with metastatic colon cancer, 18 (4.4%) had skin metastases. Eleven of the 18 had only local metastases, most of them located in the abdominal incision site.

We found 28 cases⁷⁻²⁷ of cutaneous metastases from rectal cancer in the English-language literature, including 2 case series comprising 6 cases each^{18,20} (Table 1). The mean age of patients was 55.5 years (range 29-79), 19 were men, and adenocarcinoma was the underlying histology in all. High-risk features such as mucinous (n = 7), signet ring cell (n = 4), and poorly differentiated (n = 4) were present in 54% of patients. Most of the patients presented with advanced-stage disease (stage III in 10 patients and stage IV in 11 patients). Surgical resection, either low anterior resection or



Figure 3. Perineal, bilateral groin, and genital skin metastases (86 mm × 69 mm).

Table 1. Cases of rectal cancer with cutaneous metastasis

Author, year	Age, years	Sex	Histology	Stage	Primary cancer treatment	Interval, ^a months	Skin mets location	Skin mets morphology	Skin mets treatment	Survival (follow-up time in months)
Gray and Das, ⁷ 1989	79	F	Adenocarcinoma	—	Radiation	0 ^b	Leg	Nodules	None	No (18)
Reed and Stoddard, ⁸ 1992	68	F	Adenocarcinoma, poorly differentiated	—	LAR	4	Perineum	Nodules	APR	—
De Friend et al, ⁹ 1992	49	F	Adenocarcinoma	III	LAR	7	Perineum	Nodules	WLE	—
Kauffman and Sina, ¹⁰ 1997	50	M	Adenocarcinoma, signet ring	IV	LAR+ACR	36	Multiple	Plaques	None	No (3)
Adani et al, ¹¹ 2001	70	F	Adenocarcinoma	III	APR + AC	36	Leg	Nodules	CR	Yes (14)
Tsai et al, ¹² 2002	47	M	Adenocarcinoma, signet ring	III	APR + AC	11	Multiple	Nodules	C	No (4)
Melis et al, ¹³ 2002	41	M	Adenocarcinoma	IV	NCR	1	Perineum	Plaques	None	—
Damin et al, ¹⁴ 2003	44	M	Adenocarcinoma	II	LAR	6	Groin	Zosteriform	R	No (5)
Hayashi et al, ¹⁵ 2003	50	M	Adenocarcinoma, mucinous	—	LAR	4	Perineum	Nodules	None	—
Sarid et al, ¹⁶ 2004	60	F	Adenocarcinoma, mucinous	III	NR+LAR+ACR	16	Chest, abdomen	Ulcers	WLE	No (56)
Reuter et al, ¹⁷ 2006	69	M	Adenocarcinoma	II	APR+ ACR	5	Perineum	Plaques	None	No (6)
Tan et al, ¹⁸ 2006	70	M	Adenocarcinoma, mucinous	IIIB	LAR+AC	24	Back	Nodules	WLE, C	—
Tan et al, ¹⁸ 2006	53	F	Adenocarcinoma	IIIB	APR	10	Perineum	Nodules	WLE, CR	No (26)
Kilickap et al, ¹⁹ 2006	29	M	Adenocarcinoma, signet ring	IIIA	LAR+APR+ ACR	14	Chest wall, axilla	Nodules	WLE + C	Yes (4)
Gazoni et al, ²⁰ 2008	55	F	Adenocarcinoma, poorly differentiated	IV	Colostomy+CR	0 ^b	Perineum	—	CR	No (3)
Gazoni et al, ²⁰ 2008	66	M	Adenocarcinoma, poorly differentiated	IV	Colostomy+ CR	0 ^b	Perineum	—	CR	No (4)
Gazoni et al, ²⁰ 2008	68	M	Adenocarcinoma, poorly differentiated	IV	Colostomy+CR	0 ^b	Thigh, axilla	—	CR	No (3)
Gazoni et al, ²⁰ 2008	72	M	Adenocarcinoma	IV	Colostomy+CR	0 ^b	Perineum	—	CR	No (5)
Gazoni et al, ²⁰ 2008	65	M	Adenocarcinoma	IV	Colostomy+CR	0 ^b	Perineum	—	CR	No (7)
Gazoni et al, ²⁰ 2008	78	M	Adenocarcinoma	IV	Stent+CR	0 ^b	Perineum	—	CR	No (1)
McWeeney et al, ²¹ 2009	72	M	Adenocarcinoma	III	Ileostomy+NCR	6	Perineum	Nodules	WLE	—
Saladzinskas et al, ²² 2010	64	M	Adenocarcinoma, mucinous	IIA	NR+ LAR	42	Face	Ulcers	WLE	Yes (7)
Ismaili et al, ²³ 2011	50	F	Adenocarcinoma, signet ring	IV	None	0 ^b	Multiple	Zosteriform	None	No (1)
Balta et al, ²⁴ 2012	46	M	Adenocarcinoma, mucinous	IIIB	Colostomy	12	Perineum	Ulcers	None	—
de Miguel Valencia et al, ²⁵ 2013	55	M	Adenocarcinoma, mucinous	IIIB	NCR+APR+ AC	18	Multiple	Nodules	None	No (—)
Ozgen et al, ²⁶ 2013	65	M	Adenocarcinoma	IIA	NCR+LAR+ACR	18	Perineum	Nodules	CR	Yes (12)
Akpak et al, ²⁷ 2013	47	F	Adenocarcinoma	IV	APR	36	Perineum	Ulcers	WLE + CR	—
Dehal et al, 2015 ^c	47	M	Adenocarcinoma, Mucinous	IV	CR	1	Perineum	Nodules	R	Yes (12)

^a Interval between cancer treatment/diagnosis and skin metastasis presentation.

^b In those patients, skin metastasis was the first sign of the underlying malignancy. Therefore, there was no interval between the primary cancer diagnosis and the onset of the skin metastasis.

^c Described in this article.

— = data not reported; AC = adjuvant chemotherapy; ACR = adjuvant chemoradiation; APR = abdominoperineal resection; C = chemotherapy; CR = chemoradiation; F = female; LAR = low anterior resection; M = male; mets = metastasis; NCR = neoadjuvant chemoradiation; NR = neoadjuvant radiation; R = radiation; WLE = wide local excision.

abdominoperineal resection, was performed in 16 patients, with chemoradiation given either preoperatively or postoperatively. Skin metastasis presented as a recurrence in 20 patients, with an average time to recurrence of 18 months (range 1-42). Skin metastasis was the first sign of the underlying malignancy in the remaining 8 patients. The perineum was the site of the skin metastases in 11 patients. Among the rest, skin metastases occurred at multiple sites, with frequent involvement of the chest and axillae. The face and extremities were infrequently involved. Among reports describing morphology, skin nodules were most common. Most patients (20/28) received treatment for skin metastasis: excision with or without chemoradiation (n = 8), chemotherapy and/or radiation therapy alone (n = 11), or abdominoperineal resection (n = 1). Vital status was reported for 20 patients. Among these, 15 died. The duration of follow-up was reported for only 19 patients. The average time from skin metastasis diagnosis to death was about 10 months (median 4, range 1-56).

Although cutaneous metastasis typically signifies widespread disease and a poor prognosis, several cases of isolated rectal metastases to the skin without evidence of visceral disease have been reported.^{7,9,11,13,15-17,26,27} Also, in a minority of patients, cutaneous disease may precede metastasis to other organs.^{14,18,19} In these cases, it is imperative that the skin lesion be detected early, biopsied, and properly diagnosed. Alternately, skin metastasis could be the first sign of an underlying advanced rectal cancer.^{20,23} Gazoni et al²⁰ reported a series of 6 patients with concurrent diagnoses of advanced stage IV rectal cancer and skin metastases. None survived more than 7 months after diagnosis, regardless of the treatment modality.²⁰ Therefore, recognition of suspicious skin lesions as possible harbingers of undiagnosed visceral malignancy is important in treating patients with or without a history of cancer.

Several mechanisms of cutaneous metastasis have been postulated. Kauffman and Sina¹⁰ suggested that metastatic spread of adenocarcinoma to the skin and subcutaneous tissue could be caused by lymphatic and hematogenous spread, direct extension, or implantation during surgery. They reported a case of adenocarcinoma of the rectum with inflammatory metastases to skin on the thigh. They were able to show through immunohistochemical evaluation that the dermal vessels containing neoplastic cells were both lymphatic and capillary vessels and thus concluded that the tumor cells travelled to the skin via lymphatics and blood vessels. All three mechanisms of metastasis occurred in our patient. Considering that skin metastases developed close to the primary cancer in a setting of heavy nodal disease, the likely pathophysiology is a combination of intravascular and lymphatic dissemination. However, the possibility of implantation during the biopsy of the left inguinal lymph nodes cannot be excluded.

CONCLUSION

Cutaneous metastases are a rare and usually signify disseminated disease. Their presence warrants a thorough metastatic workup. Clinicians treating patients with internal carcinomas should look for skin involvement even after a long asymptomatic period, paying special attention to all skin nodules, nonhealing ulcers, and persistent indurate erythema. Early detection and recognition of metastatic disease in the skin can dramatically alter treatment and prognosis. A high index of suspicion is recommended when new skin lesions are found in cancer patients. Patient education plays a major role in this early detection. Patients with a history of rectal carcinoma should be taught to inspect all areas of their skin several times annually, to recognize the signs of cutaneous metastases, and to take appropriate action if they find a questionable lesion. It is extremely important that patients with cancer receive regular dermatologic examinations and that practitioners remain aware of the potential for metastasis to the skin. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

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Juvenile Delinquents

In the community of living tissues, the uncontrolled mob of misfits that is cancer behaves like a gang of perpetually wilding adolescents. They are the juvenile delinquents of cellular society.

— Sherwin B Nuland, MD, 1930-2014, American surgeon and author, professor of bioethics, history of medicine, and medicine