Skin involvement as the presenting sign of anorectal adenocarcinoma

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ABSTRACT

Cutaneous involvement as the presenting sign of internal carcinoma is rare and is associated with poor prognosis. Here we present the case of a 66-year-old woman with anorectal adenocarcinoma who presented with tumor involvement of the skin.

KEYWORDS Anorectal adenocarcinoma; cutaneous metastasis; dermal lymphatic invasion

A variety of tumors originate within the anal canal, with squamous cell cancer being the predominant histologic type.¹ Other rare anal malignancies include melanoma and adenocarcinoma. As a consequence of their rarity, their management is generally not defined by prospective data.² Up to 10% of patients with any form of metastatic disease will develop skin metastases. Very few patients with internal organ malignancies initially present with skin involvement; the vast majority of these cases arise from a breast primary.³ In this report, we describe the presentation and clinical course of a patient with anorectal adenocarcinoma who initially presented with cutaneous lesions.

CASE PRESENTATION

A 66-year-old woman with limited past medical history and no family history of gastrointestinal malignancy presented with a pruritic, raised erythematous rash on her left labia major, extending to the perineum (*Figure 1a*). She was treated with valacyclovir for suspected shingles with no response. On exam, the right labia majora and urethral meatus were unremarkable. The vagina was atrophic with an intact vaginal cuff. Anorectal examination was notable for a 1 × 2 cm area of thickening along the left anal canal wall, 2 cm proximal to the anal verge. Left vulva biopsy and anal

canal biopsy revealed invasive, moderately differentiated adenocarcinoma with evidence of dermal lymphatic invasion (*Figure 1c, 1d*). The tumor cells stained diffusely with CK7, CK20, and CDX-2, with intact MMR proteins.

Staging magnetic resonance imaging of the pelvis demonstrated a 2 cm semiannular mass involving the anal sphincter 2 cm from the anal verge. Subsequent positron emission tomography–computed tomography scan confirmed the anal canal tumor, with fludeoxyglucose avidity extending to the vulva along with mildly fludeoxyglucose-avid sub-centimeter left inguinal lymph nodes. There were no sites of metastatic disease outside of the pelvis.

After multidisciplinary evaluation, the patient received neoadjuvant therapy with radiation and concurrent capecitabine, with intent to manage the tumor similarly to established standards for rectal adenocarcinoma.⁴ The radiation clinical target volume included the primary tumor, at-risk pelvic and inguinal lymph node regions, and the site of genital skin involvement with margin. The patient developed expected erythema in the treated skin region during the chemoradiation course. Although posttreatment magnetic resonance imaging showed partial response at the site of the primary tumor, 1 month following treatment the patient had biopsy-proven persistent skin disease in the vulva. The initial plan for extensive surgical resection was abandoned when she rapidly developed further progression of the disease to skin

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Figure 1. (a) Patient's skin prior to chemoradiation treatment, showing erythematous, raised lesions involving the vulva. (b) The patient's tumor progressed extensively to involve the skin of the lower abdomen, pelvis, thighs, and buttocks. The suprapubic catheter is shown as well; this was placed for palliation. (Figure provided by patient's spouse.) (c, d) Punch biopsy of skin (hematoxylin and eosin, 40× and 100× total magnification) showing malignant glandular structures in the dermis and dermal lymphatics.

of the lower abdomen. The tumor progressed subsequently through treatment with multiple types of systemic therapy, including cytotoxic therapies and immunotherapy, as well as a second course of palliative radiation, with, ultimately, extensive involvement of the surrounding skin surfaces from the lower abdomen to her bilateral thighs (*Figure 1b*). The tumor demonstrated no response to the nontargeted systemic agents trialed. Sequencing did not reveal an actionable mutation. The patient underwent placement of a suprapubic catheter and loop colostomy formation. No distant visceral or bone disease developed based on repeat imaging. Her performance status declined, and she enrolled in hospice care. She died approximately 2 years after her initial diagnosis.

DISCUSSION

Adenocarcinoma involvement of the anal canal is rare and often represents the downward growth of a low-lying rectal cancer. Tumor immunoprofiling can aid in differentiating low-lying rectal from true anal adenocarcinoma. The patient's tumor was CK7⁺, CK20⁺, and CDX2⁺, indicating likely rectal origin, as anal glands are usually CK20⁻.⁵ Anal adenocarcinomas are managed along paradigms established for rectal adenocarcinoma, with surgery playing a role in

curative-intent treatment, unlike the case for squamous cell carcinoma of the anal canal, where combined radiation therapy and chemotherapy are the primary radical treatment, with surgery reserved for salvage therapy. In one case series spanning 1976 to 1998, disease-free and overall survival at 5 years was 19% (anal adenocarcinoma) and 77% (squamous cell anal cancer), and 64% (adenocarcinoma) and 85% (squamous cell), respectively.⁶

Skin involvement by internal epithelial tumors is rare. In one review of 7316 patients, 1.3% of patients had cutaneous involvement at diagnosis.³ Involvement of the skin was seen at presentation in 0.5% of patients with colon and rectal adenocarcinoma. The patient in our report appeared to have developed the skin involvement by way of dermal lymphatic invasion. The tumor invasion of dermal lymphatics, and indeed the patient's overall clinical course, is similar to what is commonly seen in cases of inflammatory breast cancer.⁷ Although not a requirement for its diagnosis, inflammatory breast cancer is often associated with tumor emboli in the dermal lymphatics, with a resulting "inflamed" appearance of the surrounding skin (so-called carcinoma erysipeloides). The diffuse spread of these tumors through the skin complicates the application of local therapies, such as radiation therapy and surgery.

Tumors in the distal anal canal can spread via lymphatics to the inguinal regions, and it is most likely that the tumor in the present case spread via lymphatics of the perineal skin to skin of the genitalia in a similar process. Curiously, despite the aggressive nature of this patient's cancer, it did not clearly metastasize, based on imaging studies, to distant organs or bone sites. This patient's presentation and clinical course emphasize the intersection of biological and anatomical factors involved in cancer progression and spread.

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