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Metachronous adenocarcinoma of the anal canal after anterior resection for sporadic primary rectal adenocarcinoma: A rare case report

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ABSTRACT

INTRODUCTION: Anal canal adenocarcinoma is an extremely rare malignancy with poorly defined diagnostic and treatment criteria.
PRESENTATION OF CASE: A 42-year-old women was diagnosed with primary anal canal adenocarcinoma 11 months after undergoing anterior resection for primary sporadic rectal adeocarcinoma. Transanal excision was performed and additional adjuvant chemotherapy was given. Immunohistology showed positivity for cytokeratin (CK) 20 and CDX2, and negative CK7, which is compatible with colorectal subtype anal adenocarcinoma. At 6 months follow-up the patient has no evidence of recurrent or metastatic disease.
DISCUSSION: Diagnosis of primary anal adenocarcinoma is typically delayed because of its rarity, and vague clinical presentation. Exact histologic criteria remain poorly defined but the use of immunohistology has improved the overall diagnostic accuracy of anal adenocarcinoma and it also helps define its correct origin. Reports on the management and outcomes of this cancer consist mainly of retrospective studies with no consistent treatment strategy and limited comparison data. Most authors currently recommend neoadjuvant chemoradiotherapy and radical resection. Despite aggressive therapy, rates of local failure and distant recurrence remain high.
CONCLUSION: Diagnosis of adenocarcinoma of the anal canal is difficult but specific immunohistolgic patterns help to correctly identify its correct origin and subtype. Defining the correct subtype of anal adenocarcinoma may impact treatment strategies of this rare cancer.

1. Introduction

Anal canal adenocarcinoma is a rare gastrointestinal tumor; comprising 5–19% of all anal canal malignancies.[1] Standard treatment for adenocarcinoma of the anal canal has not been clearly defined, mainly because of the rarity of this malignancy. Treatment modalities include combined chemoradiotherapy, local excision, and radical excision with abdominoperineal resection. Treatment outcomes are scarce and limited to small retrospective studies and case reports, with no prospective and limited comparative data. We present a case of metachronous anal canal adenocarcinoma occurring after anterior resection and adjuvant chemoradiotherapy for a primary rectal adenocarcinoma.

2. Presentation of case

A 42 year old women with no significant past medical history presented with intermittent hematochezia of 1 month duration. She denied abdominal pain, constipation, or family history of colorectal cancer. Physical examination revealed mild hemorrhoidal disease and a normal digital rectal exam. Colonoscopy was performed and demonstrated a 4-cm long circumferential and ulcerated rectal mass, 12 cm from the anal verge. These findings were confirmed with rigid proctoscopy; and endoscopic biopsies confirmed adenocarcinoma and high-grade dysplasia arising in a tubulovillous adenoma. Pelvic magnetic resonance imaging (MRI) showed a tumor confined to the rectal wall with no evidence of adenopathy or a threatened circumferential resection margin. Further oncologic work-up, including a positron emission tomography – computed tomography (PET-CT) did not show evidence of locally invasive or metastatic disease.

After preoperative clearance, the patient underwent a hand-assisted laparoscopic anterior resection of the rectum without complications. The patients' postoperative course was uncomplicated and she was discharged on postoperative day seven. Final

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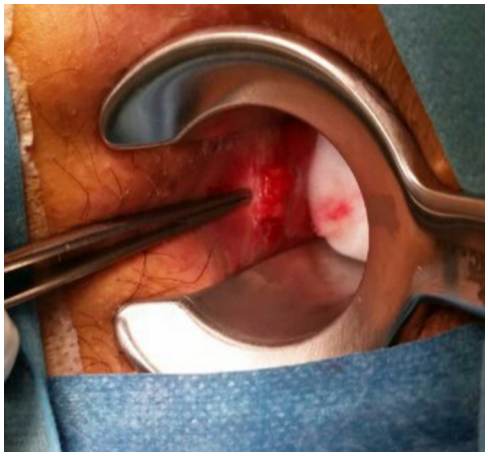

Fig. 1. Intraoperative photograph showing a nodular lesion at the left lateral position of the upper anal canal.

pathology reported a 6/4.5/1.7 cm moderately differentiated adenocarcinoma arising in a tubulovillous adenoma with positive lymphovascular and perineural invasion, as well as intra and peritumoral lymphocytic infiltrate. Twelve of 29 perirectal lymph nodes showed evidence of metastatic disease (TNM classification T3N2b, stage IIIC). Mesorectal grading for completeness of resection was "good" and all resection margins were negative for malignancy. Given the patients' pathologic staging and the recommendations by medical oncology, she received adjuvant chemotherapy (leucovorin, fluorouracil, and oxaliplatin [FOLFOX]), and long-course radiotherapy (total of 45 Gy fractioned over five weeks). She tolerated her adjuvant therapy well with no severe complications or need for hospital admission.

During post-treatment follow-up, the patient remained asymptomatic. Eleven months after surgery she underwent a follow-up colonoscopy that showed a normal appearing and patent colorectal anastomosis at 15 cm from the anal verge. The rest of the colonoscopy was normal. Digital rectal exam showed a mobile, pale-yellow, 1-cm nodular lesion at the left lateral position of the upper anal canal with a smooth surface (Fig. 1). There was no evidence tumor fixation, tethering, or ulceration. There was no evidence of inguinal adenopathy. Biopsy of the anal canal lesion showed poorly differentiated adenocarcinoma. Endoanal ultrasound demonstrated a 1 by 0.6 cm nodule at the left lateral position of the upper anal canal without evidence of sphincter involvement or adenopathy (Fig. 2). Pelvic MRI and PET-CT did not show evidence of locally invasive or metastatic disease. Shortly thereafter, the patient underwent a transanal excision of the lesion with 1-cm margins of normal-appearing tissue (Figs. 3 and 4). Additional margins were excised and evaluated intraoperatively and showed no evidence of malignancy. The patient tolerated the procedure well and there were no complications. Final pathology showed a high-grade poorly differentiated adenocarcinoma with positive lymphovascular and perineural invasion (TNM classification T1N0, stage I). No lymphocytic infiltrate was noted and all margins were negative for malignancy. Tissue staining showed positivity for cytokeratin (CK) 20 and CDX2, and negative CK 7. Additional adjuvant chemotherapy was recommended and the patient tolerated this well. Six months after surgery, the patient is asymptomatic with no evidence of recurrent or metastatic disease.

3. Discussion

Carcinomas of the anal canal are rare malignancies comprising approximately 1–2%of all gastrointestinal carcinomas.[1] Most anal canal carcinomas are squamous cell carcinomas, with less than

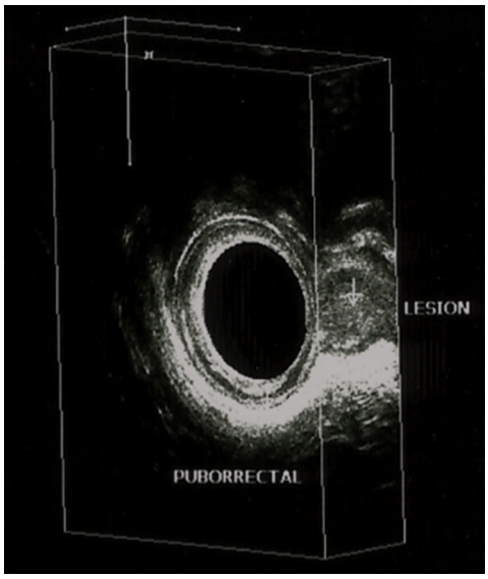

Fig. 2. Endoanal ultrasound demonstrating the location and position of a metachronous adenocarcinoma of the anal canal.

20% being adenocarcinomas.[2] There are two subtypes of anal canal adenocarcinomas: (1) Colorectal (mucosal-based), and (2) Extramucosal (fistula-associated or anal gland). The colorectal subtype originates in the mucosa of the anal canal and is histologically identical to colorectal adenocarcinomas. The extramucosal subtype has no overlying mucosal lesion and arises from the columnar epithelium lining of anal glands. These glands open into the transitional zone of the anal canal through the internal anal sphincter.[3,4] This subtype is more aggressive and has been frequently reported in association with chronic anorectal fistulas and Crohn's disease.[5,6] Adenocarcinomas extending down from the rectum are considered rectal adenocarcinomas. Risk factors for the development of anal canal adenocarcinoma include cigarette smoking, human immunodeficiency virus infection, human papilloma virus infection and anal intercourse.[1,7–9]

The differentiation of anal canal adenocarcinoma from other adenocarcinomas is difficult and diagnostic criteria have not been well established. The utility of immunohistochemistry has been

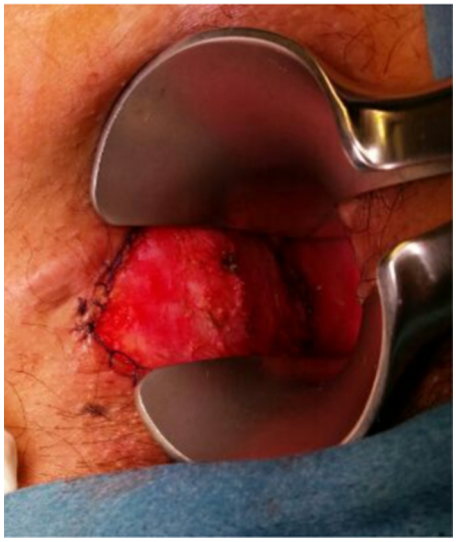

Fig. 3. Intraoperative photograph after wide local excision of a metachronous adenocarcinoma of the anal canal.