ACG CASE REPORTS JOURNAL

CASE REPORT | COLON

Recurrence of Urothelial Bladder Carcinoma in the Colon Presenting as Hematochezia

Youssef El Douaihy, MD[1], Michael Krzyzak, MD[1], Iskandar Barakat, MD[2], and Liliane Deeb, MD[2]

[1]*Department of Internal Medicine, Staten Island University Hospital, Staten Island, NY*
[2]*Department of Gastroenterology, Staten Island University Hospital, Staten Island, NY*

ABSTRACT

Patients with superficial bladder cancers remain clinically indolent after treatment with even a modicum of urologic intervention. However, with more invasive disease, the majority of patients experience recurrence. The conventional route of metastasis and recurrence in primary urothelial cell carcinoma is through lymphatic system, with regional lymph nodes, lungs, liver, brain, and bone being the most common sites. Isolated intraluminal colonic recurrence in the absence of local invasion is extremely rare. We report a unique case of urothelial cell carcinoma presenting with an isolated colonic mass, which unexpectedly, on immunohistostaining, proved to be primarily of urothelial rather than colonic origin.

INTRODUCTION

Urothelial bladder cancer accounts for greater than 90% of all cancers of the urinary tract.[1] Early-stage bladder cancer can be treated effectively; however, patients must be monitored carefully after treatment because the chance of bladder cancer returning is as high as 50%–80%.[2] Patients who have had a bladder tumor resected often subsequently have recurrent tumors locally in the bladder (51%) or in the remaining urinary tract (18%), as in the renal pelvises or ureters. Isolated intraluminal colonic recurrence is rarely described in the literature.

CASE REPORT

A 67-year-old man, formerly a heavy smoker with history of invasive urothelial bladder cell cancer pT3a N0 M0, Stage III disease, treated with bladder resection, reconstruction and adjuvant cisplatin-based chemotherapy, presented 4 years later to our hospital with intermittent rectal bleeding and worsening weakness. Review of systems was otherwise unremarkable. Physical examination revealed bright red blood on rectal exam, and was otherwise grossly unremarkable. Colonoscopy disclosed a large, fungating, ulcerated and friable tumor at 20 cm in the sigmoid colon (Figure 1). Pathology showed high-grade/poorly differentiated carcinoma invading and undermining the colonic mucosa, favoring a metastatic high-grade urothelial cell carcinoma. Immunohistochemical studies were performed on the specimen and showed the following: cytokeratin (CK7) strongly and diffusely positive in tumor cells, CK20 negative in tumor cells and positive in colonic mucosa, pancytokeratin positive in both tumor cells and colonic mucosa cells, villin negative in tumor cells, and caudal type homeobox antibody (CDX2) negative in tumor cells (Figures 2-6). This staining pattern did not support a diagnosis of primary colonic adenocarcinoma, rather a metastatic high-grade urothelial cell carcinoma.

F2-F6

Abdominal and pelvic computed tomography showed a complex-appearing left iliac chain adenopathy with associated inflammatory changes. The sigmoid colon also appeared thickened at the site of the recurring tumor. A positron emission tomography was thereafter obtained to show the highest uptake in the left lower quadrant, with a standardized uptake value (SUV) of 23.9, coinciding with the site of the tumor. The left iliac enlarged lymph nodes

ACG Case Rep J 2016;3(4):e99. doi:10.14309/crj.2016.72. Published online: August 17, 2016.

Correspondence: Youssef El Douaihy, Department of Internal Medicine, Staten Island University Hospital, North Shore–Long Island Jewish Health System, 475 Seaview Ave, Staten Island, NY 10305 (youssef.dou@gmail.com).

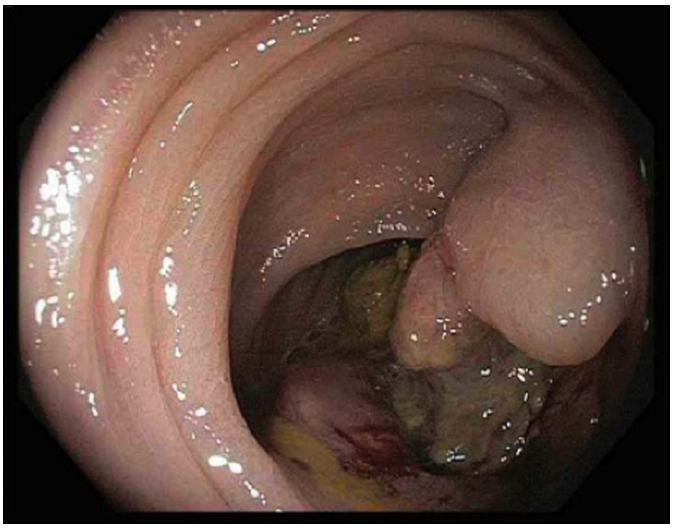

Figure 1. Endoscopic image of the colonic mass present at 20 cm from the entrance site at the anus.

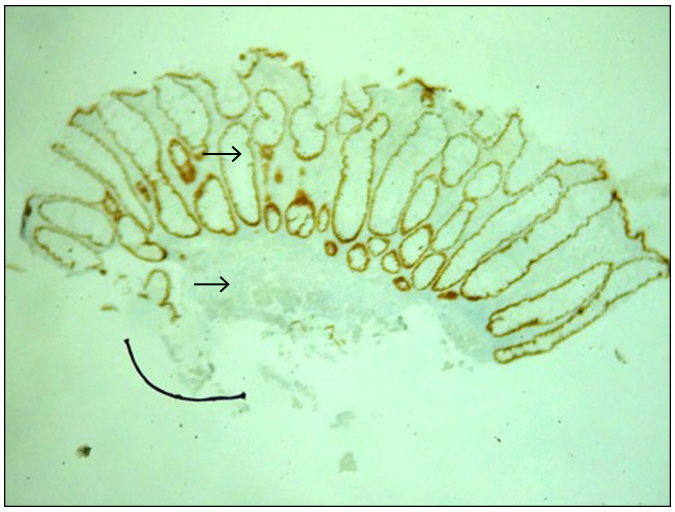

Figure 3. Low-power (40x) CDX2 staining (intestinal epithelial marker) positive for normal small bowel mucosa (top arrow), and negative for tumor cells (bottom arrow).

did not show any increased uptake confirming their nonneoplastic feature. Surgery followed by chemotherapy was suggested, but the patient refused and he agreed to receive gemcitabine and carboplatin. Bleeding resolved thereafter, and a positron emission tomography 6 months later showed regression of the colonic mass.

DISCUSSION

Bladder cancer accounts for 74 690 cases diagnosed annually with a mortality approaching 15 580 patients yearly. With more developed and targeted treatment options, the 5-year survival rate has considerably increased.[3] As the number of bladder cancer survivors continues to increase, the recurrence of this disease is also likely to increase. Direct extension of urothelial cancer has been well described in the literature. It is thought to be the major mode of spread through metalloproteinase-mediated basement membrane breakdown.[4,5] Tumor spilling has been associated with recurrence at surgical sites[6] as well as in the bladder in patients treated with transurethral resection when compared with patients treated by radical cystectomy. Moreover, direct extension impacts staging,[7] thus serving as a major predictor of prognosis. The ability of cancer cells to migrate and invade through the extracellular matrix is a critical step for tumor metastasis.[8] The extent of layer invasion correlates directly with recurrence, distant metastasis, and disease-related

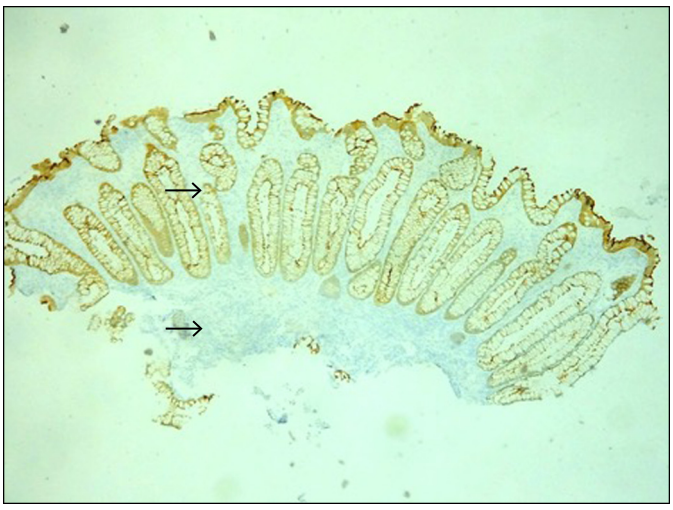

Figure 2. Low-power (40x) villin staining (GI epithelium microvilli marker) positive for normal small bowel mucosa (top arrow), and negative for tumor cells (bottom arrow), consistent with a nonintestinalorigin of the tumor cells.

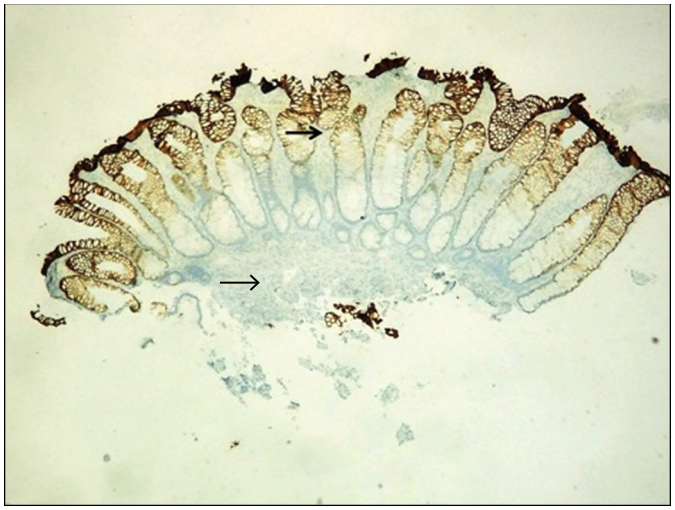

Figure 4. Low-power (40x) CK20 staining (an intestinal mucosal marker) positive for normal small bowel mucosa (top arrow), and negative for tumor cells (bottom arrow).

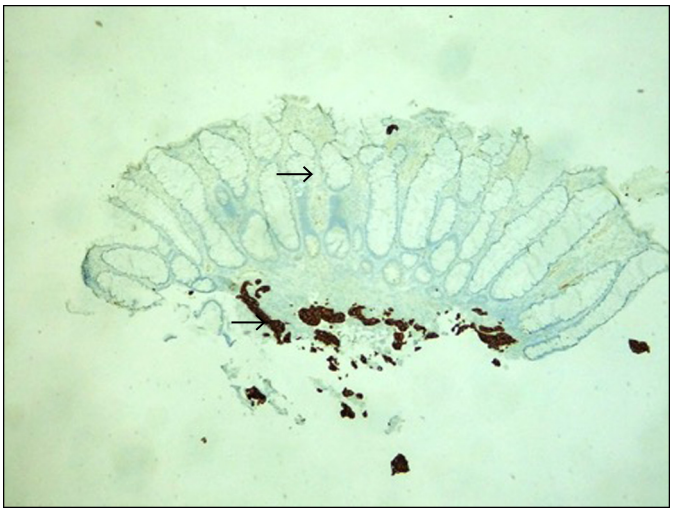

Figure 5. Low-power (40x) CK7 staining (a urothelial epithelial marker) negative for normal small bowel mucosa (top arrow), and positive for tumor cells (bottom arrow).

mortality.[9] Our patient had Stage III disease (muscle invasion), which carries 45%– 69% risk of recurrence.[9]

Angiolymphatic spread is postulated to be the commonly accepted pathway of metastasis. Abdel-Latif et al reported that lympho-vascular invasion is a predictor of lymph node metastasis, and many reported that lympho-vascular invasion is an independent predictor of overall and cancer-specific survival.[10,11] Even in patients with early subepithelial connective tissue tumors (cT1), lympho-vascular invasion may suggest a more aggressive clinical course with an increased risk of tumor recurrence and progression. Nodal status is an independent predictor of distal recurrence.[10]

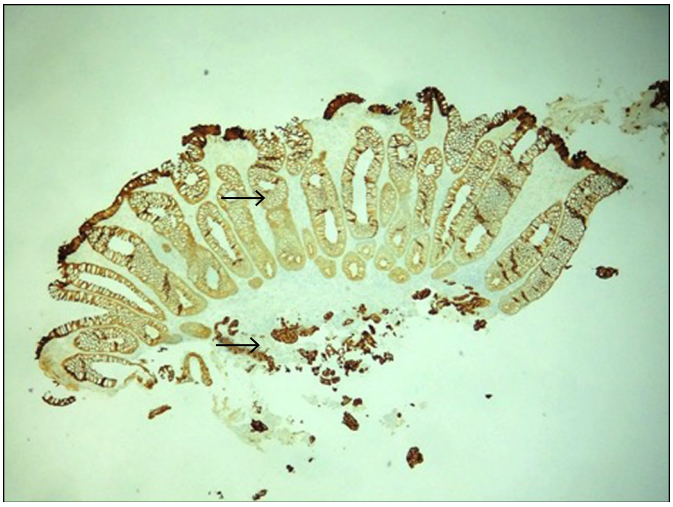

Figure 6. Low-power (40x) pancytokeratin staining (pancytokeratin) positive for both normal small bowel mucosa (top arrow) and tumor cells (bottom arrow).

On the other hand, intraluminal recurrence in the colon in the absence of peritoneal or locoregional disease is rarely described in the literature. Our case was unique in that recurrence was experienced intramucosally in the colon along with absence of any locoregional spread. This might be attributed to the high stage (T3) on final pathology rather than the N0 status at the time of operation. Many series have studied the behavior of disease recurrence in locally invasive and superficial urothelial bladder cancer (pT1 through pT4). Recurrence can occur locally or distally. Common distal recurrence and metastasis sites are lungs, liver, and lymph nodes (nonpelvic).[6,9] However, local recurrence is more common. Whether local recurrence sites were nodes, soft tissue, bone, or masses in the retroperitoneum, the clinical presentations leading to the diagnosis were lumbar pain, pelvic pain, abdominal pain, leg pain, a fistula, alteration of performance status, venous compression, or no symptoms (evidence on preplanned imaging).[12] Our patient presented with frank hematochezia, which, to our knowledge, is yet to be reported. Additionally, we have found no evidence of abdominal masses on imaging conducted prior to colonoscopy. An isolated intraluminal mucosal recurrence in the colon is a rarely described scenario that has been otherwise reported, to our knowledge, only once in the English literature.[13]

Pathology in our case revealed an urothelial neoplastic process in the colon. Immunohistochemistry for a colon cancer is typically a negative CK7, and positive CK20, villin, and CDX2. On the other hand, as shown in our patient, a urothelial cell bladder carcinoma would stain positive for CK7, and negative for CK20, villin, and CDX2.[14]

DISCLOSURES

Author contributions: Y. El Douahihy wrote the manuscript and reviewed the literature. M. Krzyzak and L. Deeb wrote and revised the manuscript. I. Barakat revised the manuscript. Dr. Deeb is the article guarantor.

Financial disclosure: None to report.

Informed consent was obtained for this case report.

Received September 2, 2015; Accepted March 12, 2016

REFERENCES

1. Ploeg M, Aben KK, Kiemeney LA. The present and future burden of urinary bladder cancer in the world. *World J Urol*. 2009;27(3):289–93.
2. Hall MC, Womack S, Sagalowsky AI, et al. Prognostic factors, recurrence, and survival in transitional cell carcinoma of the upper urinary tract: A 30-year experience in 252 patients. *Urology*. 1998;52(4):594–601.
3. Siegel R, Ma J, Zou Z, Jemal A. Cancer statistics, 2014. *CA Cancer J Clin*. 2014;64(1):9–29.

4. Bianco FJ, Gervasi DC, Tiguert R, et al. Matrix metalloproteinase-9 expression in bladder washes from bladder cancer patients predicts pathological stage and grade. *Clin Cancer Res*. 1998;4(12):3011–6.
5. Ozdemir E, Kakehi Y, Okuno H, Yoshida O. Role of matrix metalloproteinase-9 in the basement membrane destruction of superficial urothelial carcinomas. *J Urol*. 1999;161(4):1359–63.
6. Kim B, Choi HJ, Kim MH, Cho KS. Recurrence patterns of bladder transitional cell carcinoma after radical cystectomy. *Acta Radiol*. 2012; 53(8):943–9.
7. Edge SB, Byrd DR, Compton CC. *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010.
8. Wein AJ, Kavoussi LR, Campbell Mf, ebrary Inc. *Campbell-Walsh Urology*. 10th ed. Philadelphia, PA: Elsevier Saunders; 2012.
9. Wallmeroth A, Wagner U, Moch H, et al. Patterns of metastasis in muscle-invasive bladder cancer (pT2-4): An autopsy study on 367 patients. *Urol Int*. 1999;62(2):69–75.
10. Abdel-Latif M, Abol-Enein H, El-Baz M, Ghoneim MA. Nodal involvement in bladder cancer cases treated with radical cystectomy: Incidence and prognosis. *J Urol*. 2004;172(1):85–9.
11. Lotan Y, Gupta A, Shariat SF, et al. Lymphovascular invasion is independently associated with overall survival, cause-specific survival, and local and distant recurrence in patients with negative lymph nodes at radical cystectomy. *J Clin Oncol*. 2005;23(27):6533–9.
12. Cornu J-N, Neuzillet Y, Hervé J-M, et al. Patterns of local recurrence after radical cystectomy in a contemporary series of patients with muscle-invasive bladder cancer. *World J Urol*. 2012;30(6):821–6.
13. Wang HL, Lu DW, Yerian LM, et al. Immunohistochemical distinction between primary adenocarcinoma of the bladder and secondary colorectal adenocarcinoma. *Am J Surg Pathol*. 2001;25(11):1380–7.
14. Yang MH, Sun GH, Yu DS, Chang SY, Ma CP, Cha TL. CEA-producing urothelial cell carcinoma with metastasis presenting as a rectal adenocarcinoma. *Kaohsiung J Med Sci*. 2012;28(11):624–7.