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Esophageal adenocarcinoma with metastasis to the prostatic urethra and bladder

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ABSTRACT

Metastatic esophageal adenocarcinoma to the urinary bladder is extremely rare and aggressive. We discuss here the case of an 83-year-old male with history of esophageal adenocarcinoma treated with chemoradiation therapy and esophagectomy who presented with gross hematuria and lower urinary tract symptoms. Pathology of the bladder tumor after transurethral resection demonstrated invasive adenocarcinoma of both the bladder and the prostatic urethra consistent with metastatic esophageal adenocarcinoma.

1. Introduction

Esophageal cancer (EC) is a highly aggressive disease representing about 1% of all cancers diagnosed and 2.7% of all cancer deaths in the United States.[1] Squamous cell carcinoma and adenocarcinoma are the most common histological variants of EC. With a rising rate of risk factors, esophageal adenocarcinoma accounts for >60% of all EC cases in the United States.[1] The 5-year survival rate is 4% in patients with metastatic disease.[1]

Metastasis primarily follows a lymphatic pattern but direct invasion and hematogenous has been described.[2] Adenocarcinoma most frequently metastasize to intraabdominal sites.[1,3]

Esophageal metastasis to the urinary system is rare, with only 4 previously published cases in the United States, each demonstrating poor survival. In each case survival was reported as less than 9 months and the metastasis had been confined to the bladder urothelium.[4] Here, we report the case of a patient with invasive bladder and prostatic urethral adenocarcinoma from a primary esophageal cancer despite undergoing neoadjuvant chemoradiation therapy and esophagectomy.

2. Case presentation

2.1. Clinical history

The patient is an 83-year-old male with a history of benign prostatic hyperplasia (BPH) and esophageal intramucosal adenocarcinoma of the lower third of esophagus and distal gastroesophageal junction. There was no evidence of metastatic disease on imaging at the time of diagnosis. Patient was treated with neoadjuvant chemotherapy (carboplatin/Taxol) and radiation therapy, followed by minimally invasive esophagectomy 10 months after diagnosis. Final pathological staging after therapy was T3N3 adenocarcinoma representing moderately to poorly differentiated tumor growth into the adventitia of the esophagus. The oncologic follow up plan entailed a CT chest/abdomen/pelvis within a month postoperatively, which showed no evidence of disease recurrence or metastasis, with subsequent plan for follow up CT imaging every 3 months for 2 years. Eight months postoperatively, the patient presented with gross hematuria with clots, requiring continuous bladder irrigation, for which he underwent a cystoscopy, clot evacuation, and TURBT.

2.2. Diagnosis

Grossly, the patient was found to have a papillary frondular tumor involving the prostatic urethra and bladder neck. Pathology from the TURBT revealed intestinal-type mucinous glandular columnar cells consistent with invasive adenocarcinoma like patient's known esophageal adenocarcinoma (Fig. 1). Immunohistochemical stain was positive for CAM 5.2, CDX-2, weakly positive for GATA-3, and negative for CK7, CK20, PSA and NKX3.1, suggestive of metastatic carcinoma of the

Abbreviations: EC, Esophageal cancer; TURBT, transurethral resection of bladder tumor; GERD, gastroesophageal reflux disease; CT, Computerized tomography; FDG, Fluorodeoxyglucose; PET, Positron Emission Tomography; FOLFOX, folinic acid/fluorouracil/oxaliplatin; BPH, benign prostatic hyperplasia.

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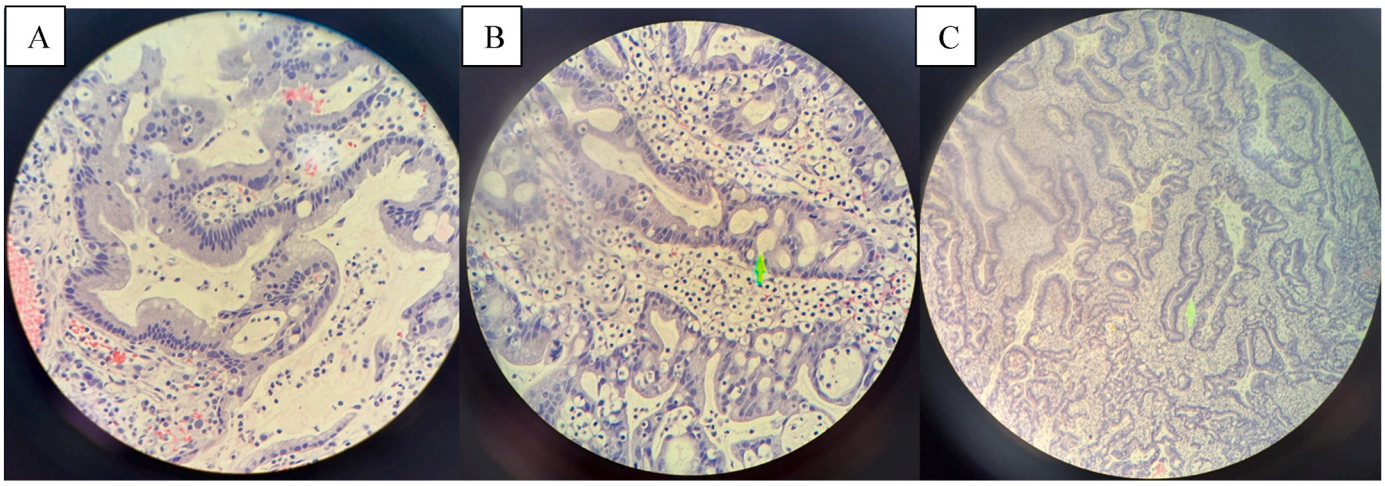

Fig. 1. Bladder tumor resection histology demonstrating intestinal-type (A) mucinous glandular (B) columnar cells (C) consistent with invasive adenocarcinoma.

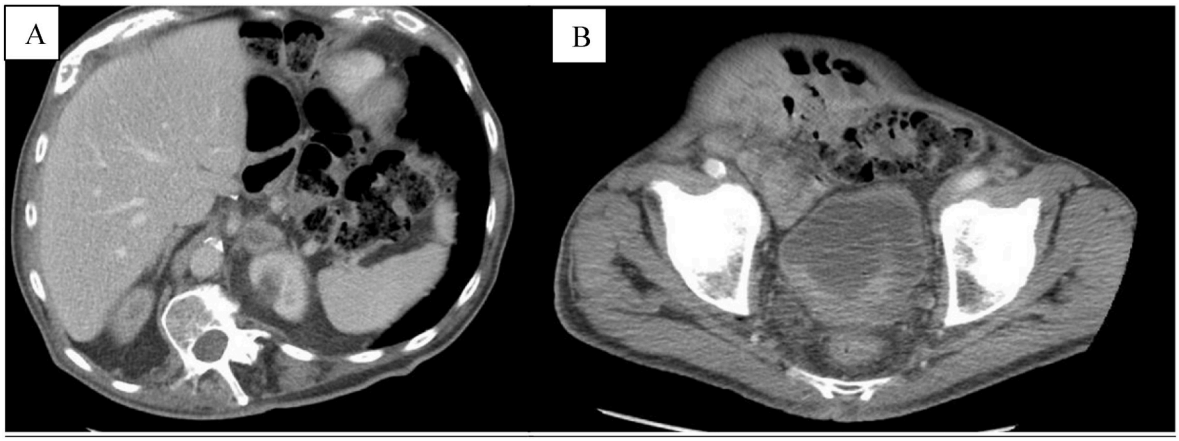

Fig. 2. CT abdomen and pelvis demonstrating left adrenal lesion (A) and irregular thickening of the urinary bladder (B).

bladder of esophageal origin. Cross sectional FDG-PET/CT imaging demonstrated hypermetabolic thoracoabdominal lymph nodes, a 1.9 cm left adrenal lesion, and an irregularly thickened urinary bladder consistent with metastatic disease.

2.3. Intervention and follow-up

The patient was started on systemic chemotherapy (FOLFOX/nivolumab). Treatment was complicated by urinary retention. Two months after initiation of chemotherapy, the patient presented with hematuria without improvement on continuous bladder irrigation. Repeat cystoscopy, clot evacuation, and TURBT revealed significant friable frondular tumor within the prostatic urethra, bladder neck and trigone. A complete resection of the tumor within the bladder was performed. The patient's hematuria cleared postoperatively. CT imaging of the chest/abdomen/pelvis one month after repeat TURBT revealed enlargement of the left adrenal metastasis and increased irregular thickening of the bladder suggesting progression of disease (Fig. 2). Genomic profiling of

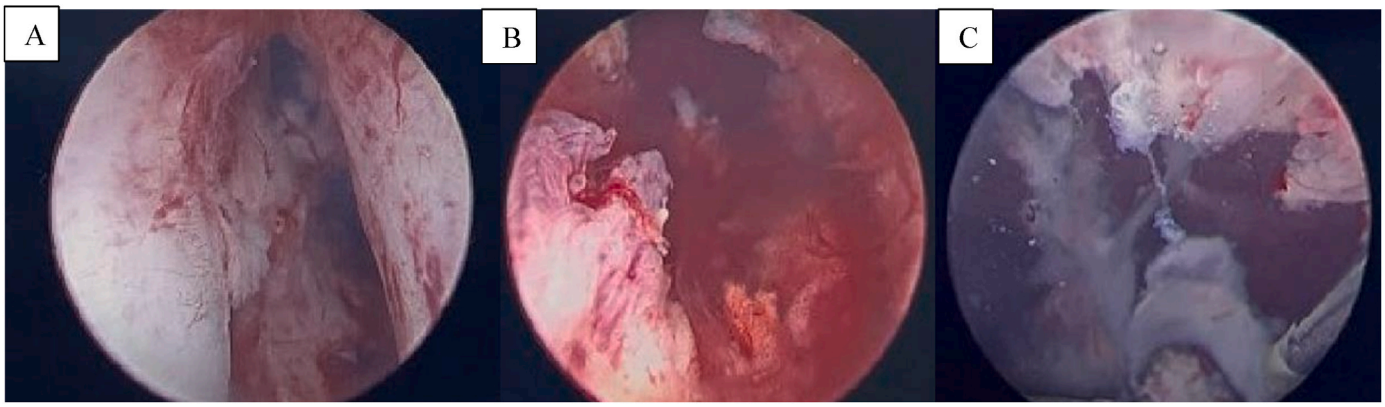

Fig. 3. Cystoscopy with friable papillary mass in prostatic urethra (A, B) and bladder neck (C).

his bladder tumor revealed amplification of MDM2, which is a negative regulator of p53 tumor suppressor. Given progression of disease, he was transitioned from FOLFOX/nivolumab to experimental chemotherapy with MDM2 inhibitor monotherapy and underwent palliative radiation therapy to the bladder, prostate, and surrounding soft tissues to assist with long-term hemostasis and preservation of the patient's functional status. Patient presented nine months after initial diagnosis with urinary retention due to tumor obstruction of bladder neck.

Cystoscopy revealed tumor burden over 5cm around the prostatic urethra and bladder neck (Fig. 3). A complete resection was not possible and nephrostomy tube was placed to relieve obstruction. He remains alive almost 3 years from his initial cancer diagnosis and over 12 months from his initial TURBT with diagnosis of esophageal cancer metastatic to bladder and prostatic urethra.

3. Discussion

Bladder carcinoma secondary to metastasis represents about 2% of all bladder tumors.[1] The rare phenomenon is most commonly due to direct extension from nearby organs such as the colon, prostate, rectum, cervix, and less often, from distant metastases or hematopoietic malignancies.[3] Bates and Baithun, in a study of 282 secondary bladder neoplasms, found that the most common site of origin of distant metastases were the stomach, skin (melanoma), lung, and breast. 54% of such tumor deposits were in the bladder neck or trigone and were histologically adenocarcinomas.[3] Esophageal adenocarcinoma spreading to the urinary bladder however is extremely rare, with only 4 previously reported cases worldwide, with our case being the first to show involvement of the prostatic urethra and with survival over 12 months since diagnosis.[5] The mechanism of spread from the esophagus to distal organs such as the bladder is unknown. Shaheen et al. suggest an arterial route of spread where an esophageal tumor embolus liberates and follows a main artery to reach distal terminal organs.[2] The prognosis of metastatic esophageal adenocarcinoma is poor, and with the rarity of metastasis to the bladder, there are minimal guidelines on the most appropriate treatment but likely require multidisciplinary coordination of medical and surgical care with chemoradiation as in this case. This unique case brings into consideration metastasis to the bladder as etiology of gross hematuria in patients with a history of primary esophageal cancer.

4. Conclusion

We present the case of a patient with esophageal adenocarcinoma with metastasis to the prostatic urethra and bladder. Cancer metastasis to the bladder is rare and usually occurs from direct invasion from prostate, colorectal, or cervical cancers. Similar to our case, gross hematuria is the most common reported symptom of metastatic cancer to the bladder. Metastatic tumor to the bladder and urethra should be within the differential in patients with gross hematuria and a history of primary esophageal cancer. The combination of palliative chemotherapy, radiation and TURBT can ultimately be offered to these patients with progressive metastatic disease to preserve quality of life.

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