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Pulmonary and hepatic metastases of low-grade urothelial cell carcinoma; A case report

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ABSTRACT

Bladder cancer is a commonly encountered malignancy of the genitourinary tract. Bladder cancer is categorized as high or low grade depending on histological analysis. Low grade urothelial cell carcinoma has an indolent clinical course as compared to high grade, with low rates of progression of disease. We present a case where a patient was identified to have low grade bladder cancer and subsequently found to have low grade bladder cancer metastases to the lung and liver. Although uncommon, low grade urothelial cell carcinoma has the potential for progression and metastasis, highlighting the importance of regular follow-up and surveillance.

1. Introduction

Bladder cancer is the 7th most commonly diagnosed cancer in males worldwide and is the most common neoplasm of the urinary tract. Urothelial cell carcinoma (UCC) is the most common histologic type of bladder cancer. A variety of factors are taken into consideration when classifying bladder cancer including Tumor, Node, Metastasis classification, molecular classification, and histological classification. The World Health Organization (WHO) guidelines define non-muscle-invasive bladder cancers as either Papillary urothelial neoplasm of low malignant potential, low grade papillary urothelial carcinoma, or high-grade urothelial carcinoma. This stratification is based on microscopic analyses of the neoplastic tissue which classifies them according to degree of nuclear anaplasia and architectural abnormalities.[1] High grade tumors have both high rates of recurrence and high rates of progression, whereas low grade tumors, despite high rates of recurrence, 15–70% at one year, have low rates of progression to higher grade disease, with less than 5% of cancers invading the lamina propria, and exceedingly rare incidence of metastasis.[2] In this report, we describe a patient found to have low grade urothelial cancer in the bladder who went on to develop biopsy-confirmed low grade pulmonary and hepatic metastases.

2. Case presentation

A 71-year-old African American female presented in 2018 with malaise and was found to have acute renal failure. CT scan of the abdomen and pelvis without IV contrast showed moderate right hydronephrosis with obstruction at the level of the ureteropelvic junction. Follow up CT of the chest, abdomen, and pelvis with IV contrast showed a 1.2 × 1.6 cm hyperattenuating mass within the right, posterior urinary bladder and no obvious metastatic disease. The patient was then scheduled to undergo elective cystoscopy with transurethral resection of bladder tumor (TURBT); however, was lost to follow-up until she presented to the hospital in April 2019 with a lower gastrointestinal bleed. At this time, her bladder mass had enlarged to measure 2.3 × 3.7 cm on CT (Fig. 1). Treatment was deferred until all acute processes were controlled, and the patient was again lost to follow-up due to multiple missed appointments. The patient was then readmitted in July 2019 for gross hematuria presumably due to bladder mass. Cystoscopy with TURBT was performed at this time. Pathologic analysis revealed low-grade, non-invasive papillary urothelial cell carcinoma (Fig. 2).

In November 2019, the patient presented with a urinary tract infection and gross hematuria. CT of the chest, abdomen, and pelvis showed persistent severe right hydroureteronephrosis with heterogeneous appearance of the urinary bladder. Multiple scattered bilateral pulmonary nodules, measuring up to 1.8 cm were noted in the posterior

Abbreviations: WHO, World Health Organization; UCC, Urothelial cell carcinoma; TURBT, Transurethral resection of bladder tumor; CT, Computerized tomography.

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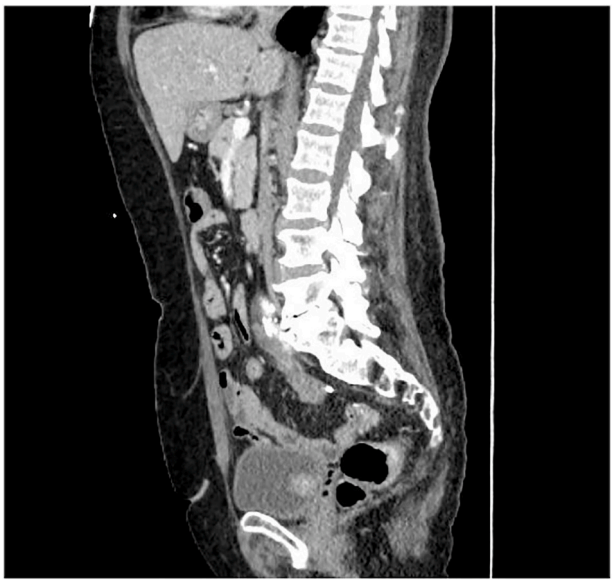

Fig. 1. Sagittal view of CT abdomen and pelvis showing intravesical mass.

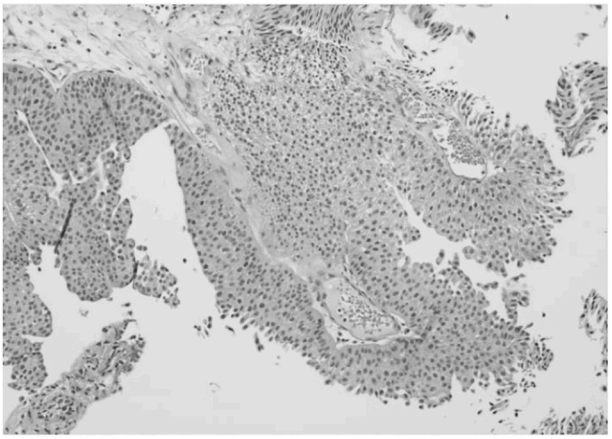

Fig. 2. Hematoxylin and eosin stained tissue sample showing papillary tumor architecture.

lower lobe of the right lung, suspicious for metastases. Cystoscopy with TURBT was performed, which revealed low-grade, diffuse multifocal papillary urothelial cell carcinoma with areas of focal high-grade urothelial cell carcinoma. A CT-guided transthoracic core needle biopsy was performed on the largest pulmonary nodule in the right lower lobe with pathology confirming metastatic low grade urothelial cell carcinoma of the bladder (Fig. 3). No surgical interventions were recommended at this time, given the unfortunate progression and recurrence of her cancer and metastasis.

In March 2020, the patient again presented to the hospital. A CT scan revealed worsened bilateral pulmonary masses. Additionally, marked hepatomegaly was noted with large masses concerning for metastatic disease. A needle biopsy of the right liver lobe was performed revealing metastatic carcinoma with necrosis, most consistent with urothelial carcinoma. Histologic analysis of the tissue sample revealed epithelioid tumor cells with some focal papillary features and extensive coagulative necrosis. The tumor cells expressed AE1/AE3, CK7, CK20, p63, GATA-3, and uroplakin (strong).

3. Discussion

Metastatic spread from high grade bladder cancer is well

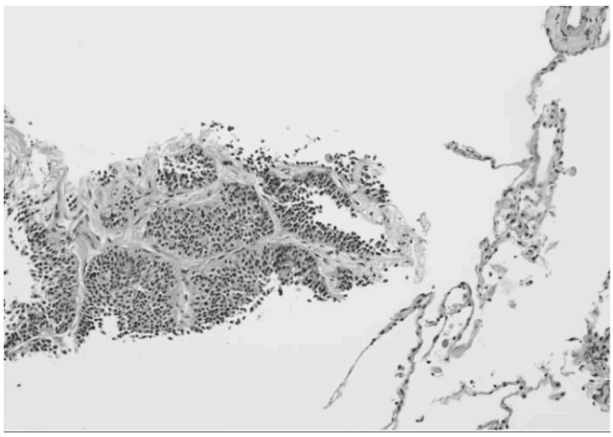

Fig. 3. Lung biopsy showing low grade appearing urothelial carcinoma within lung tissue.

documented and often metastasizes to certain organs at a higher rate. The most common locations for metastasis of bladder cancer are pelvic lymph nodes, liver, lung, and bone. Reports of metastatic disease associated with low grade UCC however, are exceedingly rare. It is quite unusual in the case of this patient that the low grade urothelial cancer was the histologic variant that had metastasized to the liver and lungs, rather than the high grade foci seen on her third TURBT. Less than 30 cases have been reported in the literature worldwide. The primary locations where low grade, non-muscle invasive bladder cancer has been observed to metastasize include: the lungs, liver, bones, ovaries. Other sites of metastasis that have been observed include: eyes, thyroid gland, and brain.[3,4]

Several theories have been described in the literature that may help to explain distant organ metastasis of low grade UCC. These include staging inaccuracies, sampling errors during TURBT, and intravascular spread of cancer cells during and after TURBT.[4]

Clinical understaging of low grade bladder cancer is always a possibility when diagnosing low grade UCC. One study estimated that in 78 patients who underwent radical cystectomy for clinical stage T1 or less, 40% were grade pT2 or higher upon review of the final pathology.[5] Despite this trend, the likelihood of clinical understaging is unlikely in our case given the multiple tissue samples from TURBT and the biopsies of the metastatic lesions which were diagnosed by a different pathologist at a separate institution.

Sampling errors during TURBT also remain a concern when resecting any intravesical mass. Non-resection of certain areas of bladder tumor could potentially miss areas of higher-grade pathology that could lead to upstaging. Despite the concern for sampling errors, this is extremely unlikely in our case given the multiple resections of the bladder tumor showing predominantly low grade UCC.

4. Conclusion

Low grade bladder cancer is mostly considered to have an indolent course with usually only local recurrence and slow progression. Despite a low potential for metastases, our case illustrates that wide metastatic spread to the lungs and liver is possible even with a low-grade bladder malignancy.

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Consent

Written informed consent was obtained from the patient for publication of this[1–5] ase report and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Authors' contributions

MS – compiled clinical data and was primary author, TP – contributing author and assisted in compilation of data, MV – Assembled pathologic slides and reviewed article, JS – conducted clinical orchestration and reviewed article.

Declaration of competing interest

No financial or non-financial competing interests were present in this study.

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