Is radical cystectomy an overtreatment for T1 high-grade transitional cell carcinoma of the bladder? Lesson learnt from case series

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Abstract

The introduction of intravesical bacillus Calmette–Guérin (BCG) made a breakthrough in the treatment of high-grade nonmuscle-invasive bladder cancer. Indeed, the intravesical immunotherapy helped many patients in preserving their bladder for a period of time. However, many studies revealed that <50% of the patients will be able to maintain their bladder in 5 years of follow-up. The shortage of BCG adds to the odds of cancer progression and patient suffering. We present a series of three cases of disease progression despite the confirmed pathologic local staging of the bladder cancer to be nonmuscle disease. The message we would like to address from this review is that radical cystectomy is not an overtreatment of this potentially lethal disease.

Keywords: Bacillus Calmette–Guérin, metastasis, positron emission tomography-computerized tomography, progression, radical cystectomy, transitional cell carcinoma

INTRODUCTION

Approximately 75% of patients with bladder cancer present with a disease confined to the mucosa (stage Ta and Cis) or submucosa (stage T1), i.e., nonmuscle-invasive bladder cancer (NMIBC).[1] T1 high-grade transitional cell carcinoma (TCC) of the bladder presents as a challenge to urologists to manage. The disease is well known for its high risk of recurrence and progression. The morbidity and mortality of the disease is well reported but underappreciated. Transurethral resection (TUR) is the gold standard for the initial diagnosis and treatment of NMIBC.[1] Adjuvant intravesical therapy with bacillus Calmette–Guérin (BCG) is considered the standard of care for these types of tumors. However, immediate radical cystectomy should be considered for high grade multiple T1 tumors, T1 tumors located at a site difficult to resect, residual T1 tumors after resection, or high-grade tumors with Cis and lymphovascular invasion.[1] There is long-standing controversy about the optimal treatment of the T1 high-grade TCC. Some urologists may consider initial cystectomy to be an overtreatment since more than half of patients with T1 high-grade TCC of the urinary bladder do not progress. However, others consider radical cystectomy as underutilized for this disease. Many patients with T1 high-grade bladder cancer are likely to have recurrence and the tumor will often progress, metastasize, and cause death due to the lack of BCG and alternative,

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nonexperimental effective treatment options.[1] In this case series, we present three cases of metastatic T1 high-grade TCC from our department to shed light on the ominous nature of the disease.

CASE REPORTS

Case 1
A 72-year-old Caucasian female presented with intermittent gross hematuria for 2 years before being evaluated. She has a more than 50-year history of smoking 1–2 packs of cigarettes per day. She was evaluated with cystoscopy and computed tomography (CT) urogram. Both revealed a filling defect in the bladder with no lymph node enlargement. She underwent TUR, revealing T1 high-grade TCC with no muscle involvement. Treatment options were discussed with her, and she was given the choice between radical cystectomy and adjuvant immunotherapy with intravesical instillation of BCG; she elected to have a bladder preservation approach. She underwent weekly instillation of BCG for 6 weeks and was evaluated after 3 months with cystoscopy. The cystoscopy was negative, so she was put on maintenance BCG. However, on the second surveillance cystoscopy done 6 months after the initial resection, she was found to have recurrence with T1 high-grade TCC. At this point, she opted to have radical cystectomy with bilateral pelvic lymph node dissection. Final pathology revealed T1N1M0, TCC with the involvement of the left internal iliac lymph nodes. On that adverse pathology, her positron emission tomography (PET)-CT revealed multiple periaortic lymph nodes. She subsequently underwent adjuvant chemotherapy with cisplatin-based therapy.

Case 2
A 58-year-old male presented to our service with T1 high-grade bladder cancer after failing intravesical chemotherapy. The patient had a long smoking history with about 50 packs per year. He also had occupational exposure to benzene compounds. Radical cystectomy was offered after his CT urogram was negative. He underwent radical cystectomy with bilateral extended pelvic lymph node dissection. His final pathology revealed T1N2 high-grade TCC of the bladder with the involvement of both internal and common iliac lymph nodes. Thankfully, his PET-CT was negative for additional metastatic disease.

Case 3
A 63-year-old female presents with gross hematuria for 2 years. She smoked for more than 40 years, averaging 1 pack per day. She had a remote history of hematuria 8 years prior and underwent hematuria workup with cystoscopy and CT urogram. The workup revealed a 3 cm lateral wall lesion at the level of the right ureteral orifice. She underwent TUR of that lesion and the final pathology revealed an invasive high-grade Ta TCC of the bladder. She was noncompliant and never followed through on initial management. She reestablished care after her hematuria returned. Repeat CT urogram showed a large bladder masses at the anterior wall and the dome. Second, TUR was performed and the final pathology revealed T1 high-grade TCC. Cystectomy versus BCG was discussed with her, and she elected to undergo bladder preservation with immunotherapy. Due to the lack of immunotherapy, she was offered intravesical gemcitabine and was re-evaluated 3 months later. Another T1 high-grade TCC was seen at this time, and since the patient was complaining of right flank pain, a CT urogram was performed that revealed multiple enlarged pelvic lymph nodes. PET-CT was ordered that revealed multiple enhancing pulmonary nodules, and a subsequent biopsy of the lung revealed metastatic TCC. The patient was not considered a candidate for radical cystectomy and was sent for chemotherapy.

These three consecutive cases of T1 high-grade TCC of the bladder all were accompanied by extravesical disease. All of these patients had a very strong history of smoking. One patient failed BCG; two did not receive BCG due to a shortage of the medication.

DISCUSSION

Each year approximately 80,000 new cases of bladder cancer are encountered in the United States, making it the 4th most common cancer.[2] Most of the patients are over 55 years old, and men are 4 times more likely to be affected than women. [3] Most of the cases present as nonmuscle invasive disease and only about 20% present as muscle-invasive disease. Bladder cancers are generally classified as high-grade and low-grade, invasive and noninvasive, and some present as Cis.[1,2] The initial treatment of any bladder mass involves TUR.[1] The presence of high-grade disease, multiple tumor, large tumor, and CIS represents a risk for recurrence and progression. The risk of recurrence within 5 years after diagnosis is approximately 31%–75% regarding NMIBC[3] It is estimated that 1/3 of all patients will eventually progress into a muscle-invasive disease.[1,3] According to the guidelines, the presence of high-risk disease should be treated with either adjuvant immunotherapy using BCG or immediate radical cystectomy.[6] Radical cystectomy, although having the highest cure rate, is considered an aggressive approach to this disease and an over treatment according to some authorities. Chalasani et al. aimed to look at T1 high-grade disease and highlight its severe aggressiveness. In the 306 cases of T1 high-grade NMIBC that underwent...
radical cystectomy following failed immunotherapy, they discovered that at the time of cystectomy, 48% of cases were upstaged to T2–T4 disease and that the majority of those upstaged had extravesical disease. This concurs with our observation from three consecutive cases; we encountered at our center. On reviewing all the evidence that we have, we still recommend radical cystectomy for T1 high-grade TCC of the bladder, especially in the era of BCG shortage and the lack of effective alternative treatment.

CONCLUSION

We presented three cases of T1HG NMIBC with lymph node involvement, with two cases progressing to lung metastasis. The reality is, while cT1 is considered nonsystemic disease, radical cystectomy should be offered upfront to the patients due to the shortage of BCG and lack of other effective disease control measures. Indeed, upfront cystectomy, while a significant life-changing event, offers patients a chance at longer disease-free survival.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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