

Complete Response to Intravesical Gemcitabine in Non-Muscle Invasive Bladder Cancer Patient after BCG Failure A Case Report and Literature Review

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Abstract

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Abstract

Bladder cancer treatment remains a challenge to every oncologist. We report the case of a 57-year-old man with BCG-refractory bladder cancer, who had a complete response to the intravesical Gemcitabine to shine the light on the role of Gemcitabine as a bladder sparing treatment in BCG-failure patients.

Introduction

Bladder cancer is the 10th most common cancer worldwide and has a steadily increasing incidence [1]. It is more common among men, for whom it ranks the 6th most diagnosed and the 9th most fatal cancer [1]. At presentation, 75% of cases confined to the urothelium or lamina propria (non-muscle invasive bladder cancer, NMIBC) [2]. Then, the initial treatment includes a transurethral resection (TUR) followed by an intravesical adjuvant therapy with Bacillus Calmette–Guérin (BCG) for intermediate and high-risk patients [3]. In case of BCG failure, radical cystectomy is the standard of care in high-risk patients. However, many of them are unfit or refuse to undergo such an intervention, so other treatment options are required [4]. Herein, we report the case of a bladder cancer patient who had a complete response to intravesical gemcitabine after BCG failure, to highlight the potential effectiveness of gemcitabine as a bladder sparing treatment in BCG-failure patients who cannot undergo or refuse surgery.

Case Report/Case Presentation

A 57-year-old man, 45 pack-year smoker presented to the clinic complaining of gross hematuria. His medical history was significant for diabetes mellitus, peripheral vascular disease, cardiomyopathy, and prior cerebral hemorrhage. Also, he underwent a coronary artery bypass graft (CABG) in September 2019. Otherwise, clinical examination was insignificant.

The cystoscopy and CT scan (shown in Fig. 1) showed a multifocal bladder tumor. Transurethral resection (TUR) was performed. The TUR pathology revealed a stage-T1G3 transitional cell carcinoma, the muscularis was present but free of tumor, so non-muscle invasive bladder cancer (NMIBC) was diagnosed. The tumor involved the prostatic urethra. The CT scan excluded any distant metastases.

After that, the patient received one vial of intravesical Bacillus Calmette-Guerin (BCG)-Medac once a week for 6 weeks. Three months later, the TUR showed residual tumor fragments, so the patient was considered BCG-refractory.

Radical cystectomy is the standard of care in such situations. However, due to the cardiomyopathy, the patient was unfit for the surgery and also refused it. So, other treatment options were required.

Another TUR was performed and followed by the intravesical injection of 2 g of Gemcitabine once a week for 6 weeks. After 3 months, the cystoscopy and taken biopsies showed complete response to the treatment and no evidence of tumor. No side effects were encountered during the therapeutic course.

Discussion/Conclusion

Non-muscle invasive bladder cancer (NMIBC) remains a therapeutic challenge, especially in the era of BCG shortage. Although the transurethral resection (TUR) of the tumor followed by intravesical BCG injection has long been the standard of care for NMIBC, the treatment fails in about 40-50% of patients [5].

The classifications of BCG failure are shown in Table 1. [6] [7]

Radical cystectomy is indicated in cases of BCG failure and provides a 92% disease-free survival when early performed [8]. However, post-surgical quality of life assessment showed many physical, mental, and social health problems in patients who underwent the surgery [9]. So many people refuse such intervention. On the other hand, many of them are unfit for surgery due to cardiac or other health issues.

As an alternative to surgery, bladder-sparing treatments include a second course of BCG, intravesical mitomycin C (MMC), intravesical chemotherapy with gemcitabine, and a few other options [10].

Gemcitabine (GEM) has now level-one evidence as an effective drug for bladder cancer [11]. When used intravesically, GEM reaches low plasma levels which reduces systemic toxicity [12].

A systematic review and meta-analysis compared the efficacy and safety of intravesical GEM versus MMC for NMIBC and demonstrated that using GEM is associated with a statistically significant decrease in tumor recurrence rate and reduction in local toxicity compared with MMC [13]. In addition, MMC is an expensive drug that cannot be affordable in some low-income countries.

Ye et al conducted a similar meta-analysis on five clinical trials with an overall 386 bladder cancer patients, comparing GEM to BCG. The results showed no statistically significant difference in tumor recurrence rates, but GEM was associated with significantly lower rates of dysuria and hematuria in comparison with BCG [14].

Our patient suffers from severe cardiomyopathy that makes surgery contraindicated. He also refused the radical cystectomy due to the poor postoperative quality of life.

Considering the reasons mentioned above, we preferred GEM over other treatment options after the first BCG failure. The treatment course led to a complete pathologic response with no side effects. A 6-month follow-up showed no tumor recurrence, but a longer follow-up time is needed to determine the long-term efficacy of the treatment.

In our case, we aim to shine the light on the promising role of GEM in treating resistant bladder cancers and avoiding radical cystectomy complications.

Since our study was performed on one patient only, it provides relatively weak –but important– evidence. So, to formulate definitive recommendations, larger and higher-quality studies are required.

Author Contributions:

Fouad Nahhat: wrote the abstract, introduction, and discussion, and participated in the literature review.

Modar Doyya: wrote the case presentation, designed the figure, and participated in the literature review.

Hazem Ksiri: participated in patient's treatment and supervised the manuscript preparation scientifically and academically.

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Figure Legend

Fig. 1. The CT scan shows the multifocal bladder tumor.

Table Legend

Table 1. BCG Failure classifications.

