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Case Report

West Virginia Resident is First American to Receive Dicycloplatin Chemotherapy: A WVU Urologic Oncology Case Report

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ABSTRACT

A 65-year-old Caucasian male presented with increasing hematuria over four months in 2016. Work up and scans revealed a 1.5 cm bladder mass, with a subsequent pathologic diagnosis of non-invasive high-grade papillary urothelial carcinoma. The patient declined BCG Immunotherapy and traveled to China soon after diagnosis and transurethral resection for Dicycloplatin (DCP) chemotherapy. DCP is approved by the Chinese FDA but only available at present in military hospitals. It is similar in molecular structure to platinum-based chemotherapy drugs used in the West, its side effects reported to be more tolerable. The patient received 8 weeks of IV DCP chemotherapy – he only experienced mild nausea, myralgia, a relative leukopenia and thrombocytopenia (though within normal limits) and, importantly, no alopecia – then returned to WV for quarterly surveillance. No recurrence of tumor has been observed to date; the most recent cystoscopy was on April 24, 2018, 22 months after diagnosis and resection.

Introduction

The rate of cancer death in the United States for men and women combined fell 25% from its peak in 1991 to 2014. This decline translates to the prevention of millions of cancer deaths. That is significant progress; however, 1,685,210 new cancer cases and 595,690 cancer deaths are projected in the USA in 2016 [1, 2].

Bladder cancer (BC) causes 170,000 deaths annually worldwide. More than 50,000 men and 16,000 women are diagnosed each year in the USA [3,4]. Although quitting smoking lowers the risk, former smokers are likely always at a higher risk of BC versus never smokers [5-7]. Approximately 70 percent of new urothelial bladder cancer cases are non-muscle invasive tumors, typically removed by complete transurethral resection. To prevent recurrence of non-muscle invasive tumors (T1, Ta), resection is typically followed by intravesical immunotherapy with Bacillus Calmette–Guérin (BCG) if the tumor was high-grade urothelial carcinoma or in the event of large tumors or multifocal disease. BCG is the standard protocol. Some studies suggest that BCG is superior to standard chemotherapy. However, rate of recurrence after adjuvant BCG treatment in bladder cancer is about 50% (90% without BCG) [8-13]. Untreated non-invasive tumors may infiltrate the muscular wall, requiring cystectomy and urinary diversion into an isolated bowel loop or substitute bladder. For muscle invasive BC, the standard treatment is partial or radical cystectomy depending on tumor number and size [14-17].

Platinum drugs remain a cornerstone of chemotherapy for many cancers, including bladder cancer when immunotherapy fails to secure remission. However, the adverse effects of cisplatin and carboplatin are often

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severe, causing some patients to stop treatment. Toxic effects such as myelosuppression, nephrotoxicity, hepatotoxicity, neurotoxicity, and nausea and vomiting are often constraints to full dosage and long-term use.

Dicycloplatin (DCP) is a novel platinum analog developed in China. It was approved by the State Food and Drug Administration (SFDA) of China in March of 2012. DCP is synthesized from platinum powder and contains a host part which is carboplatin and the guest part, an additional carboxylate ligand, linked via 4 hydrogen bonds. It is a hydrogen-bond supramolecule, not a covalent-bond molecule. DCP has a stable chemical structure, good water solubility, and an excellent safety profile [18, 19].

Case Report

A 65-year-old Caucasian American male with increasing hematuria over a 4-month period, without lower urinary tract symptoms, was seen in June of 2016 at West Virginia University (WVU) Hospital, Morgantown, WV, USA. Work-up, including CT-Urogram and cystoscopy revealed a 1.5 cm bladder mass. Transurethral resection was performed on June 30, 2016. The pathologic diagnosis was non-invasive high-grade papillary urothelial carcinoma involving the right lateral wall bladder tumor (Ta). Immunotherapy with BCG and surveillance cystoscopy were recommended to the patient. The patient declined BCG treatment course but elected cystoscopic surveillance every three months at WVU after dicycloplatin chemotherapy in Beijing, China [20].

Of note, the patient is a former smoker. His mother died of ovarian cancer at age 50 and his father had advanced prostate cancer at the time of his death at age 81 from other causes. The patient's family history and his familiarity with DCP through his work as a medical writer led him to elect DCP. In July 2016, the patient traveled to Beijing where he received eight weekly DCP IV infusions.

Baseline blood counts and chemistry were evaluated prior to chemotherapy, then weekly before each treatment. The DCP treatment at Beijing 301 Hospital began July 21, 2016. Dicycloplatin 300 mg was dissolved in 250 ml 5% glucose solution and infused over one hour. The patient was treated in the Day Ward of the Tumor Building at Beijing 301 Hospital and observed for 30 min afterwards. The patient received one cycle of 300 mg of DCP by IV weekly for eight weeks.

Adverse effects of DCP in this patient included mild nausea at the outset, moderate fatigue, and (in the last 2-3 weeks) back and leg aches. There was no emesis or hair loss. Weekly hematological monitoring showed mild effects on blood cells. Noticeable decreases in red blood cells, white blood cells, and platelets were observed. However, all remained within normal limits (Figure 1).

After completion of DCP treatment, the patient returned to the United States for regular surveillance at West Virginia University Hospital. CT IVP was performed on August 3, 2017, thirteen months after resection; no upper tract or metastatic lesions were visualized. Cystoscopies every 3 months up to April 24, 2018 showed no evidence of tumor recurrence.

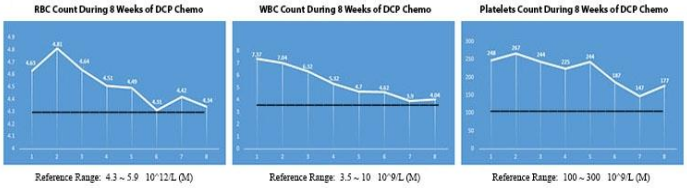

Figure 1: Hematologic Data - CBC with Differential (July-Sept. 2016 in Beijing 301 Hospital, China**)**

Cystoscopies performed on October 13, 2016, January 16, 2017, April 20, 2017, August 3, 2017 and on April 24, 2018 revealed no recurrence of tumor, and the resection area was observed to be clear of new growth on each occasion. Wash solutions collected during each cystoscopy were examined by a Cytologist and no malignant cells were observed.

Figure 2 shows the images taken during cystoscopy before resection (top left panel) and after resection (top middle panel) on June 30, 2016. The residue of bladder tumor lesion observed 1-year after DCP treatment is shown in the top right panel, and during the 22-month post DCP chemotherapy in the bottom panels. The resection site appeared to be healing. The DCP chemotherapy received by this patient – and follow-up observations of his resection site - may not prove DCP efficacy is superior. However, the patient only received DCP chemotherapy during his course of treatment since diagnosis, and there is no evidence to date of tumor recurrence. Also, of note, the patient experienced tolerable side effects during DCP chemotherapy.

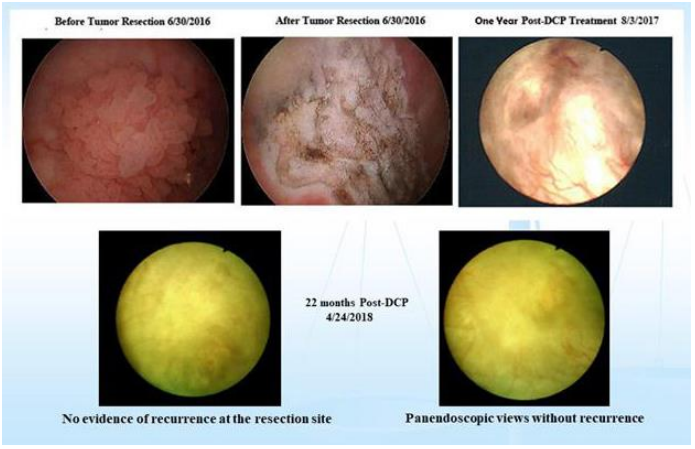

Figure 2: Cystoscopy Images of Bladder Tumor and Resection Site
Images taken during cystoscopy before and after tumor resection, 1-year after DCP chemotherapy and 22-month follow-up.

Conclusion

DCP has sustained remission in this patient with bladder cancer for more than 22 months. The adverse effects profile was tolerable with minimal myelosuppression.

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Conflict of interest

The authors declare that they have no competing interests.

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