

Remarkable Response to Neoadjuvant Therapy with Methotrexate, Vinblastine, Adriamycin, and Cisplatin for Undifferentiated Bladder Carcinoma: A Case Report and Literature Review

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Key Words

Undifferentiated bladder carcinoma · Methotrexate, vinblastine, adriamycin, and cisplatin · Neoadjuvant chemotherapy

Abstract

We report a case of primary undifferentiated bladder carcinoma, which revealed a remarkable response to methotrexate, vinblastine, adriamycin, and cisplatin (MVAC) therapy. A 46-year-old Japanese woman presented at the hospital with the chief complaints of gross hematuria and pain during urination. Cystoscopy revealed a large smooth-surfaced tumor in the urinary bladder. The histopathological diagnosis was undifferentiated carcinoma. The patient then received 3 courses of MVAC over a 3-month period. Hydronephrosis disappeared after the first course, and the tumor shrank rapidly. After completion of the third MVAC course, radical cystectomy and ileal conduit surgery were performed. After 7 years, the patient has still had no recurrences or metastases. We retrospectively review the relative efficacy of the two popular chemotherapeutic regimens in the management of muscle-invasive bladder cancer in patients who had had radical cystectomy. © 2014 S. Karger AG, Basel

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Introduction

Radical cystectomy is the standard treatment for invasive bladder cancer but cannot be considered for advanced cases because the tumor sometimes remains after this procedure and lymph node metastasis may occur. Adjuvant treatments have been performed as part of efforts to improve the treatment outcome for invasive bladder cancer, and a large-scale randomized controlled trial and meta-analysis [1] revealed that adjuvant regimens including cisplatin produce good results. Thus, the effectiveness of cisplatin is gradually becoming apparent.

The prognosis of undifferentiated bladder tumors is generally poor, but we treated a patient in whom no recurrence was observed for 7 years after a surgical procedure following neoadjuvant therapy with methotrexate, vinblastine, adriamycin, and cisplatin (MVAC).

Case Report

A 46-year-old Japanese woman presented at the hospital with the chief complaints of gross hematuria and pain during urination. Cystoscopy revealed a large smooth-surfaced tumor in the urinary bladder, reaching from the posterior wall to the dome (fig. 1). The patient underwent transurethral resection of the bladder tumor, and the histopathological diagnosis was undifferentiated carcinoma. The tumor expanded rapidly as the patient was examined in preparation for total cystectomy. Bilateral hydronephrosis manifested after approximately 1 month. Due to doubts regarding permeation of the digestive tract as shown by CT, the option of further surgery was abandoned and a nephrostomy was performed in conjunction with chemotherapy (cT4N0M0).

The patient then received 3 courses of MVAC over a 3-month period. The hydronephrosis disappeared after the first course, and the tumor shrank rapidly (fig. 2). After completion of the third MVAC course, total cystectomy and ileal conduit surgery were performed. Intraoperatively, no anomalies were found in the abdominal cavity, but the bladder was shown to be firmly accreted to the pelvic wall, which was separated incrementally. An isolated preparation revealed what was thought to be white necrotic tissue (pT1, pN0, ew0, ly0, v0, n0). After 7 years, the patient has still had no recurrences or metastases.

Discussion

A complete pathologic response was obtained in this patient, and our review of the relevant literature revealed some interesting observations. At present, there is no consensus regarding the significance of metastasectomy after chemotherapy for advanced urothelial carcinoma [2]. Gemcitabine plus cisplatin (GC) therapy was used in many cases, although there is no significant evidence that it is any more effective than MVAC therapy as neoadjuvant chemotherapy. It was reported that a group of patients who underwent MVAC therapy as neoadjuvant chemotherapy had a lower mortality rate than a surgery-alone group [3]. Typically, due to the high incidence of side effects accompanying the use of agents, reduced doses are administered, and thus in recent years some regimens with fewer and/or less severe side effects tended to be the preferred choice.

Although regimens that include new anticancer agents (e.g., gemcitabine) may be considered to be as effective as MVAC and to have superior tolerability, it is important to continue investigating such regimens as neoadjuvant chemotherapy. Some recent studies of

neoadjuvant chemotherapy comparing GC therapy and MVAC therapy were reported [1]. Dash et al. [4] provided a positive report stating that, as preoperative chemotherapy, GC therapy was as effective as MVAC therapy in reducing the progression of the disease and the disease-free survival rate. However, other researchers published negative reports on regimens other than MVAC therapy. For example, it has been reported that chemotherapies other than MVAC therapy that included GC were ineffective in increasing the complete response (CR) rate pathologically compared to immediate cystectomy, and that the chemotherapies did not improve the overall survival rate [5]. We can anticipate the results of further prospective studies that will enable us to better compare the results of neoadjuvant chemotherapies.

In a study of MVAC therapy as neoadjuvant therapy for lymph node metastasis-positive patients, it was reported that, of 51 patients who underwent cystectomy, 14 achieved a pathologic CR (pCR) [6]. In that study, the subjects were patients who had been pathologically diagnosed as having lymph node metastasis of bladder cancer and patients who had undergone a needle biopsy or a lymphadenectomy because of swollen lymph nodes prior to cystectomy. It is highly interesting that of the patient group that did not include false-positive cases, 27.5% achieved a pCR.

Herr et al. [7] conducted a median of 4 courses (range 2–6) of chemotherapy (MVAC in 60 cases) for 80 patients with bladder cancer with unresectable regional lymph node metastasis, and pCR was achieved in 24 cases (30%). These authors concluded that there was a CR for the therapeutic value of chemotherapy and that with a reduction ratio of 50% or more of the cases, patients with bladder cancer were well adapted to surgical treatment after chemotherapy. Sweeney et al. [8] observed 2 CRs among 11 patients who were treated surgically after 2 courses of chemotherapy (the regimen is not clear in their report), and they concluded that benefits could be obtained from surgery when there were two or fewer areas of lymph node metastasis after chemotherapy. Using only the above-cited studies as a reference, it seems that, in cases in which the evaluation of the patient after 2–6 courses of chemotherapy shows a CR or an effect close to a CR, one option is to embark on surgical treatment.

Although there are occasional documents stating that MVAC therapy is useful in cases involving lymph node metastasis, no documents were found discussing which regimen is best in terms of tissue type or differentiation. However, there were reports demonstrating that when MVAC therapy was implemented towards poorly-differentiated bladder tumors associated with small cell carcinoma, it resulted in CRs. In our patient, after clear benefits were seen with 3 courses of MVAC treatment, surgical treatment was conducted. The fact that radical cystectomy was performed swiftly after the chemotherapy is considered to be one reason for the effectiveness of the treatment. As shown in our patient, it appears that even in the case of progressive or metastatic cancer, chemotherapy can have significant effectiveness, and as long as the patient's overall condition is good, surgical treatment can be an option.

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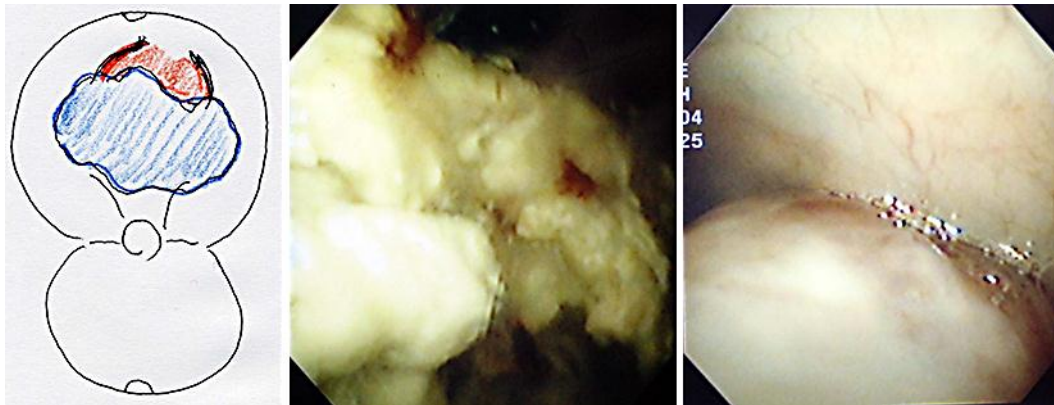


Fig. 1. Cystoscopy revealed a large smooth-surfaced tumor in the urinary bladder, reaching from the posterior wall to the dome.

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Pre MVAC treatment



After MVAC 3 courses

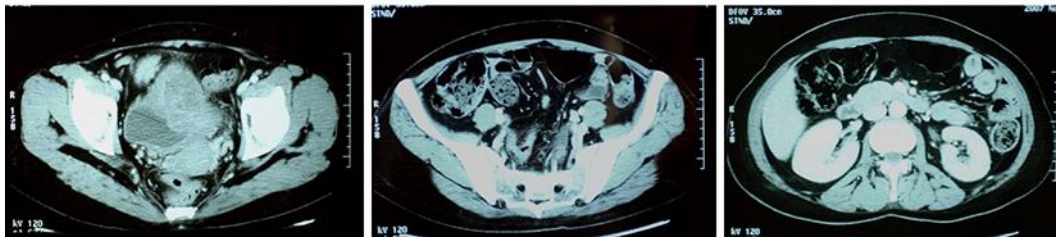


Fig. 2. CT findings before MVAC treatment and after 3 courses of MVAC. The hydronephrosis disappeared after the first course of MVAC treatment, and the tumor shrank rapidly.