Case Report

Successful Treatment of a Large Superficial Bladder Cancer with Neoadjuvant Arterial Infusion Chemotherapy: A Case Report

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Large superficial bladder cancer · Neoadjuvant arterial Infusion chemotherapy · Bladder preservation

Abstract
We present a case in which neoadjuvant arterial infusion chemotherapy was effective in treating a large superficial bladder cancer. A 50-year-old male was admitted to the Kanazawa Medical Center with the complaint of dizziness. The patient exhibited severe anemia, and his computer tomography showed a large bladder tumor. Cystoscopy revealed a large papillary tumor. Magnetic resonance imaging showed no muscle invasion and no metastasis. To avoid a prolonged operation time and excessive blood loss, we performed neoadjuvant arterial infusion chemotherapy for tumor volume reduction before transurethral resection of the bladder tumor (TUR-BT). The arterial infusion chemotherapy was performed twice, and the tumor size gradually reduced from 275 to 28 cm³. After neoadjuvant chemotherapy, TUR-BT was safely performed without blood transfusion. The tumor was staged as T1 with G1. This is the first report demonstrating that neoadjuvant arterial infusion chemotherapy is effective in treating large superficial bladder cancer and is a possible strategy for bladder preservation.

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**Introduction**

Bladder cancer is a common disease of urothelial carcinoma, and transurethral resection of bladder tumor (TUR-BT) is the gold standard treatment strategy for superficial bladder cancer [1].

However, in case of a very large bladder cancer, TUR biopsy is sometimes performed to check the tumor pathology, and if found to be noninvasive, the tumor is treated by radical cystectomy rather than by radical TUR-BT to avoid excessive blood loss and prolonged operation time [2]. There are no established guidelines for determining whether to perform radical total cystectomy or radical TUR-BT for a large superficial bladder cancer; thus, treatment depends on the individual surgeon’s skill and judgment.

In this report, we describe the successful use of neoadjuvant arterial infusion chemotherapy in association with radical TUR-BT for treating a large superficial bladder cancer.

**Case Presentation**

A 50-year-old male was admitted to the Kanazawa Medical Center with the complaint of dizziness. The patient exhibited severe anemia (hemoglobin, 3.9 g/dL); his computed tomography (CT) showed a large bladder tumor measuring 9.2 × 7.4 × 8.1 cm, originating from the right lateral wall of the bladder and occupying the entire bladder (Fig. 1). Cystoscopy revealed a large papillary tumor. CT and magnetic resonance imaging did not show muscle invasion and metastasis. Consequently, the patient was diagnosed with primary superficial bladder cancer (cT1, N0, M0). We thought that the best treatment choice would be performing radical TUR-BT for the initial treatment rather than immediately performing radical cystectomy because there was no evidence of muscle invasion and the patient had a history of “schizophrenia.” However, we also took into account the prolonged operation time associated with radical TUR-BT and the risk of failure in arresting bleeding considering the large bladder cancer. Consequently, we planned neoadjuvant arterial infusion chemotherapy before radical TUR-BT in anticipation of tumor volume reduction.

Arterial infusion chemotherapy was performed twice. First, cisplatin (100 mg/body) was injected into the superior vesical artery, and the patient was observed for 5 weeks to check for any adverse events. Following this, cisplatin was injected into the internal pudendal artery. CT performed 7 weeks after the day of the first arterial infusion chemotherapy showed that the tumor volume had reduced from 275 to 28 cm$^3$ (Fig. 2). On the day of surgery, the internal iliac artery was embolized, and TUR-BT was safely performed (operation time: 161 min). No blood transfusion was required. Pathology revealed a low-grade urothelial cell carcinoma (stage T1). Consequently, intra-arterial chemotherapy was selected for the neoadjuvant therapy, and we were able to preserve the bladder.

**Discussion**

To the best of our knowledge, the treatment strategy for large “superficial” bladder cancer is undefined for the following reasons:

First, there is no common agreement regarding what size a bladder tumor constitutes a “large tumor.” In the literature, a large tumor has been variously defined as one with a total resected weight >50 g, a weight ≥15 g, and a diameter >5 cm [2-4].
Second, there is no association between tumor size and prognosis in a superficial bladder cancer. In case of an “invasive” bladder cancer, radical cystectomy is mainly performed. Cheng et al. reported that for a cancer with pathological stage T2, tumor size is one of the important predictor of survival [5]. However, while assessing superficial bladder cancer, Gupta and Parr [3] reported that tumor size is not an adverse prognostic factor. In their study, 56 patients with large superficial tumors (any tumor with a resected weight of ≥15 g) were enrolled, including 24 patients with Ta and 32 with T1 tumors. The group as a whole comprised 13 G1, 39 G2, and 4 G3 tumors; the progression rate for G1 tumors was 0%. Therefore, in patients with superficial bladder cancer, it is important to try to preserve the bladder.

However, in the treatment of a large superficial bladder cancer, TUR-BT is associated with 2 major problems: a prolonged operation time and excessive blood loss.

Hamasaki et al. [2] defined tumors weighing >50 g as large tumors and reported 6 cases of large bladder cancer treated with radical TUR-BT. This study did not describe the amount of blood loss, but 5 patients received blood transfusions, and the data showed that patients with a tumor volume >250 g required a blood transfusion. The median operation time was 300 min (160–481 min). In another study, Gupta and Parr [3] reported that for patients with a tumor volume >100 g, TUR-BT was required to be performed more than 3 times. Daley et al. [6] reported a clear association between the operation time, excessive blood loss, and the risk of complications.

Given these results, it is important to consider neoadjuvant treatment for large superficial bladder cancers. Intra-arterial chemotherapy for a bladder tumor is mainly performed in cases of muscle-invasive bladder cancer for bladder preservation or as neoadjuvant therapy intended to achieve tumor down-staging [7]. Intra-arterial chemotherapy has been used instead of intravenous chemotherapy to improve local response because higher drug concentrations at the infused tumor site and lower systemic toxicities of drugs have been observed with the former compared with the latter [8].

There are some studies reporting the performance of intra-arterial infusion chemotherapy for superficial bladder cancer, but the treatment effectiveness has not been guaranteed. However, Kakizaki et al. [9] conducted an in vivo canine study in which the concentrations of intra-arterially injected cisplatin and doxorubicin were significantly higher in the bladder mucosa than in the bladder muscles. Kobayashi et al. [7] reported 18 patients with superficial bladder cancer in whom cancer could not be completely controlled with TUR and/or intravesical systemic chemotherapy; these patients were treated with intra-arterial infusion chemotherapy including cisplatin and doxorubicin, with some of the patients treated case with angiotensin II as well. Of the 18 patients, 8 showed pathologically proven complete response, 5 showed partial response, and 5 showed no change; the overall response rate (complete response + partial response) was 72%. This study indicates that intra-arterial infusion chemotherapy is effective for a superficial tumor that cannot be completely controlled by TUR and/or intravesical systemic chemotherapy [7].

This is the first report demonstrating the effectiveness of neoadjuvant intra-arterial chemotherapy for volume reduction of a large superficial bladder cancer. In our patient, chemotherapy performed twice reduced the tumor volume from 275 to 28 cm³, and we could safely perform radical TUR-BT without blood transfusion.

Neoadjuvant arterial infusion chemotherapy is effective for large superficial bladder cancers and is a possible strategy for bladder preservation. We should perform neoadjuvant chemotherapy aimed at volume reduction especially when treating tumors weighing >250 g to avoid a prolonged operation time and the need for blood transfusion.
Statement of Ethics

The authors have no ethical conflicts to disclose.

Disclosure Statement

The authors have no conflicts of interests to declare.

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Fig. 1. CT showed a large bladder tumor.

Fig. 2. The tumor volume had reduced to 28 cm³.