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Case Report

The First Case of Stage IVB Vulvar Cancer Treated with Carboplatin Plus Paclitaxel-based Neoadjuvant Chemotherapy Followed by Definitive Radiotherapy

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Abstract

Systemic chemotherapy or palliative external beam radiotherapy (RT) remains the main treatment modality for patients with stage IVB vulvar cancer accompanied by metastasis beyond the pelvis. However, long survival is rarely achieved by this treatment modality in such patients. In this report, we describe the first case of a patient with stage IVB metastatic vulvar cancer, who was successfully treated with carboplatin plus paclitaxel (TC)-based neoadjuvant chemotherapy followed by TC-based definitive chemoradiotherapy (external beam radiotherapy and high-dose-rate interstitial brachytherapy).

Keywords: Paclitaxel; Carboplatin; Neoadjuvant chemotherapy; Concurrent chemoradiation; Interstitial brachytherapy

Abbreviations: RT: Radiotherapy; TC: Carboplatin plus paclitaxel; NAC: Neoadjuvant chemotherapy CCRT: Concurrent chemoradiotherapy; MRI: Magnetic resonance imaging; CT: Computed tomography; SCC: Squamous cell carcinoma antigen; EBRT: External beam radiotherapy; HDR-ISBT: High-dose-rate interstitial brachytherapy; 5-FU: 5-fluorouracil; MMC: Mitomycin C

Introduction

Stage IVB vulvar cancer is defined as a cancer that has spread to the lymph nodes in the pelvis or to other parts of the body, and it accounts for less than 5% of invasive vulvar cancer [1]. For patients with stage IVB vulvar cancer, especially for those with visceral metastasis, systemic chemotherapy with palliative intent remains the main treatment modality [2]. however, this treatment modality rarely results in long survival.

Due to the rarity of reported cases, information regarding the role of systemic chemotherapy for treating vulvar cancer has been limited. Although previous studies conducted in the 1990's or early 2000's involving small number of patients had suggested a relatively chemoresistant nature of vulvar carcinoma when compared with cervical cancer [3,4], recent investigations have suggested that newly diagnosed, advanced vulvar cancer is sensitive to systemic platinum-based combination chemotherapies [5,6]. We occasionally experience cases of stage IVB vulvar cancer, in which metastatic tumors beyond the pelvis disappeared after chemotherapy, although a viable vulvar tumor persisted. For such patients, a curative treatment modality for the persisting vulvar tumor needs to be proposed.

Surgical resection can be a treatment modality in such patients. In patients with locally advanced vulvar cancer, neoadjuvant chemotherapy followed by surgery seems to have a curative

therapeutic efficacy [5-7]. Even for large vulvar lesions that invade or cross the borders of surrounding structures, such as the urethra, anus, bladder, and other adjacent organs, exenterative surgeries may have a curative therapeutic efficacy. However, when a vulvar tumor involves the pelvic bone, the tumor cannot be removed with an adequate surgical margin, even by pelvic exenteration.

Definitive radiotherapy with or without concurrent chemotherapy may be another potentially curative treatment option in such patients. Although it has been associated with considerable toxicity, including frequent skin damage, theoretically, radiotherapy has a curative therapeutic efficacy even for vulvar tumors that involve the pelvic bone or surrounding organs, without sacrificing the structure and functions of the pelvic organs [8,9]. At present, external beam radiotherapy for locoregional control/symptom palliation is recommended as a treatment modality for patients with stage IVB vulvar cancer accompanied by metastasis beyond the pelvis [2]. However, the feasibility, safety, and efficacy of neoadjuvant chemotherapy (NAC) followed by definitive concurrent chemoradiotherapy (CCRT) have never been investigated.

We herein describe the first case of a patient with large vulvar cancer successfully treated with carboplatin plus paclitaxel-based neoadjuvant chemotherapy followed by definitive CCRT.

Case Presentation

A 58-year-old woman, gravida 3 para 3, presented with a large vulvar tumor. Her past medical history was unremarkable except for a hysterectomy for that was performed a myoma measuring 74 × 51 × 56 mm. On evaluation, her vagina and uterine cervix were normal, whereas a giant subcutaneous nodule on the vulvar was observed. There was no accompanying vaginal or rectal bleeding. Histological analysis of a biopsy specimen from the vulvar lesion demonstrated a squamous cell carcinoma. Pelvic magnetic resonance imaging (MRI) revealed a vulvar tumor measuring 74 × 51 × 56 mm, which involved rectum, urethra and pubis (Figure 1). Computed tomography (CT) of the chest and abdomen suggested a pulmonary metastatic nodule and lymphadenopathy in the bilateral obturator and inguinal regions, all of which were greater than 1 cm in diameter. The patient's squamous cell carcinoma antigen (SCC) level of the patient was evaluated up to 5.3 ng/ml. These findings confirmed the diagnosis of an International Federation of Gynecology and Obstetrics (FIGO) Stage IVB vulvar cancer, and systemic chemotherapy consisting with paclitaxel and carboplatin (TC) was initiated.

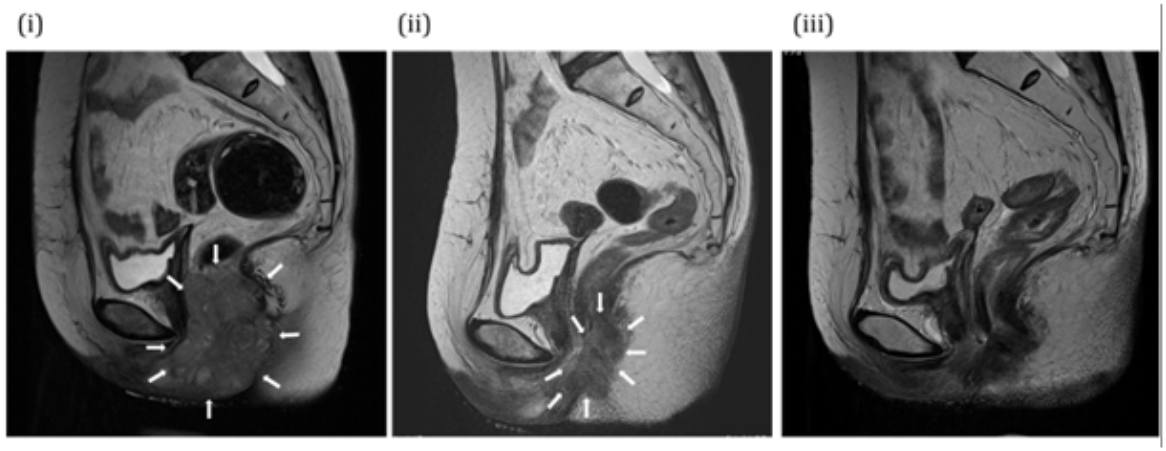

Figure 1: T_2-weighted magnetic resonance imaging images of vulvar cancer. (i) Pretreatment, (ii) After six cycles of chemotherapy, and (iii) After CCRT.

At the completion of six cycles of TC-based chemotherapy, a significant reduction in tumor size was noted. As shown, a pelvic MRI revealed a vulvar tumor measuring 24 × 34 × 30mm, which still involved the rectum and urethra. In addition, CT of the abdomen and chest revealed the complete resolution of the pulmonary metastatic nodules and lymphadenopathy. The SCC level was also normalized. However, a recto-vaginal fistula was developed, presumably because of the rapid resolution of the vulvar tumor involving the rectum.

As the metastatic disease completely resolved, we had decided to recommend her curative treatment options for the remaining vulvar tumor. As the patient desired to preserve the bladder function, we proposed a definitive RT concurrently with TC and colostomy thereafter. The patient received with concurrent TC-based chemotherapy and radiotherapy (CCRT) consisting of external beam radiotherapy (EBRT: 50 Gy given in 25 fractions) and high-dose-rate interstitial brachytherapy (HDR-ISBT) (25 Gy given in 5 fractions). The treatment was well tolerated and yielded a complete remission of the vulvar lesion and successful bladder preservation (Figure 1). Colostomy is performed after CCRT, as scheduled. After 10 months of follow-up, the patient was currently alive without any recurrence.

Discussion

In this report, we described the first case of a patent with large vulvar cancer successfully treated with carboplatin plus paclitaxel-based TC-based multimodal treatment, i.e, NAC followed by definitive CCRT consisting of external beam RT plus ISBT.

It has been difficult to achieve long survival in patients with Stage IVB vulvar cancer having metastatic disease beyond the pelvis. At present, systemic chemotherapy, EBRT with palliative intent, and the best supportive care are recommended for this disease [2]. Despite a historical belief that vulvar cancer is not chemosensitive [3,4], recent studies have shown that advanced vulvar cancer is sensitive to chemotherapy, although durable responses with long survival are rarely achieved [5,6]. The recommended regimens include both single agent (cisplatin, carboplatin or paclitaxel) and combination chemotherapy (cisplatin/paclitaxel or carboplatin/paclitaxel with or without bevacizumab, cisplatin/vinorelbine, and cisplatin/gemcitabine) [2]. However, only limited information is available concerning the role of chemotherapy in treating patients with Stage IVB vulvar cancer having metastatic disease beyond the pelvis.

In the patient in our study, we employed carboplatin/paclitaxel as a systemic chemotherapy as bevacizumab has not been approved for the treatment of vulvar cancer in Japan. The significant activity of carboplatin/paclitaxel observed in our study was consistent with previous reports showing that NAC can minimize the size of vulvar tumor. Moreover carboplatin/paclitaxel improved the resection rate of subsequent surgery in patients with locally advanced vulvar cancer [5,6,8].

As the metastatic disease completely disappeared in the present case, we decided to perform curative treatment for the remaining vulvar cancer. As the patient desired to preserve the function of the pelvic organs as much as possible, we decided to perform definitive CCRT to irradicate the remaining vulvar tumor, instead of performing surgical resection. However, radiotherapy in combination with 5-fluorouracil (5-FU) and mitomycin C (MMC) or cisplatin as a single agent or in combination, has been the most successful and feasible treatment in patients with vulvar cancer [9,10]. Significant responses shown by patients to TC and our previous studies involving patients with cervical cancer suggested that CCRT using TC might be more efficacious than conventional CCRT using single platinum agent [11,12]; therefore, we employed TC as a concurrent chemotherapy during radiotherapy. Furthermore, to the best of our knowledge, there are no studies directly comparing patient outcomes after EBRT plus BT vs. EBRT alone for inoperable vulvar cancer. However, based on our experience using TC-based CCRT consisting of EBRT and HDR-ISBT in patients with primary vaginal cancer [13], we employed EBRT plus HDR-ISBT as a definitive RT for this patient. As expected, the TC-based CCRT was safely performed, successfully irradicated vulvar lesion. The patient is currently alive without disease 10 months after completion of treatment.

In gynecologic malignancies, the TC-based definitive CCRT has been employed only in patients with cervical cancer and vaginal cancer [11-13]. Thus, this is the first report of TC-based CCRT employed in patients with vulvar cancer. Our case may indicate that systemic chemotherapy consisting of TC is active against metastatic vulvar cancer and may also suggest that neoadjuvant TC followed by TC-based CCRT (EBRT plus HDR-ISBT) may be a promising treatment to achieve long survival in such patients. The efficacy and safety of this treatment should be investigated further in future clinical studies, preferably in a prospective setting.

Conclusion

In conclusion, we describe the case of a patient with stage IVB vulvar cancer successfully treated with TC-based NAC followed by definitive RT. Given the rarity of stage IV vulvar cancer, we believe that reporting even individual cases in which complete remission could be achieved is important for establishing a potentially curative treatment.

Acknowledgement

None.

Conflict of Interest

The authors declare no competing interests.

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