Primary small cell carcinoma of the bladder

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KEY WORDS

bladder ◗ small cell carcinoma ◗ hematuria

ABSTRACT

Primary small cell bladder carcinoma is an extremely rare and highly aggressive tumor. It is usually characterized by early systemic dissemination and death from metastatic disease. Because of its rarity, an optimum treatment strategy has not been established and various combinations of surgery, radiotherapy, and chemotherapy have been described in published studies. We report a case of small cell carcinoma of the urinary bladder that was successfully treated with a combination of TURT, adjuvant platinum-based chemotherapy, and radiotherapy. The patient remains disease free after 3 years of follow-up.

INTRODUCTION

Primary small cell carcinoma of the bladder (SCCB) is an infrequent neoplasm accounting for less than 1% of all urinary bladder carcinomas [1]. The first case was reported in 1981 by Cramer et al. [2]. Since then, cases diagnosed according to the World Health Organization's criteria have been published [3]. Metastases are often present at the time of diagnosis and prognosis is generally poor [1, 4]. Here, we present a new case of a primary SCCB and discuss the clinical, diagnostic, and therapeutic aspects of this uncommon and highly aggressive tumor.

CASE REPORT

A 67 year old white male presented with macroscopic hematuria of two weeks duration. He is an ex smoker and has a medical history of epilepsy and osteoarthritis. Physical examinations were unremarkable. Urine cytology was suspicious for neoplastic cells. Flexible cystoscopy revealed both solid and papillary tumors in the right lateral wall of the bladder around the right ureteric orifice. CT-urography showed a 5 cm mass involving the right lateral wall of the bladder above the right ureteric orifice (Fig. 1). Both kidneys were normal. Transurethral resection of bladder tumor (TURT) was performed. Histological examination of the tumor revealed extensive infiltration with muscular involvement by malignant cells with scanty cytoplasms, nuclear molding, and necrosis (Fig. 2). The cells exhibited positive staining for the neuroendocrine marker CD56. All these features were that of small cell carcinoma. After a detailed staging work-up; including bone scan and CT scan of the chest, abdomen, and pelvis; there was no evidence of metastasis. This case was discussed at our multidisciplinary meeting (MDT) and clinical stage T3N0M0 was established. Moreover, it was decided that the best course of treatment in this case of localized disease would be chemo-radiotherapy with aggressive cystoscopic surveillance after radiotherapy to identify any local relapse. This would allow for effective local control and, most importantly, allows for a bladder preserving method. The patient was treated with four cycles of Carboplatin/Etoposide. A check cystoscopy performed after the chemotherapy treatment revealed no evidence of recurrent disease. Consolidation radiotherapy with 60 Gy was then given to the patient without any major complications. The patient remained disease free and asymptomatic in 3 years follow-up as a result of this combined treatment modality.

DISCUSSION

There is no difference in the clinical presentation of SCCB from other tumors of the urinary bladder. A predilection for males over females with a 5:1 proportion is characteristics of this neoplasm [5]. Patients with SCCB are typically elderly men and they usually boast a history of smoking. The clinical presentation includes macroscopic hematuria and is less often found with pain or obstructive symptoms. In most cases, the initial diagnosis is made at the metastatic or progressive stage of the disease. Rare cases of paraneoplastic syndromes have been reported. Long term outcome for patients with SCCB remains poor and most patients experience early systemic recurrence. In one large series, disease specific survival at 1, 3, and 5 years was 56%, 23%, and 16%, respectively [4]. Histologically, SCCB is similar to the SCC of the lung (SCCL) and characterized by sheets and nests of small round cells containing hyperchromatic nuclei. Immunostaining for neuroendocrine differentiation markers are usually positive, however, none of them correlate with treatment outcome or prognosis. CD56 has become the marker antibody of choice in many laboratories including ours because the sensitivities for other markers in small cell carcinoma can vary [6] and comparative studies suggest that CD56 is one of the most sensitive markers in this situation [7].

Some studies have demonstrated the coexistence of elements of transitional cell carcinoma in up to two-thirds of patients diagnosed with SCCB [3, 5]. Because of the rarity of SCCB, an optimal therapy has not yet been developed.

The available data indicate that SCCB has a poor prognosis, which may only be influenced by the extent of the disease at the time of diagnosis paired with the combination chemotherapy as the cornerstone of treatment with surgery or radiation treatment as adjunctive [8, 9]. As with SCCL, surgical resection alone, in the form of a cystectomy, is unlikely to be curative owing to micrometastases, which are usually present at the time of diagnosis. In addition, relapse after resection of apparent organ confined disease is well documented [10]. Cheng et al., in his large series demonstrated no difference in survival between patients who underwent cystectomy compared with those that did not [4]. Consequently, the authors raised doubt about the effectiveness of cystectomy as initial treatment.

Platinum-based chemotherapy as adjuvant or neoadjuvant therapy combined with radical cystectomy has been associated with significantly improved survival in two large series [11, 12]. Based on this evidence, most authors recommend a platinum

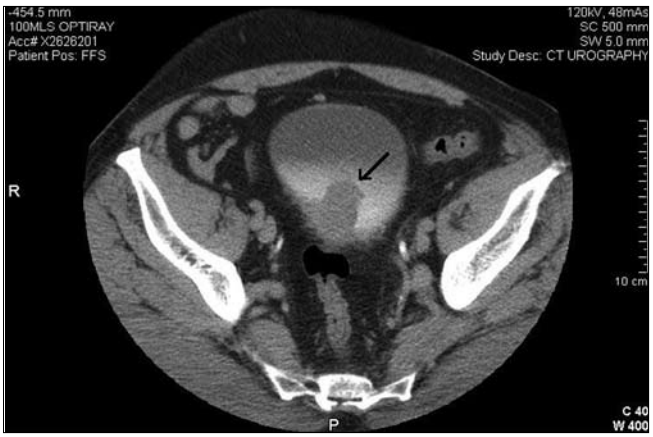

Fig. 1. CT-urography showing a large tumor on the posterior wall of the bladder (arrow).

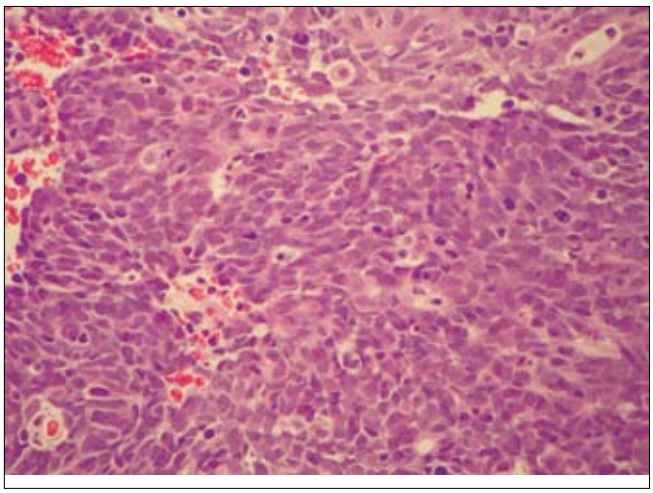

Fig. 2. Photomicrograph of a small cell carcinoma demonstrating the typical features of hyperchromatic nuclei with scanty cytoplasm and nuclear molding. Numerous mitotic figures are present (H&E 100x).

containing regimen as an essential component of SCCB management, particularly when the disease has spread outside the bladder [3, 10, 11].

On the other hand, SCCB shares many clinicopathological features with the more common SCCL whose clinically relevant two stage system of limited and extensive disease is widely used to determine prognosis and treatment. The current treatment of limited SCLC comprises a combination of cisplatin based chemotherapy coupled with chest irradiation [13]. Due to the dismal prognosis of SCCB, just as its pulmonary counterpart, an organ sparing treatment strategy of chemotherapy and radiotherapy is an attractive concept after considering the extent of disease. Oblon et al. first described a bladder preserving approach using sequential chemo- and radiotherapy [14]. Several investigators reported long term survival when radiation therapy was combined with chemotherapy in a bladder preserving approach. In a series of four patients treated with chemo-radiotherapy, Bastus et al. reported no relapse with a mean follow-up of >4 years. Lohrisch et al. reported an overall survival of 44% at 5 year follow-up using this combined approach [9, 15]. Therefore, the bladder sparing treatment strategy of chemo- and radiotherapy subsequent to a macroscopically comprehensive TURT can achieve long-term remission or even a cure in those with localized disease. In addition, this bladder sparing approach will preserve normal bladder function while maintaining an exceptional quality of life.

For patients presenting with metastasis, palliative chemotherapy supplemented with radiotherapy for local control can be used in selected patients.

To summarize, SCCB, like its pulmonary counterpart, has the potential for rapid growth and widespread metastasis. Moreover, the possibility of SCCL that has metastasized to the bladder should always be carefully ruled out. The prognosis is uniformly poor due to early invasion and high metastatic potential. However, for localized disease, a combined treatment using platinum-based combination chemotherapy and consolidation radiotherapy can achieve long term remission and cure.

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