Effect of Surgery Combined with Gemcitabine and Oxaliplatin Chemotherapy on Primary Signet Ring Cell Carcinoma of Bladder: A Case Report

Shaocheng Wang; Xiaoyu Huang; Guangyu Zhang; Wensheng Zhou*
Department of Urology, The First Affiliated Hospital of Bengbu Medical College, Bengbu 233000; China.

Abstract

Background: Primary signet ring cell carcinoma of the bladder is an extremely rare and highly invasive variant of primary bladder cancer. When tumors are found, they usually show high-level and high-stage lesions and diffuse invasion of the bladder wall, and most tumors do not grow in the cavity. Most patients have no specific symptoms at the beginning, which leads to delayed diagnosis and treatment and poor prognosis.

Case introduction: We report a case of painless gross hematuria in Bengbu City, Anhui Province, China. Ultrasound and enhanced CT scanning showed that there were 33 x 23 mm hypoechoic and punctate blood flow in the bladder wall. Histopathological examination of the tumor after partial cystectomy showed signet ring cell adenocarcinoma. Gastrointestinal examination did not reveal any other tumor localization. Therefore, regular infusion chemotherapy of gemcitabine can make the patients have no metastasis within the 36 month survival period and have a good quality of life; After 48 months, the patient found tumor recurrence, mainly manifested in hematuria and palpable lower abdominal lumps. The patient requested surgery. Oxaliplatin + gemcitabine chemotherapy was performed regularly after operation. Extensive metastasis was found after 10 months of follow-up.

Conclusion: In the treatment of primary signet ring cell carcinoma of the bladder, the rarity and success of oxaliplatin and gemcitabine as adjuvant chemotherapy are two important features described in this case report, which are rarely reported in the literature.

Keywords: Primary signet ring cell carcinoma; Bladder; Bladder perfusion chemotherapy; Intravenous chemotherapy; Surgery; Gemcitabine; Oxaliplatin.
Primary Signet Ring Cell Carcinoma of The Bladder (PSRCC) is a rare bladder tumor. In 1955, Saphir reported the first two cases, and less than 100 cases were described later [1]. Signet Ring Cells Carcinoma (SRCC) are usually considered to be a small group of high-grade urothelial carcinoma. The pure morphology of these cells is extremely rare [2].

Microscopically, signet ring cells are described as crescent cells, the nuclei of which are compressed to the side of the cell edge by a large number of cytoplasmic mucins. In some tumors, they appear as single clear vacuoles, while in others, they appear as foam like multivesicular cytoplasmic material [3-5]. The cumulative distribution of mucin in cytoplasm and nucleus is uneven [6]. SRCC first invades the bladder mucosa and submucosa, and finally the whole layer is involved [7]. It is difficult for this kind of tumor to grow like an extrusive tumor, but it is more likely to spread around. In the previous cognition, it is not easy to identify in cystoscopy because its growth mode is invasive rather than exogenous growth. In order to make a diagnosis, we often need to biopsy the whole bladder [5]. In recent years, with the deepening of the understanding of the disease, the results of cystoscopic pathological biopsy diagnosis have become more and more reliable. We now report a case of primary signet ring cell carcinoma of the bladder and briefly review the current literature.

Case introduction

A 59 year old man from Bengbu City, Anhui Province, China came to our hospital for treatment due to painless gross hematuria. Ultrasound and enhanced CT scan showed that there were 33 x 23 mm low echoes and punctate blood flow on the bladder wall. History and family history were not significant. Ultrasound showed that the anterior wall of bladder was thickened, and space occupying possibility was suspected. On enhanced CT scan, 33 x 23 mm low echo was found on the bladder wall, punctate blood flow was found, and no lymph node enlargement or distant metastasis was found. Cystoscopy revealed a non papillary mass in the anterior wall of the bladder, with normal micturition at both ureteral orifices. After communicating with patients and their families, partial cystectomy was considered. Histopathological examination showed that this was a poorly differentiated signet ring cell adenocarcinoma that had invaded the deep musculars. We compared tumor markers and performed a complete digestive system examination. Finally, the team made an assessment and analysis, and the possibility that the tumor of extraneous origin in the bladder was excluded. Therefore, this tumor is considered as PSRCC. According to AJCC stage and postoperative pathology, the patient’s stage can be judged as t2bn0m0. The patient was followed up for a long time after the operation, and regularly re-examined for half a year. The reexamination item was chest and abdomen CT scan, and systemic gemcitabine intravesical infusion chemotherapy was carried out. The single dose was 1.0 g/50 mlns. After the preparation of normal saline, it was injected into the bladder, once a week, eight times later it was changed to once a month, and continued the long-term infusion chemotherapy. After 24 months of follow-up, there was no recurrence and the infusion chemotherapy was stopped. It can be judged that the treatment method has a significant effect, and the survival period of patients has been successfully prolonged.

Discussion

Primary Signet Ring Cell Carcinoma of The Bladder (PRSCC) is a rare bladder tumor Only 0.24%~2% of the incidence rate of bladder cancer [8]. In 1955, Saphir reported the first two cases, and less than 100 cases were described later [1]. Recent studies [9] have described the pathogenesis of signet ring cell carcinoma, which is a highly malignant dedifferentiated adenocarcinoma. Between these round cells, there is no interaction between them. The tumor contains a large number of vacuoles filled with mucus, which is secreted by tumor cells. The mechanism of this phenomenon is that in well differentiated adenocarcinoma, erbb2/erbB3 complex activity is increased, and then phosphatidylinositol 3-kinase (PI3K) is activated. Then p38MAP kinase was activated downstream of PI3K, and the adhesion junction was destroyed by Rac1 activation. The loss of adhesion leads to the disappearance of tight junctions, which leads to the loss of cell-cell interaction. Activation of PI3K can promote mucin secretion. Mucin MUC4 can activate erbB2. In normal cells, MUC4 and erbB2 are separated by adhesions, but in signet ring cells, because these connections have been lost, they can interact. As a result, erbb2/erbB3 signaling pathway was activated, and cell-cell interaction was lost, leading to the formation of signet ring cell carcinoma. At the same time, the cell growth activity was enhanced due to the structural activation of erbb2/erbB3 complex. And E-cadherin gene mutations can be found in some signet ring cell carcinomas, which is
consistent with the above hypothesis. However, it is not clear why erbb2/erbb3 pathway is important in signet ring cell carcinoma. This may be because ERBB3 strongly activates PI3K. Further research is needed to explore its mechanism.

Most of these tumors occur in middle age and are usually detected later. The prognosis of most patients is unsatisfactory [10]. In this case study, the patient’s initial age of onset was 51 years. The common clinical presentation of this disease is very similar to that of other bladder malignancies [11]. Common symptoms are irritation of urination and hematuria. Associated symptoms such as urinary retention, low back pain, and ureteral obstruction are rare. Signet ring cell carcinoma of the bladder is the most common invasive cancer, most involving all levels of the bladder. On cystoscopy, lesions are generally described as pedunculated, polypoid, sessile, and ulcerative filtering phenotypes, among others [12]. Bladder adenocarcinoma can occur anywhere in the bladder, but the most common site is the fornix of the bladder. In the histopathological cases reported in the literature, histological sections may show urothelial carcinoma with glandular/signet ring cell differentiation, or signet ring degeneration in primary urachal or nonurachal bladder adenocarcinoma Body [13-17]. Due to the rarity and dispersion of these cells, malignant signet ring cells are rarely found in urine excretions or instrumental urine samples, so they can easily be missed or misinterpreted. Therefore, the diagnosis of signet ring cell carcinoma from urine cytology is not the method of choice [18]. Distinguishing this cancer from metastatic cancer is important because different treatment strategies are often necessary. Histologic testing of signet ring cell carcinoma of the bladder correlates with findings at sites such as the gastrointestinal tract, breast, lung, gallbladder, and prostate; therefore, further evaluation must be performed to rule out metastatic tumors [10-12]. In this patient, no foreign bodies were found in other parts from imaging, pathology, immunohistochemistry, and surgical exploration. Can be identified as primary signet ring cell carcinoma.

The treatment group divided the treatment of this case into two types, and formulated different treatment methods according to the onset and recurrence. The first diagnosis showed that his tumor was small and invading, and the patient’s symptoms were relatively mild and his age was relatively young. Therefore, the patient underwent partial cystectomy plus intravesical chemotherapy with gemcitabine. Systematic follow-up was performed. No recurrence was found during the 24-month follow-up. Therefore, the patient’s metastasis-free survival was at least 24 months, and the time to recurrence of symptoms was 48 months, and the patient’s quality of life was extremely high. This is a huge breakthrough in the treatment of PSRCC. By the time the patient found recurrence, the tumor had grown so large that it had invaded surrounding tissues, and the patient’s symptoms had begun to worsen. According to the patient’s desire for further treatment, the patient received tumor reduction surgery + gemcitabine combined with oxaliplatin intravesical chemotherapy. Currently, the patient has survived for more than 10 months and will continue chemotherapy. The treatment effect is obvious, and the quality of life of the patients has been significantly improved. Both treatments performed better than expected. The patient’s survival time has reached five years, which can be regarded as a successful treatment in this case.

Conclusion

PSRCC of the bladder is a rare histological variant of mucinous adenocarcinoma. It is generally characterized by low differentiation, high grade and late stage. Its prognosis is generally poor. Recently, studies [19] showed that cisplatin and gemcitabine were successfully used for chemotherapy. The treatment method of this case is similar to that of this case. The operation combined with chemotherapy (including intravesical chemotherapy with gemcitabine and intravenous chemotherapy with gemcitabine and oxaliplatin) was used, so that the patient did not relapse for at least 24 months, and the survival time was successfully up to five years. It has great guidance for the treatment of patients in the future. We can consider further optimizing the operation mode, and cooperate with other advanced treatment methods to further improve the relevant treatment methods.

References


