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Case Report

Intra-Arterial Chemotherapy in Liver Metastatic Bladder Cancer Refractory to Standard Therapy: Two Case Reports

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Abstract

Bladder cancer is the commonest malignancy of the urinary tract. Unfortunately most patients develop metastases during the course of their medical history. In this setting, chemotherapy treatment remains the only therapeutic option. Today, there is not standard therapy over the second line chemotherapy.

We reported our experience with intra-arterial chemotherapy in two patients with metastatic bladder cancer liver progression disease after standard chemotherapy. The schedule used consisted in epirubicin 35 mg/mq and cisplatin 42 mg/mq administered into hepatic artery proper by bolus injection through a catheter inserted in the femoral artery with the Seldinger method, with cycles repeated every 21 days. Intra-arterial chemotherapy provided a good liver disease control, allowing to treat disease progression with radiotherapy, without important adverse events. Interesting, intra-arterial chemotherapy was well tolerated despite age, previous treatment and related residual toxicities.

Keywords: Bladder; Cancer; Chemotherapy; Intra-arterial; Liver; Metastases

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Introduction

Bladder cancer is the commonest malignancy of the urinary tract, with the incidence being four times higher in men than in women [1]. About 50% of patients who underwent radical cystectomy for invasive bladder cancer develops recovery of local or distant disease, while approximately 10-15 % of patients present with metastatic disease at time of diagnosis [2], especially in liver, bone and lung. In metastatic setting, chemotherapy treatment remains the only therapeutic option. Although recent advances have improved outcomes in second line therapy, the vast majority of patients have disease recurrence or progression within few months, with a 5years survival rate of less than 10%. Furthermore, treatment options in subsequent lines are limited, partly because patient clinical conditions are deteriorated and chemotherapy is often burdened by significant side effects. We reported our experience with intra-arterial chemotherapy in two patients with metastatic bladder cancer liver progression disease.

Materials and Methods

We described two case reports of metastatic pre-treatted bladder cancer subjected to intra-arterial chemotherapy. The first patient was 80 years old; in his medical history myocardial infarction six years ago, with an actual ejection fraction of 45%. In December 2012 he underwent to radical cystectomy with lymphadenectomy and prostatectomy due to infiltrating urothelial carcinoma pT2N1G3, followed by 5 cycles of adjuvant chemotherapy with carboplatin plus gemcitabine in other oncological department. Following the appearance of worsening low back pain, in March 2015 he performed a bone scan and CT scan that showed the presence of right pelvis, liver and lymph nodes metastasis. Given the time elapsed since the term adjuvant therapy and the good general condition (ECOG PS 0), the patient has been subjected to 3 cycles of carboplatin first-line chemotherapy in association with gemcitabine, followed by concomitant gemcitabine-pelvis radiotherapy (33 Gy total dose). The treatment was discreetly tolerated with just a grade 1 peripheral neurotoxicity. The next restaging CT scan evidenced a liver and bone progression disease, with lymph nodes disease stability. So, from July to September 2015, he underwent to a vinfluina second-line chemotherapy. After 3 cycles of chemotherapy, a total body CT showed bone and lymph nodes disease partial response but a liver progression disease. Therefore, vinfluina therapy was not well tolerated due to G4 neutropenia and severe asthenia. In October 2015, the patient went in our Oncological Department: considering general condition (ECOG PS 2), age, recent side effects and previous received therapies, as well as the only site of hepatic progression, we decided to subject the patient to cisplatin-epirubicin intra-arterial chemotherapy with the Seldinger method. Regional chemotherapy were administered through an angiographic catheter (Simmons 2; 5 Fr) introduced via the femoral artery into hepatic artery. The schedule used consisted in epirubicin 35 mg/mq and cisplatin 42 mg/mq diluted in 100 ml of normal saline and then infused over a period of 10 minutes, with cycles repeated every 21 days. After 3 cycles, restaging CT scan showed a right hepatic lobe metastasis reduction and a slight increase of those left. We decided to proceed the subsequent 3 cycles with a selective catheterization of

the right and left hepatic arteries, infusing respectively 40 and 60% of the drugs, in order to better perfuse the left lobe, where there has been a minor response. CT scan performed in February 2016, showed a liver stable disease but a bone progression. Loco regional treatment was well tolerated, with the exception of a grade 2 transient increases in transaminases and mild asthenia. Due to bone progression disease with pain and physically disabled, patient underwent to palliative sacral radiotherapy in March 2016, and continued intra-arterial treatment for additional 2 cycles, until May 2016. Unfortunately, restaging CT scan showed an important liver, bone and lung progression disease, furthermore the patient had a severe deterioration of the general conditions (ECOG PS 3), so we decided to continue just supportive care. The patient died in September 2nd, 2016.

The second patient is 64 years old without comorbidities .In March 2013 he had diagnosis of infiltrating urothelial carcinoma, cT4N2M1 (metastasis in abdominal lymph nodes and bone). From May to October 2013, he performed 6 cycles of first-line cisplatin-gemcitabine chemotherapy with good tolerance and stability disease. In March 2014, due to lymph nodes and bone progression disease, he was subjected to weekly paclitaxel second-line chemotherapy, followed by concomitant chemo-radiotherapy on abdominal lymph nodes and on first and second lumbar vertebrae, until October 2014. Treatment was discreetly tolerated, except for the grade 2 peripheral neuropathy and moderate asthenia and anorexia appearance. Unfortunately, restaging CT scan performed in December 2014 showed the appearance of liver metastases, with stability of the remaining lesions. Considering general condition (ECOG PS 2), residual grade 2 peripheral neurotoxicity, persistent moderate asthenia and anorexia, previous received therapies and the only site of hepatic progression, we proposed to the patient a loco regional approach with cisplatin-epirubicin intra-arterial chemotherapy. So, from January to July 2015, he received 6 cycles of epirubicin 35 mg/mq and cisplatin 42 mg/mq chemotherapy, administered into hepatic artery proper by bolus injection through a catheter inserted in the femoral artery with the Seldinger method (each cycle was repeated every 21 days). Loco regional treatment was well tolerated without any side effect, patient general condition improved with resolving of anorexia and residual grade 1 asthenia and reduction of hepatic lesions. In August 2015, treatment was temporarily suspended due to enforcement of antalgic palliative pelvis radiotherapy and it was restarted for further 2 cycles, until October 2015. The next revaluation CT scan showed a lung progression disease, so the patient resumed weekly paclitaxel. Chemotherapy was finally stopped in February 2016, due to general condition progressive deterioration.

Results

Both patients received platinum combination first-line chemotherapy with a PFS of 3.23 months for the first elderly patient (carboplatin plus gemcitabine) and 10.13 months for the second younger patient (cisplatin plus gemcitabine). At the progression, also second-line chemotherapy had poor effect in patient 1 (PFS 2.5 month with vinfluina), while paclitaxel second-line chemotherapy awarded a PFS of 9.1 month in patient 2. Third-line therapy loco regional approach with cisplatin-epirubicin intra-arterial chemotherapy (epirubicin 35 mg/mq plus cisplatin 42 mg/mq chemotherapy, administered into hepatic artery proper by bolus injection through a catheter inserted in the femoral artery with the Seldinger method. Each cycle was repeated every 21 days) awarded a PFS of 8.97 and 12.1 month in the first and second patient, respectively. Notable, no grade 3-4 toxicities were reported, rather, patient ECOG PS improved during treatment. Globally, OS was 45.7 month for patient 1 and 38.7 for patient 2.

Discussion

Bladder cancer is one of the most aggressive and a poor prognosis tumor. Cisplatin containing first-line chemotherapy can prolong median OS until 14 months, especially in patients with only lymph nodes disease and good PS [3-11]. Vinfluina second-line chemotherapy showed an advantage of just 2.6 months versus best supportive care (6.9 vs 4.3 months respectively), at expense of significant haematological and not toxicities [12,13]. Despite these survival data, some patient is candidates to a third-line regime. Obviously, a further course of treatment should take into account the previous received therapies, residual toxicities, patient general condition and any future side effects. Considering that, today, there is no consensus schedule in these patients and our experience with loco regional chemotherapy [14,15], we submitted two pre-treated patients with hepatic metastasis bladder cancer to intra-arterial chemotherapy. Both patient received a platinum combination first-line chemotherapy with a PFS of 3.23 months for the first elderly patient (carboplatin plus gemcitabine) and 10.13 months for the second younger patient (cisplatin plus gemcitabine). At the progression, also second-line chemotherapy had poor effect in patient 1 (PFS 2.5 month with vinfluina), while paclitaxel second-line chemotherapy awarded a PFS of 9.1 month in patient 2. Considering the subsequent progression disease just in the liver, residual toxicities and general condition, we proposed to both patients a loco regional approach with cisplatin-epirubicin intra-arterial chemotherapy (epirubicin 35 mg/mq plus cisplatin 42 mg/mq chemotherapy, administered into hepatic artery proper by bolus injection through a catheter inserted in the femoral artery with the Seldinger method. Each cycle was repeated every 21 days). Restaging CT scan showed a good liver disease controls in both cases, with a third-line therapy PFS of 8.97 and 12.1 month in the first and second patient, respectively. Very important, no grade 3-4 toxicities were reported, rather, patient ECOG PS improved during treatment. Globally, OS was 45.7 month for patient 1 and 38.7 for patient 2. Our experience showed that intra-arterial chemotherapy is feasible and effective, so it could be considered a therapeutic option in pre-treated hepatic metastatic bladder cancer, regardless of age and residual toxicities. Of course, we need to collect more case reports to confirm our data and plan an ad hoc trial in this patient setting.

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