Cardiac Failure Caused by the Association of Carboplatin and Gemcitabine Chemotherapy in a Patient with Metastatic Urothelial Cancer: A Case Report

Tiong FL*, Cornillet L2 and Houede N1
1Oncology Unit, University of Nimes, France
2Cardiology Unit, University of Nimes, France

Abstract

Introduction: Carboplatin is one of the most frequently drug, used in the treatment of many cancers. Several agents are known to cause cardiomyopathy and myocardial ischemia such as Anthracyclines and Fluorouracil. Descriptions of cardiac events associated with platinum agents are less common.

Case Report: We report the case of a seventy-seven year-old man, who had no cardiovascular comorbidity. He was treated with Carboplatin and Gemcitabine infusions for a metastatic urothelial cancer. He presented a heart failure after blood infusion two weeks after the end of chemotherapy.

Discussion: A few cases of cardiovascular toxicity due to Carboplatin have been reported immediately during the treatment or some weeks later. The increased oxidative stress could be one of the mechanisms.

Conclusion: More studies are needed to evaluate the prevalence of these toxicities and to guide practitioners in decision making.

Keywords: Cardiac failure; Carboplatin; Bladder cancer

Introduction

Carboplatin and Gemcitabine are two of the most commonly used chemotherapeutic agents in clinical oncology practice. Several agents are known to cause cardiomyopathy and myocardial ischemia, like Anthracyclines and Fluorouracil. However, descriptions of cardiac events associated with platinum agents are less common. There are no consensus guidelines regarding prevention, monitoring, or treatment of patients at risk for chemotherapy-induced cardiomyopathy. We report the case of dilated myocardopathy revealed by cardiac failure in a patient with metastatic bladder cancer, treated with Carboplatin and Gemcitabine regimen.

Case Report

The patient was a seventy-seven year-old man with a history of hypertension and hypercholesterolemia. He was a heavy smoker. He had no history of myocardial infarction or angina. His mother died after a blood transfusion when she was 53 year-old, but the patient didn’t know exactly how. Before he was diagnosed a urologic cancer he complained of epigastric pain for eleven months and was subjected to stress test which resulted normal. In December 2013, he was diagnosed a pT2 urothelial carcinoma. In fact, he suffered from macroscopic hematuria since one year. The Computered Tomography scanner showed a 62 mm mass syndrome without any pulmonary, hepatic or bone metastasis. Two months later the patient underwent cystoprostatectomy without neoadjuvant chemotherapy. Tumor (removed) was classified as pT2b pN0 G3.

In November 2014, the patient suffered from pain in the hips. A bone scan showed no bone metastases. Shortly after, the patient presented to the Emergency Department (ED) with fever and pain. He was admitted in the oncology unit where he had CT scan and MRI. Multiple metastases were found: in liver, lungs, bones and retroperitoneal lymph nodes. The patients suffered from disseminate pains. He was not able to stand up. He had fever 38°5 every day since his hospitalization. Blood test revealed anemia and inflammatory syndrome. The patients was therefore treated with opioids, large spectrum antibiotics and given blood infusions.

He began and Carboplatin AUC 4.5 + Gemcitabine 1000 mg/m² chemotherapy regimen. Rapidly the pain decreased. He received six cycles of chemotherapy. The chemotherapy was quite well tolerated although the anemia and thrombopenia, which required transfusions. The CT scan at the end of treatment showed a partial response. Two weeks after the end of chemotherapy the patient received two packs of red cells because of symptomatic anemia (8.3 g/dl). A few hours after, the patient suffered from severe dyspnea with high blood pressure (210/110 mmHg). Echocardiography revealed a sinus rhythm, fine complex QRS and repolarization abnormalities in lateral and inferior territory. The left ventricular function was altered at 25 to 30%. N-Terminal proBNP (Brain Natriuretic Peptide) levels were very high at 12 171 pg/ml (normal value <125 pg/ml) and cardiac Troponin I levels was low at 42 µg/l (normal value <14 µg/l), strengthening the diagnosis of cardiac decompensation. He was transferred to intensive care unit and was treated with a medical treatment with high dose loop diuretics such as furosemide (LASILIX), isosorbide dinitrate (RISORDAN), beta blockers, converting enzyme inhibition and non-invasive ventilation. The left ventricular function was altered of 25 to 30%.

The patient was stabilized within a few days. Two weeks later he went to the cardiologist. Although the left ventricular function was 40%, the patient had orthopnea. At the transthoracic echocardiography it was found a global hypokinesia. Left ventricle was dilated at 61 mm while the right remained normal. The coronary angiography showed dilated cardiomyopathy but the arteries were normal. It was decided a medical treatment. In July 2015 the patient presented to the ED with of seizure. The brain CT scan showed multiple metastases that were confirmed by the MRI. The BODY scan showed bone and liver metastases in progression. After discussion of the case during...
Gomez et al., described the case of a patient who developed severe chest pain and left heart failure signs ten minutes after Carboplatin infusion for an ovarian carcinoma [3]. Naitoh and colleagues reported a patient who suffered from acute myocardial infarction during Carboplatin and Gemcitabine therapy for a non-small cell lung cancer [4]. Sakai et al., [5] discussed a patient who experienced symptoms of congestive heart failure two weeks after Carboplatin therapy [5]. Shaheer Khan et al., [6] described the case of unstable angina associated with Cisplatin and Carboplatin in a patient with advanced melanoma [6]. One of the explanations from Cheng et al. is an increased oxidative stress through a mitochondrial pathway in rat cardiomyocytes exposed to Carboplatin [7]. Gemcitabine-induced acute coronary syndromes are rarely described in the literature. Bdair et al. reported a case of a patient with previous myocardial infarction history, which developed acute myocardial infarction three days after Gemcitabine therapy [8].

Conclusion

Unlike Cisplatin, no caution for cardiac toxicities is taken with Carboplatin. However, our case shows that chemotherapeutic agents must be administered with cardiac monitoring to prevent cardiac complications, even if the agent is not known as “cardiotoxic”.

To the best of our knowledge, no assessment of cardiac events associated to Carboplatin has been made so far, therefore a large retrospective study is needed to evaluate the prevalence of these toxicities and to help physicians in monitoring patients at risk.

References


Discussion

Cardiotoxicity is a significant complication due to chemotherapy. Cardiovascular events may consist in blood pressure changes, thrombosis, electrocardiographic changes, arrhythmias, myocarditis, pericarditis, myocardial infarction, cardiomyopathy, cardiac failure (left ventricular failure) and congestive heart failure [1]. They may occur during or shortly after treatment or years after the completion of chemotherapy.

Here, we report the case of an elderly patient with metastatic disease, treated by the association of Carboplatin and Gemcitabine chemotherapy. In the literature we found five case reports describing cardiac toxicities attributable to Carboplatin. In the case we presented the patient experienced heart failure after completing six cycles of chemotherapy. Given the rarity of cardiovascular toxicity associated with Carboplatin, the heart failure was unexpected. Indeed the patient had a normal cardiac test and had no symptoms. The fact that his mother was dead after a blood transfusion could suggest that he had a not diagnosed hereditary heart disease. Similar to our case, Yano and Shimada reported a case of angina in a patient five hours after receiving Carboplatin and Etoposide for a small cell lung cancer. The patient had no previous cardiovascular disease [2].

a multidisciplinary genito-urinary round, treatment with cerebral radiotherapy and Vinflunine chemotherapy were initiated. The patient completed his cerebral radiotherapy and received one cycle of Vinflunine. Fifteen days after the last cycle of chemotherapy the patient was hospitalized in oncology day unit for moderate hypercalcemia. The left ventricular test was at 55%. Rapidly, the patient developed severe dyspnea and died (Figure 1).

Figure 1: Bones and liver metastasis.