Tumor lysis syndrome associated with docetaxel and carboplatin in a case with recurrent endometrial cancer

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ABSTRACT

Tumor lysis syndrome (TLS) is an oncological life-threatening complication characterized by hyperuricemia, hyperphosphatemia, and hyperkalemia, which can lead to acute renal failure, cardiac arrhythmias, cardiac arrest and seizures. Although TLS is a rare complication in patients with non-hematological malignancy, the mortality rate of TLS in solid tumors is higher than that in hematological malignancies. Acute renal injury is the most common cause of mortality associated with TLS in solid tumors. We report a case of TLS following chemotherapy for a recurrent uterine serous carcinoma. In this case, we speculated that the cause of death might be a pul-

1. Introduction

Tumor lysis syndrome (TLS) is an oncological life-threatening complication resulting from lysis of tumor cells with the release of their intracellular components into the bloodstream. They sometimes occur spontaneously, but more often after chemotherapy (Cario and Bishop, 2004). TLS consists of hyperuricemia, hyperphosphatemia and hyperkalemia, and leads to acute renal injury, cardiac arrhythmias, cardiac arrest and seizures (Cario and Bishop, 2004). Although the association between hematological malignancies and TLS has been well described, it is uncommon for patients with solid tumors to have complicated TLS (Gemic, 2006). However, the mortality associated with TLS in patients with solid tumors is higher than that in patients with hematologic cancer. Acute renal injury is the most common cause of death of TLS in solid tumors (Gemic, 2006). We describe a patient who developed TLS following docetaxel and carboplatin for recurrent endometrial cancer.

2. Case report

A 63-year-old woman with a two-month history of right hip pain was referred to our hospital with suspected sacroiliitis. Eleven months before admission, she was diagnosed with a FIGO stage III C2 uterine serous carcinoma, which was treated using surgical treatment and six cycles of adjuvant carboplatin and paclitaxel therapy. The laboratory data on admission are summarized in Table 1. Computed tomography (CT) showed masses at the left lung base, at superior space of right kidney and on the right side of descending aorta (Fig. 1). Positron emission tomography (PET) showed high density in the thoracolumbar spines and pelvis (Fig. 2). Bone biopsy was performed; we discovered adenocarcinoma in histology. We diagnosed recurrent uterine cancer which had metastasized to bones and multi organs. The time between completion of chemotherapy and recurrence of tumor was five months.

We proposed chemotherapy or that she seek the best supportive care and she selected the former. Tri-weekly docetaxel (70 mg/m²) and carboplatin (AUC 5) was administrated as her previous regimen resulted in peripheral neuropathy. Nineteen hours after chemotherapy, she complained of chest pain and dyspnea. The transthoracic echocardiogram (TTE) showed a D-shaped left ventricle and inferior vena cava not collapsing with inspiration, suggesting right heart overload. Enhanced CT images also showed right heart strain with no evidence of a pulmonary embolism (PE, Fig. 3). There was an increase in increase of 0.76 mg/dL in the serum creatinine level compared to baseline. Arterial blood gas sampling revealed the result as follows: pH 7.26; PaCO₂ 24.6 mm Hg; PaO₂ 73.7 mm Hg; BE -14.5; HCO₃ 10.9 mEq/L. She presented with hypotension, tachycardia, tachypnea, and oliguria. Finally, we diagnosed her with TLS which led obstructive shock and acute renal injury. We also suspected a PE caused by undetectable micro clots or tumor fragments spreading into the bloodstream. She received intensive care including a massive infusion (200 ml/h), noninvasive positive pressure ventilation with 50% oxygen and administration of a
vasopressor. We gave her a calcium gluconate injection and glucose-insulin therapy for hyperkalemia. Sodium bicarbonate and heparin were administrated to improve metabolic acidosis and undetectable PE, respectively. Despite the correction of hyperkalemia and metabolic acidosis (pH 7.387 and K 4.96 mEq/L), her right heart failure and low cardiac index (1.7 L/min/m²) continued. We were not able to perform hemodialysis due to hypotension. Her condition deteriorated rapidly and she died 54 h after chemotherapy.

3. Discussion

TLS is infrequently encountered in the patients with solid tumors; we only found one reported case in a patient with endometrial cancer (Godoy et al., 2010). The woman with a history of FIGO stage 2B uterine cancer developed TLS after receiving paclitaxel and carboplatin for recurrent endometrial cancer with multiple mesenteric and peritoneal implants. Our case was similar in that there was recurrence with multiple metastasis and a regimen containing chemotherapeutic agents (platinum and taxane) was used. TLS associated with docetaxel has also been reported in only three cases: two patients with multiple metastatic prostate cancer (Bhardwaj and Varma, 2017; Sorscher, 2004) and a patient with non-small-cell lung cancer (Ajzensztejn et al., 2006).

Acute renal injury is the most common cause of mortality associated with TLS in solid tumors (Gemic, 2006). In our case, the patient presented with acute renal injury, however, we speculated that her cause of death might be obstructive shock caused by a pulmonary tumor embolism. We can consider the development of it by TLS in our patient for the following reasons. First, she presented with chest pain and dyspnea, and hypoxia. These symptoms were consistent with a PE, and were improved by administration of heparin. Second, enhanced CT images showed right heart overload and no evidence of clots in pulmonary arteries. Third, the patient had no pre-existing heart disease and the elevation of serum creatine phosphokinase (CPK) levels, which is marker for myocardial infarction (MI), was not suggestive of MI after several examinations following chemotherapy. Finally, the time to the development of TLS after chemotherapy was more rapid than that in previously reported cases of fatal acute renal injury. Collectively, we considered that fragments of tumor invaded the vessels, spread and then obstructed pulmonary arteries. However, we were not able to administer lung perfusion scintigraphy and PET, thus we had to conduct an autopsy to diagnose the pulmonary tumor embolism. Therefore, it remains a matter of speculation. If patients who received chemotherapy...
complained chest pain and dyspnea, we have to consider the possibility of a pulmonary tumor embolism and provide the patient with intensive care. We again realize that it is most important to assess the risk of TLS prior to chemotherapy, which should be administrated among the high risk patients appropriately for prevention.

Optimal management of TLS is prevention. Effective prevention of TLS involves monitoring fluid and electrolyte conditions, active hydration, and diuresis with administration of allopurinol or rasburicase before chemotherapy (Cario and Bishop, 2004; Cario et al., 2010; Coiffier et al., 2008; Howard et al., 2011). These preventive mechanisms can also prevent renal injury and metabolic derangements. In most cases of TLS, hemodialysis is necessary for treatment to improve renal injury and metabolic derangements (Cario et al., 2010). Risk factors for TLS have been well documented (Cario et al., 2010; Coiffier et al., 2008). In our institution, we check laboratory data a week prior to the administration of chemotherapy and allopurinol to the patients with azotemia. We provide chemotherapy in the hospital for patients with high risk of TLS, and we also provide aggressive hydration for such patients after chemotherapy.

Our management of high risk of TLS patients is similar to that for those with hematological malignancies (Cario and Bishop, 2004; Howard et al., 2011); it is not based on substantial evidence for solid tumors. Therefore, it remains unclear as to which subgroups of patients are at the highest risk of developing TLS and if allopurinol or rasburicase not only reduces uric acid levels but also reduces morbidity and mortality from TLS in solid tumors. Further guidance is necessary to standardize the definition of TLS and simply predict the risk of it for each type of cancer.

We report a case of TLS in the patient who received docetaxel and carboplatin for recurrent endometrial cancer. The cause of her death was speculated the development of a pulmonary tumor embolism. Despite the infrequency of its occurrence in gynecologic malignancy, clinicians need to assess the risk of TLS before chemotherapy which should be administrated among high risk patient appropriately due to its potential lethality.

Disclosure statement

The authors declare that they have no conflicts of interest to disclose.

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