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Tumor lysis syndrome in a patient with metastatic non-small cell lung cancer: Case report and literature review

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Abstract
Tumor lysis syndrome (TLS) is a potential complication in cancer therapy. It may occur in highly treatment sensitive tumors, especially in childhood cancers and hematologic malignancies, whereas it is rare in the treatment of adult solid tumors. We report a case of TLS during chemotherapy in a patient with metastatic non-small cell lung cancer (NSCLC, squamous cell carcinoma) and review the literature regarding the occurrence of TLS in patients with NSCLC. Reviewing the literature, a total of 120 patients with solid tumors who developed TLS have been reported. There are only 9 other reported cases of NSCLC complicated with TLS. TLS is a potentially fatal complication especially in solid tumors because of its poor clinical outcome.

1. Introduction

Tumor lysis syndrome (TLS) is an oncologic emergency characterized by severe metabolic derangements that occur when a large amount of malignant tumor cells breakdown rapidly and release their intracellular contents into the systemic circulation [1,2]. Laboratory tumor lysis syndrome is defined as metabolic abnormalities (hyperuricemia, hyperkalemia, hyperphosphatemia and hypocalcemia) with initiation of therapy [1]. Clinical tumor lysis syndrome is defined as laboratory tumor lysis syndrome accompanied by an increased creatinine level, seizures, cardiac dysrhythmia, or death [1]. Known risk factors for TLS are greater tumor mass and having highly effective anticancer therapy for a particular tumor [1].

TLS is at risk primarily in hematologic malignancies and rapidly growing solid tumor such as germ cell tumors or small cell carcinomas that are exposed to chemotherapy,

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radiation, corticosteroids, or may occur spontaneously. TLS is becoming more frequently reported in solid tumors [1-4]. To the best of our knowledge, the present study case is the 10th report describing TLS in non-small cell lung cancer (NSCLC).

2. Case report

A 68-year-old Caucasian male with multiple comorbidities including severe peripheral vascular disease (PVD), diabetes mellitus, and chronic obstructive pulmonary disease was incidentally found to have a tumor in the right lower lobe of the lung and multiple lesions within the liver on a routine CT scan of the abdomen performed prior to scheduled aorto-femoral bypass surgery at another hospital. The outside hospital work-up included an ultrasound-guided biopsy of a liver lesion reported as a low-grade neuroendocrine carcinoma. As a result, aorto-femoral bypass surgery was performed at the outside hospital given the patient's severe PVD. Postoperatively, the patient had respiratory failure and following a several month recovery, a PET/CT scan was performed and revealed uptake in a single lesion in the right lower lung without definite hilar or mediastinal adenopathy and two liver lesions. Biopsy of the lung lesion revealed poorly differentiated squamous cell carcinoma confirmed by immunohistochemical staining for p63 (Figure 1a and b). Staining for chromogranin and synaptophysin was negative making small cell neuroendocrine tumor unlikely.

Because of the patient's significant co-morbid conditions, he was initially treated with stereotactic body radiation therapy to the right lower lung lesion and yttrium-90 spheres to the liver. Due to progression of his liver metastases, a repeat treatment with yttrium-90 spheres was performed several months later. To our knowledge, there were no reported symptoms or biochemical disturbances consistent with TLS during the yttrium-sphere therapy. With continued progression of his liver disease, the patient then underwent chemoembolization to several of the hepatic lesions. However, during the ensuing months, follow-up CT scan revealed progressive hepatic metastases and the patient sought further therapy at our institution. Given his progressive liver disease, he underwent a repeat liver biopsy which revealed poorly differentiated squamous cell carcinoma. The pathology slides of the liver and lung lesions from the outside hospital were reviewed at our institution and were consistent with the diagnosis of poorly differentiated squamous cell carcinoma.

With the confirmation of progressive metastatic lung carcinoma, chemotherapy was discussed with the patient and intravenous cisplatin 75 mg/m^2 (158 mg total dose) and gemcitabine 1000 mg/m^2 (2110 mg total dose) was administered. On the day of treatment, laboratory results revealed normal electrolytes, calcium, and phosphorus. Abnormal laboratory results included a LDH 5164 IU/L, AST 158 IU/L, ALT 72 IU/L, alkaline phosphatase 198 IU/L, and total bilirubin 2.7 mg/dL. On day 7 following treatment, the patient was admitted to the intensive care unit with increasing shortness of breath, fatigue, confusion, and lower extremity edema. His medications on admission included aspirin, fluticasone-salmeterol, tiotropium inhaler, furosemide, glipizide, guaifenesin, metformin, naproxen, prednisone, ranitidine, and antiemetics as needed. On physical examination, he was tachycardic, tachypneic despite home oxygen therapy, and hypotensive. His laboratory results revealed a creatinine 3.2 mg/dL, potassium 6.7 mmol/L, bicarbonate 15 mmol/L, calcium 5.7 mg/dL, phosphorus 10.9 mg/dL, uric acid 20.9 mg/dL, lactic acid 2.8 mmol/L, and LDH 4512 U/L. An electrocardiogram demonstrated borderline QT prolongation. Blood cultures were obtained and revealed no growth.

The patient was initially maintained on non-invasive ventilation but ultimately required intubation for his hypoxic respiratory failure. He was treated with intravenous fluids, insulin, sodium polystyrene sulfonate, calcium gluconate, allopurinol, rasburicase, wide-spectrum antibiotics, and vasopressors. Despite aggressive medical management, he remained oligoanuric and subsequently required continuous renal replacement therapy. Given his poor prognosis, he was transitioned to comfort care within 30 hours of presentation and died shortly after.

3. Discussion

Tumor lysis syndrome is a life-threatening condition of multiple metabolic derangements that occur due to the rapid destruction of tumor cells with release of cellular breakdown products, most frequently following the treatment of various malignancies [1,2]. In 2012 and 2014, Vodopivec et al. and Mirrakhimov et al. reviewed the literature and reported 100 and 120 patients with solid tumors complicated with TLS [5,6] respectively. Since their

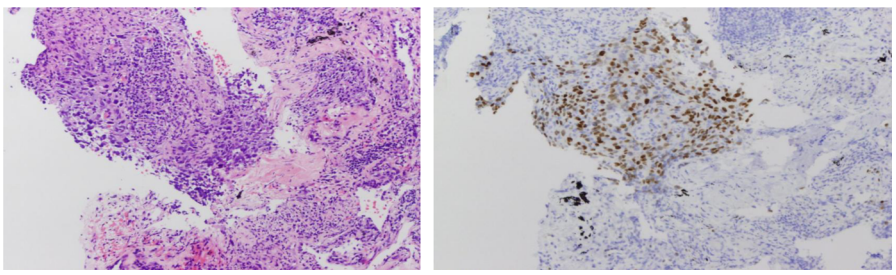

Figure 1 (a and b) The lung biopsy revealed infiltrative small clusters of tumor cells with hyperchromatic and pleomorphic nuclei (center of field and 10 o'clock). A small amount of uninvolved alveolar lung tissue was also sampled (lower right corner). The tumor cells expressed p63 by immunohistochemistry, supporting a diagnosis of squamous cell differentiation.