Tumor Lysis Syndrome in a Low-Risk Pancreatic Cancer Patient

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Tumor lysis · Risk stratification · Malignancy

Abstract
Tumor lysis syndrome (TLS) is the most common hematologic emergency encountered during the treatment of high-grade malignancies. While it can lead to death, the prognosis is typically excellent if caught early on in the course. Risk stratification prior to treatment initiation is paramount in deciding the utility of prophylaxis and ultimately in reducing morbidity and mortality. The following case describes the development of TLS in a patient categorized as low risk and highlights the need for further elucidation of a unified risk stratification system.

Introduction
Tumor lysis syndrome (TLS) is a hematologic emergency most commonly encountered during the treatment of high-grade hematologic malignancies [1]. It is rarely seen in cases of solid tumors; however, as therapies continue to become more effective and more targeted, its frequency in these cases has been increasing [2, 3]. The syndrome occurs following rapid lysis of tumor cells causing release of intracellular contents into the bloodstream and can be classified as either laboratory or clinical via the Cairo and Bishop classification system [4]. Laboratory TLS is defined as the development of 2 of the following 4 laboratory abnormalities, in the same 24-h period, within 3 days prior to starting treatment and within 7 days after initiation of chemotherapy: hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. Clinical TLS is defined as the presence of laboratory TLS plus acute kidney injury, cardiac arrhythmia, or symptomatic hypocalcemia (seizure and tetany). We present a rapidly fatal case of clinical TLS in a patient with stage IV pancreatic adenocarcinoma following palliative treatment with gemcitabine and nab-paclitaxel.

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Case Presentation

A 76-year-old female with a past medical history of stage III renal cell carcinoma status after right nephrectomy which did not require adjuvant treatment presented for follow-up to an outpatient clinic when she was found to have severe abdominal pain, tachycardia, and pallor. She had recently been diagnosed with pancreatic adenocarcinoma with metastatic disease to the liver complicated by splenic vein thrombosis. Upon admission to the hospital, she was found to have a leukocytosis count of 21,000 μL and was started on broad-spectrum antibiotics for concern of spontaneous bacterial peritonitis. Creatinine was found to be mildly elevated at 1.10 mg/dL, so she was started on maintenance fluids. Further laboratory tests were within normal limits. CT abdomen/pelvis was obtained which showed re-demonstration of the liver metastasis and peritoneal stranding, which was concerning for peritoneal carcinomatosis (Fig. 1). A family meeting was held, and the decision was made to move forward with palliative chemotherapy with gemcitabine and nab-paclitaxel.

Overnight following her first dose of chemotherapy, her potassium increased to 6.1 mmol/L, uric acid increased to 9.2 mg/dL, phosphorus increased to 6.2 mg/dL, and creatinine increased to 0.72 mmol/L, and creatinine increased to 2.27 mg/days (Table 1). A diagnosis of TLS was made, and the patient was given rasburicase and allopurinol for hyperuricemia, D50 and insulin for hyperkalemia, and nephrology was consulted for initiation of urgent hemodialysis. The electrolyte abnormalities resolved following hemodialysis, but the patient’s kidney function remained poor, reaching a maximum creatinine level of 3.28 mg/dL 2 days later. Calculated GFR had dropped over the course of the hospital stay from a baseline of 64 mL/min/1.73 m² to 13 mL/min/1.73 m². A family meeting was held, and the decision was made to place the patient on comfort care. She died 7 days following her chemotherapy. No follow-up imaging or CA 19-9 levels were obtained.

Discussion

TLS is the most common hematologic emergency consequence of chemotherapy, primarily seen in cases of hematologic malignancies treated with aggressive drug regimens. Patients with solid tumors have previously been found to only be at 1% risk of getting TLS [5]. Additionally,
there are specific risk factors which have been shown to correlate with TLS. These tumor risk factors include having high tumor proliferation rate, high sensitivity to chemotherapy, bulky disease >10 cm, and/or white blood cell count >50,000 and/or LDH >2 times the upper limit of normal [6]. Increased risk also depends on whether or not there is other organ or bone marrow infiltration. Other clinical indications are an elevated uric acid level or phosphate levels, any prior exposure to nephrotoxic drugs, acidic urine and/or oliguria, and lastly dehydration [7]. Additionally, those with underlying impaired renal function prior to starting chemotherapy have also been found to have an increased risk for developing TLS [7].

Based on the above information, prior to receiving chemotherapy treatment, our patient had minimal signs to suggest a possible increased risk for development of TLS. At the time of diagnosis, primary tumor size was noted to be 3.5 cm × 3.8 cm × 3.2 cm, located in the tail of the pancreas, which remained largely unchanged throughout the hospital course (3 weeks). Lab values were never suspicious for an elevated risk of TLS development. Known risk factors that were present in this patient were metastatic lesions, specifically involving the liver and the peritoneum, and impaired renal function due to history of renal cell carcinoma requiring a nephrectomy. At the time of treatment initiation, it was felt that the patient was at low risk for TLS.

**Conclusion**

While TLS can lead to death, the prognosis is typically excellent if caught early on in the course. This case demonstrates the need for high clinical suspicion when initiating any course of chemotherapy, even when the dosing is for palliation. It is particularly important to be acutely aware of electrolyte changes in the setting of bulky solid tumor such as pancreatic adenocarcinoma and other malignancies with a high burden of metastatic disease. Currently,
guidelines for TLS prophylaxis are lacking. Further work is necessary to elucidate a truly beneficial risk stratification system to identify patients that would benefit from prophylaxis. This case highlights the importance of considering TLS prophylaxis in a patient with a highly aggressive, fast-growing tumor and widespread metastatic disease.

**Statement of Ethics**

All research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The subject discussed in the above case report has given written informed consent to publish information regarding the case. All patient information has been de-identified.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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**Author Contributions**

Paul Travers made substantial contributions to the conception or design of the work as well as acquisition, analysis, and interpretation of the data; drafted the work and revised it critically for important intellectual content; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Alexandra Goodman drafted the work and revised it critically for important intellectual content and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Bernard Poiesz gave final approval of the version to be published.

**Data Availability Statement**

All data underlying the results are available as part of the article and no additional source data are required.

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