A Rare Case of Tumor Lysis Syndrome

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INTRODUCTION

Tumor lysis syndrome (TLS) is a metabolic disturbance caused by the destruction of rapidly dividing cancer cells following administration of cytotoxic chemotherapy. The subsequent release of intracellular material results in hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia.[1] The clinical presentation of TLS, including acute kidney injury, results from these electrolyte abnormalities and can be life-threatening.[2] Here we present the second reported case of TLS in a woman with endometrial cancer.

CASE PRESENTATION

A 63 year old woman with newly-diagnosed endometrial cancer (International Federation of Gynecology and Obstetrics, FIGO, stage IVB) who received her first dose of carboplatin and paclitaxel four days earlier presented to the emergency room with shortness of breath and lower extremity swelling. Her physical examination was significant for a heart rate of 132 beats per minute and a respiratory rate of 26 breaths per minute. She was noted to have a harsh systolic murmur loudest at the right second intercostal space and a mildly distended abdomen. Chest radiography was unremarkable. A ventilation perfusion scan was negative for pulmonary embolism. Her labs at time of admission (Table 1) were consistent with tumor lysis syndrome. Based on the Cairo-Bishop criteria (described below), the diagnosis of tumor lysis syndrome was made.

OUTCOME AND FOLLOWUP

The patient received vigorous intravenous hydration with normal saline solution and treatment with intravenous rasburicase. After two doses of rasburicase her labs began to normalize (Table 1), and her symptoms dissipated. On the day of discharge all lab abnormalities had resolved, and the patient was discharged in stable condition.

Table 1. Laboratory Values

Lab Parameter (normal range at TJU)	Pre- chemotherapy	Admission	2 days after rasburicase
Serum potassium (3.5-5.0 mmol/L)	4.4	5.5	4.5
BUN (7-27 mg/dL)	14	68	65
Serum creatinine (0.7-1.4 mg/dL)	0.8	2.4	1.9
Serum phosphate (2.4-4.5 mg/dL)	n/a*	6.1	4.3
Serum calcium (8.5-10.5 mg/dL)	n/a*	8.3	8.3
Serum Urate (2.5-6.0 mg/dL)	n/a*	15	5.1

*values were not measured

Table 2. Clinical Characteristics of Patients at High Risk for Tumor Lysis Syndrome
Tumors with a high proliferation rate and sensitivity to cytotoxic agents
Large tumor masses
Renal insufficiency and obstructive uropathy
Elevated serum lactate dehydrogenase or uric acid level
Dehydration

TABLE 3. Cairo-Bishop definition of laboratory tumor lysis syndrome in adults. Diagnosis requires two or more of the following abnormalities observed within three days before to seven days after initiation of chemotherapy:	
Uric acid	Greater than or equal to 8.00 mg/dL or 25% increase from baseline
Potassium	Greater than or equal to 6.00 mmol/L or 25% increase from baseline
Phosphorous	Greater than or equal to 4.5 mg/dL or 25% increase from baseline
Calcium	Less than or equal to 7.0 mg/dL or 25% decrease from baseline

Table 4. Cairo-Bishop definition of clinical tumor lysis syndrome in adults. Diagnosis requires meeting criteria of laboratory tumor lysis syndrome plus one or more of the following not directly or probably attributable to a therapeutic agent:	
1	Creatinine greater than 1.5 times upper limit of normal (our ULN = 1.4 mg/dL)
2	Cardiac arrhythmia/sudden death
3	Seizure

DISCUSSION

TLS is a rare but serious complication of cytotoxic chemotherapy. Malignancies with the highest risk of TLS are those with both high proliferative rates and tumor burden, particularly hematologic malignancies.[3] Solid tumors have a much lower incidence of TLS. A literature review found the highest incidence of TLS in small-cell carcinoma and breast carcinoma, with a few reported cases each in neuroblastoma, germ cell tumors, melanoma, and others.[4] While a few cases of TLS have been reported in association with gynecologic cancers,[5,6] there has been only one reported case associated with endometrial cancer. In this case from 2010, a 60 year old woman with recurrent FIGO stage IIB endometrial cancer developed TLS four days after receiving carboplatin and paclitaxel. The patient required hemodialysis and expired despite aggressive management.[7]

While TLS remains a rare complication of chemotherapy in patients with solid tumors, the clinical characteristics of patients at high risk for TLS should be recognized (Table 2).[8] In 2004, Cairo and Bishop proposed a system for diagnosing and classifying tumor lysis syndrome.

Table 3 describes the laboratory definition of TLS, and Table 4 describes the clinical definition of TLS. Acute kidney injury in TLS results from the release of nucleic acids from lysed tumor cells, which are degraded by xanthine oxidase to hypoxanthine, xanthine, and uric acid.[9] In the acidic environment that often occurs as a result of volume depletion, uric acid solubility decreases[10] and crystallization occurs in the distal tubules and collecting ducts. This crystallization obstructs the tubular lumen and leads to inflammation.[11] Uric acid may also contribute to acute kidney injury by crystal-independent mechanisms, due to its vasoconstrictive, anti-angiogenic, pro-inflammatory, and pro-oxidative properties.[12] The other features of clinical tumor lysis syndrome - tetany, cardiac arrhythmias, and seizures – also result from the metabolic derangements that occur when cancer cells are lysed by cytotoxic chemotherapy.[13] The patient described here did not exhibit these manifestations.

The treatment of tumor lysis syndrome is mainly supportive and includes cardiac and electrolyte monitoring, correction of electrolyte abnormalities, intravenous fluids (isotonic saline solution at 2500-3000 mL/m^2/24 hours), and renal replacement therapy if indicated.[14] Urinary alkalinization is controversial. The patient described here received four liters of normal saline and two doses of rasburicase. Rasburicase decreases uric acid levels by catalyzing the conversion of uric acid to allantoin, which is more soluble in urine.[15] This is in contrast to allopurinol, a prophylactic medication, which competitively blocks xanthine oxidase, preventing the conversion of purines to uric acid.[16,17] Once TLS is diagnosed, rasburicase is the appropriate therapy to eliminate the excess uric acid.[13]

KEY POINTS

Successful management and treatment of TLS is highly dependent on the prompt identification of clinical and laboratory characteristics, signs, and symptoms of patients at risk. The initiation of prophylactic measures, especially hydration and administration of allopurinol, and the early recognition and treatment of metabolic abnormalities using rasburicase can prevent the severe and life-threatening complications associated with TLS.

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