Acute spontaneous tumor lysis syndrome in a patient with squamous cell carcinoma of the lung

Sir,

A 74-year-old man presented to the emergency room after he had not urinated for over 24 h. He had noticed decreasing urine output over the last couple of days. A week prior, he was seen by his primary care physician for worsening cough and weight loss, and was diagnosed with stage IV squamous cell carcinoma of the lung. He was scheduled to start chemotherapy later in the week of his presentation. He had a history of chronic obstructive lung disease, coronary artery disease and hypertension. His medications were aspirin and metoprolol. He had a long history of tobacco use.

His vital signs on presentation were—temperature of 37.5°C (99.5°F), pulse of 102 beats/min, respiratory rate of 18/min and blood pressure of 166/74 mmHg. The physical examination was remarkable only for dehydration, lethargy and generalized weakness. Blood counts revealed leukocyte count of 12 300 cells/μl, hemoglobin of 9.6 g/dl and platelet count of 326 000 cells/μl. Chemistries were remarkable for hyperkalemia with a serum potassium of 5.2 mmol/l, a serum creatinine of 4.7 mg/dl (baseline—0.8 mg/dl), mild hyperphosphatemia with a serum phosphate of 4.7 mg/dl (normal 2.4–4.1 mg/dl), and significant hyperuricemia with a serum uric acid of 15.4 mg/dl (normal 2.1–8.5 mg/dl). A random ratio of urine uric acid to creatinine was 1.4.

A diagnosis of acute spontaneous tumor lysis syndrome with uric acid nephropathy was made. Given the anuria, he was urgently started on hemodialysis. He was also promptly initiated on vigorous hydration and allopurinol. The uric acid level normalized after one cycle of hemodialysis, the electrolyte imbalances were corrected by the next morning, and the renal dysfunction completely resolved over the next 3 days. Allopurinol was continued and he was started on chemotherapy a few days later.

Discussion

Acute tumor lysis syndrome is a catastrophic condition of multiple metabolic derangements that occur due to the rapid destruction of tumor cells with massive release of cellular breakdown products, typically seen following the treatment of malignancies. The syndrome is characterized by the rapid development of hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, metabolic acidosis and acute renal failure. The electrolyte imbalances can lead to serious and potentially fatal arrhythmias. The renal failure occurs due to uric acid precipitation within the tubules and calcium phosphate deposition in the renal parenchyma and vessels.

When the syndrome is seen prior to the institution of therapy, it is termed pretreatment or more commonly, spontaneous tumor lysis syndrome. The spontaneous form of the tumor lysis syndrome is less likely to involve hyperphosphatemia. It is possible that the phosphate released by the rapid nucleoprotein turnover in the spontaneous form is reused for synthesis of new tumor cells in contrast to the post-treatment form where there are no new tumor cells to reutilize the large amounts of released phosphate.

Acute spontaneous tumor lysis syndrome has been usually described in association with hematologic malignancies such as leukemia and lymphoma. Rare reports of acute spontaneous tumor lysis syndrome in solid tumor malignancies involved gastrointestinal adenocarcinoma, germ cell tumors, gastric carcinoma, inflammatory breast carcinoma, colon carcinoma, malignant pheochromocytoma, hepatocellular carcinoma, prostate cancer, and adenocarcinoma of the lung. To our knowledge, acute spontaneous tumor lysis syndrome has never been reported with squamous cell carcinoma of the lung.

Management after the onset of acute renal failure consists of attempting to wash out the obstructing uric acid crystals with a loop diuretic and vigorous fluids, and of late, rasburicase. Hemodialysis and/or continuous venovenous hemofiltration to remove...
the excess circulating uric acid should be considered in anuric patients and in those patients in whom a diuresis cannot be induced.1

Risk factors for the development of acute spontaneous tumor lysis syndrome in patients with solid tumor malignancies are noted in Table 1. Our patient had advanced bronchogenic carcinoma with a bulky and necrotic tumor (Figure 1), precipitating acute spontaneous tumor lysis syndrome with renal failure. We speculate that his use of aspirin might also have contributed to the uric acid nephropathy by inhibiting uric acid secretion.

This case illustrates the need to identify and risk-stratify all patients with solid tumor malignancies for their risk of developing acute spontaneous tumor lysis syndrome. Patients with any risk factors should be treated prophylactically, even prior to the initiation of chemotherapy. Those with low risk should be treated with allopurinol and hydration. For patients at high risk, such as those with multiple risk factors or hyperuricemia prior to the start of chemotherapy, rasburicase should be the treatment of choice.14

In conclusion, since early recognition and aggressive management can lead to complete recovery of renal function,4 acute spontaneous tumor lysis syndrome should be considered in the differential diagnosis of patients with any malignancy and acute renal dysfunction. Equally critical is the recognition of patients at risk and the effective use of prophylactic therapy to prevent this catastrophic syndrome.

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References

Table 1  Risk factors for development of acute spontaneous tumor lysis syndrome in patients with non-hematologic solid tumor malignancies

<table>
<thead>
<tr>
<th>Risk Factor</th>
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<tbody>
<tr>
<td>Large tumor burden (bulky tumor mass or disseminated disease) with necrosis</td>
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<td>Rapidly proliferating tumor</td>
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<td>Extensive bone marrow involvement</td>
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<td>Hepatic metastasis</td>
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<td>Elevated white cell count (&gt;50 K/µl; e.g. as a leukemoid reaction)</td>
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<td>Elevated lactate dehydrogenase level (&gt;1000 IU/l)</td>
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<tr>
<td>Elevated uric acid level</td>
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<td>Impaired renal function</td>
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<td>Use of potentially nephrotoxic drugs such as contrast media, non-steroidal anti-inflammatory drugs, antibiotics, and drugs which inhibit uric acid excretion (aspirin, thiazides, probenecid)</td>
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<tr>
<td>Extrinsic compression of the urinary tract by the tumor</td>
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<tr>
<td>Underlying problems such as dehydration, infection or urinary obstruction</td>
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Figure 1. Chest CT showing a large tumor with extensive necrosis.


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