

# Spontaneous Tumor Lysis Syndrome in a Critically Ill Patient With Cytology Favoring Small Cell Carcinoma: A Case Report

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## Abstract

Tumor lysis syndrome (TLS) is a life-threatening metabolic emergency most commonly associated with hematologic malignancies and is rarely reported in solid tumors. We describe spontaneous TLS in a woman in her late 70s with chronic kidney disease, diabetes mellitus, and atrial fibrillation who presented with vasopressor-dependent shock and was found to have a large necrotic mediastinal mass with mediastinal lymphadenopathy and bilateral pulmonary nodules. Endobronchial ultrasound-guided transbronchial needle aspiration of mediastinal lymph nodes demonstrated malignancy favoring small cell carcinoma. She had received no anticancer therapy. Available pre-bronchoscopy laboratory measurements included potassium 4.5 mEq/L, phosphorus 3.0 mg/dL, uric acid 4.0 mg/dL, and calcium 8.8 mg/dL, without the characteristic biochemical pattern of TLS. Subsequently, she developed progressive hyperkalemia, hyperphosphatemia, modest hypocalcemia, severe metabolic acidosis, oliguria progressing to anuria, and worsening renal failure. Uric acid increased to a documented peak of 12 mg/dL, and lactate dehydrogenase reached 3,608 U/L. Rasburicase was administered, and continuous renal replacement therapy was initiated; however, the patient developed refractory shock and progressive multiorgan failure and died. This case highlights spontaneous tumor lysis syndrome (STLS) as a rare but potentially fatal complication of a bulky thoracic malignancy with cytology favoring small cell carcinoma, particularly in the setting of markedly impaired renal reserve. Bronchoscopy serves as a temporal landmark in the biochemical evolution of TLS, but a causal relationship cannot be established, and pre-existing shock, acute kidney injury, and possible sepsis were important concurrent contributors.

**Categories:** Oncology, Pulmonology, Internal Medicine

**Keywords:** acute kidney injury, bronchoscopy, critical care, small cell lung cancer, spontaneous tumor lysis syndrome, tumor lysis syndrome

## Introduction

Tumor lysis syndrome (TLS) is a life-threatening oncologic emergency caused by rapid destruction of malignant cells and the release of intracellular contents into the circulation. The resulting hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia can lead to acute kidney injury, cardiac arrhythmias, seizures, and multiorgan failure [1-3]. TLS is classically associated with rapidly proliferating hematologic malignancies, particularly acute leukemias and high-grade lymphomas, and most commonly occurs after the initiation of cytotoxic therapy [4,5].

TLS has also been reported in solid tumors, including breast, colorectal, hepatocellular, and lung malignancies [6,7]. Spontaneous tumor lysis syndrome (STLS), in which TLS develops without preceding anticancer therapy, is considerably less common [8]. High tumor burden, rapid tumor turnover, and impaired renal function may increase the risk and clinical severity of tumor lysis [1-3,6,7]. Recognition of STLS can be particularly challenging in critically ill patients because shock, acute kidney injury, and infection may independently produce metabolic abnormalities that overlap with those of TLS.

Small cell lung cancer (SCLC) has a distinct clinical course and epidemiology [9] and is characterized by rapid proliferation and early dissemination [10]. These features may predispose patients with substantial disease burden to tumor lysis. Jallad et al. [11] described spontaneous TLS in SCLC and reviewed previously reported cases of TLS associated with this malignancy, most of which occurred after cytotoxic therapy. TLS associated with SCLC was reported as early as 1983 following induction chemotherapy [12]. Although uncommon, these reports demonstrate that tumor lysis can occur in association with SCLC even before anticancer treatment is initiated.

We report a case of STLS in a woman in her late 70s with a large necrotic mediastinal malignancy, lymph

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node cytology favoring small cell carcinoma, a solitary functioning kidney, and underlying chronic kidney disease (CKD). She had received no anticancer therapy and was already critically ill with shock, acute kidney injury, and metabolic acidosis before the biochemical evolution of TLS became apparent. Pre-bronchoscopy laboratory testing did not demonstrate the characteristic biochemical pattern of TLS; subsequent testing showed hyperkalemia, hyperphosphatemia, hyperuricemia, modest hypocalcemia, and progressive renal failure. Bronchoscopy serves as a temporal landmark in the documented laboratory sequence rather than an established precipitant. This case highlights the importance of considering STLS in critically ill patients with substantial tumor burden and limited renal reserve, particularly when shock, infection, and acute kidney injury may coexist and complicate interpretation of the metabolic abnormalities.

## Case Presentation

A woman in her late 70s with a medical history of atrial fibrillation treated with apixaban, type 2 diabetes mellitus, stage 3b CKD, hypertension, hyperlipidemia, coronary artery disease, aortic stenosis, hypothyroidism, and renal cell carcinoma treated with right radical nephrectomy presented to a referring emergency department after the sudden onset of dizziness, a spinning sensation, severe nausea, and epigastric pain. She became lightheaded and experienced a near-syncope episode with a fall onto her buttocks without loss of consciousness. She reported neck pain but denied dyspnea, fever, or urinary symptoms. She was a former smoker with an approximately 15-pack-year smoking history.

Her baseline renal function before the acute illness included a blood urea nitrogen (BUN) level of 28 mg/dL, serum creatinine of 1.7 mg/dL, and estimated glomerular filtration rate (eGFR) of 30 mL/min/1.73 m<sup>2</sup>. At presentation, the white blood cell count was  $17.6 \times 10^9/L$ , BUN was 28 mg/dL, serum creatinine was 2.4 mg/dL, and eGFR was 20 mL/min/1.73 m<sup>2</sup>, consistent with acute kidney injury superimposed on CKD. Potassium was 4.0 mEq/L, phosphorus 4.9 mg/dL, and calcium 10.2 mg/dL. N-terminal pro-B-type natriuretic peptide was 2,268 pg/mL, alkaline phosphatase was greater than 1,000 U/L, and high-sensitivity troponin was within the reference range.

Computed tomography (CT) of the head and cervical spine showed no acute traumatic abnormality, and CT angiography of the head and neck demonstrated no acute vascular lesion. Initial CT angiography of the thorax demonstrated a 9.1 × 7.0 cm heterogeneous necrotic posterior mediastinal mass causing substantial mass effect on adjacent cardiomeastinal structures, including the posterior wall of the heart and left lower lobe bronchovascular structures, with possible invasion of the left atrium. The mass obstructed the left lower lobe bronchus and was associated with post-obstructive pulmonary changes and pulmonary venous congestion. Mediastinal lymphadenopathy and bilateral pulmonary nodules were also present (Figure 1).

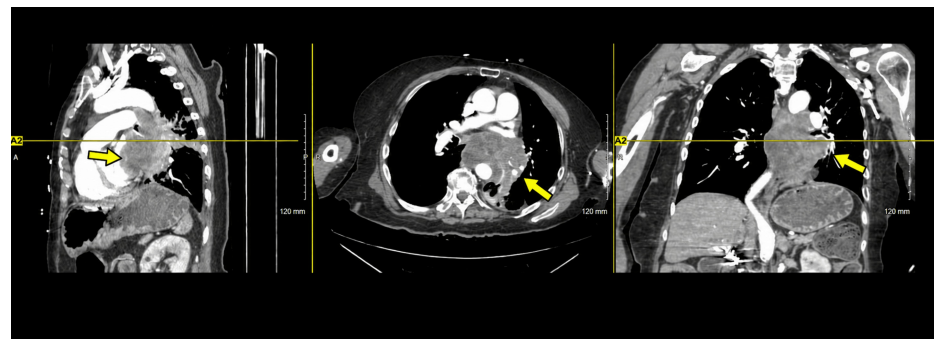


**FIGURE 1: Initial contrast-enhanced computed tomography angiography of the thorax obtained at presentation, demonstrating a large heterogeneous necrotic posterior mediastinal mass (arrows) with mass effect on adjacent cardiomeastinal structures.**

CT angiography of the abdomen and pelvis showed postoperative changes from right nephrectomy without evidence of local recurrence, no hepatic metastatic disease, and descending and sigmoid colonic wall thickening concerning for infectious or inflammatory colitis. Although initially hemodynamically stable, the patient subsequently developed profound hypotension. She received approximately 1.5 L of intravenous crystalloid with an incomplete response, followed by a push dose of epinephrine and initiation of norepinephrine. Persistent shock required concurrent norepinephrine and vasopressin support before bronchoscopy. The clinical differential included septic shock in the setting of post-obstructive pneumonia and possible colitis. Lactate reached 6.1 mmol/L and procalcitonin was 47.85 ng/mL. Broad-spectrum antimicrobial therapy was initiated. Blood, respiratory, and urine cultures remained negative at 48 hours; however, negative cultures alone could not exclude infection.

Transthoracic echocardiography demonstrated hyperdynamic left ventricular systolic function with an

ejection fraction greater than 65%, mild diastolic dysfunction, normal right ventricular systolic function, and no pericardial effusion. Progressive encephalopathy and inability to protect the airway prompted endotracheal intubation and mechanical ventilation on day 2. Thus, substantial critical illness, including vasopressor-dependent shock, acute kidney injury, and metabolic derangement, clearly preceded bronchoscopy.

The extensive mediastinal disease raised concern for a primary pulmonary malignancy, lymphoma, or recurrent metastatic renal cell carcinoma. Cardiothoracic surgery evaluated the patient and determined that surgical intervention was not appropriate because of the extensive invasive mediastinal process with associated hilar and pulmonary lesions. Bronchoscopy with endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was therefore recommended to establish a diagnosis.

Bronchoscopy was performed on day 3. Exact clock times for several laboratory measurements relative to the procedure were unavailable; therefore, laboratory values are presented according to their documented clinical sequence. Available laboratory measurements obtained before bronchoscopy included potassium of 4.5 mEq/L, phosphorus of 3.0 mg/dL, uric acid of 4.0 mg/dL, and calcium of 8.8 mg/dL. Exact collection times for these measurements relative to bronchoscopy were unavailable. BUN was 45 mg/dL, serum creatinine was 2.6 mg/dL, and eGFR was 18 mL/min/1.73 m<sup>2</sup>. Serum carbon dioxide was 16 mEq/L, the anion gap was 19 mEq/L, and lactate was 2.9 mmol/L. Arterial blood gas analysis demonstrated a pH of 7.30, a partial pressure of carbon dioxide of 33 mmHg, and bicarbonate of 16 mEq/L. Thus, renal dysfunction and metabolic acidosis were already present before bronchoscopy, but the available pre-procedure laboratory data did not demonstrate the characteristic combination of metabolic abnormalities associated with TLS. The oncology team did not consider the patient to be experiencing TLS at that time, and prophylactic urate-lowering therapy was not initiated.

Bronchoscopy lasted approximately 35 minutes. A large exophytic and infiltrative obstructing lesion was visualized at the orifice of the left mainstem bronchus. The lesion could be traversed proximally but completely obstructed the left lower lobe bronchus. EBUS-TBNA was performed using a 21-gauge needle at lymph node stations 4R, 7, and 10L, with five passes obtained from each station. Importantly, the large necrotic mediastinal mass itself was not directly sampled. No immediate procedural complication was documented.

Final cytologic examination, reported after the patient's death, demonstrated malignancy favoring small cell carcinoma in specimens obtained from lymph node stations 4R, 7, and 10L and in the corresponding cell blocks. No separate histologic biopsy or immunohistochemical characterization was available in the records reviewed. Accordingly, the malignancy was considered cytologically consistent with, but not definitively histologically confirmed as, small cell carcinoma. Representative histologic or immunohistochemical images were therefore not available for inclusion.

Subsequent laboratory testing demonstrated marked metabolic deterioration. Potassium increased to 6.2 mEq/L and phosphorus to 7.1 mg/dL, while calcium decreased modestly to 7.7 mg/dL. BUN increased to 54 mg/dL, serum creatinine to 2.9 mg/dL, and eGFR declined to 16 mL/min/1.73 m<sup>2</sup>. Serum carbon dioxide was 15 mEq/L. Arterial blood gas analysis demonstrated severe acidemia with a pH of 7.10, bicarbonate of 9 mEq/L, and partial pressure of carbon dioxide of 48 mmHg. Urine output, which had been approximately 300 mL during the preceding 12 hours, decreased markedly, and the patient progressed to anuric acute kidney injury.

A subsequent uric acid measurement increased from the closest available pre-bronchoscopy value of 4.0 mg/dL to 12.0 mg/dL. No intermediate uric acid measurement was available, and therefore the precise trajectory of the uric acid increase could not be determined. Rasburicase 3 mg was administered intravenously, and continuous renal replacement therapy (CRRT) was initiated.

With continued deterioration, potassium reached 6.4 mEq/L, phosphorus 9.0 mg/dL, calcium 7.6 mg/dL, BUN 59 mg/dL, and serum creatinine 3.4 mg/dL. Serum carbon dioxide fell below 10 mEq/L, the anion gap exceeded 26 mEq/L, lactate increased to 5.8 mmol/L, and lactate dehydrogenase (LDH) reached 3,608 U/L. A subsequent uric acid measurement was 11.0 mg/dL. The serial biochemical and renal findings are summarized in Table 1.

| Parameter                                      | Historical baseline | Initial presentation | Early ICU course | Available pre-bronchoscopy values | Subsequent deterioration | Late deterioration |
|------------------------------------------------|---------------------|----------------------|------------------|-----------------------------------|--------------------------|--------------------|
| Potassium (mEq/L)                              | 3.8                 | 4.0                  | 4.0              | 4.5                               | 6.2                      | 6.4                |
| Phosphorus (mg/dL)                             | 3.5                 | 4.9                  | 4.5              | 3.0                               | 7.1                      | 9.0                |
| Uric acid (mg/dL)                              | -                   | -                    | -                | 4.0                               | -*                       | 12.0 <sup>†</sup>  |
| Calcium (mg/dL)                                | 9.5                 | 10.2                 | 9.6              | 8.8                               | 7.7                      | 7.6                |
| BUN (mg/dL)                                    | 28                  | 28                   | 36               | 45                                | 54                       | 59                 |
| Creatinine (mg/dL)                             | 1.7                 | 2.4                  | 2.4              | 2.6                               | 2.9                      | 3.4                |
| eGFR (mL/min/1.73 m <sup>2</sup> )             | 30                  | 20                   | 20               | 18                                | 16                       | -                  |
| Serum CO <sub>2</sub> (mEq/L)                  | -                   | -                    | 18               | 16                                | 15                       | <10                |
| Anion gap (mEq/L)                              | -                   | 14                   | -                | 19                                | 17                       | >26                |
| Lactate (mmol/L)                               | -                   | -                    | 6.1              | 2.9                               | -                        | 5.8                |
| Arterial pH                                    | -                   | -                    | -                | 7.3                               | 7.1                      | -                  |
| Arterial HCO <sub>3</sub> <sup>-</sup> (mEq/L) | -                   | -                    | -                | 16                                | 9                        | -                  |
| Arterial pCO <sub>2</sub> (mmHg)               | -                   | -                    | -                | 33                                | 48                       | -                  |
| LDH (U/L)                                      | -                   | -                    | -                | -                                 | -                        | 3,608              |
| Hemoglobin (g/dL)                              | 12                  | 13.1                 | 12.2             | -                                 | 10.3                     | 6.8                |
| AST (U/L)                                      | 28                  | 40                   | -                | -                                 | 628                      | 2,648              |
| ALT (U/L)                                      | 35                  | 28                   | -                | -                                 | 595                      | 1,674              |

**TABLE 1: Serial biochemical, renal, hepatic, and hematologic findings during the clinical course**

\*No intermediate uric acid measurement was available between the pre-bronchoscopy value of 4.0 mg/dL and the subsequently documented peak.

<sup>†</sup>The peak documented uric acid concentration was 12.0 mg/dL before rasburicase administration; the exact collection time relative to bronchoscopy was unavailable. A subsequent uric acid measurement was 11.0 mg/dL.

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CO<sub>2</sub>, carbon dioxide; eGFR, estimated glomerular filtration rate; HCO<sub>3</sub><sup>-</sup>, bicarbonate; ICU, intensive care unit; LDH, lactate dehydrogenase; pCO<sub>2</sub>, partial pressure of carbon dioxide.

Compared with the closest available pre-bronchoscopy measurements, potassium increased by 37.8%, phosphorus by 136.7%, and uric acid by 200%, whereas calcium decreased by 13.6%. These changes occurred in the setting of progressive anuric renal failure and no preceding anticancer therapy.

The patient's hemodynamic status deteriorated concurrently, ultimately requiring norepinephrine, vasopressin, epinephrine, and phenylephrine. During this period, hemoglobin decreased from 10.3 g/dL to 6.8 g/dL, prompting packed red blood cell transfusion and investigation for hemorrhage. Apixaban had been held, and intravenous heparin was also held during portions of the hospitalization because of markedly prolonged activated partial thromboplastin time. CT angiography of the thorax obtained during the evaluation for possible bleeding did not identify an active thoracic hemorrhagic source. The cause of the acute hemoglobin decline could not be definitively established.

Abdominal distention also developed during worsening shock and acidosis. Bladder pressure was 16 mmHg, raising concern that intra-abdominal hypertension might be contributing to impaired renal and systemic perfusion. General surgery evaluated the patient. The abdomen remained soft with minimal distention, limited imaging showed no evidence of pneumoperitoneum, and further abdominal imaging was deferred because of profound hemodynamic instability. A specific contribution of intra-abdominal pressure to the renal or hemodynamic deterioration could not be established.

Aspartate aminotransferase and alanine aminotransferase increased progressively during the period of worsening shock and ultimately reached 2,648 U/L and 1,674 U/L, respectively. Initial abdominal imaging had demonstrated no hepatic metastatic disease. The marked aminotransferase elevation occurred in parallel with escalating vasopressor requirements and multiorgan hypoperfusion and was considered compatible with hypoperfusion-related hepatic injury, although medication-related and other potential contributors could not be excluded.

A follow-up contrast-enhanced CT angiogram of the thorax obtained during the deterioration on day 3 demonstrated interval enlargement of the necrotic mediastinal mass and mediastinal/hilar lymphadenopathy, worsening left lower lobe post-obstructive atelectasis, increasing pleural effusions, and new bilateral pulmonary abnormalities (Figure 2).

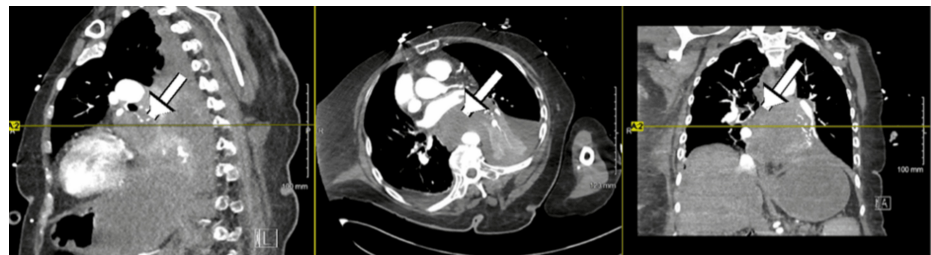


**FIGURE 2: Follow-up contrast-enhanced computed tomography angiography of the thorax obtained after bronchoscopy, demonstrating interval enlargement of the necrotic mediastinal mass and associated mediastinal/hilar lymphadenopathy (arrows), with worsening left lower lobe post-obstructive atelectasis and bilateral pulmonary abnormalities.**

The combination of progressive hyperkalemia, marked hyperphosphatemia, a threefold increase in uric acid, modest hypocalcemia, markedly elevated LDH, and worsening anuric renal failure in the absence of preceding anticancer therapy was considered consistent with STLS. However, the patient's metabolic deterioration occurred in the context of profound critical illness. Septic shock remained an important competing and potentially contributing process because of the radiographic post-obstructive pneumonia, possible colitis, markedly elevated procalcitonin, and vasopressor-dependent shock. The absence of growth from blood, respiratory, and urine cultures at 48 hours did not exclude infection.

Despite rasburicase, CRRT, broad-spectrum antimicrobial therapy, mechanical ventilation, blood transfusion, albumin administration, and escalating support with four vasopressors, the patient developed refractory shock and progressive multiorgan failure. Following discussion with the family regarding her poor prognosis and lack of response to maximal supportive therapy, goals of care were transitioned to comfort-focused treatment. Mechanical ventilation was withdrawn, and the patient died on day 4. No anticancer therapy was administered.

## Discussion

### Diagnostic framework and biochemical evolution

The Cairo-Bishop classification remains the most widely used framework for describing TLS [13]. Laboratory TLS is defined by the development of at least two qualifying abnormalities involving uric acid, potassium, phosphorus, or calcium, whereas clinical TLS incorporates laboratory TLS together with clinically significant complications such as acute kidney injury, cardiac arrhythmia, or seizures [13,14]. Although these criteria were developed primarily in the setting of anticancer therapy, they are frequently used as a descriptive framework for STLS [15]. Prompt recognition and management are essential because TLS can progress rapidly to severe electrolyte abnormalities, acute kidney injury, and multiorgan dysfunction [16].

Application of these biochemical thresholds to the available laboratory sequence supports the diagnosis of TLS in this case. Compared with the available pre-bronchoscopy measurements, potassium increased from 4.5 to 6.2 mEq/L, representing a 37.8% increase; phosphorus increased from 3.0 to 7.1 mg/dL, a 136.7%

increase; and uric acid increased from 4.0 to a documented peak of 12.0 mg/dL, a 200% increase. Each of these abnormalities exceeded both a 25% change and the corresponding adult absolute threshold used in the Cairo-Bishop classification. Calcium decreased from 8.8 to a nadir of 7.6 mg/dL, a 13.6% reduction, and therefore did not independently satisfy the calcium criterion. Thus, at least three biochemical criteria were met.

Interpretation of these findings requires consideration of the patient's pre-existing renal and hemodynamic abnormalities. Acute kidney injury and metabolic acidosis were already present before the biochemical evolution of TLS, and subsequent anuria could itself exacerbate hyperkalemia and hyperphosphatemia by impairing renal clearance. The marked increase in uric acid from 4.0 to 12.0 mg/dL provides additional evidence of tumor lysis that is not explained as readily by the electrolyte consequences of renal failure alone. However, no intermediate uric acid measurement was available, so the precise timing and rate of the urate increase cannot be established. LDH subsequently reached 3,608 U/L. Although elevated LDH is recognized as a marker of high tumor burden and increased TLS risk [17], it is nonspecific and may also have reflected systemic tissue injury in the setting of profound shock.

The patient ultimately developed progressive anuric renal failure requiring CRRT. Nevertheless, attribution of the renal failure exclusively to TLS would be inappropriate because she already had CKD, a solitary functioning kidney, acute kidney injury, and vasopressor-dependent shock. The available data therefore support STLS as an important component of a complex and multifactorial critical illness rather than as the sole cause of organ failure.

#### *Critical Illness, Shock, and Limited Renal Reserve*

A central feature of this case is that substantial critical illness clearly preceded bronchoscopy and the subsequently recognized biochemical evolution of TLS. The patient developed profound hypotension despite intravenous fluid resuscitation and required concurrent norepinephrine and vasopressin support before bronchoscopy. She also had acute kidney injury, metabolic acidosis, post-obstructive pneumonia, possible colitis, an elevated lactate, and markedly elevated procalcitonin. These findings establish that severe systemic illness was already present before the later metabolic deterioration.

Several mechanisms could have contributed simultaneously to the development and severity of tumor lysis. The patient had a large, extensively necrotic mediastinal malignancy, suggesting substantial tumor burden and ongoing cellular turnover. Severe shock may have further compromised tumor perfusion and promoted ischemic necrosis, while acute kidney injury and markedly limited renal reserve reduced the capacity to excrete potassium, phosphate, and uric acid. She had undergone prior right radical nephrectomy and had underlying CKD, with a baseline creatinine of 1.7 mg/dL and eGFR of 30 mL/min/1.73 m<sup>2</sup> that had worsened before bronchoscopy. Renal dysfunction is a recognized risk factor for clinically significant TLS because reduced clearance can magnify the metabolic consequences of tumor breakdown [14,17].

Sepsis remained an important competing and potentially contributing process. Imaging demonstrated post-obstructive pulmonary disease and possible colitis, and the patient had vasopressor-dependent shock with substantial inflammatory abnormalities. Blood, respiratory, and urine cultures remained negative at 48 hours, but negative cultures do not exclude infection. Conversely, sepsis and renal failure alone do not fully account for the marked rise in uric acid occurring together with hyperphosphatemia, hyperkalemia, modest hypocalcemia, and markedly elevated LDH. The clinical deterioration is therefore best interpreted as multifactorial, with STLS occurring in the setting of severe critical illness rather than as an isolated process.

The patient's subsequent course further reflected systemic hypoperfusion and multiorgan dysfunction. Aspartate aminotransferase and alanine aminotransferase ultimately increased to 2,648 U/L and 1,674 U/L, respectively, during escalating vasopressor requirements, a pattern compatible with hypoperfusion-related hepatic injury, although additional contributors could not be excluded. Hemoglobin also declined substantially, prompting transfusion and investigation for hemorrhage; thoracic CT angiography did not identify an active thoracic bleeding source. These findings reinforce the severity and multifactorial nature of the underlying critical illness.

#### *STLS in a Malignancy Favoring Small Cell Carcinoma*

SCLC is characterized by rapid proliferation and early dissemination [9,10], biological properties that may increase susceptibility to tumor lysis in patients with substantial disease burden. TLS associated with SCLC was reported after induction chemotherapy as early as 1983 [12]. Jallad et al. [11] subsequently described spontaneous TLS in SCLC and reviewed 11 previously reported cases, most of which occurred following cytotoxic therapy. These observations demonstrate that spontaneous tumor lysis can occur in association with SCLC even in the absence of anticancer treatment.

The malignancy in the present case, however, must remain appropriately qualified. EBUS-TBNA specimens from lymph node stations 4R, 7, and 10L, including corresponding cell blocks, were positive for malignancy favoring small cell carcinoma. A separate histologic biopsy and immunohistochemical characterization were

not available. Consequently, this case cannot be regarded as definitively histologically confirmed SCLC, particularly given the patient's prior history of renal cell carcinoma and the broader differential diagnosis considered before cytologic evaluation.

Irrespective of the precise tumor subtype, several disease-related features favored susceptibility to tumor lysis. Initial imaging demonstrated a  $9.1 \times 7.0$  cm heterogeneous necrotic mediastinal mass with extensive mediastinal and hilar disease and bilateral pulmonary nodules. Massive liver metastases are recognized as another disease-related risk factor for TLS [17], but hepatic metastatic disease was not identified in this patient. Her combination of bulky necrotic malignancy and severely impaired renal reserve may therefore have been particularly important in determining the clinical consequences of tumor breakdown.

#### *Bronchoscopy as a Temporal Landmark*

Bronchoscopy is best regarded in this case as a temporal landmark rather than an established precipitant of TLS. The procedure was performed to obtain diagnostic material after the patient had already developed vasopressor-dependent shock, acute kidney injury, and metabolic acidosis. EBUS-TBNA sampled lymph nodes at stations 4R, 7, and 10L; the large necrotic mediastinal mass itself was not directly sampled, and no immediate procedural complication was documented.

Procedures that intentionally produce substantial tumor necrosis, such as transcatheter embolization of solid tumors, have been associated with TLS [18]. Diagnostic EBUS-TBNA is fundamentally different because it involves limited tissue sampling rather than intentional destruction of a large tumor burden. In this patient, the presence of extensive spontaneous tumor necrosis, profound shock, and impaired renal clearance provides a more biologically plausible setting for STLS than the limited needle aspiration of remote lymph nodes.

The available laboratory sequence remains clinically informative because the characteristic TLS metabolic pattern was not evident in the available pre-bronchoscopy studies and became apparent later in the clinical course. However, exact clock times for several laboratory measurements relative to bronchoscopy were unavailable, and no intermediate uric acid measurement was obtained between 4.0 and 12.0 mg/dL. Accordingly, the data establish temporal sequence but do not support a causal relationship between bronchoscopy and tumor lysis. The procedure should therefore not be interpreted as the trigger for STLS.

#### *Risk Assessment, Prophylaxis, and Clinical Implications*

Preventive strategies for patients considered at increased risk for TLS include adequate hydration, close biochemical monitoring, and urate-lowering therapy with agents such as allopurinol or rasburicase according to the estimated level of risk [14,16,17]. Risk-stratification approaches, however, are best established for hematologic malignancies and patients about to receive highly effective anticancer therapy. The optimal approach for untreated solid tumors presenting with spontaneous critical illness is less clearly defined.

Before bronchoscopy, the oncology team did not consider the patient to be experiencing TLS, and the available uric acid, potassium, phosphorus, and calcium measurements did not demonstrate the characteristic biochemical pattern of TLS. Prophylactic urate-lowering therapy was therefore not initiated. Once the metabolic pattern evolved, rasburicase was administered, and CRRT was initiated. This case does not establish that prophylactic rasburicase or allopurinol should routinely be administered before diagnostic bronchoscopy or other minimally invasive procedures. Rather, it highlights the importance of maintaining awareness of STLS in critically ill patients with bulky, rapidly proliferating or necrotic malignancies, particularly when renal reserve is markedly impaired.

The clinical significance of STLS in solid tumors is substantial despite its rarity. A scoping review of spontaneous TLS in adult solid tumors reported acute kidney injury in 83.1% of cases, renal replacement therapy in 37.3%, STLS-related mortality in 55.4%, and all-cause mortality in 80.0% [19]. Reliable estimates of population prevalence and hospital length of stay remain limited because the available literature consists predominantly of case reports and small observational series.

Severe TLS is associated with substantial morbidity and mortality, and acute renal injury has been associated with adverse outcomes [11,20]. In this patient, progressive anuric renal failure, refractory shock, severe metabolic acidosis, and multiorgan dysfunction developed despite rasburicase, CRRT, antimicrobial therapy, mechanical ventilation, transfusion, and escalating vasopressor support. STLS should therefore be considered when otherwise unexplained hyperuricemia, hyperphosphatemia, and hyperkalemia develop in a patient with substantial tumor burden, even when competing explanations such as septic shock and acute kidney injury are present.

## **Limitations**

Several limitations should be acknowledged. First, the malignancy was not definitively characterized by

histology and immunohistochemistry. Cytologic specimens from multiple mediastinal lymph node stations and corresponding cell blocks were positive for malignancy favoring small cell carcinoma, but definitive histopathologic confirmation was unavailable.

Second, the exact clock times of several laboratory measurements relative to bronchoscopy were unavailable, and no uric acid value was obtained between the available pre-bronchoscopy concentration of 4.0 mg/dL and the subsequent peak of 12.0 mg/dL. The precise onset and rate of biochemical tumor lysis therefore cannot be reconstructed.

Third, the patient's critical illness substantially complicates causal attribution. Vasopressor-dependent shock, pre-existing CKD, acute kidney injury, post-obstructive pneumonia, possible colitis, and severe systemic hypoperfusion were already present or evolved during the same hospitalization. Hyperkalemia and hyperphosphatemia may have been amplified by anuric renal failure, and septic shock could not be excluded despite negative blood, respiratory, and urine cultures at 48 hours. STLS should therefore be viewed as an important component of a multifactorial deterioration rather than the sole cause of multiorgan failure.

Finally, this single case cannot establish a causal relationship between bronchoscopy and tumor lysis. The procedure sampled lymph nodes rather than the necrotic primary mass, while extensive tumor necrosis and severe hemodynamic compromise were already present. The bronchoscopy therefore provides a useful temporal landmark in the documented laboratory sequence but should not be interpreted as an established precipitating event.

Taken together, the marked evolution of uric acid, phosphorus, and potassium, the substantial necrotic tumor burden, absence of preceding anticancer therapy, and progressive anuric renal failure support STLS as an important component of this patient's deterioration. The case also illustrates the diagnostic difficulty of recognizing STLS when severe shock and acute kidney injury coexist and independently contribute to the same metabolic abnormalities. In such patients, careful interpretation of serial biochemical trends and early consideration of tumor lysis may facilitate timely recognition and management.

## Conclusions

STLS is a rare but potentially fatal complication that can occur in association with aggressive solid malignancies before the initiation of anticancer therapy. In this case, a bulky necrotic mediastinal malignancy with lymph node cytology favoring small cell carcinoma, markedly limited renal reserve, and severe critical illness was followed by progressive hyperuricemia, hyperphosphatemia, hyperkalemia, modest hypocalcemia, worsening renal failure, and multiorgan dysfunction. The characteristic biochemical pattern of TLS was not evident in the available pre-bronchoscopy laboratory data but became apparent later in the clinical course. Although bronchoscopy provides a useful temporal landmark, causation cannot be established, and shock, acute kidney injury, and possible sepsis were important concurrent contributors to the patient's deterioration. STLS should therefore be considered in critically ill patients with substantial tumor burden and impaired renal reserve when characteristic metabolic abnormalities develop before anticancer therapy. Serial monitoring of uric acid, potassium, phosphorus, calcium, and renal function may facilitate earlier recognition and prompt management.

## Additional Information

### Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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