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Spontaneous Tumor Lysis Syndrome Secondary to Iatrogenic Acute Kidney Injury: A Case Report

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Abstract

Spontaneous Tumor Lysis Syndrome (STLS) is a rare oncologic condition caused by the breakdown of neoplastic tissue in the absence of traditional anti-tumor therapy. It is postulated that cancers with rapidly dividing cells lead to increased cell turnover which exceeds the kidneys' ability to adequately filtrate by-products of cellular breakdown (*i.e.*, phosphate, potassium, anduric acid), leading to end organ damage. It has been reported in the past that kidney failure is a sequelae of Tumor Lysis Syndrome (TLS), but there have been no reports that demonstrate acute kidney injury (AKI) preceding TLS. The case presented here demonstrates TLS in a patient with no formal cancer diagnosis, who had received no chemotherapy or radiation that was precipitated by an iatrogenic AKI with chlorthalidone and ibuprofen. This unusual pattern of AKI preceding STLS may provide insight into the pathophysiology of the condition and could possibly lead to greater understanding of this phenomenon.

Keywords

Spontaneous Tumor Lysis, Acute Kidney Injury, Lymphoma, Chlorthalidone, NSAID

1. Introduction

Tumor Lysis Syndrome (TLS) is an oncologic emergency related to massive neoplastic breakdown. It is typically related to hematologic malignancies, though it has been noted in solid tumors such as melanoma, neuroblastoma, small cell

lung cancer as well as others [1]. TLS occurs when tumor cells release their intracellular contents into the bloodstream following the initiation of chemotherapy, radiation, or from medications (e.g., steroids, hormonal therapies). This results in characteristic findings of hyperuricemia, hyperkalemia, hyperphosphatemia, hypocalcemia, and metabolic acidosis. Without intervention this cascade can lead to multiorgan failure including renal insufficiency, cardiac arrhythmias, and/or seizures. Due to the life-threatening nature of this illness, rapid identification is critical [2].

TLS may occur unrelated to the initiation of cancer-specific therapy. These rare cases of TLS are referred to as "spontaneous." The precise pathophysiology leading to the onset of STLS is not definitively known, although it is postulated that cancers with rapidly dividing cells lead to increased cell turnover which exceeds the kidneys' ability to adequately filtrate by-products of cellular breakdown (*i.e.* phosphate, potassium, and uric acid), thus leading to end organ damage [3]. While acute renal failure typically follows the onset of TLS, the case presented with the patient's consent in this report follows a timeline that supports acute renal failure as the catalyst for STLS—an exceedingly rare phenomenon that is not well-documented.

2. Case Presentation

A 42-year-old man with type two diabetes mellitus, hyperlipidemia, hypertension, thyroid nodule, morbid obesity (*i.e.*, body mass index [BMI] of 71.9), and anxiety presented to the emergency department with four days of worsening leg pain associated numbness and tingling. His home medications included bupropion XL 300 daily, chlorthalidone 25 mg daily, metformin 1000 mg BID, omeprazole 40 mg daily, and trazodone 50 mg daily. He had back pain and spasms that started approximately one month before presentation, and he had been prescribed cyclobenzaprine as an outpatient without much improvement. The week prior to presentation he had increased his chlorthalidone to 50 mg daily and was taking 800 mg of ibuprofen three times daily.

At the time of admission, the patient had serum creatine elevated enough to warrant an admission for Acute Kidney Injury (AKI) (see **Figure 1**). Additionally, he met Systemic Inflammatory Response Syndrome (SIRS) criteria although there was no obvious source of infection. The patient was placed on intravenous (IV) antibiotics with ampicillin-sulbactam. Two months prior to the patient's admission to the hospital he had an annual exam which showed a 54 pound weight loss over the year prior. Two weeks following this exam he presented at the emergency department for abdominal pain. At that time, a computerized tomography (CT) scan of his chest, abdomen, and pelvis showed retroperitoneal and bilateral inguinal lymphadenopathy (see **Figure 2**). During this interval he also had an ultrasound of the scrotum, and the reading physician noted "abnormal appearance of the testicles, right greater than left, which may represent edematous changes, however an infiltrative lymphomatous process cannot be entirely excluded."

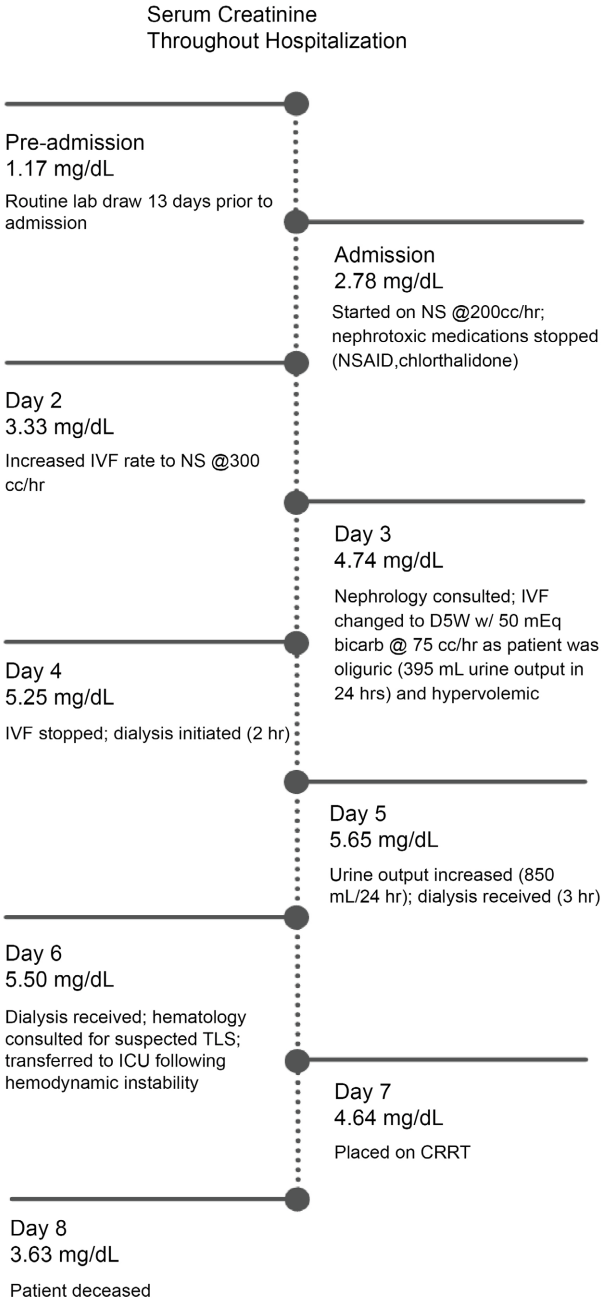

Figure 1. Serum creatine trend with interventions throughout admission.

Repeat labs on his second day of admission were remarkable for an increase in creatinine and an elevation in white blood cell count. IV hydration was increased and antibiotics were broadened to cefepime and daptomycin. His creatinine and white blood count continued to increase accompanied by decrease in urinary output over the following hours, and it was at this time that nephrology was consulted. As he was clinically hypervolemic and oliguric, IV fluid was transitioned from 300 cc/hr NS to D5W w/50 mEq bicarb at 75 cc/hr. Over the following 48 hours, he continued to be oliguric with still rising creatinine and

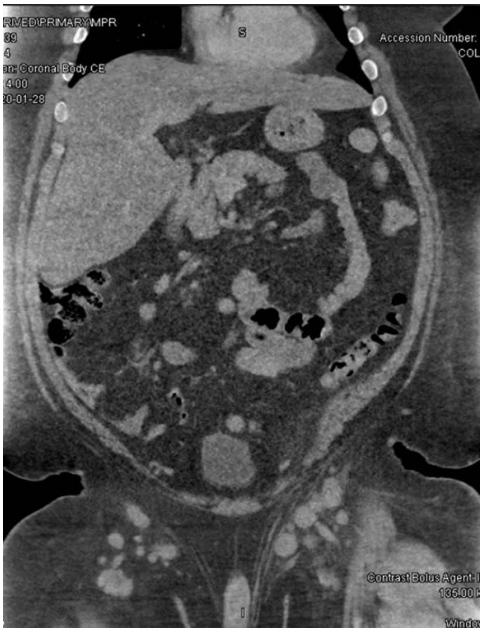

Figure 2. CT scan showing marked retroperitoneal and bilateral inguinal lymphadenopathy.

WBC. On day 4 of admission, hemodialysis was initiated.

Table 1 displays the lab values from the patient's sixth day of hospitalization. Based on these lab values in addition to lymphadenopathy on previous CT scans, STLS was considered. Hematology/oncology concurred with the concern for lymphoma given the above labs as well as his leukocytosis with neutrophil and monocyte predominance. Ultimately, interventional radiology (IR) was consulted for biopsy as the patient was deemed a poor surgical candidate for surgical excision of a lymph node. He underwent IR-guided lymph node biopsy following dialysis. After the procedure, he became persistently hypotensive despite fluid resuscitation and was intubated and transferred to the MICU where he was started on Levophed and continuous renal replacement therapy. A CT scan was performed and read with diffuse adenopathy within the chest, abdomen and pelvis. In the setting of his outstanding inguinal lymph node biopsy results, the radiologist noted "findings concerning for lymphoma in the appropriate clinical setting."

Over the next 24 hours, the patient's condition continued to deteriorate and increasingly required vasopressor support. Given his likely diagnosis of TLS and declining condition, his wife and family decided to make the patient DNR/DNI and transition to comfort measures. He passed away several hours later. An autopsy was performed, which showed widespread anaplastic large cell lymphoma. Both nodal (mesenteric, para-aortic, inguinal, para-esophageal and mediastinal) and extranodal (bilateral psoas muscles, urinary bladder, peritoneum, and pleural) involvement were present. The final pathology report was as follows:

"Based on the information that is available to us at this time and the autopsy findings, Mr. *** died as a result of widespread anaplastic large cell lymphoma

Table 1. Laboratory values consistent with TLS.

Test/Marker	Patient Value	Normal Reference Range
WBC	23.8 × 10^3/uL	3.7 - 11.0 × 10^3/uL
HGB	11.3 g/dL	11.5 - 16.0 g/dL
HCT	34.6%	34.8% - 48.0%
PLT CT	87 × 10^3/uL	150 - 400 × 10^3/uL
Na	126 mmol/L	135 - 145 mmol/L
K	5.9 mmol/L	3.5 - 5.0 mmol/L
Cl	94 mmol/L	98 - 111 mmol/L
Carbon Dioxide	16 mmol/L	21 - 35 mmol/L
BUN	108 mg/dL	10 - 25 mg/dL
Creatnine	5.68 mg/dL	0.60 - 1.05 mg/dL
GLUCOSE	125 mg/dL	70 - 110 mg/dL
ANION GAP	16 mmol/L	4 - 13 mmol/L
Ca	7.8 mg/dL	8.8 - 10.3 mg/dL
Mg	2.5 mg/dL	1.6 - 2.6 mg/dL
Phos	10.4 mg/dL	20 - 130 mg/dL
URIC ACID	12.8 mg/dL	4.0 - 8.5 mg/dL

with probable spontaneous tumor lysis syndrome, causing SIRS and multiorgan failure. Anaplastic large cell lymphoma, while uncommon, characteristically occurs in young adults, with a slight male predominance. Extranodal involvement to include the skin, soft tissue, and lungs is common. The tumor, as in this case, is composed of large lymphocytes with markedly irregular, eccentric nuclei and prominent nuclear grooves. Mr. *** already had widespread disease at the time of presentation. His condition rapidly deteriorated because of the large tumor burden resulting in superimposed systemic inflammatory response syndrome." [4] [5].

3. Discussion and Conclusions

TLS is most widely defined using the criteria from Cairo *et al.* in 2004 which uses clinical features or laboratory work up. Lab work requirements include elevation of uric acid, phosphorus, or potassium by 25% or decrease of calcium by 25%. There must be two or more of these findings three days prior to or within seven days after chemotherapy with adequate hydration and use of a uric acid lowering agent. Additionally, clinical diagnosis is defined as one of the lab defining factors with one or more of the following: Creatinine ≥ 1.5× ULN, cardiac arrhythmia/sudden death, or seizure [6].

The patient's clinical scenario is consistent with both clinical and laboratory definitions of TLS. With his profound weight loss in the year prior to hospitalization, underlying malignancy had likely been present during this time. What

truly makes this case unique is the timing of the patient's tumor lysis in regard to his renal failure. He presented with acutely worsened renal function attributed to him taking Ibuprofen and doubling his chlorthalidone dosage for the four days prior to admission. It is postulated that his renal injury was the catalyst to worsened inability to clear intracellular by-products (*i.e.* phosphorus, potassium, and uric acid). On admission, his creatinine had increased to 2.78 mg/dL from 1.2 mg/dL two weeks prior to admission. At that time his potassium and calcium levels were not abnormal enough to fit the lab work definition for TLS. Phosphorus was not tested until day two of admission, which was found to be elevated at that time. As TLS was not on the initial differential, uric acid was not tested until several days into the admission.

Cumulatively, this argues for the idea that the AKI preceded the spontaneous tumor lysis syndrome. While tumor lysis syndrome remains a serious oncologic issue, this timing of AKI preceding tumor lysis is something that should be considered by medicine teams and nephrologists as they take care of patients with known or suspected underlying malignancies with renal failure refractory to traditional management. This case may help to shed light on the still unknown pathophysiology of TLS, and may support the suggestion of Schiff in a recent paper to use predictive factors such as type and burden of malignancy, anticipated response to cytoreductive therapy, kidney disease, and pretreatment uric acid and lactate dehydrogenase prior to initiating antineoplastic therapy [7].

Tumor Lysis Syndrome is an oncologic emergency most often seen after the initiation of cancer-specific therapy. We document a case of Spontaneous Tumor Lysis Syndrome, which we believe was secondary to acute renal failure rather than causative of it.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Dar, L., Gendelman, O. and Amital, H. (2014) Tumor Lysis Syndrome Presenting in a Patient with Metastatic Melanoma Treated with Radiation Therapy. *Israel Medical Association Journal*, **16**, 456-457. https://www.ima.org.il/FilesUploadPublic/IMAJ/0/87/43917.pdf

[2] Mirrakhimov, A.E., *et al.* (2015) Tumor Lysis Syndrome: A Clinical Review. *World Journal of Critical Care Medicine*, **4**, 130-138. https://doi.org/10.5492/wjccm.v4.i2.130

[3] Roque, W., Rehman, A., Suero-Abreu, G.A., Danek, B.A., Colao, J., Fayngersh, A., Srinivas, S., Kra, J., Cai, D. and Chang, V.Y. (2019) Spontaneous Tumor Lysis Syndrome in T-Cell Malignancy: Two Case Reports. *Stem Cell Investigation*, **6**, 24. https://doi.org/10.21037/sci.2019.07.01

[4] Gangireddy, M., *et al.* (2019) Spontaneous Tumor Lysis Syndrome in Diffuse Large B-Cell Lymphoma: Early Diagnosis and Management. *Cureus*, **11**, e4679.

[5] Hsu, H.H. and Huang, C.C. (2004) Acute Spontaneous Tumor Lysis in Anaplastic

Large T-Cell Lymphoma Presenting with Hyperuricemic Acute Renal Failure. *International Journal of Hematology*, **79**, 48-51. https://doi.org/10.1007/BF02983533

[6] Cair, M.S. and Bishop, M. (2004) Tumor Lysis Syndrome: New Therapeutic Strategies and Classification. *British Journal of Hematology*, **127**, 3-11. https://doi.org/10.1111/j.1365-2141.2004.05094.x

[7] Joshua, P. and Schiff, M.M. (2022) Tumor Lysis Syndrome in a Patient with Metastatic Endometrial Cancer Treated with Lattice Stereotactic Body Radiation Therapy. *Advances in Radiation Oncology*, **7**, Article ID: 100797. https://doi.org/10.1016/j.adro.2021.100797