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Case Report

Spontaneous Tumor Lysis Syndrome in a Patient with Bulky Chronic Lymphocytic Leukemia Diagnosed after Resolution of Symptoms

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Keywords
Chronic lymphocytic leukemia · Spontaneous tumor lysis syndrome · Acute kidney injury · Electrolyte abnormalities · Large tumor burden

Abstract
Tumor lysis syndrome (TLS) is an oncologic emergency characterized by the destruction of tumor cells leading to an influx of large amounts of uric acid, potassium, and phosphorus into systemic circulation. It most often occurs after the initiation of cytotoxic therapy in high-grade lymphomas and leukemias; however, rarely it may occur spontaneously. The authors report a case of spontaneous tumor lysis causing electrolyte abnormalities and acute kidney injury in a patient with subsequently diagnosed large chronic lymphocytic leukemia tumor burden. Spontaneous TLS can be the first presentation of underlying malignancy; therefore, physicians should be aware of the associated findings.

Introduction

Spontaneous tumor lysis syndrome (STLS), defined as cell lysis in the absence of treatment, is often seen in solid malignancies, acute lymphocytic leukemia, and diffuse large B-cell lymphomas, but it rarely presents with chronic lymphocytic leukemia (CLL) [1]. CLL, the most common leukemia in the western hemisphere, is defined as a mature B-cell hematologic neoplasm characterized by monoclonal B lymphocytes [2]. Tumor lysis syndrome (TLS) occurs after the initiation of chemotherapy and has been seen more often in CLL due

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to the emergence of targeted anticancer drugs, such as venetoclax [3]. Metabolic disturbances occur due to lysis of tumor cells leading to the release of intracellular contents resulting in hyperphosphatemia, hyperkalemia, hyperuricemia, and hypocalcemia. These electrolyte disturbances can lead to sequelae such as acute renal failure, seizures, and fatal arrhythmias. Here, we report a rare case of a 72-year-old man who developed STLS on the second day of admission that required intermittent hemodialysis and was diagnosed with CLL after STLS resolution.

Case Report/Case Presentation

A 72-year-old man presented to the hospital with complaints of weakness, shortness of breath, vomiting, and diarrhea for 3 days. He did not have any significant past medical history, did not take any medications, and had not seen a physician in over 20 years. He was not vaccinated for COVID-19 and said that he had close contact with a family member who was diagnosed as COVID-19 positive. A COVID-19 polymerase chain reaction was ordered, which came back positive. The laboratories were drawn at admission and included a complete blood count and a complete metabolic panel (Table 1). Laboratory analysis revealed leukocytosis with an elevated lymphocyte count which was attributed to COVID-19 but was otherwise unremarkable. Physical examination revealed superficial lymphadenopathy but was otherwise within normal limits. The patient was admitted to observation status and was treated supportively without the usage of steroids for COVID-19 as he was saturating at 95% on room air.

The following day, the patient's condition deteriorated, he was in distress, dyspneic, anxious, and oliguric. Laboratory findings were abnormal as well, demonstrating hyperkalemia, hyperuricemia, hypocalcemia, and elevated creatinine (Table 1). Given that the patient had findings of lymphadenopathy, coupled with laboratory abnormalities, suspicion was high for the possibility of TLS. He was transferred to the intensive care unit and was started on aggressive IV fluids, furosemide, sodium bicarbonate for urinary alkalinization, and rasburicase. Hematology-oncology was consulted and recommendations were given. He met the criteria for both laboratory and clinical TLS according to the Cairo and Bishop classification system. Continuous cardiac monitoring and frequent measurements of electrolytes, creatinine, and uric acid every 6 h were ordered as well. Hyperkalemia was treated with patiromer and hypocalcemia was replaced with calcium gluconate. Our patient did not develop hyperphosphatemia. Due to a lack of improvement in his kidney

Table 1. The laboratory values that were seen on admission, day 1, day 2, day 3, at discharge, and on 30-day follow-up

Laboratory variable	On admission	Day 1	Day 2	Day 3	At discharge	After 30 days	Reference range
WBC, $\times 10^3/\mu L$	27	184	135	92	48	11	4.5–11.5
Uric acid, mg/dL	–	48.2	26.4	24.4	6.9	5.9	2.6–6.0
Potassium, mg/dL	4.1	6.5	5.9	5.3	4.2	4.4	3.5–5.1
Calcium, mg/dL	9.7	6.7	7.8	8.0	8.9	9.5	8.5–10.5
Phosphorus, mg/dL	2.8	3.5	3.3	3.2	3.1	2.9	2.5–5.0
Creatinine, mg/dL	0.86	8.7	7.98	5.26	0.92	0.81	0.51–0.95
BUN, mg/dL	10	102	89	32	27	19	8.5–21.5
LDH, U/L	–	1,022	876	563	485	505	230–480

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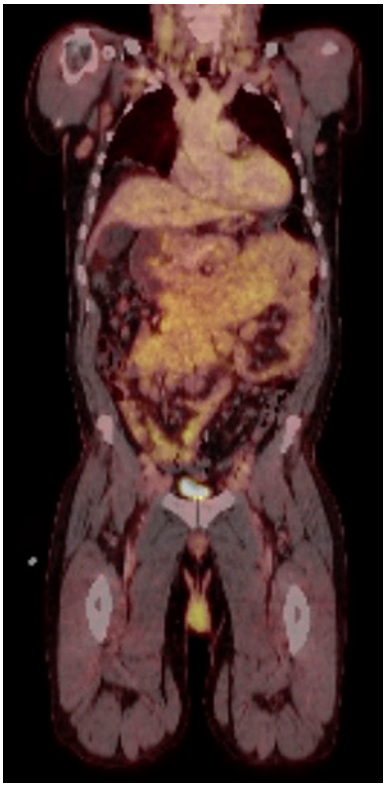

Fig. 1. PET-CT showing bulky lymphadenopathy with the largest lymph node conglomerate being 8.4 × 15.6 × 16 cm. PET-CT, positron emission tomography-computed tomography.

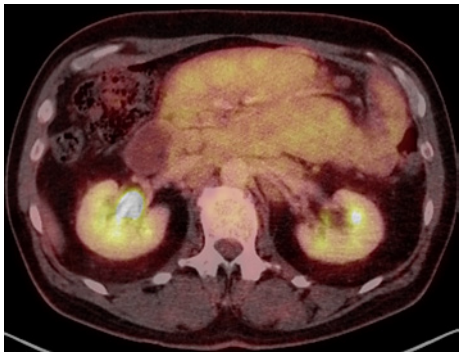

Fig. 2. PET-CT showing bulky lymphadenopathy with the largest lymph node conglomerate being 8.4 × 15.6 × 16 cm. PET-CT, positron emission tomography-computed tomography.

function and persistent low urine output for 24 h, he was started on intermittent hemodialysis.

After adequate treatment and 4 sessions of hemodialysis, urine output increased, creatinine steadily improved from 8.7 mg/dL to 1.4 mg/dL, and all other laboratory abnormalities were corrected within the next 6 days. Given the patient's abnormal laboratory investigations and lymphadenopathy, suspicion for malignancy was high, thus a positron emission tomography-computed tomography was ordered. The finding showed extensive cervical, thoracic, and intra-abdominal adenopathy compatible with possible lymphoma, with predominant activity equal to or below the liver (Deauville score 4). The largest nodal conglomerate measured 8.4 × 15.6 × 16 cm and showed a max standardized intake activity of 3.1 [shown in Fig. 1, 2]. There was no splenic or extranodal involvement. A biopsy of a peripheral lymph node revealed chronic lymphoid leukemia. The gross specimen showed atypical lymph nodes that were positive for

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PAX-5 and CD5, but negative for Cyclin D-1 and CD-3 stained a few lymphocytes. Ki-67 showed an increase in mitotic activity of 18%. Flow cytometry analysis of peripheral blood demonstrated a monoclonal B-cell population with an expression of CD19, CD22, CD23, CD5, lambda light chain, and diminished CD20. His CLL was characterized as Rai stage 1, Binet stage 2, immunoglobulin heavy chain mutation was present, and fluorescence in situ hybridization showed a normal karyotype. The findings of this case were consistent with CLL causing STLS. He was referred for outpatient follow-up with hematology-oncology who started treatment with ibrutinib.

Discussion/Conclusion

TLS is associated with hematological malignancies such as aggressive non-Hodgkin lymphoma and acute lymphoblastic leukemia after initiation of chemotherapy. Spontaneous tumor lysis occurs without an inciting event; however, it can occur in tumor types that have a high proliferative rate, large tumor burden, or in tumors with a high sensitivity to cytotoxic therapy [4]. In chronic hematologic malignancies such as CLL, TLS is rarely observed due to a slow rate of proliferation and response to chemotherapy [5]. In the case presented, we believe that STLS occurred due to the large tumor burden present as the lymph node conglomerate was 8.4 × 15.6 × 16 cm. TLS due to CLL is rare, it has been observed after treatment with either venetoclax, obinutuzumab, alvocidib, fludarabine, ibrutinib, rituximab, or steroids; however, STLS due to CLL is extremely rare as there are fewer than 5 cases currently reported in the literature [6].

STLS is an infrequent occurrence; however, it is often more severe compared to TLS due to lack of pretreatment with agents such as allopurinol and rasburicase [7]. Tumor cell lysis leads to the release of large amounts of potassium, phosphate, and uric acid into the systemic circulation which can cause acute kidney injury. However, STLS studies have shown that hyperphosphatemia and hypocalcemia do not occur as often as in TLS, which may lead to an underestimation of the incidence of the syndrome [8]. As in our case, large amounts of uric acid led to derangements in the patient's renal function causing him to develop an acute kidney injury which resolved with intermittent hemodialysis. Hyperkalemia may lead to cardiac arrhythmias and therefore close cardiac monitoring with telemetry is needed as well as laboratory analysis of the patient's electrolytes, creatinine, and uric acid every 6 h [9]. Treatment consists of intensive supportive care, binding agents such as patiromer, rasburicase, uric acid crystal removal with aggressive IV hydration combined with a loop diuretic, and renal replacement therapy if indicated [4]. If left untreated, death can occur from fatal arrhythmias, seizures, and severe acute renal failure.

Conclusion

STLS should be high on a differential diagnosis, even in malignancies it is not commonly associated with, such as CLL. It should be suspected if a patient's clinical condition points to a picture of acute kidney injury with electrolyte abnormalities, and a possibility of an undiagnosed malignancy. In our case, the patient presented with symptoms of COVID-19 infection; however on the second day, he developed electrolyte abnormalities highlighting the fact that STLS can occur at any time. We cannot conclude whether coinfection with COVID-19 precipitated STLS, but as the virus is known to cause a variety of conditions, it may be a possibility. The authors believe physicians' knowledge about the presentation, early diagnosis, and prompt treatment of STLS is of utmost importance as it is an oncological emergency.

Statement of Ethics

Ethical approval was not required to write this case report as the patient was not identified. This decision was made by the Ball Memorial Hospital Ethical Review Committee. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Sasmith R. Menakuru saw the case and wrote the paper, Adelina Priscu helped write and edit the paper. Ibrahim Khan helped write the paper. Amir Beirat helped write the paper.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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