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Case Report

A Case of Acute Lymphoblastic Leukemia with Spontaneous Tumor Lysis Syndrome after Adenosine Injection

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Abstract

Tumor lysis syndrome (TLS) is a life-threatening oncological emergency that usually occurs after cytotoxic therapy in patients with a large tumor burden, for example, patients with high-grade lymphoma or acute lymphoblastic leukemia (ALL). We report a case of a patient with ALL who spontaneously developed TLS without having undergone cytotoxic therapy. The mechanisms of spontaneous TLS are unclear, and the relationship between adenosine and cell growth/cell death is controversial. Several literature reviews have revealed that adenosine plays a role in the survival signal pathway. Although rare, our case is an example of a patient developing spontaneous TLS after adenosine treatment.

Keywords: Acute lymphoblastic leukemia, oncologic emergencies, tumor lysis syndrome

Introduction

Acute lymphoblastic leukemia (ALL) is a hematologic malignancy, and patients with genetic abnormalities generally have poor outcomes.[1] Tumor lysis syndrome (TLS) is a life-threatening oncological emergency caused by severe electrolyte imbalance with hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia.[2] TLS usually occurs after cytotoxic therapy in patients with a large tumor burden, such as in those with high-grade lymphoma and ALL.[3] The prevention and treatment of TLS are contingent on patient-risk factors, and clinical practitioners must be able to identify the clinical presentations and diagnose TLS. We report a case of a patient with ALL who spontaneously developed TLS after adenosine treatment without cytotoxic therapy.

Case Report

A 20-year-old male with ALL presented to the emergency department (ED) with epigastralgia in November 2016.

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In the ED, his initial vital signs were as follows: blood pressure 122/95 mmHg, heart rate 128 beats/minute (bpm), respiratory rate 20 cycles/minute, and body temperature 36.9°C. A laboratory test revealed leukocytosis with blastocystosis (white blood cell [WBC] count: 226,000/μL and blast: 80%), anemia (hemoglobin: 7.7 g/dL and mean corpuscular volume: 92.8%), and thrombocytopenia (platelet count: 40,000/μL). The serum creatinine (SCr) content was 1.02 mg/dL on arrival to the ED. However, a sudden onset of tachycardia of 170–180 bpm with a regular narrow QRS complex was noted, and 12 and 6 mg doses of adenosine were administered in the ED for suspected paroxysmal supraventricular tachycardia. After his condition stabilized, he was admitted for further management.

Decreased urine output with a deterioration in renal function (SCr: from 1.02 to 4.97 mg/dL), hyperuricemia (uric acid: from 3.5 to 29.4 mg/dL), hyperphosphatemia (P: 8 mg/dL), and hypocalcemia (ion Ca^{++}: from 4.7 to 3 mg/dL) were noted 2 days after the administration of adenosine. Decreases in WBC count and blast (WBC: from 226,000/μL to 11,710/μL; blast: from 86% to 8%) were also noted. Spontaneous TLS with severe hyperuricemia, hypocalcemia, hyperphosphatemia, and acute kidney injury combined with metabolic acidosis was diagnosed. Urgent hemodialysis was arranged to treat renal failure with oliguria secondary to uric acid nephropathy. After hemodialysis, his renal function improved (SCr: from 4.97 to 1.84 mg/dL), and serum uric acid and calcium levels returned to normal range; however, leukocytosis (WBC: 238,860/uL) and blastocystosis (blast: 76.5%) were noted. Figure 1 displays the laboratory test results and medication yields.

Conclusion

TLS with end-organ damage affects approximately 5% of patients with hematologic malignancies and up to 25% of high-risk patients, such as those with ALL or Burkitt's lymphoma.[4] TLS often occurs within 7 days of cytotoxic treatment, and patients with chronic kidney disease are at increased risk.[5] Spontaneous TLS involves cell lysis with excessive nucleic acids in patients who have not undergone cytotoxic therapy. This uncommon complication has been described in only a few case reports. In this study, we present the case of a patient who spontaneously developed TLS after adenosine treatment without cytotoxic therapy.

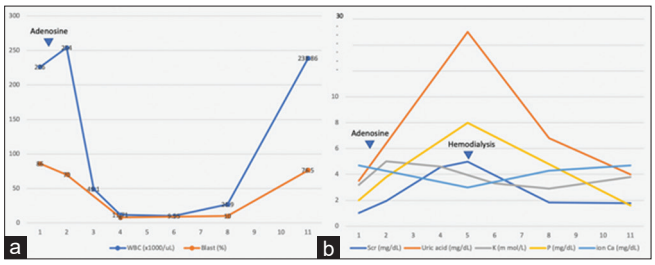

Figure 1: (a) Changes in white blood cell count and blast ratio. (b) Changes in creatinine, electrolyte, and uric acid levels of the patient with tumor lysis syndrome before and after adenosine treatment

Considering the risk of developing TLS, tumors are classified as being high, intermediate, and low risk. Burkitt's lymphoma, acute lymphocytic leukemia with a WBC count >100,000/μL, acute myeloma leukemia with a WBC count >10,000/μL, and diffuse large B-cell lymphoma with bulky disease are classified as high-risk tumors.[4] TLS is diagnosed according to the criteria of Cairo and Bishop, which entail laboratory and clinical diagnoses. The principal treatments for managing TLS are aggressive hydration to expand volume, correcting electrolyte imbalances, and avoiding any agents toxic to the kidneys such as intravenous contrast media and nonsteroidal anti-inflammatory drugs. Allopurinol can be considered for use in low-risk patients with TLS, and rasburicase (0.1–0.2 mg/kg) can be used for patients with an extremely high uric acid level or aggressive malignancy. Alkalinization of urine with isotonic sodium bicarbonate to increase the solubility of uric acid can also be considered. Hyperkalemia, hyperphosphatemia, and symptomatic hypocalcemia must all be treated appropriately. Hemodialysis may be necessary for patients with renal insufficiency or acute renal failure.[6]

Mechanisms such as hypoxia and hyperthermia are thought to cause tumor cell death. Adenosine is a purine nucleoside that interacts with cells through cell surface receptors such as A1, A2a, A2b, and A3.[7] The relationship between adenosine and cell growth/death is unclear and controversial. Merighi *et al*. demonstrated that adenosine is a mediator of both cell proliferation and cell death of cultured human melanoma cells through different receptors. For example, adenosine initiates a survival signal pathway through the activation of A3 receptors and induces cell death through A2a receptors, which involves protein kinase C and mitogen-activated protein kinases.[8,9] Lokshin *et al*. found that adenosine may induce cell death through apoptosis and that the mechanism is attributed to growth inhibition and cytotoxicity achieved through the depletion of pyrimidine nucleotides, which is the pathway of pyrimidine starvation.[10,11] Similarly, the administration of a chemotherapeutic agent and exposure to hypoxia have been demonstrated to activate A2b receptors to amplify cell death mediated by p53. Moreover, the accumulation of endogenous[12] and TP53 mutations has been detected in 8.2% of adult ALL cases.[1] In a few cases, TLS has occurred in patients under general anesthesia, pregnant patients, or patients with a high fever.[4] Although rare, our case is an example of spontaneous TLS after adenosine treatment.

To better prevent the occurrence of spontaneous TLS, further studies are warranted to identify its causes and determine the definite risk factors.

Ethical approval

Ethical approval for this study (KMUHIRB-E(I)-20190294) was provided by the Institutional Review Board of Kaohsiung Medical University Chung-Ho Memorial Hospital on November 14th, 2019.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. By completing the form, the patient has given consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published and due efforts will be made to conceal his identity but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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