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Case Report

Relapse of Lung Adenocarcinoma Manifested by Spontaneous Tumor Lysis Syndrome

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Keywords
Tumor lysis syndrome · Non-small cell lung cancer · Pulmonary adenocarcinoma · Spontaneous lysis · Case report

Abstract

Introduction: Tumor lysis syndrome (TLS) is an oncologic emergency characterized by several metabolic derangements, such as hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. TLS is typically observed in hematologic malignancies, especially after starting the first administration of antineoplastic therapies. TLS in a solid malignancy is very unusual, and exceedingly rare when occurring spontaneously, in the absence of chemotherapy. ***Case Presentation:*** We report a case of a 76-year-old man with lung adenocarcinoma, which started as a cancer with indolent behavior and small tumor burden but relapsed in 5 months with rapidly proliferating metastatic disease. Spontaneous TLS was the presenting clinical manifestation of the tumor relapse, and it led to the patient's death. ***Conclusion:*** To our knowledge, this is the first case of spontaneous TLS in a relapsed adenocarcinoma of the lung reported in the medical literature. The development of the metabolic derangements of TLS should prompt the consideration of tumor relapse during the follow-up of patients with solid malignancies.

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Introduction

Tumor lysis syndrome (TLS) is a syndrome characterized by several clinical and laboratory findings due to the release into the circulation of large amounts of intracellular contents, such as potassium, phosphate, and deoxyribonucleic acid. TLS is considered an oncologic emergency because patients typically develop acute hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia, which can be complicated by acute renal failure (ARF), arrhythmia, seizure, and death [1]. In rapidly growing hematologic malignancies, such as acute leukemias and aggressive non-Hodgkin's lymphomas, the incidence of TLS is as high as 36% [2]. In those cases, TLS is usually "induced," because it develops within hours to a few days after starting the first cycle of chemotherapy. Occasionally, TLS can also be "spontaneous," when it develops without chemotherapy, only because of a very high proliferation rate and cell turnover of the underlying cancer. TLS is observed in solid malignancies only rarely, with an estimated incidence of less than 1%. In these tumors, spontaneous TLS is even rarer, as shown by a recent review which listed a total of 63 published cases over 43 years [3]. Here we report a case of a lung adenocarcinoma which initially presented as an indolent tumor, but it later progressed with an aggressive behavior. TLS was the presenting clinical manifestation of the tumor's relapse.

Case Presentation

A 76-year-old male, former paper mill worker with 40-pack-year smoking history, was diagnosed with lung adenocarcinoma. His past medical history included hepatic steatosis, coronary artery disease requiring the insertion of an implantable cardiac defibrillator, and benign prostatic hyperplasia. During a screening computed tomography (CT) chest, he was incidentally found to have an 11 × 9 mm nodule in the left upper lobe of the lungs (shown in Fig. 1). The nodule slowly grew over time, with a 3 mm increase over 6 months, which made it suspicious for malignancy. The positron emission tomography and CT obtained 6 months after the initial detection of the nodule were negative for lymphadenopathy or distant metastatic disease. The patient underwent surgical resection with wedge lobectomy, using video-assisted thoracoscopic surgery (VATS), with curative intent. The pathology of the nodule was consistent with non-small cell lung cancer, adenocarcinoma type, with immunohistochemical stains positive for TTF-1 and napsin A and negative for CK 5/6 and p40. No involvement was found in the 18 resected regional lymph nodes, and the pathologic stage of the malignancy was IA2 (T1b N0 M0).

Five months after VATS, the patient developed acute dyspnea, fatigue, and general malaise. Repeat positron emission tomography and CT showed diffuse metastatic disease in the liver (shown in Fig. 2) and bones. The results of the complete blood counts were unremarkable, and there was no clinical or laboratory evidence of sepsis. The metabolic profile revealed hyperuricemia (16.4 mg/dL, normal 3.5–7.2 mg/dL), hyperkalemia (6.4 mmol/L, normal 3.5–5.1 mmol/L), hyperphosphatemia (5.9 mg/dL, normal 2.5–4.5 mg/dL), and normocalcemia (10.0 mg/dL). There was ARF (serum creatinine 4.3 mg/dL, normal 0.67–1.17 mg/dL), along with metabolic acidosis (bicarbonate level 12 mmol/L, normal 22–29 mmol/L). The results of the laboratory tests were consistent with TLS complicated by ARF. The patient was admitted to the intensive care unit, where he was given intravenous fluids and a dose of rasburicase (0.2 mg/kg intravenously over 30 min). The medical staff was planning to initiate hemodialysis, but the patient and his family elected to comfort care only, in view of the poor clinical conditions and the incurable nature of the disease. The patient died

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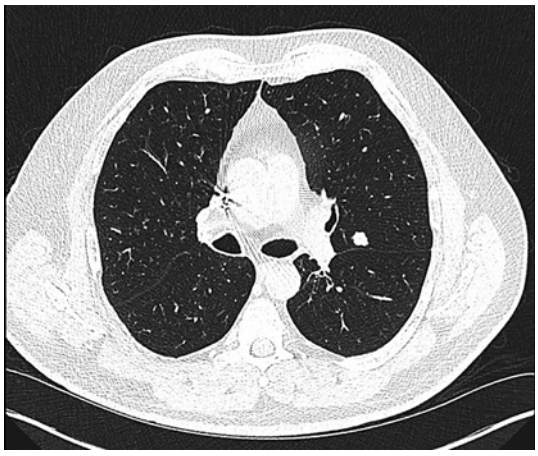

Fig. 1. Axial view of the CT scan of the lungs, 6 months prior to the development of TLS. A solid nodule of 11 mm × 8 mm is visible in the inferior portion of the left upper lobe.

2 days later. An autopsy was not performed. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000534398).

Discussion

In cancers with high tumor burden and rapid cell turnover, the lysis and death of the tumor cells release into the circulation large amounts of intracellular contents, such as phosphorus, potassium, and uric acid. This condition is called TLS, and it can be distinguished into "laboratory TLS", characterized by hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, and "clinical TLS," where those metabolic abnormalities are complicated by ARF, cardiac arrhythmias, seizures, and death. The pathophysiology of TLS is complex. The large quantities of cellular contents, mostly filtered by the kidneys, may exceed the renal compensatory mechanisms and induce obstruction of the renal tubules. The metabolism of purines from the DNA leads to the production of xanthine, which is metabolized to urate. When the conversion to urate overwhelms the enzymatic pathway, crystallization occurs within the renal tubules, and these results in obstructive uropathy and decreased glomerular filtration rate, leading to ARF [4]. Moreover, animal models have displayed increased pressures in the proximal and distal tubules as well as in the peritubular capillaries, further potentiating renal dysfunction [5], and a pro-inflammatory effect of uric acid [6].

The treatment of TLS is largely supportive, and it consists in the management of electrolyte imbalances, aggressive intravenous hydration, intravenous rasburicase in cases of significant hyperuricemia, and hemodialysis as clinically indicated. In view of the potentially life-threatening nature of the metabolic derangements, early diagnosis is essential for decreasing the mortality risk (which is usually due to seizures and arrhythmias).

Although TLS is a commonly observed medical condition in the treatment of hematologic malignancies, TLS in solid tumors is very rare, especially when it is spontaneous, i.e., not induced by chemotherapy. This is because most solid malignancies have a doubling time in the order of weeks or months, whereas some hematologic malignancies, like acute myelogenous leukemia, can have a tumor doubling time in the order of days [7]. Our case is interesting not only because it describes the development of TLS in a solid tumor but also because the TLS developed de novo and was not induced by chemotherapy. In our case, TLS was the first clinical manifestation that led to the diagnosis of tumor relapse, in a cancer which previously

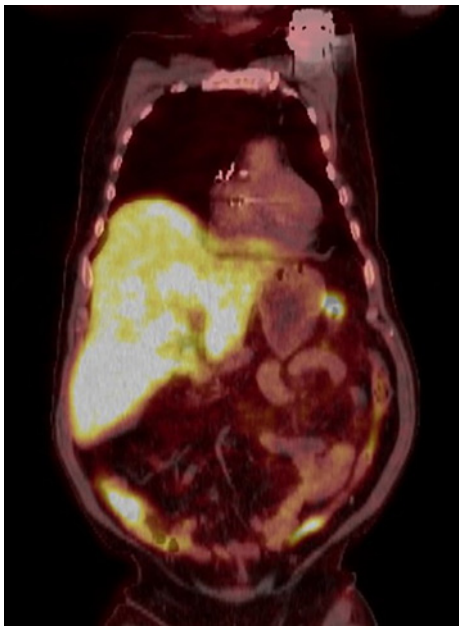

Fig. 2. PET/CT scan at the time of the TLS, showing hepatomegaly and diffuse metabolic activity in the liver, consistent with active metastatic disease. PET, positron emission tomography.

had indolent behavior and was treated with curative intent. To our knowledge, no similar cases of spontaneous TLS upon tumor relapse of a pulmonary adenocarcinoma have been reported in the medical literature.

Conclusions

The laboratory detection of certain metabolic abnormalities, namely hyperphosphatemia, hyperkalemia, hypocalcemia, hyperuricemia, and elevated LDH (either alone or in various combinations) in a patient with a history of cancer should always prompt the inclusion of TLS in the differential diagnosis, even when the malignancy is a solid tumor. The laboratory tests of TLS should be obtained even in those patients who did not receive prior antineoplastic treatment.

Statement of Ethics

This study, based on a single chart review of patient data, did not require ethical approval, in accordance with institutional and national guidelines. Written informed consent was obtained from the wife of the deceased patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Daebin Im drafted the manuscript, obtained consent from the patient's spouse, and collected the patient's data. Katie Alsheimer was responsible for the critical care of the patient and contributed to the discussion. Joyson Poulose wrote the outline of the oncologic aspect of the discussion and did a literature search. Violeta Zeykan and Giampaolo Talamo supervised the case preparation, provided insight to the discussion, and finalized the report. All authors read and approved the final manuscript.

Data Availability Statement

All data described in this study are included in this article. Further inquiries can be directed to the corresponding author.

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