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Spontaneous tumor lysis syndrome in the setting of small cell lung cancer: Report of two cases and review of the literature

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ABSTRACT

Tumor lysis syndrome (TLS) is a life-threatening condition characterized by massive lysis of malignant cells after treatment, which results in hyperuricemia, hyperkalemia, hyperphosphatemia and hypocalcemia. These metabolic abnormalities may cause acute kidney injury (AKI), seizures, cardiac arrhythmia and sudden death. Spontaneous TLS (STLS), which occurs in the absence of chemotherapy or radiotherapy, is a rare entity that has particularly been described in the setting of hematological malignancies. STLS has been exceptionally associated with solid tumors; however it could be an underdiagnosed entity and should certainly be considered in the differential diagnosis of AKI in patients with solid tumors. Moreover, due to further delay in diagnosis this entity could be associated with worse prognosis. Early management with intravenous hydration, hypouricemic agents and correction of electrolyte disorders are essential, although clinical course may be aggressive.

We describe two unusual cases of STLS in the setting of small cell lung cancer who developed STLS. A high index of suspicion is needed in order to initiate necessary prophylactic precautions and avoid fatal consequences.

1. Introduction

Tumor lysis syndrome (TLS) is an oncologic emergency characterized by a constellation of metabolic abnormalities secondary to the release of tumor cells content into the systemic circulation [1]. This can result in hyperkalemia, hyperphosphatemia, hypocalcemia and hyperuricemia, and eventually can lead to systemic consequences (particularly acute kidney injury (AKI)) [2]. TLS has usually been described in hematological malignancies (especially Burkitt's lymphoma and acute lymphoblastic leukemia), and much less frequently in solid tumors, following the initiation of chemotherapy or radiotherapy [3]. The reported incidence of TLS in patients with hematological malignancies is 4–42% [4], although prophylactic measures seem to have reduced the incidence [5].

Spontaneous TLS (STLS), which occurs in the absence of chemotherapy or radiotherapy, is exceptional in solid tumors though it has been described in the setting of malignancies with a high proliferative index and large tumor burden, such as germ cell tumors or gastrointestinal carcinomas [6–9]. Early recognition and preventive treatment are essential to minimize the potential fatal complications. We present two unusual cases of STLS in the setting of small cell lung cancer.

2. Case reports

2.1. Case 1

A 64-year-old man with a previous history of heavy smoking (80 pack-year) presented to the emergency department with a history of progressive epigastric pain, loss of appetite and unintentional weight loss of 5 kg over a period of three weeks. Physical examination only revealed a painful hepatomegaly. The initial laboratory data showed a slight increase in total bilirubin along with elevated levels of liver enzymes (LE) and lactate dehydrogenase (LDH). Complete laboratory findings are summarized in Table 1. An abdominal ultrasound revealed hepatomegaly with heterogeneous echogenicity and multiple hepatic hilar lymphadenopathies.

The patient was admitted to the hospital and further diagnostic procedures were performed over the next days. A body computed-tomography (CT) scan showed a 60 mm mass in the upper lobe of the left lung invading the left pulmonary artery, with hilar and mediastinal lymphadenopathies (Fig. 1). It also showed a severe hepatomegaly with multiple small metastases (miliary pattern),

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Table 1
Blood results of Case 1.

Description	*Day* 1	*Day* 2	*Day* 9	*Day* 10
Creatinine (mg/dL)	0.99	1.12	2.45	3.03
Urea (mg/dl)	45	68	136	186
Sodium (mmol/l)	142	137	131	128
Potassium (mmol/l)	4.6	5.2	5.6	6.3
Corrected calcium level (mg/dl)	10.3	10.4	9	8.6
Phosphorus (mg/dL)	–	–	6.2	10.7
Uric acid (mg/dL)	–	–	15	22.6
Bicarbonate (mmol/l)	–	–	17	13
Total bilirubin (mg/dl)	1.6	1.4	5.4	6.5
AST (U/l)	204	449	1056	1641
ALT (U/l)	124	152	314	490
GGT (U/l)	702	1124	1100	1223
LDH (U/l)	1516	2341	2720	3875
Alkaline Phosphatase (U/l)	357	376	901	934
Hemoglobin (g/dl)	15	14.5	14.2	14.8
White blood cell count ($\times 10^9$/l)	9	9.5	16	13
Thrombocyte count ($\times 10^9$/l)	342	340	219	225
INR	0.9	–	1.47	1.85

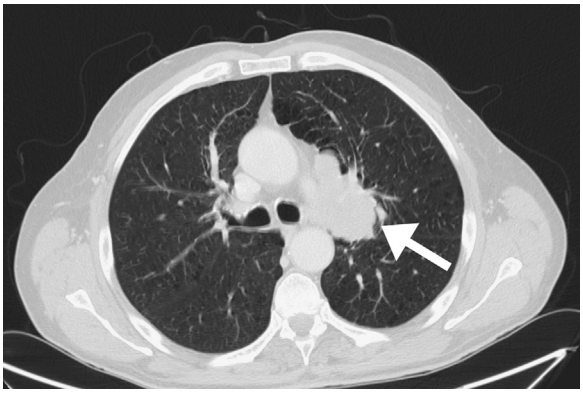

Fig. 1. Computed tomography scan showing a large left hilar mass with extensive mediastinal lymphadenopathy.

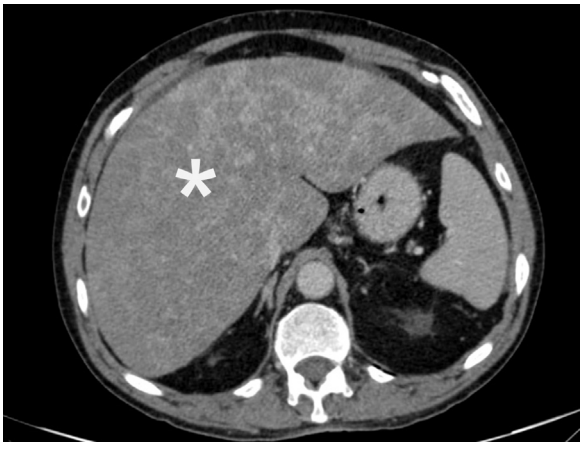

Fig. 2. CT scan showing extensive metastatic liver involvement with miliary pattern.

but no intestinal or retroperitoneal involvement (Fig. 2). A percutaneous liver biopsy revealed a highly proliferative neoplasia (Ki67 of 90%), with small and hyperchromatic cells, positive for synaptophysin and CD56, compatible with metastatic small cell carcinoma.

Between the second and ninth day the patient was normotensive, afebrile, and did not receive nephrotoxic medications. Liver function impairment was considered as an expression of the extensive liver involvement.

On the ninth day of admission the patient developed progressive confusion and agitation. Blood tests showed severe renal impairment, hyperkalemia with metabolic acidosis and severe hyperuricemia, together with a gradual increase in LE and LDH levels (Table 1). Post-renal obstruction was excluded with renal and bladder ultrasound, and urinalysis demonstrated 5–10 red blood cells (RBCs) per high powered field (hpf), 15–20 WBCs/hpf, and uric acid crystals. The severity of hyperuricemia could not be explained by the degree renal impairment, which raised the suspicion of STLS. Therefore, we initiated vigorous intravenous hydration, rasburicase and treatment for specific electrolyte abnormalities. Unfortunately, the patient clinical course was complicated with progressive liver dysfunction, multiple organ failure and died 24 h later.

2.2. Case 2

A 60-year-old man with a previous history of hypertension, hypercholesterolemia and former smoking (30 pack-year) was admitted to our hospital with abdominal pain, confusion and somnolence over the last two days. The patient had been diagnosed one month earlier with small-cell lung carcinoma (35 mm mass in left upper pulmonary lobe with mediastinal adenopathies) with extensive liver metastases, and had not received treatment yet.

Physical examination on admission revealed severe cachexia, a Glasgow Coma Scale of 11 (E3V3M5), blood pressure of 120/64 mmHg, temperature of 36 °C and a tender hepatomegaly on abdominal exam. Initial laboratory work showed an AKI with hyperpotasemia, hyperphosphatemia and hyperuricemia, along with severe impairment of liver function test. Laboratory findings are summarized in Table 2.

Intravenous hydration and close monitoring were initiated, but AKI progressed over the next 12–24 h. The whole clinical course and laboratory findings were consistent with STLS complicated with acute hepatic failure and therefore aggressive hydration, rasburicase and loop diuretics were initiated in an attempt to limit the impact of this condition. Despite all these measures, anuric AKI developed with progressive mental status impairment and respiratory failure. The patient was not considered suitable candidate for dialysis given the poor prognosis, thus palliative measures were adopted, and died within hours.

Table 2
Blood results of Case 2.

Description	*Day* 1	*Day* 2
Creatinine (mg/dL)	2.4	4.6
Urea (mg/dl)	100	158
Sodium (mmol/l)	131	129
Potassium (mmol/l)	5.6	6
Corrected calcium level (mg/dl)	9	8.5
Phosphorus (mg/dL)	5.1	6.7
Uric acid (mg/dL)	12.6	16.9
Bicarbonate (mmol/l)	19	17
Total bilirubin (mg/dl)	17.1	16.8
AST (U/L)	408	396
ALT (U/L)	167	161
GGT (U/L)	1241	1176
LDH (U/L)	1940	2092
Alkaline Phosphatase (U/L)	646	648
Hemoglobin (g/dl)	10.7	10,3
White blood cell count ($\times 10^9$/l)	6.6	6
Thrombocyte count ($\times 10^9$/l)	192	147
INR	1.3	1.6