TUMOUR LYSIS SYNDROME IN SOLID TUMOURS: CLINICAL CHARACTERISTICS AND PROGNOSIS

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Introduction and Aims

- Tumour 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.
- TLS is an uncommon complication in solid tumors following the initiation of treatment, and its spontaneous development (STLS) before treatment is exceptional.
- Aims: to analyze the main clinical and prognostic features of a case series with TLS and STLS.

Patients and Methods

- Single-center observational retrospective study in which we included all patients with solid tumours diagnosed with TLS and STLS between 2000-2016, according to Cairo-Bishop criteria.
- Baseline characteristics including demographics, ECOG (*Eastern Cooperative Oncology Group*) scale on admission, as well as the type of cancer and the extent of metastatic involvement, were collected from medical records.
- The creatinine change criteria proposed by the Acute Kidney Injury Network (AKIN) was used to stratify acute renal failure.
- According to Cairo-Bishop classification, TLS laboratory abnormalities include the development of 2 or more of the following abnormalities within 3 days prior or 7 days after initiation of treatment: hyperuricemia, hyperkalaemia, hyperphosphatemia, hypocalcaemia. TLS is clinically defined by increased serum creatinine, development of cardiac arrhythmia or sudden death, or seizures.

Cairo-Bishop Classification

Laboratory criteria			Clinical criteria
Uric acid	≥ 8.0 mg/dL	or 25% increase	1. Creatinine x 1.5 times the upper limit of normal.
Potassium	≥ 6.0 mmol/L	or 25% increase	2. Cardiac arrhythmias.
Phosphorus	≥ 4.6 mg/dL	or 25% increase	3. Seizures
Calcium	≤ 7.0 mg/dl	or 25% increase	

Results

Etiology of neoplasms in each group

Neoplasm	Histology	TLS, n (%)	STLS, n (%)
Lung	Small cell lung cancer	3 (16%)	2 (11%)
	Lung adenocarcinoma	2 (11%)	1 (5%)
Digestive tract	Oesophageal adenocarcinoma	1 (5%)	
	Oesophageal squamous cell carcinoma		1 (5%)
	Gastric adenocarcinoma		1 (5%)
	Colon adenocarcinoma		1 (5%)
Gynaecological	Endometrial adenocarcinoma	1 (5%)	1 (5%)
	Infiltrating ductal breast carcinoma	1 (5%)	
Urological	Prostatic adenocarcinoma	1 (5%)	
Other	Extragonadal germ cell tumour	1 (5%)	
	Quadriceps myxoid liposarcoma		1 (5%)
	Tumour of unknown origin		1 (5%)

Clinical and biochemical characteristics of all the patients and according to etiologic subgroup

	Total	TLS	STLS	p
Number, n (%)	19	10 (53)	9 (47)	
Age, years	63 (16)	62 (18)	63 (13)	0.815
Sex, male (%)	15 (79)	7 (70)	8 (89)	0.656
ECOG scale on admission [a]	2 [1-3]	2 [2-3]	2 [1-3]	0.847
Time from diagnosis of the tumour, days	28 [12-63]	26 [5-38]	37 [12-49]	0.191
Arrhythmia, n (%)	5 (26)	2 (20)	3 (33)	0.628
Confusion-lethargy, n (%)	3 (16)	2 (20)	1 (11)	1.000
Seizures, n (%)	8 (42)	3 (30)	5 (55)	0.370
Symptomatic hypocalcaemia, n (%)	3 (16)	2 (20)	1 (11)	1.000
Acute renal failure, AKIN classification:				0.869
AKIN 1	10 (53)	5 (50)	5 (55)	
AKIN 2	3 (16)	2 (20)	1 (11)	
AKIN 3	6 (32)	3 (30)	3 (33)	
Serum creatinine, mg/dl	3.3 (1.6)	3.6 (1.7)	2.9 (1.5)	0.380
eGFR, ml/min/1,73 m^2	23 (13)	19 (7)	28 (16)	0.138
Uric acid, mg/dl	16 (6)	16 (7)	16.3 (5)	0.928
Potassium, mM/L	6 (0.9)	6 (0.7)	6.2 (1)	0.498
Calcium, mg/dl	7.9 (0.8)	7.5 (0.8)	8.3 (0.8)	0.046
Phosphorus, mg/dl	8.3 (3.3)	9.3 (3)	7.3 (3.3)	0.194
Bicarbonate, mM/L	17 (6)	18 (5)	17 (7)	0.655
Total bilirubin, mg/dl [a]	1.7 [0.9-3.3]	2 [0.9-4]	1.3 [0.8-3.8]	0.497
GGT, U/L	518 (390)	468 (328)	571 (466)	0.640
LDH, U/L	1713 (890)	1872 (787)	1554 (1010)	0.645
Haemodialysis, n (%)	3 (16)	3 (30)	0 (0)	0.211
Renal function recovery, n (%)	7 (37)	6 (60)	1 (11)	0.057
Death during admission, n (%)	12 (63)	5 (50)	7 (78)	0.350

- All patients were treated with intensive intravenous hydration (physiological saline and bicarbonate) and diuretics (furosemide). A uricolytic agent (rasburicase) was used in 63% of patients, and xanthine oxidase inhibitors (allopurinol) in 26%.
- Renal replacement therapy with haemodialysis was only performed in 3 patients (16%) with TLS who were on chemotherapy, 2 of them recovering renal function afterwards. The median time on haemodialysis was 8 days. Seven patients (37%) recovered renal function after 9 days (median, interquartile range: 4–12 days), and this recovery was more frequently seen among the TLS group.
- Mortality during hospitalization was high, especially in the STLS group. Overall, 9 patients (47%) died after tumour lysis syndrome and 3 (16%) for different reasons despite having recovered from tumour lysis (acute myocardial infarction, pneumonia, and gastrointestinal bleeding).
- Patients with an unfavourable outcome were younger, with a more severe renal impairment, and more frequently with STLS, although the differences did not reach statistical significance.

Clinical characteristics according to outcome of TLS

	Favourable	Unfavourable	p
Number, n (%)	10 (53)	9 (47)	
Age, years	67 (14)	58 (16)	0.226
Sex, male (%)	7 (70)	8 (89)	0.582
Spontaneous TLS, n (%)	3 (30)	6 (67)	0.179
Multiple liver metastases, n (%)	7 (70)	6 (67)	0.892
Serum creatinine, mg/dl	2.3 (1.6)	3.8 (1.5)	0.142
eGFR, ml/min/1,73 m^2	25 (12)	20 (13)	0.152
Uric acid, mg/dl	17 (7)	15 (5)	0.624
Potassium, mM/L	5.8 (1)	6.4 (1)	0.156
Serum calcium, mg/dl	7.7 (1)	8.1 (1)	0.220
Phosphorus, mg/dl	7.8 (3.7)	8.9 (3)	0.465
Bicarbonate, mM/L	20 (6)	14 (4)	0.051
LDH, U/L	1728 (1100)	1713 (1000)	0.813

Conclusions

- TLS and STLS are rare entities that may occur in solid tumors and result in acute kidney injury.
- Its development is associated with increased mortality, and therefore a high index of suspicion is essential to early recognize and treat.

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