

# Renal Cell Carcinoma with Extensive Rhabdoid Features: Case Report of Spontaneous Tumor Lysis Syndrome and Review of Literature

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## ABSTRACT

Tumor Lysis Syndrome (TLS) is an oncologic emergency which consists of a constellation of electrolyte imbalances, acute renal failure, seizure, and arrhythmias. It is most commonly seen with hematologic malignancies after the initiation of chemotherapy. However, it can also occur spontaneously, prior to treatment with cytotoxic agents. To our knowledge, only few cases of TLS in Metastatic Renal Cell Carcinoma (mRCC) were reported in the literature. Herein, we present the case of a 55-year-old man with metastatic RCC with rhabdoid features who developed Spontaneous Tumor Lysis Syndrome (STLS). He developed acute oliguric renal failure and multiple electrolyte abnormalities requiring hemodialysis. This case highlights the importance of evaluation of potential risk factors of STLS and preventive therapies needed even before treatment of solid tumors.

### Background

Tumor Lysis Syndrome (TLS) is a metabolic oncologic emergency that can occur following the release of intracellular components either spontaneously or after the administration of anti-neoplastic therapy. The sudden influx of electrolytes and nucleic acids into circulation can lead to hypocalcemia, hyperkalemia, hyperphosphatemia, and hyperuricemia – all of which can have life-threatening end-organ effects on the central nervous system, myocardium, and kidneys. Patients may present with oliguria, dysuria, vomiting, seizures, altered mental status, weakness, arrhythmias, and/or paralysis [1].

TLS has been rarely described with non-hematologic solid tumors, and it is even more uncommon to have Spontaneous Tumor Lysis Syndrome (STLS) in solid tumors. To our knowledge, only few cases of STLS in Metastatic Renal Cell Carcinoma (mRCC) were reported in the literature [2,3].

We present a case of STLS in a patient with mRCC with rhabdoid features, together with a review of literature regarding the occurrence of STLS in patients with metastatic RCC and solid tumors.

### Case Presentation

A 55-year old male with no past medical history who was admitted to the hospital on October 27th, 2017 for shortness of breath, left flank and right

upper quadrant pain. Urinary Analysis (UA) completed with his primary care physician two weeks prior to this admission revealed microscopic hematuria. The patient reported low-grade fever, nausea, shortness of breath, and poor appetite for two days prior to hospitalization. Baseline Complete Blood Count (CBC) on the day of admission revealed a White Blood Count (WBC) of 8.0 K/mm<sup>3</sup> (Normal Range 4.8 – 10.8), hemoglobin of 14.2 gm/dL (NR 14 – 18), and platelet count of 305 K/mm<sup>3</sup> (NR 130 – 400). Other pertinent laboratory studies included: potassium of 4.6 mmol/L (NR 3.6 - 5.0), calcium 8.7 mg/dL (NR 8.5 – 10.3), creatinine 0.96 mg/dL (NR 0.57 – 1.11), ALT 315 units/L (NR 13 – 40), AST 166 units/L (NR 10 – 59), and Alk Phos 310 units/L (NR 38 – 126). His previous blood work from seven months ago was unremarkable.



**Figure 1:** Contrast-enhanced computed tomographic scan, obtained at diagnosis showed bilateral pleural effusion, left renal mass and liver metastases.

A Computed Tomography (CT) of the abdomen and pelvis revealed a left renal mass, compatible with renal cell carcinoma, as well as liver metastases (Figure 1). CT angiogram of the chest showed numerous bilateral lung nodules and moderate size of pleural effusion. The

patient was seen by Interventional Radiology (IR) and underwent ultrasound-guided diagnostic/therapeutic thoracentesis and CT guided liver biopsy. The pathology finding of the biopsy was consistent with Metastatic Renal Cell Carcinoma (mRCC) with rhabdoid features (Figure 2). Laboratory values yielded a uric acid of 6.0 mg/dL (NR 4.5 – 8.0) and a Lactate Dehydrogenase (LDH) of 1,584 units/L (NR 125 – 243).

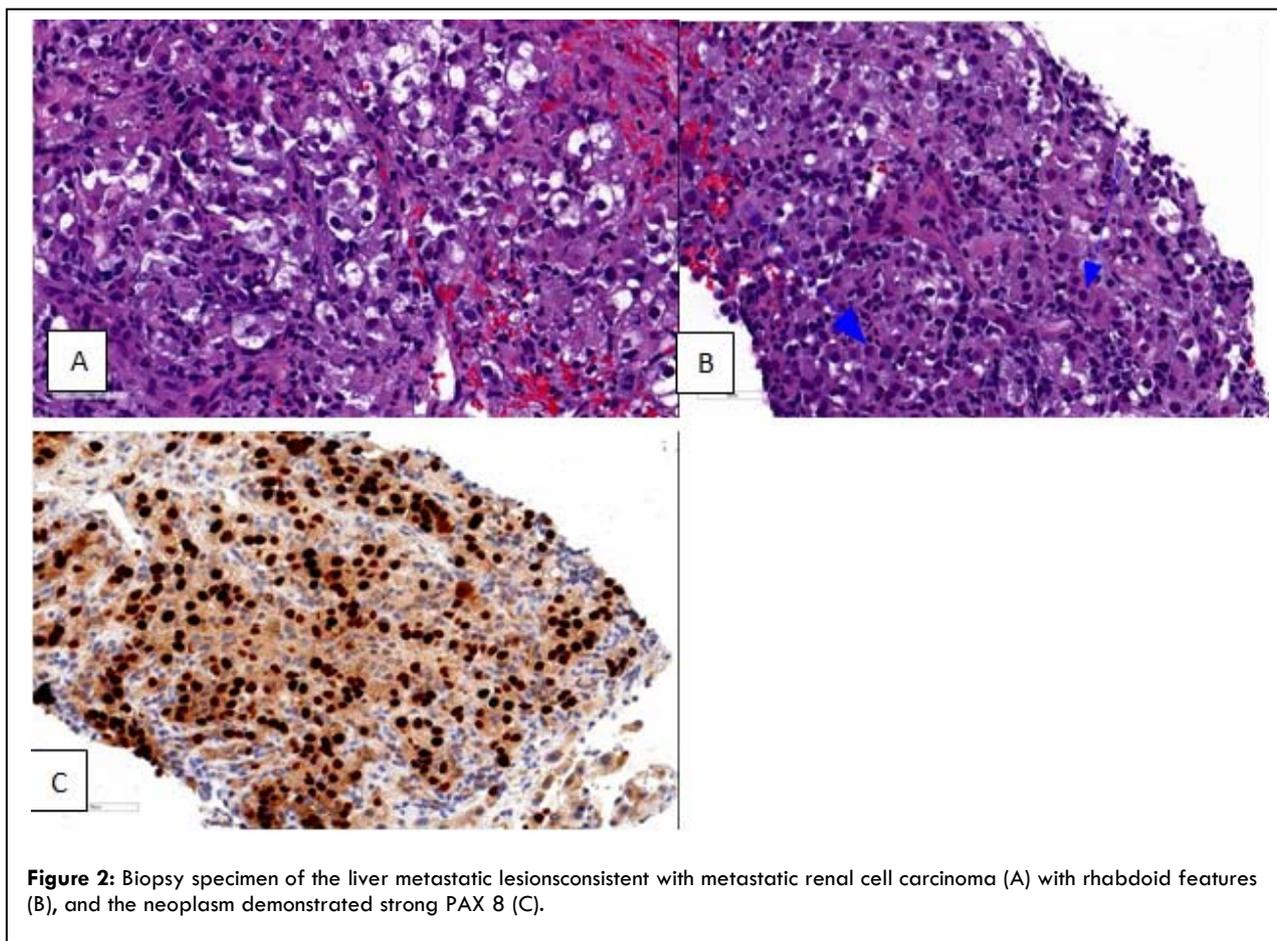
The patient developed progressively worsening shortness of breath and abdominal distension. Lab studies showed: WBC count of 12.7 K/mm<sup>3</sup> (NR 4.8 – 10.8), sodium 132 mmol/L (NR 135 – 145), potassium 4.5 mmol/L (NR 3.6 – 5.0), chloride 91 mmol/L (NR 100 – 110), BUN 44 mg/dL (NR 8 – 25), creatinine 2.16 mg/dL (NR 0.57 – 1.11), calcium 8.2 mg/dL (NR 8.5 – 10.3), albumin 3.3 gm/dL (NR 3.5 – 5.0), phosphorus 4.4 mg/dL (NR 2.4 – 4.7), magnesium 2.9 mg/dL (NR 1.6 – 2.9), eGFR 32 mL/min (NR > 60), ALT 257 units/L (13 – 40), AST 234 units/L (NR 10 – 59), Alk Phos 599 units/L (NR 38 – 126), uric acid of 13 mg/dL (NR 4.5 – 8.0) and LDH 2,244 units/L (NR 125 – 243).

The patient was treated with aggressive hydration using normal saline, intravenous antibiotics and rasburicase. Nephrology was consulted and a Hemodialysis (HD) catheter was placed. The patient became hypotensive during his first HD, subsequently was transferred to the Intensive Care Unit (ICU) and started on vasopressors. Despite aggressive supportive measures his condition deteriorated and he died of multiple organ failure.

### Discussion

We present here a fatal case of STLS as complication of mRCC. Evidence of TLS in solid tumors is limited to case reports and small case series [1-6] because the risk of this syndrome in these patients was thought generally low. There is, however, a growing number of reported cases of TLS in such patients after the initiation of cancer treatment [2,3]. It is also possible that STLS is under diagnosed/ underreported if many cases are misdiagnosed as metabolic or electrolyte disturbances [2,3].

Although it occurs rarely, TLS can occur spontaneous in patients with solid tumors [1-3]. Our extensive literature



**Figure 2:** Biopsy specimen of the liver metastatic lesions consistent with metastatic renal cell carcinoma (A) with rhabdoid features (B), and the neoplasm demonstrated strong PAX 8 (C).

**Table 1:** Pertinent laboratory findings in a 55-year old male with metastatic renal cell carcinoma with rhabdoid features and Spontaneous Tumor Lysis Syndrome (STLS).

Parameter (Normal Range)	10/27/17	11/6/17 (before rasburicase)	11/7/17 (after rasburicase)	11/8/17	11/9/18 (before rasburicase)	11/10/18 (after rasburicase)
Serum Creatinine (0.57 - 1.11 mg/dL)	0.96	2.16	2.71	4.64	5.05	5.09
GFR (> 60 mL/min)	> 60	32	25	13	12	12
Potassium (3.6 - 5.0 mmol/L)	4.6	4.5	4.5	5.6	5.4	4.5
Calcium (8.5 - 10.3 mmol/L)	8.8	8.3	8.8	8.2	7.9	7.8
Albumin (3.5 - 5.2 g/dL)	3.5	3.3	3.5	3.1	3.2	3.1
Phosphorus (2.4 - 4.7 mg/dL)	--	4.4	--	--	6.4	6.2
Uric Acid (3 - 6 mmol/L)	6.0	13	11	--	13.3	2.3
Lactate dehydrogenase (125 - 243 IU/L)	--	2244	2627	--	2903	--

search of Pub Med yielded 132 cases of TLS in solid tumors [2-3]; 32 cases (24%) were STLS. (Table 1). There was a male predominance with 24 of 32 patients being male. Although there was a variation in origin of primary tumors, extensive liver involvement is noted in 82.8% of total cases reported. TLS in solid tumors is unpredictable and carries a worse prognosis when compared to hematologic malignancies [2,3,7]. There is a 20%–50% mortality in all cases of TLS in solid tumors if undiagnosed or if diagnosed too late [7-12]. Our analysis of published cases suggests that STLS may have higher rate of Acute Renal Injury (AKI) (88% vs 86%,  $p=0.001$ ) and elevated LDH (75% vs 70%,  $p=0.003$ ). In our review, 24% of all cases of TLS in solid tumors are spontaneous, which similar to previous reports [7, 8]. Hyperphosphatemia was previous thought less frequently in STLS; this is hypothesized to be because in highly proliferative tumor cells actually recycles the phosphorus for the synthesis of new cells [10]. However, the difference of frequency of hyperphosphatemia in STLS and treatment related TLS (TTLS) was not statistically significant in our analysis (Table 2). Similar to treatment induced TLS, the development of STLS is associated with very high mortality [2-3].

**Table 2:** Comparison of Spontaneous Tumor Lysis Syndrome (STLS) and treatment related Tumor Lysis Syndrome (TTLS).

Variable	STLS (N = 32)	TTLS (N = 100)	p Value
Age ≥ 60	15 (47%)	43 (43%)	0.701
Male	24 (75%)	59 (59%)	0.103
Liver Metastases	26 (75%)	71 (71%)	0.253
Hyperphosphatemia	22 (69%)	80 (80%)	0.401
Acute renal injury	28 (88%)	86 (86%)	0.013
Elevated LDH	24 (75%)	70 (70%)	0.030
Hyperuricemia	27 (84%)	87 (87%)	0.930
Death	18 (56%)	54 (54%)	0.975

Only six cases of TLS in mRCC have been previously reported [6-17]. In all cases, patients presented with bulky metastases, high grade disease and hepatic metastases. In three cases, TLS occurs after treatment with sunitinib, a tyrosine kinase inhibitor. Another two cases occurred spontaneously. Our case represents the sixth case of TLS and the third cases of STLS in mRCC

(Table 3). In this particular patient, the two most prominent risk factors for the development of STLS were rapid proliferation rate and aggressive histology (mRCC with rhabdoid features), as well as large tumor burden (as evidenced by liver metastases). Rhabdoid renal cell carcinoma (RRCC) morphology is currently defined as any histologic type of RCC that has foci of high-grade malignant cells with rhabdoid morphology – large eccentric vesicular nuclei, globular eosinophilic paranuclear intracytoplasmic inclusion bodies, abundant eosinophilic cytoplasm, and prominent nucleoli [11-13]. In a small study investigating the effect of rhabdoid morphology on RCC, the mean survival of patients with RCC with rhabdoid features was found to be 8 months. 10 out of 14 (71%) patients developed metastases, while 6 out of 14 (43%) patients died from the disease [14]. It was concluded that RCC with rhabdoid features is an aggressive cancer with a poor prognosis [13].

### Conclusion

In conclusion, TLS is a life-threatening oncological emergency that requires rapid identification and aggressive supportive measures, as it can be reversible if treated early. STLS is not common in solid neoplasms, but the incidence may be higher in mRCC. Clinicians should maintain a high index of suspicion for patients with malignancies who demonstrate the known pretreatment risk factors, including renal impairment, hyperuricemia, and increased LDH, even in the absence of chemotherapy. Our case and literature review underscore the importance of continued awareness, risk assessment, and prevention to reduce this fatal potential complication in patients with solid tumors.

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