

## Spontaneous Tumor Lysis Syndrome in Primitive Neuroectodermal Tumor

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### Abstract

Tumor lysis syndrome is caused by the massive lysis of tumor cells. It frequently occurs in rapidly proliferating malignancies and less often after solid tumor treatment. Spontaneous tumor lysis syndrome is extremely rare and only occurs in bulky, advanced, and metastatic tumors. Electrolyte abnormalities in tumor lysis syndrome could be life-threatening without prompt recognition and treatment. In this case, we present a spontaneous tumor lysis syndrome in a 22-year-old man with primitive neuroectodermal tumor.

When managing bulky, advanced solid tumors, especially with liver metastasis, cautious observation should be sought because of the possibility of spontaneous tumor lysis syndrome.

**Keywords:** Spontaneous tumor lysis syndrome, Solid tumors, PNET

### Introduction

Tumor lysis syndrome (TLS) is a life-threatening complication caused by massive lysis of tumor cells and release of significant amounts of nucleic acids, proteins, and electrolytes.<sup>1-3</sup>

TLS most commonly occurs in tumors that have a short doubling time, rapid proliferation, and large tumor burden, in addition to disseminated tumors and high sensitivity to anti-neoplastic drugs.<sup>1</sup>

It is characterized by hyperuricemia, hyperphosphatemia, hyperkalemia, and hypocalcemia,

and leads to seizures, renal failure, cardiac arrhythmia, and ultimately death.<sup>4-6</sup>

TLS often occurs in rapidly proliferating malignancies and is common in hematologic malignancies,<sup>7</sup> but less frequently after treatment of solid bulky tumors.<sup>8</sup> However, spontaneous TLS is very rare in solid tumors. Here, we describe a rare case of spontaneous TLS with primitive neuroectodermal tumor (PNET).

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## Case presentation

A 22-year-old man was hospitalized due to constipation and difficulty with defecation since 4 months prior, in addition to constant abdominal pain with occasional vomiting one month prior to his admission. His abdominal pain was chronic and not relieved with NSAIDs.

During physical examination, the patient was extremely cachectic with temporal wasting. Ascites and a voluminous palpable mass were detected in the lower part of his abdomen.

Abdominopelvic ultrasonography showed a normal size liver with heterogeneous parenchymal echogenicity and multiple various size ill-defined hypoechoic lesions. Additional findings included mild to moderate ascites with large heterogenous lesions throughout the abdominopelvic cavity, which favored peritoneal seeding.

Colonoscopy was impossible due to stricture in the rectal region, but an endorectal ultrasonography showed narrowing in the rectum with external pressure effect. There was a large heterogeneous mass (approximately 7.5×7 cm) observed adjacent to the rectum without any invasion. The mass was superior to and seemed to be invading the prostate.

According to Cairo-Bishop criteria, his laboratory results revealed a significant alteration in favor of the diagnosis of TLS (Tables 1, 2). Immediately, hydration and urine alkalization were initiated. Only 3 mg rasburicase was available in our hospital, which we prescribed for the patient. Within 2 days, uric acid levels decreased to 3.5 mg/dl and creatinine to 0.9 mg/dl.

Abdominopelvic spiral CT scan with contrast revealed multiple low attenuated liver masses in favor of metastasis. It also showed inferior vena cava thrombosis and heterogeneous masses in the pelvic cavity with a cystic component with pressure on the anterior rectum (Figure 1).

A bone scan revealed bone metastasis of the neck and trochanteric regions of the left femur.

The patient underwent an ultrasound guided liver biopsy. Sections from the needle biopsy showed infiltration of small round cell tumors with scant cytoplasm and high N/C ratio with

**Table 1.** Laboratory trends in the study patient

Parameter	
WBC (K/ $\mu$ L)	10,000
Hemoglobin (g/dL)	9.6
Platelets (K/ $\mu$ L)	472000
Potassium (mmol/L)	4.5
BUN (mg/dL)	49
Creatinine (mg/dL)	1.7
Phosphorus	5.7
Calcium (mg/dL)	8.2
ALT (U/L)	67
AST (U/L)	93
Uric acid (mg/dL)	15.5
LDH (U/L)	2234

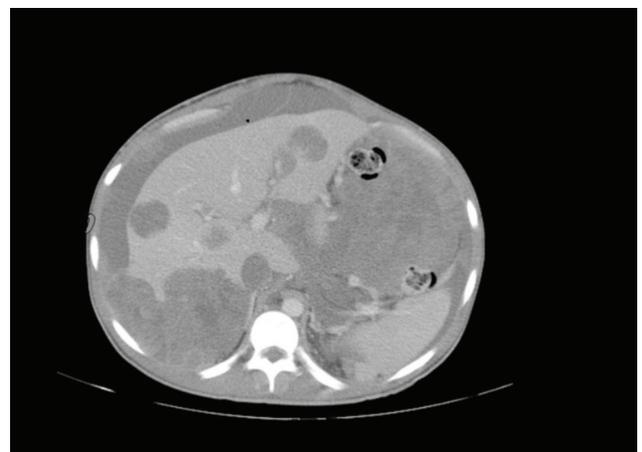
ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase.

frequent foci of necrosis (Figure 2a).

The immunohistochemical (IHC) study revealed that the malignant cells expressed microneme protein 2 (MIC2) in a membranous pattern (Figure 2b) with cytoplasmic staining of vimentin and neuron-specific enolase (NSE) as seen in Figure 2c. The tumor cells had a high proliferative index of Ki67 more than 90% (Figure 2d). Other IHC markers were assessed to rule out small cell tumor with MIC2 expression such as lymphoblastic lymphoma, leukemia, and rhabdomyosarcoma. However, there was no expression of MyoD1, desmin, LCA, TdT, CD3, CD20, or cytokeratin.

According to both histology and IHC, the diagnosis was in favor of PNET.

The patient received the VAC chemotherapy regimen (vincristine, doxorubicin and cyclophos-



**Figure 1.** Abdominopelvic spiral CT scan with contrast revealed multiple low attenuated liver masses in favor of metastasis.

**Table 2.** Cairo-Bishop criteria for tumor lysis syndrome in adults

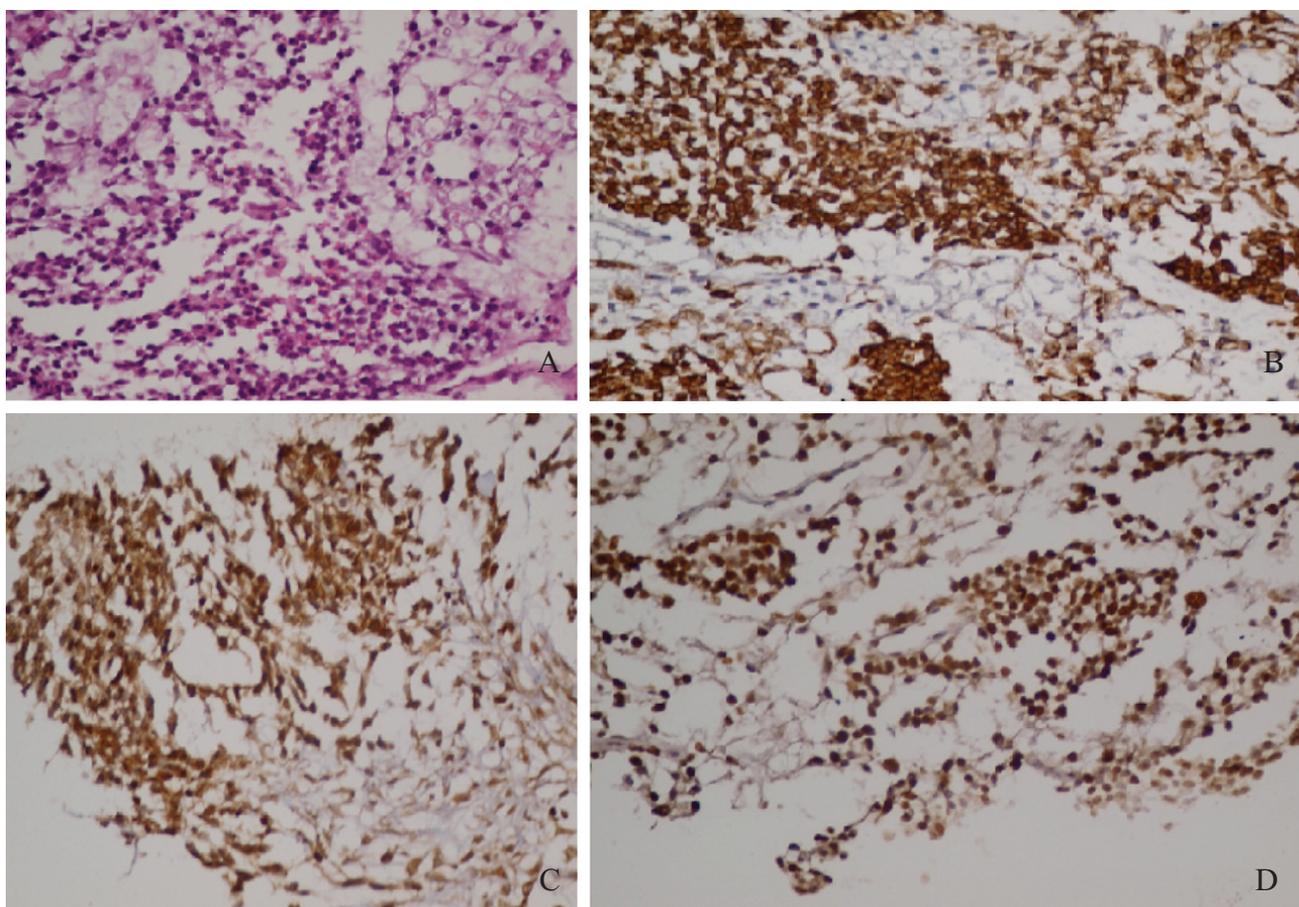
	Factor	Value
Laboratory tumor lysis	Uric acid	$\geq 8$ mg/dL or 25% increase from baseline
	Potassium	$\geq 6$ mEq/L or 25% increase from baseline
	Phosphorus	$\geq 4.5$ mg/dL or 25% b emincrease from baseline
	Calcium	$\leq 7$ mg/dL or 25% decrease from baseline
Clinical tumor lysis	Creatinine	$\geq 1.5 \times$ ULN
	Arrhythmia/sudden cardiac death	
	Seizures	

phamide) and was discharged in good condition after 10 days. After two courses of VAC/IE protocol (vincristine, doxorubicin and cyclophosphamide alternating with Ifosfamide+etoposide) chemotherapy, a follow-up abdominopelvic ultrasound showed that all metastases had disappeared in the liver and the mass size in the pelvic cavity was reduced to 5.5×6 cm.

## Discussion

Although TLS is commonly observed in hematologic malignancies, it can be seen in solid tumors, especially after cytotoxic chemotherapy, radiotherapy, targeted antibody therapy, and even glucocorticoids.<sup>6</sup>

The classic findings of TLS are hyperkalemia, hyperphosphatemia with secondary hypocalcemia, and hyperuricemia. These electrolyte abnormalities



**Figure 2.** A. The tumor is composed of small malignant cells (H&E, 400×). B. Cytoplasmic staining of microneme protein 2 (MIC2), (IHC, 400×). C. Cytoplasmic expression of neuron-specific enolase (NSE), (IHC, 400×). D. High proliferative index (IHC, 400×). IHC: Immunohistochemical.

can lead to cardiac arrhythmia, seizures, or acute renal failure, which could be life-threatening without prompt recognition and/or treatment.<sup>7</sup> In solid tumors, TLS has a poor prognosis with a mortality rate between 20-50%.<sup>9,10</sup>

Spontaneous TLS which occurs in the absence of any definitive therapy is a rare event in patients with solid tumors.<sup>11</sup> Advanced tumor and metastasis might be potential risk factors for TLS.<sup>12</sup>

Sommerhalder et al., in a literature review, reported 28 cases of solid tumors with spontaneous TLS.<sup>9</sup>

Extensive liver metastases have been reported in 82.8% of total cases.<sup>9</sup> This might be due to a high purine pool in the liver that can be released during necrosis or impaired uric acid metabolism if hepatic function is impaired by a high tumor burden.<sup>13</sup> In the aforementioned study, patients without liver metastasis had a large tumor burden and necrosis. It is unclear whether liver metastasis represents an individual risk factor for TLS or is a marker of advanced disease.<sup>9</sup>

In this case report, the patient demonstrated spontaneous TLS caused by PNET. The patient had renal failure, hyperuricemia, and hyperphosphatemia according to clinical TLS criteria, in the setting of widespread metastatic disease. It seemed that TLS in our patient was due to tumor bulkiness and advanced disease, liver metastasis, and a high LDH level.

To the best of our knowledge, only one case of spontaneous TLS associated with PNET has been reported in the literature,<sup>14</sup> in a 10-year-old boy. Our patient was the first case of spontaneous TLS in an adult with PNET.

## Conclusion

Caution should be taken when managing bulky, advanced solid tumors, especially those with liver metastasis. Early diagnosis and aggressive management should be performed to prevent fatal outcomes.

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## Conflict of Interest

None declared.

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