Case Report

Spontaneous tumor lysis syndrome in a patient with advanced gastric adenocarcinoma: a case report

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Abstract: Tumor lysis syndrome (TLS) is an oncologic emergency that usually occurs after initial treatment of a malignant tumor. It manifests as hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia, ultimately resulting in acute kidney failure, seizures, cardiac arrhythmias, and even death. Here, we report a very rare case of spontaneous TLS in a patient with advanced gastric adenocarcinoma who eventually succumbed to renal failure. Extra vigilance towards electrolyte imbalances should be given during initiation of therapy in cases of large gastric cancer with severe distant metastasis. Risk assessment prior to surgery, early diagnosis and comprehensive treatment strategies are vital in improving the prognosis of gastric cancer patients with TLS. Urgent hemodialysis should be implemented as soon as possible in order to prevent further renal deterioration.

Keywords: Tumor lysis syndrome (TLS); gastric cancer; renal failure; risk assessment; hemodialysis

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Introduction

Tumor lysis syndrome (TLS) is an oncologic emergency that usually occurs after the initial treatment of a malignant tumor. Chemotherapy often causes lysis of large quantities of tumor cells, leading to the release of intracellular contents into the blood which causes hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia. These electrolyte and metabolic abnormalities ultimately result in symptoms such as acute kidney failure, seizures, cardiac arrhythmias, and even sudden death (1-3).

TLS commonly occurs in hematologic cancers in view of their high cell turnover, rapid proliferation rates and increased chemosensitivity (4). While the incidence of TLS has been increasingly reported in solid tumors (5-9), TLS in gastric cancer is uncommon (10). TLS usually occurs within a week of initiation of cytotoxic therapy and may occur spontaneously in certain circumstances (11-13). Here, we report a rare case of spontaneous TLS in a patient with advanced gastric cancer.

Case presentation

A 62-year-old gentleman was admitted in the Second Affiliated Hospital of Zhejiang University, School of Medicine, with a 20-day history of worsening weakness and poor appetite. This was associated with discomfort of the right flank, hard stools and a loss of weight of 5 kg over one month. No nausea, vomiting or fever were reported. The patient had no history of renal disease. Physical examination on admission revealed BMI of 24.2 (a height of 172 cm and a weight of 71.6 kg). Left cervical lymph nodes were not palpable. Mild tenderness was present in the epigastric region. Gastroscopy showed a huge annular irregular mass on the wall of lower two thirds of the gastric body with peripheral mucosa edema (*Figure 1*). Biopsy confirmed the presence of a low-grade adenocarcinoma. Abdominal enhanced CT scan revealed a large-scale thickness (size of 9 cm) of the gastric wall with serosa invasion, infiltration of the left lower ureter, multiple enlarged perigastric lymph nodes (lymph nodes No. 2, 4, 5, 6), suspicious metastatic

nodes in greater omentum, and a small amount of pelvic effusion (*Figure 2*). Furthermore, ^{18}F-fluorodeoxyglucose (FDG) PET/CT scan showed that diffuse enhancement in the stomach (SUVmax =6.72), perigastric lymph nodes (SUVmax =4.22), a blurry omentum and a small amount of pelvic effusion (*Figure 2*).

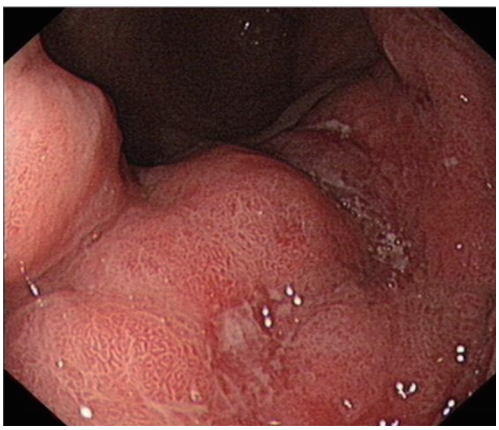

Figure 1 Gastroscopy showed a huge annular irregular swelling mass on the gastric body.

Laboratory findings at admission are as follows: white blood cells: 13.8×10^9/L (normal range, 4.0–10.0×10^9/L), hemoglobin: 143 g/L (normal range, 131–172 g/L), sodium:137.4 mmol/L (normal range, 135–145 mmol/L), potassium: 5.32 mmol/L (normal range, 3.50–5.50 mmol/L), calcium: 2.37 mmol/L (normal range, 2.08–2.60 mmol/L), phosphorus: 2.20 mmol/L (normal range, 0.81–1.45 mmol/L), serum creatinine (Cr): 437 μmol/L (normal range, 40–106 μmol/L), uric acid: 8.74 mg/dL (normal range, 3.50–7.20 mg/dL), urea nitrogen: 23.76 mmol/L (normal range, 2.80–7.20 mmol/L), lactic dehydrogenase (LDH): 353 U/L (normal range, <248 U/L), tumor marker CA-199: 926.9 U/mL (normal range, <37 U/mL) and tumor marker CA-242: 20.4 U/mL (normal range, <20 U/mL). Laparoscopic exploration was performed on the ninth day of admission, revealing numerous white nodules in the peritoneum, ligamentum teres hepatis, and pelvic cavity (*Figure 3*). Intraoperative frozen section one nodule revealed metastatic low-grade adenocarcinoma. Numerous free tumor cells were observed upon microscopic inspection

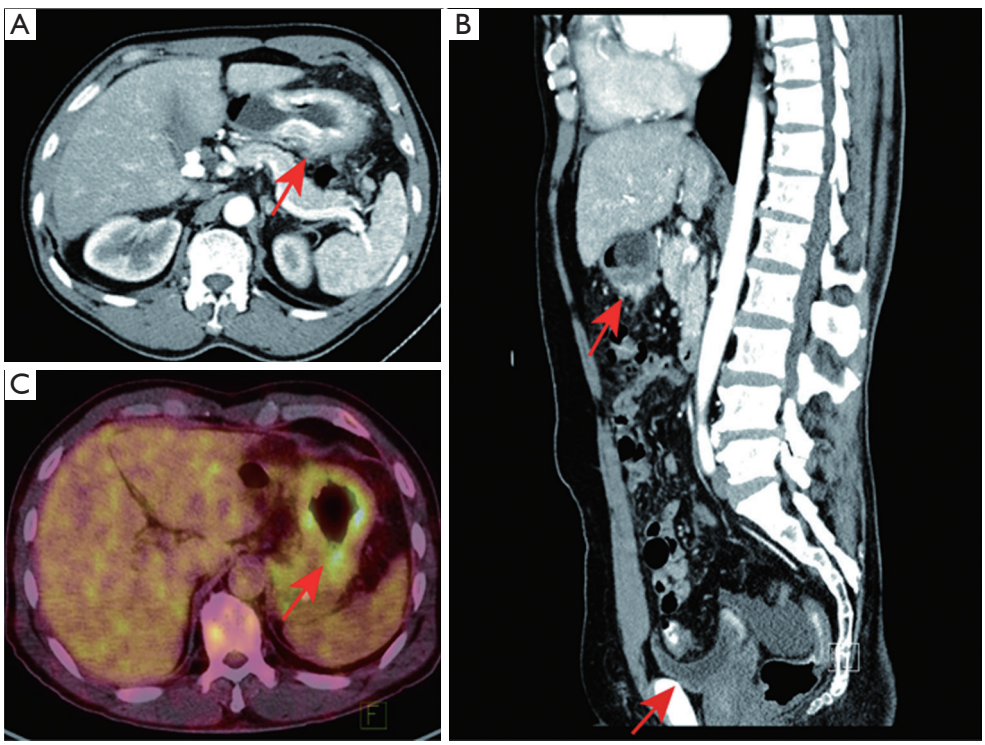

Figure 2 Radiological examinations. (A,B) Abdominal enhanced CT scan revealed a large-scale thickness of gastric wall with serosa invasion (red arrow), multiple enlarged perigastric lymph nodes, suspicious metastatic nodes in greater omentum, and a small amount of pelvic effusion (red arrow); (C) ^{18}F-fluorodeoxyglucose (FDG) PET/CT scan showed diffuse enhancement in stomach (red arrow), perigastric lymph nodes, and a blurry omentum.

of the peritoneal lavage fluid (*Figure 4*).

An intraabdominal catheter was inserted in preparation of subsequent intraperitoneal chemotherapy. Surprisingly, the patient's renal function deteriorated immediately after surgery, as evidenced by a serum creatinine level of 746 μmol/L. On the nineteenth day of admission, bilateral ureteral stents were inserted in order to alleviate ureteral obstruction. Subsequently, serum creatinine declined to 150 μmol/L. Nevertheless, this decrease was short-lived as serum creatinine began to rise gradually again. Potassium and phosphorus levels were slightly increased, while calcium levels remained low during the entire course of treatment. Inflammatory biomarkers such as white blood cells and C-reactive protein (CRP) were relatively high despite anti-infection therapy (*Table 1*) (*Figure 5*). The patient was diagnosed as having TLS during multi-disciplinary team (MDT) discussion of the case. Subsequently, the patient was treated with volume expansion, diuretics, sodium bicarbonate, anti-infective therapy, with the aim to improve his electrolyte imbalances. Despite these interventions, serum creatinine continued rising, reaching a peak of 1,005 μmol/L. The patient refused hemodialysis and eventually succumbed to renal failure a month after his initial surgery.

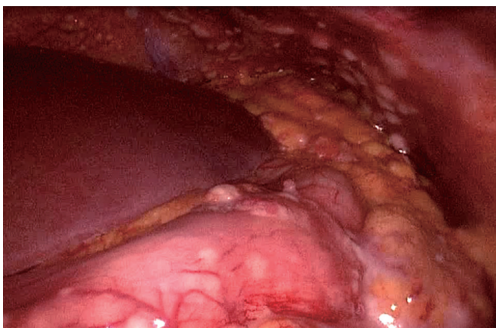

Figure 3 Laparoscopy observed numerous white nodules in abdominal cavity.

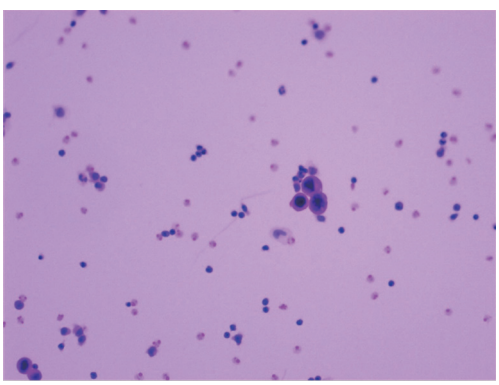

Figure 4 Free tumor cells observed under microscopical examination of the peritoneal lavage (H&E stain, ×400).

Discussion

TLS is frequently reported during initiation of therapy against malignant tumors. It comprises of a series of metabolic abnormalities caused by massive release of intracellular contents into the blood that exceeds the ability of renal clearance. It is manifested by hyperuricaemia, hyperkalaemia, hyperphosphataemia and hypocalcaemia (1-3). While there is currently no universal definition of TLS, the most accepted TLS classification was proposed by Cairo and Bishop, which was modified from works of Hande and Garrow (14). Based on the Cairo and Bishop

Table 1 Laboratory examinations during the time of hospital

Date	Serum creatinine (μmol/L)	Uric acid (mg/dL)	Potassium (mmol/L)	Phosphorus (mmol/L)	Calcium (mmol/L)	White blood cells ($\times 10^9$/L)	CRP (mg/L)	Urine output per day (mL/kg)
Day 1	437	8.74	5.32	2.20	2.37	13.8	–	–
Day 18	746	–	6.22	–	2.12	6.1	0.5	48.6
Day 26	150	–	3.83	–	–	8.3	–	41.9
Day 32	372	–	5.10	–	–	18.8	75.5	38.2
Day 37	777	–	6.12	–	–	12.5	64.6	23.5
Day 39	834	–	6.04	1.95	2.03	12.9	80.4	36.2
Day 43	1,005	6.17	5.24	2.25	1.79	10.1	156.1	8.3

CRP, C-reactive protein.

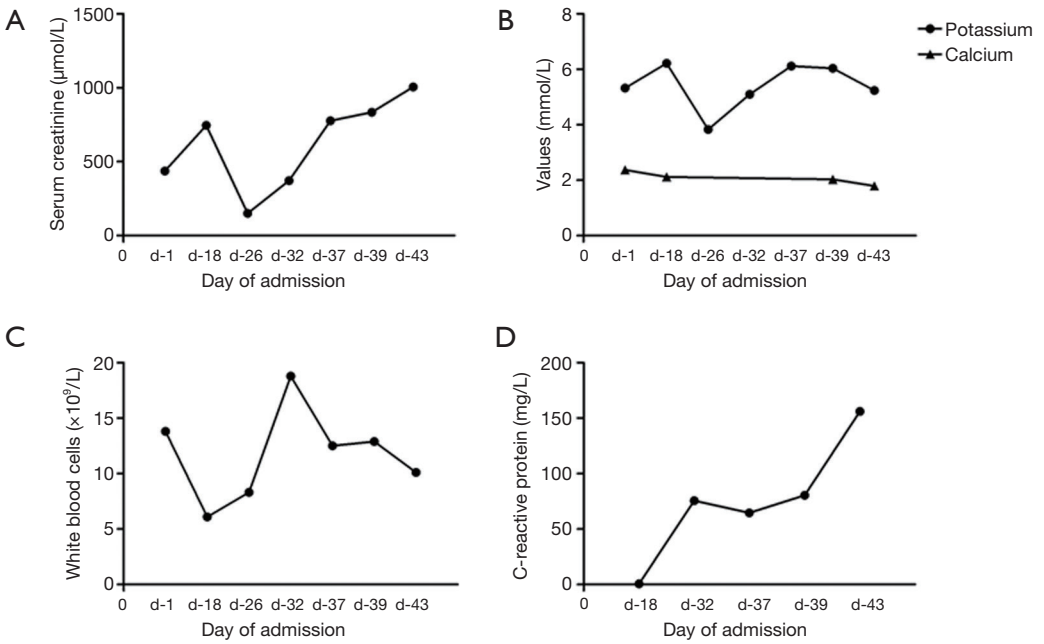

Figure 5 Trends of serum creatinine (A), potassium, calcium (B), white blood cells (C) and C-reactive protein levels (D).

classification, TLS is stratified into laboratory TLS (L-TLS) and clinical TLS (C-TLS). L-TLS is defined as changes in any two or more measurable values, including uric acid of 8 mg/dL or greater, potassium 6 mmol/L or greater, phosphorus 2.1 mmol/L or greater, calcium 1.75 mmol/L or less, or a 25% change from baseline in any of these electrolytes. C-TLS is defined as presence of L-TLS and at least one clinical manifestation including renal insufficiency, arrhythmia, seizure or sudden death (15). The patient in our case suffered from hyperuricemia (8.74 mg/dL) and hyperphosphataemia (2.20 mmol/L) at baseline, and experienced a decrease in calcium at almost 25% from baseline as well as along with renal insufficiency (1,005 μmol/L). These findings fulfill the criteria of both L-TLS and C-TLS.

TLS is usually associated with haematological malignancies in view of the large cell turnover, higher proliferation rates and increased chemosensitivity of these cells (4,14,16,17). Despite the increasing reports of TLS in solid tumors, the incidence of TLS in gastric adenocarcinoma is very rare (10). To the best of our knowledge, there were only 5 reports of TLS in gastric adenocarcinoma (10,18-21). Three of them were chemotherapy-induced while another two developed spontaneous TLS. However, the patient in one of the case reports of spontaneous TLS was noted to have received chemotherapy 2 months prior to the development of TLS, while the other case report of a patient with spontaneous TLS was diagnosed at time of presentation. While the risk factors for the development of spontaneous TLS has yet to be identified, previous studies have revealed several risk factors that may be associated with spontaneous TLS in solid tumor, such as tumor extension, a large initial tumor burden, bulky tumors, extensive metastasis, extrinsic compression of the genitourinary tract by the tumor, tumor cells with high proliferative rate, and abnormal pretreatment laboratory findings such as elevated LDH, serum creatinine, and uric acid. Patient-related factors such as preexisting nephropathy, hypotension, and obstructive uropathy are also risk factors for developing TLS (10). In this report, the patient was diagnosed with metastatic gastric cancer, an indication of a large tumor burden. Furthermore, this patient was found to have elevated LDH, serum creatinine, and uric acid levels at the point of presentation. Ureteral obstruction was also present in this patient. All these factors placed this patient at a high risk of developing TLS. Additionally, surgical procedures and severe infection may have further increased the risk of TLS in this patient as operative procedures have the potential to trigger tumor cell death or to stimulate tumor cell growth.

The metabolic abnormalities in TLS, if untreated, will lead to life-threatening complications such as acute kidney

failure, seizures, cardiac arrhythmias, and even death. A study by Vodopivec *et al.* estimates the mortality of TLS in solid tumors to be approximately 41% (10). Early recognition and prevention are especially crucial for patients at high risk. Treatment of TLS focuses on correction of electrolyte disturbances and preservation of renal function. A typical TLS treatment regimen involves volume expansion, urinary alkalinisation, allopurinol, rasburicase, or even dialytic modalities if necessary (1,22). Our patient received volume expansion, urinary alkalinisation and correction of electrolyte disturbances as soon as he was diagnosed as TLS. Nevertheless, his renal function continued to deteriorate, and without the initiation of life-saving haemodialysis, this patient eventually succumbed to his disease.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/tcr.2019.07.53). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the relatives of the patient for publication of this case report and any accompanying images.

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