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Chemotherapy-Induced Tumour Lysis Syndrome in Gastric Adenocarcinoma with Diffuse Liver Metastases: A Case Report

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Abstract

Tumour Lysis Syndrome (TLS) is an important oncological emergency case which is often found together with haematological malignities and, much less often, with solid tumours. While TLS seen in solid tumour cases usually develops following a cytotoxic chemotherapy and its prognosis is poor. We present the case of a 60-year-old man with gastric adenocarcinoma with diffuse liver metastases (image shows diffuse liver metastatic lesions) and high serum LDH levels, who developed TLS after systemic chemotherapy. With urgent and proper supportive treatment (intravenous intensive hydration, sodium bicarbonate, diuretic, calcium gluconate, allopurinol and haemodialysis), an impressive recovery from TLS was achieved in the patient with an advanced stage gastric cancer. The purpose of this report is to emphasize that although the present case was a rare, high physician attention is required because significant morbidity or mortality may occur when the syndrome is not duly considered during the pre-cytotoxic evaluation of the patient, when preventive measures are not taken, or if the appropriate treatment is not applied immediately once the syndrome appears, especially in patients who have high tumour burden solid cancer.

Keywords

Tumour Lysis Syndrome, Gastric Cancer, Chemotherapy, Solid Tumour

1. Introduction

Tumour Lysis Syndrome (TLS) is an oncometabolic syndrome which initially appears as the tumour cells rapidly lysis, followed by metabolic anomalies which

can become life-threatening. The aforementioned metabolic anomalies arise as a result of the leakage of intracellular ions, nucleic acid, protein and metabolites into the extracellular fluid [1]. Fast-releasing metabolites cause disorder in the regular haemostatic metabolism of the body, resulting in laboratory anomalies such as hyperuricaemia, hyperkalemia, hypophosphatemia and hypocalcaemia. As a result of such anomalies the patient will often develop clinical outcomes such as renal failure and, occasionally, cardiac arrhythmias. Although TLS is usually discovered upon initiation of chemotherapy, more rarely, and particularly in cases where a fast-growing tumour is present, it can be seen before treatment as well, as a result of the malignant cells' self-lysis [2] [3]. If the required measures are not taken and the existing clinical entity is not treated immediately, metabolic anomalies of cancer patients can result in renal impairment, cardiac arrhythmia, neurological complication and sudden death. Our purpose herein is to present a case of TLS which developed after chemotherapy in a patient with metastatic gastric adenocarcinoma.

2. Case Report

A 60-year-old male patient presented with weight loss, loss of appetite, and a stomach ache which he had been experiencing for the two months prior to his consultation. The patient had not had any previously known chronic disease. The findings of the physical examination were diffuse sensitization around the abdominal region, along with solid, palpable and painful hepatomegaly.

Laboratory testing produced the following results: ALT: 70 U/L (normal range: 0 to 41 U/L), AST: 89 U/L (normal range: 0 to 31 U/L), WBC: 9.4×10^3/mL (normal range: 4×10^3/mL to 11×10^3/mL), hemoglobin: 12.2 gr/dL (normal range: 11 to 18 g/dL), platelets: 325×10^3/mL (normal range: 150×10^3/mL to 400×10^3/mL), total bilirubin: 0.5 mg/dl (normal range: 0.2 to 1.2 mg/dL), creatinine kinase: 384 U/L (normal range: 38 to 174 mg/dL). A chemistry panel revealed the following: Creatinine 0.7 mg/dL (normal range: 0.7 to 1.3 mg/dL), uric acid 8.5 mg/dL (normal range: 0 to 5.7 mg/dL), lactate dehydrogenase (LDH): 1538 U/L (normal range: 125 to 220 U/L), potassium: 4.7 mEq/L (normal range: 3.5 to 5.5 mEq/L), sodium was 140 mEq/L (normal range: 136 to 145 mmol/L), calcium: 8.4 mg/dL (normal range: 8.8 to 10.5 mg/dL), phosphorus: 3.5 mg/dL (normal range: 2.5 to 4.5 mg/dL).

The computerized tomography (CT) scan revealed a diffused mural thickening (tumour) of the 8 cm segment between the gastric cardia to fundus and corpus; the thickest section measured 2 cm. Multiple metastatic lymphadenopathies were observed at this level on the gastrohepatic ligament and perilesional area. There were multiple metastatic lesions filling the liver parenchyma; the largest was 6 cm in diameter. Millimetric implants were also present in the peritoneum. Intraabdominal free fluids were also observed (**Figure 1**).

Esophagogastroduodenoscopy showed a 8-cm sized ulcerofungating mass starting from the gastric cardia and leading through the posterior wall of the

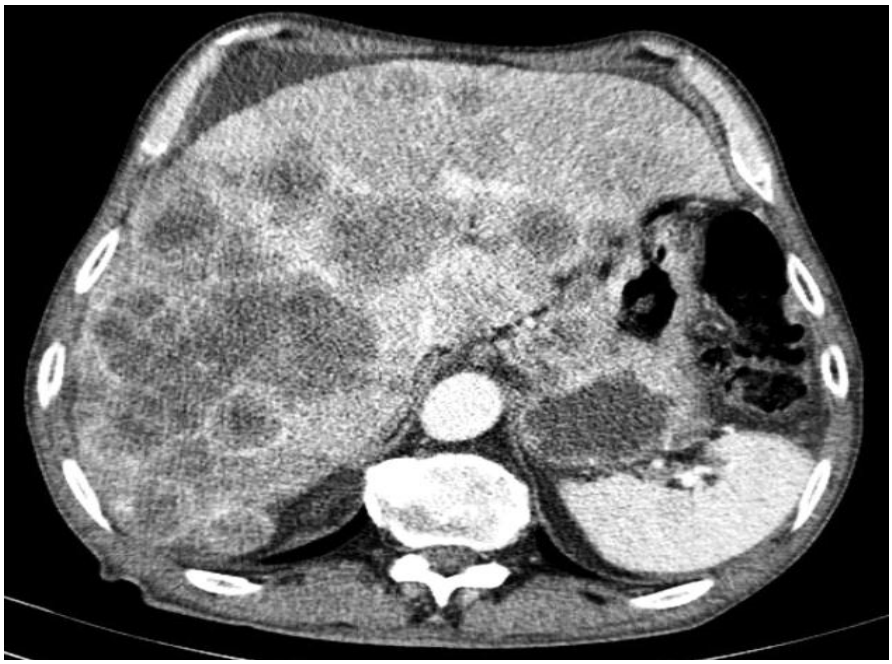

Figure 1. Computed tomography scan of abdomen showed gastric body wall thickening and extensive metastases with multiple hepatic lesions, intraabdominal fluid, perigastric and retroperitoneal lymphadenopathies.

corpus of the gastric body. The result of the endoscopic biopsy was found to correspond to poorly differentiated gastric adenocarcinoma. It was decided that the patient should be treated with palliative chemotherapy based on a diagnosis of advanced gastric cancer with multiple metastases in liver, lymph nodes of abdomen and malignant ascites. The patient began treatment with cisplatin (100 mg/m^2, intravenously, on 1 day), and 5-fluorourasil (800 mg/m^2, continuous infusion, for 1 - 4 days) in a 4-week cycle.

Laboratory findings 5 days after completion of the chemotherapy for the patient are as follows: Creatinine: 3.8 mg/dL (normal range: 0.7 to 1.3 mg/dL), uric acid: 16.9 mg/dL (normal range: 0 to 5.7 mg/dL), LDH: 1909 U/L (normal range: 125 to 220 U/L), potassium: 5.6 mmol/L (normal range: 3.5 to 5.1 mmol/L), sodium: 136 mmol/L (normal range: 136 to 145 mmol/L), calcium: 7.8 mg/dL (normal range: 8.4 to 10.7 mg/dL), phosphorus: 9 mg/dL (normal range: 2.7 to 4.5 mg/dL), ALT: 111 U/L (normal range: 0 to 41 U/L), AST: 114 U/L (normal range: 0 to 31 U/L), WBC: 15.5 × 10^3/mL (normal range: 4 × 10^3/mL to 11 × 10^3/mL), hemoglobin: 9.6 g/dL (normal range: 11 to 18 g/dL), platelets: 78.000 × 10^3/mL (normal range: 150 × 10^3/mL to 400 × 10^3/mL).

Urinary ultrasonography of the patient showed no signs of an obstruction. Based on consideration of the laboratory findings, the patient was diagnosed with tumour lysis syndrome. Treatment was initiated immediately with intensive hydration, sodium bicarbonate, diuretic, calcium gluconate, allopurinol and at the end haemodialysis treatments were carried out. Upon the patient's laboratory findings returning to normal values, the patient was duly discharged from the hospital.

3. Discussion

Clinical entities caused by cancer which result in morbidity or mortality are becoming more and more frequent, discovered either by means of technological advances or due to increasing experience in the field. TLS is an oncological emergency case which has a place among the metabolic anomalies caused by cancer. TLS usually consists of a scheme of metabolic anomalies which arise following cytotoxic chemotherapy and is life-threatening one's life when untreated [1] [4]. While cytotoxic chemotherapy is the most common trigger, it is not the sole cause of TLS. TLS can also develop spontaneously through radiotherapy, hormonotherapy, liver tumour radio-frequency ablation, corticosteroids, immunotherapy (interferon or interleukin), and following surgical treatments [5].

The disease was first defined by Hande and Garrow. This definition separates TLS into 2 groups, the first consisting only of laboratory finding anomalies, while the second specifies life-threatening clinical problems as well [4]. Taking the aforementioned classification as a basis, laboratory TLS is defined as certain minimal levels, or a more than 25% increase over pre-chemotherapy baseline levels, of uric acid, potassium, calcium, and phosphorus (**Table 1**) within the first 4 days following chemotherapy [1]. Along with the laboratory anomalies, the definition of clinical TLS consists of suffering from serious clinical toxicities such as acute renal insufficiency, cardiac arrhythmias or seizure. In order for the TLS diagnosis to be made on the basis of laboratory criteria, at least 2 of the above given criteria must have appeared 3 days prior to treatment and/or 7 days following the treatment. As for the clinical diagnosis, a minimum of 1 clinical symptom must be accompanied by at least 2 laboratory criteria.

During the treatment of haematological malignancy, the incidence frequency of TLS following chemotherapy is reported to vary between 4% and 42%, which is quite a wide range [6]. The incidence frequency of life-threatening complications in cases of haematological malignancy is as high as 13% [6]. As for patients with solid tumours, there is no clear data on the incidence frequency of TLS. However, in cases where TLS occurs in such patients, it will result in death for 1 out of every 3 patients. As a result of the increase in clinical experience, protective measures are taken more frequently and more efficiently.

Despite the fact that such tumour-related properties appear quite valid for haematological malignancy, the validity of the other aforementioned mechanisms for solid tumours has not been able to be proven thus far [5]. In some studies performed on solid tumours, despite the fact that they are known to bear some risks, the incidence frequency of TLS has been found to be quite low [7] [8]. Primary solid tumours associated with TLS include testicular cancer, small cell lung cancer, ovarian cancer, breast cancer, melanoma, medulloblastoma, leiomyosarcoma, sarcoma, vulvar cancer, neuroblastoma, rhabdomyosarcoma, hepatoblastoma, hepatocellular carcinoma, thymoma, Merkel cell carcinoma, colon cancer and gastric adenocarcinoma [5] [9]. TLS, due to gastric cancer in the literature, is limited to a few cases. TLS is observed in cases of gastrointestinal-derived poorly

Table 1. Cairo-Bishop diagnostic criteria for tumour lysis syndrome.

*Laboratory criteria	
• Uric acid ≥ 8 mg/dl (476 μmol/mL)	or a 25% increase from baseline
• Phosphorus ≥ 4.5mg/dl (1.45 mmol/L)	or a 25% increase from baseline
• Potassium ≥ 6 mEq/L (6.0 mmol/L)	or a 25% increase from baseline
• Corrected calcium ≤ 7 mg/dL (1.75 mmol/L)	or a 25% decrease from baseline
***Clinical criteria**	
• Creatinine ≥ 1.5 times the upper limit of normal	
• Cardiac arrhythmia or sudden death	
• Seizure *May not be directly related to a therapeutic agent	

Modified from Cairo MS and Bishop M (1).

differentiated anaplastic carcinomas more frequently than with solid tumours.

The most critical point with this syndrome is to determine the patient group at risk and to take prophylactic precautions before starting treatment. There are various factors which trigger the occurrence of TLS. Factors related to the tumors themselves include short tumour duplication interval, a fast-growing fraction and high cellular cycle rate, high tumour burden, a disseminated tumour, tumours which are highly sensitive to chemotherapy, tumours which apply external pressure to the genitourinary tract, and high LDH and uric acid levels. Predisposing factors related to the patient's condition are dehydration, low urine flow and renal failure.

Specifically, in solid tumors, the risk factors for the occurrence of TLS can be summarized as follows; pre-treatment azotemia, high LDH, exposure to nephrotoxic agent, oliguria, presence of an infection, dehydration, presence of liver metastases and hyperuricaemia [5]. TLS is not expected to occur in cases of chemotherapy non-sensitive solid tumours, even when the tumour size is large. However, it has a poor prognosis when it does occur [3]. One remarkable aspect regarding TLS is the presence of liver metastases (with or without liver function abnormalities) in most patients with solid tumours, just as we observed in our case. Diffuse liver involvement seems to predispose patients to TLS, either due to high purine pools, high tumour burden or impaired uric acid metabolism disorder in solid tumours [5].

Post-chemotherapy high LDH values, hyperuricaemia and decrease in renal function are warning signs for TLS and suggest the possibility of acute tumour lysis syndrome. Rapid lysis of the tumour cells, releasing the intracellular elements into the extracellular environment, leads to renal insufficiency and tumour lysis syndrome. This can cause sudden death due to the rapid increase in serum potassium and phosphorus levels and cardiac arrhythmia. Hypocalcaemia causes muscle cramps, dizziness and tetania. Reported mortality rates for TLS cases left untreated are 47% - 100% [10].

Both in cases of haematological malignity and cases where solid tumours have developed, the approach is almost the same: protection, early diagnosis, and improvement of the biochemical and clinical anomalies. High-risk patients should

be identified prior to treatment, then closely monitored and hydrated so as to obtain sufficient urination. Pharmacological agents for the purpose of prophylaxis should also be used, where necessary. Agents used for prophylaxis include allopurinol, a xanthine oxidase inhibitor which prevents the formation of uric acid out of xanthine, uricozyme (non-recombinant urate oxidase), and rasburicase (recombinant urate oxidase), which turns uric acid into allantoin, a more soluble molecule and one of the urate oxidase enzymes. Proper use of these agents reduces the rate of TLS incidence significantly. Another important point is that as soon as biological anomalies start to appear, a multidisciplinary approach should be adopted. Working in coordination with the nephrology department, hyperkalemia, hypophosphatemia, hypocalcaemia, hyperuricaemia and acute renal insufficiency cases have to be treated correctly. As seen in our case, haemodialysis, when required, should not be delayed, thereby preventing significant risk of morbidity and mortality.

4. Conclusion

In the case that we have presented herein, the patient who underwent combination chemotherapy due to advanced stage gastric adenocarcinoma (especially diffuse liver metastases) developed TLS following the treatment. As detailed above, although rarely seen with solid tumours, TLS can appear in patients with large diameter tumours, diffused liver metastasis, chemotherapy-sensitive tumours and high LDH levels, and its mortality rate is higher in comparison with haematological malignancy. Accordingly, to prevent tumour lysis syndrome in high-risk patients, the risks should be considered before treatment, biochemical parameters have to be observed, a strict monitoring should be implemented and pre-treatment preventive measures must be taken.

Conflict of Interests

The authors declare that they have no conflict of interest.

Informed Consent Statement

Informed consent has been taken from the patient.

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References

[1] Cairo, M.S. and Bishop, M. (2004) Tumour Lysis Syndrome: New Therapeutic Strategies and Classification. *British Journal of Haematology*, **127**, 3-11. https://doi.org/10.1111/j.1365-2141.2004.05094.x

[2] Davidson, M.B., Thakkar, S., Hix, J.K., *et al.* (2004) Pathophysiology, Clinical Consequences, and Treatment of Tumour Lysis Syndrome. *American Journal of Medicine*, **116**, 546-554. https://doi.org/10.1016/j.amjmed.2003.09.045

[3] Kekre, N., Djordjevic, B. and Touchie, C. (2012) Spontaneous Tumour Lysis Syndrome. *CMAJ*, **184**, 913-916. https://doi.org/10.1503/cmaj.111251

[4] Hande, K.R. and Garrow, G.C. (1993) Acute Tumour Lysis Syndrome in Patients with High-Grade Non-Hodgkin's Lymphoma. *American Journal of Medicine*, **94**, 133-139. https://doi.org/10.1016/0002-9343(93)90174-N

[5] Gemici, C. (2006) Tumour Lysis Syndrome in Solid Tumours. *Clinical Oncology*, **18**, 773-780. https://doi.org/10.1016/j.clon.2006.09.005

[6] Coiffier, B., Altman, A., Pui, C.H., *et al.* (2008) Guidelines for the Management of Pediatric and Adult Tumour Lysis Syndrome: An Evidencebased Review. *Journal of Clinical Oncology*, **26**, 2767-2778. https://doi.org/10.1200/JCO.2007.15.0177

[7] Arrambide, K. and Toto, R.D. (1993) Tumour Lysis Syndrome. *Seminars in Nephrology*, **13**, 273-280.

[8] Kattan, J., Culine, S., Tavakoli-Razavi, T., *et al.* (1994) Acute Tumour Lysis Syndrome in Poor-Risk Germ Cell Tumours: Does It Exist? *Support Care Cancer*, **2**, 128-131. https://doi.org/10.1007/BF00572095

[9] Barton, J.C. (1989) Tumor Lysis Syndrome in Nonhematopoietic Neoplasms. *Cancer*, **64**, 738-740. https://doi.org/10.1002/1097-0142(19890801)64:3<738::AID-CNCR2820640328>3.0.CO;2-Z

[10] Garnick, M.B. and Mayer, R.J. (1978) Acute Renal Failure Associated with Neoplastic Disease and Its Treatment. *Seminars in Oncology*, **5**, 155-165.