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Spontaneous Acute Tumor Lysis Syndrome with Advanced Gastric Cancer

Acute tumor lysis syndrome (TLS) occurs frequently in hematologic malignancies such as high-grade lymphomas and acute leukemia, which are rapidly proliferating and chemosensitive tumors. It occurs rarely in solid tumors and has never been reported in gastric adenocarcinoma. Typical biochemical findings of acute tumor lysis syndrome are hyperuricemia, hyperkalemia, hyperphosphatemia and hypocalcemia in patients with a malignancy. Rapid changes of these electrolytes may cause cardiac arrhythmia, seizure, acute renal failure and sudden death. Therefore, as soon as it is detected, it should be taken care of immediately. Until now almost all cases of TLS associated with solid tumor have developed after cytoreductive therapy in chemosensitive tumors. We report here a case of spontaneous acute tumor lysis in a patient of advanced gastric cancer with hepatic metastases and multiple lymphadenopathy. The biochemical finding of TLS improved with the management and tumor burden also showed slight response to the one cycled combination chemotherapy but the patient died of progressive pneumonia.

Key Words: *Tumor Lysis Syndrome; Stomach Neoplasms; Solid Tumor*

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INTRODUCTION

An oncologic emergency, acute tumor lysis syndrome (TLS) causes rapid and severe metabolic changes manifested with hyperkalemia, hyperuricemia, hyperphosphatemia and hypocalcemia. We can usually expect the tumor lysis before cytoreductive therapy in neoplasms that have high cell turnover, large tumor burdens and sensitivity to chemotherapy or radiotherapy. Hence, TLS should and can be prevented. High-grade lymphoma may accompany spontaneous tumor lysis syndrome at the time of its presentation. In solid tumors, TLS rarely occurs, but there have been reports of it associated with breast cancer (1, 2), small cell lung cancer (3), medulloblastoma (4) and adenocarcinoma (5). We describe a case of a 36-yr-old man with advanced gastric cancer who has an acute TLS, which developed spontaneously without treatment.

CASE REPORT

A 36-yr-old man was admitted with a 15-day history of abdominal fullness and pain. He had no symptoms or history of renal disease or gout. Vital signs were blood pressure 130/70 mmHg, pulse rate 116/min, respiratory rate 24/min and body temperature 36.4℃. He was alert but looked lethargic. On examination, a 3×3 cm sized lymph node enlargement at the left supraclavicular area and a big, firm, nontender hepatomegaly were also noticed. The hepatomegaly extended 11 cm distally from the end of the xiphoid process and 9 cm and 2 cm below the costal margin of the right midclavicular and midaxillary region respectively. There was no other peripheral lymphadenopathy. Laboratory findings at admission were as follows: leukocyte count 11,660/μL, hemoglobin 10.7 g/dL, hematocrit 33.9%, uric acid 16.9 mg/dL (normal; 2.9-7.3 mg/dL), blood urea nitrogen 36 mg/dL (10-26 mg/dL), creatinine 2.9 mg/dL (0.6-1.2 mg/dL), calcium 7.0 mg/dL (8.4-10.2 mg/dL), phosphorus 6.9 mg/dL (2.6-4.6 mg/dL), GOT/GPT 1467/407 IU/L, lactic dehydrogenase (LDH) 13,924 IU/L (240-460 IU/L), sodium 134 mEq/L (135-145 mEq/L), potassium 5.6 mEq/L (3.6-5.5 mEq/L) and chloride 97 mEq/L (96-106 mEq/L). Urine pH was 5.0. An arterial blood sample showed a pH of 7.393, PaO_2 of 94 mmHg, $PaCO_2$ of 31 mmHg and HCO_3^- of 18.5 mEq/L. Chest radiograph revealed a bulging contour, suggesting enlarged lymph nodes in the

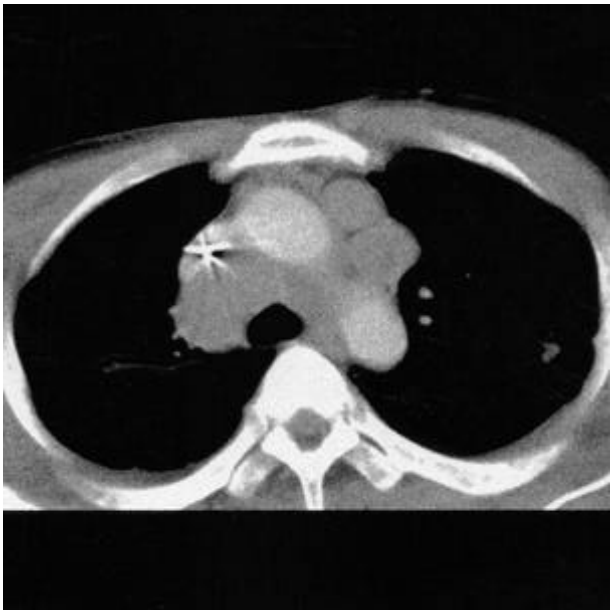

Fig. 1. Chest CT scan shows multiple lymphadenopathy in both paratracheal and aorticopulmonary area.

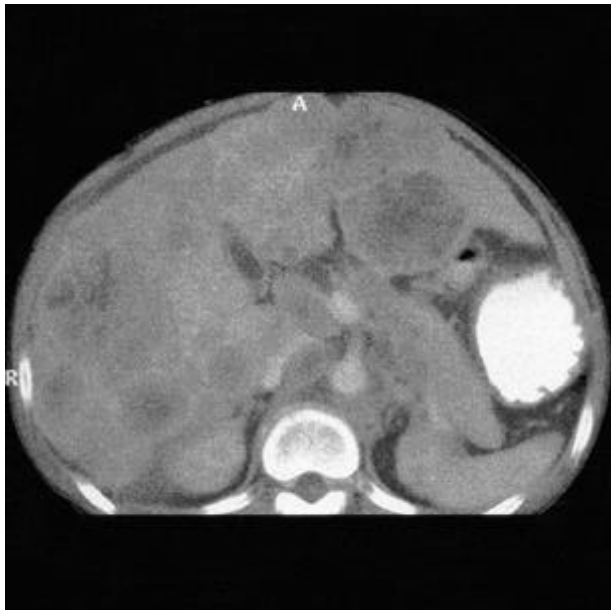

Fig. 2. Contrast-enhanced abdominal CT scan shows relatively sharp marginated hypodense masses with slight peripheral rim enhancement in both lobes of the liver. A metastatic periaortic lymph node is noted.

right paratracheal and aorticopulmonary window regions. A computerized tomography (CT) scan of the chest revealed multiple lymphadenopathy on both sides of the paratracheal and aorticopulmonary areas (Fig. 1). An abdominal CT scan showed a thickening of the gastric wall, multiple conglomerated low attenuated lymph nodes in the paraaortic, aortocaval, peripancreatic area and multiple hepatic metastases (Fig. 2). Gastrofiberscopy showed a huge ulcerating mass of more than 7 cm in diameter on the wall of the greater curvature of the lower body. Diagnosis of the TLS was easily made. Vigorous hydration, furosemide, and urine alkalinization with sodium bicarbonate were instituted to monitor the urinary pH, which adjusted to at least 7.0 before the cytotoxic therapy began. We also administered 300 mg of allopurinol per day orally. He had no signs of urinary obstruction on ultrasonography. Because diuresis did not rapidly ensue, emergency hemodialysis was initiated. Seven days later, the level of uric acid was 4.3 mg/dL, calcium 9.0 mg/dL, phosphorus 3.1 mg/dL, BUN 15.9 mg/dL, creatinine 1.0 mg/dL, LDH 9625 IU/L, GOT/GPT 100/64 IU/L, sodium 135 mEq/L, potassium 4.5 mEq/L and chloride 98 mEq/L. He was given cytoxan (500 mg/m^2 on day 1), adriamycin (20 mg/m^2 on day 1), vincristin (1 mg/m^2 on day 1 and day 8) and prednisolone (60 mg on days 1 through 5) for chemotherapy. Abdominal CT after 20 days of chemotherapy showed a decrease in the size of hepatic mass, lymphadenopathy and left supraclavicular lymph node. After 14 days of chemotherapy, chest PA showed bilateral, diffuse infiltrates involving the middle and lower lung fields. Broad spectrum antibiotics were administered, but progression to consolidation occurred. Gancyclovior was empirically administered after bronchoalveolar lavage. But he died of progressive pneumonia. Gastrofiberscopic biopsy revealed a poorly differentiated adenocarcinoma with cytokeratin (+), leukocyte

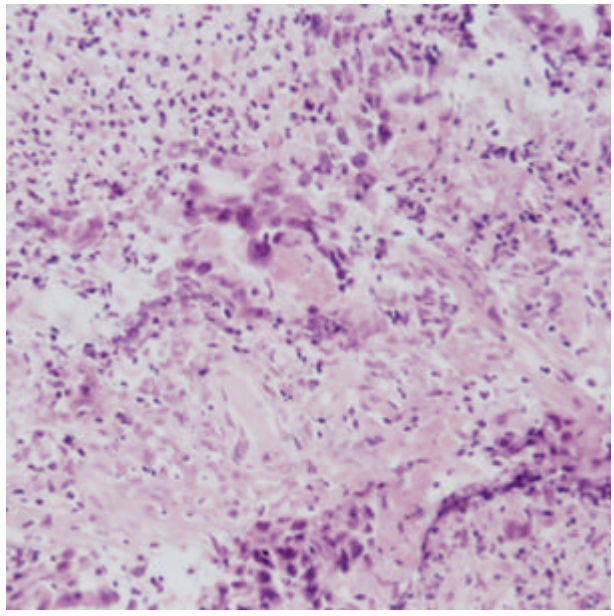

Fig. 3. Malignant epithelial cell clusters are embedded in the massive necrotic debris (H&E, ×100).

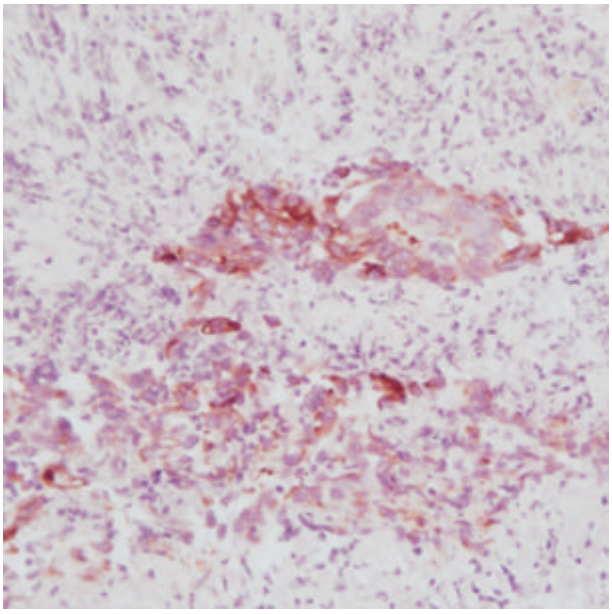

Fig. 4. The cytokeratin-positive epithelial cells are stained brown (×100).

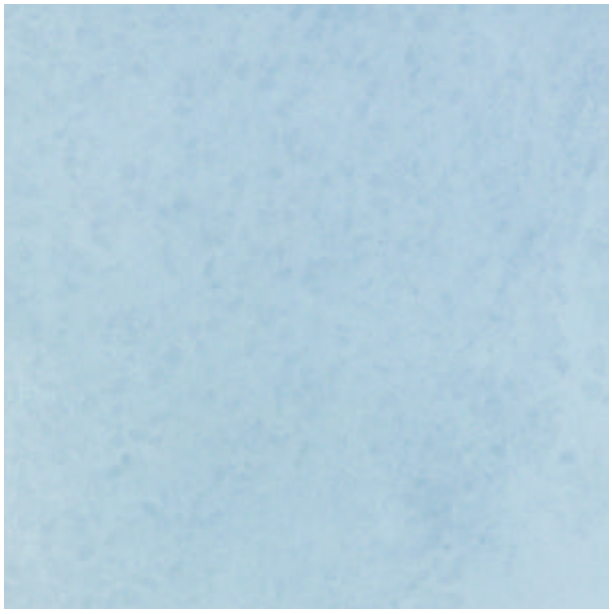

Fig. 5. The leukocyte common antigen immunostaining reveals negative finding (×100).

common antigen (LCA) (−) (Fig. 3-5). Later, the culture of specimen obtained by bronchoalveolar lavage for cytomegalovirus pneumonia was reported to be positive.

DISCUSSION

Tumor lysis syndrome is a metabolic emergency commonly described in aggressive hematologic malignancies but rare in solid tumors. Moreover, none has ever been reported in gastric cancer. According to the report by Gregory et al., there had been 25 cases of TLS in patients with solid tumor (6), seven cases of small cell carcinoma developed TLS after chemotherapy and four of them recovered. There also had been cases of breast carcinoma (2), ovarian carcinoma (7), vulva carcinoma (8), seminoma (1), melanoma (9), leiomyosarcoma (10), rhabdomyosarcoma (11), neuroblastoma (12), medulloblastoma (4) and hepatoblastoma (13). According to the report (6), azotemia, elevated LDH and hyperuricemia may become pretreatment risk factors for TLS in solid tumor patients. But it is not easy to expect tumor lysis in solid tumor, which is less sensitive to chemotherapy even though the tumor burden is large. And 36% of patients with TLS in solid tumors died despite management against TLS. In 1977, there was a report about a spontaneous acute tumor lysis without treatment in disseminated carcinoma of the abdomen. It was considered to have originated in the gastrointestinal tract. The cell type was a poorly differentiated, anaplastic carcinoma, but they could not identify the primary lesion (5). According to previous reports, TLS usually started 4 to 7 days after cytotoxic treatment (6), but only one case of adenocarcinoma of unknown primary site was reported to have developed TLS spontaneously from the tumor necrosis without treatment (5). Though we could not predict the timing of the emergence of TLS in relation to the cell type of solid tumor, our case was also adenocarcinoma of the stomach and TLS presented at the time of admission. It is well known that TLS frequently occurs in acute leukemia and high-grade lymphoma. Rapid lysis of tumor cells with the release of large quantities of intracellular products and ions may result in life-threatening acute renal failure and tumor lysis syndrome. Uric acid is relatively insoluble in the acidic environment of urine and may form uric acid crystals that result in an acute obstructive uropathy and renal failure. Rapidly increased serum potassium and phosphates can cause cardiac arrhythmia and sudden death. Hypocalcemia may result in muscle cramps, tetany and seizures. Even if TLS is not a common finding in solid tumors, there is a need to be alert for the development of TLS in the chemosensitive tumor with elevated LDH and hyperuricemia, decreased renal function. When evidence of TLS is noticed prior to chemotherapy, the metabolic abnormalities should be corrected before starting anticancer therapy. Without aggressive prevention and treatment, the mortality of acute uric acid nephropathy was reported to be 47 to 100% (14, 15). If TLS is suspected, serum electrolytes, including potassium, phosphorus, calcium, and bicarbonate have to be monitored frequently and early intervention is essential. When TLS develops spontaneously

before definite cytoreductive therapy, enough treatment for TLS is required and cytotoxic therapy should be started after serum urate is decreased. We also did chemotherapy as soon as uric acid was normalized. The reasons that we chose cytoxan, adriamycin and prednisolone as the regimen of chemotherapy were as follows; 1) TLS itself is not common in solid tumor such as gastric cancer, 2) there might have been a possibility of the anaplastic large cell non-Hodgkin's lymphoma of stomach, which may show cytokeratin positive, leukocyte common antigen negative having aggressive clinical feature similar to gastric carcinoma, even though the gastrofiberscopic biopsy turned out to be gastric cancer, 3) we were not able to exclude completely double primary tumors, non-Hodgkin's lymphoma and gastric carcinoma because autopsy was not done, 4) adriamycin is also an active agent for gastric cancer.

REFERENCES

1. Barton JC. *Tumor lysis syndrome in nonhematopoietic neoplasm. Cancer 1989; 64: 738-40.*
2. Drakos P, Bar-Ziv J, Catane R. *Tumor lysis syndrome in nonhematologic malignancies. Report of a case and review of the literature. Am J Clin Oncol 1994; 17: 502-5.*
3. Hussein AM, Feun LG. *Tumor lysis syndrome after induction chemotherapy in small cell lung carcinoma. Am J Clin Oncol 1990; 13: 10-3.*
4. Tomlinson GC, Solberg LA Jr. *Acute tumor lysis syndrome with metastatic medulloblastoma: a case report. Cancer 1984; 53: 1783-5.*
5. Crittenden DR, Ackerman GL. *Hyperuricemic acute renal failure in disseminated carcinoma. Arch Intern Med 1977; 137: 97-9.*
6. Kalemkerian GP, Darwish B, Varterasian ML. *Tumor lysis syndrome in small cell carcinoma and other solid tumors. Am J Med 1997; 103: 363-7.*
7. Bilgrami SF, Fallon BG. *Tumor lysis syndrome after combination chemotherapy for ovarian cancer. Med Pediat Oncol 1993; 21: 521-4.*
8. Shamseddine A, Khalil AM, Wehbeh MH. *Acute tumor lysis syndrome with squamous cell carcinoma of the vulva. Gynecol Oncol 1993; 51: 258-60.*
9. Minasian LM, Szatrowski TP, Rosenblum M, Steffens T, Morrison ME, Chapman PB, Williams L, Nathan CF, Houghton AN. *Hemorrhagic tumor necrosis during a pilot trial of tumor necrosis factor-alpha and anti-GD3 ganglioside monoclonal antibody in patients with metastatic melanoma. Blood 1994; 83: 56-64.*
10. Gold GE, Malamud SC, LaRosa F, Osband ME. *Adoptive chemoimmunotherapy using ex vivo activated memory T-cells and cyclophosphamide: tumor lysis syndrome of a metastatic soft tissue sarcoma. Am J Hematol 1993; 44: 42-7.*
11. Khan J, Broadbent VA. *Tumor lysis syndrome complicating treatment of widespread metastatic abdominal rhabdomyosarcoma. Pediat Hematol Oncol 1993; 10: 151-5.*
12. Hain RD, Rayner L, Weitzman S, Lorenzana A. *Acute tumor lysis syndrome complicating treatment of stage IVS neuroblastoma in infants under six months old. Med Pediat Oncol 1994; 23: 136-9.*
13. Lobe TE, Karkera MS, Custer MD, Shenefelt RE, Douglass EC. *Fatal refractory hyperkalemia due to tumor lysis during primary resection for hepatoblastoma. J Pediat Surg 1990; 25: 249-50.*
14. Garnick MB, Mayer RJ. *Acute renal failure associated with neoplastic disease and its treatment. Semin Oncol 1978; 5: 155-65.*
15. Kjellstrand CM, Campbell DC, von Hartitzsch B, Buselmeier TJ. *Hyperuricemic acute renal failure. Arch Intern Med 1974; 133: 349-59.*