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Case Report Open Access

Tumor Lysis Syndrome in a Patient with Metastatic Colon Cancer after Treatment with 5-Fluorouracil/Leucovorin and Oxaliplatin: Case Report and Literature Review

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Development of tumor lysis syndrome (TLS) may occur after chemotherapy or spontaneously in bulky or rapidly growing tumors. This syndrome is frequent but preventable in patients with hematologic malignancies. TLS following therapy has been reported infrequently in various types of solid tumors. TLS associated with oxaliplatin containing chemotherapy in a solid tumor has never been reported. A 59-year-old man received 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) chemotherapy for metastatic colon cancer. Development of TLS occurred three days after administration of chemotherapy. Two days later, his abnormal laboratory findings were recovered with appropriate management. To the best of our knowledge, the current case is the first report on development of acute TLS following oxaliplatin containing chemotherapy in a patient with colon cancer. We also review the literature on tumor lysis syndrome in patients with colorectal cancer.

Key words
Tumor lysis syndrome, Oxaliplatin, Colon

Introduction

Tumor lysis syndrome (TLS) generally occurs in patients with hematologic malignancy. It is characterized by a set of metabolic complications, including hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. These metabolic alterations, which are caused by the rapid release of intracellular components, such as potassium, phosphorus, nucleic acids, and cytokines, into the systemic circulation resulting from tumor cell lysis, can have life threatening consequences. Development of TLS rarely occurs in patients with solid tumors [1-3]. It may occur after chemotherapy or develop spontaneously in bulky or rapidly growing solid tumors. We report on the first case of development of TLS following oxaliplatin containing chemotherapy in a patient with colon cancer.

Case Report

A 59-year-old man presented with abdominal distension and dyspepsia. Marked hepatomegaly was observed on physical examination.

Abdominal 2-dimensional spiral computed tomography (CT) of the patient showed an irregularly shaped ulceroinfiltrating mass in the distal descending colon, multiple irregularly shaped extracolonic nodules with peritoneal invasion, and numerous liver metastases in both hepatic lobes. Colonoscopy showed a circular protruding mass in the distal descending colon, located 35 cm from the anal verge; biopsy of this lesion indicated that it was a moderately differentiated adenocarcinoma with the wild-type K-Ras gene.

A distal colonic stent, 22 mm in diameter and 10 cm in length (uncovered M.I. Tech stent), was inserted through the colonoscope in order to resolve colonic stenosis. First-line chemotherapy consisted of 12 cycles of 5-fluorouracil, leucovorin, and irinotecan (FOLFIRI) plus bevacizumab; upon completion, the overall tumor response was assessed as stable disease. However, seven weeks after the end of chemotherapy, the patient complained of abdominal fullness and follow-up chest and abdominal CT scans showed that his hepatic and intra-abdominal lymph node metastases had progressed and newly developed metastatic lung nodules were observed. The patient was then started on 5-fluorouracil, leucovorin, and oxaliplatin (FOLFOX) chemotherapy as second line treatment. However, three days after starting the second cycle of FOLFOX chemotherapy, his blood urea nitrogen was 21.8 mg/dL (normal range, 8.0 to 23.0 mg/dL), creatinine was 1.8 mg/dL (normal range, 0.5 to 1.2 mg/dL), potassium was 4.8 mmol/L (normal range, 3.5 to 5.1 mmol/L), calcium was 7.7 mg/dL (normal range, 8.2 to 10.2 mg/dL), phosphorus was 4.6 mg/dL (normal range, 2.5 to 4.5 mg/dL), uric acid was 12.4 mg/dL (normal range, 2.5 to 8.5 mg/dL), and lactate dehydrogenase was 4,420 IU/L (normal range, 200 to 400 IU/L); these findings were consistent with acute TLS. The patient was managed with massive intravenous hydration, diuresis, and allopurinol. Two days later, his uric acid level was 5.8 mg/dL (normal range, 2.5 to 8.5 mg/dL) and renal function was recovered, with a creatinine concentration of 1.1 mg/dL (normal range, 0.5 to 1.2 mg/dL), a potassium concentration of 3.9 mmol/L (normal range, 2.5 to 4.5 mmol/L), and a phosphorus concentration of 3.0 mg/dL (normal range, 2.5 to 4.5 mg/dL).

Two weeks later, he started his third cycle of FOLFOX chemotherapy, however, on day 3, despite efforts to prevent TLS, his renal function began to show deterioration, with a blood urea nitrogen concentration of 44.7 mg/dL (normal range, 8.0 to 23.0 mg/dL), a creatinine concentration of 3.9 mg/dL (normal range, 0.5 to 1.2 mg/dL), and a uric acid concentration of 10.7 mg/dL (normal range, 2.5 to 8.5 mg/dL). After two weeks of management for TLS, he showed a decrease in blood urea nitrogen concentration to 13.3 mg/dL (normal range, 8.0 to 23.0 mg/dL), creatinine concentration to 1.2 mg/dL (normal range, 0.5 to 1.2 mg/dL), and uric acid concentration to 3.7 mg/dL (normal range, 2.5 to 8.5 mg/dL).

After five cycles of FOLFOX chemotherapy, hyperbilirubinemia was observed. Abdominal and pelvic CT scans showed progression of the primary tumor and metastatic hepatic lesions, with newly developed peritoneal carcinomatosis. At that time, the patient's Eastern Cooperative Oncology Group (ECOG) performance status was 2. The chemotherapy regimen was switched to irinotecan plus cetuximab. Six days after administration of the first cycle of this regimen, he developed grade 4 febrile neutropenia and died from septic shock the following day.

Discussion

Development of TLS is rare in patients with solid tumors. The first such patient, who had a widespread adenocarcinoma of gastrointestinal origin with renal failure, was reported in 1977 [4], and an additional 74 patients with solid tumors who developed TLS were reported between 1977 and 2011. These solid tumors included breast cancer, small cell lung cancer, germ cell tumor, melanoma, Merkel cell carcinoma, head and neck cancer, non-small cell lung cancer, ovarian cancer, vulva cancer, prostate cancer, hepatocellular carcinoma, colorectal cancer, gastric cancer, sarcoma, neuroblastoma, medulloblastoma, hepatoblastoma, gestational trophoblastic neoplasia, renal cell carcinoma, transitional cell carcinoma, and thymoma [1,5-13].

In most patients, TLS is induced by chemotherapy, however, it may also be induced by other anti-neoplastic treatments, including radiotherapy, hormonal therapy, surgery, radiofrequency ablation, and immunotherapy, or may develop spontaneously before initiation of therapy [1,14]. Prognosis of TLS is poorer in patients with solid tumors than in patients with hematological malignancies. Its grave outcome may be due to a lack of early recognition and prevention.

Although development of TLS has been reported in several patients with colorectal cancer after treatment with irinotecan [10-13], none of these patients was receiving FOLFOX chemotherapy. To the best of our knowledge, the current case constitutes the sixth reported case of a patient with colorectal cancer who developed TLS, and is the first report in a patient undergoing FOLFOX chemotherapy (Table 1). Five of these

Table 1. Cases of patients with metastatic colon cancer who developed tumor lysis syndrome

Age (yr)	Gender	Metastasis	Treatment	Onset of TLS	Outcome of TLS	Reference
64	Male	Liver	Cetuximab	18 hr	Died	Krishnan et al. [9]
38	Female	Liver	Irinotecan	6 days	Died	Nikolic-Tomasevic et al. [10]
62	Male	Lung, bone, thyroid	FOLFIRI+bevacizumab	2 days	Died	Hentrich et al. [11]
66	Male	Liver, lung, bone	FOLFIRI	72 hr	Died	Oztop et al. [12]
42	Female	Liver	Irinotecan	8 days	Died	Boisseau et al. [13]
59	Male	Liver	FOLFOX	3 days	Died	Present case

TLS, tumor lysis syndrome; FOLFIRI, 5-fluorouracil, leucovorin and irinotecan; FOLFOX, 5-fluorouracil, leucovorin, and oxaliplatin.

six patients had liver metastases and four had been treated with an irinotecan containing regimen. These patients also had a large tumor burden, including liver, lung, or multiple metastases. In addition, cetuximab and bevacizumab can induce TLS; therefore, careful monitoring is required when these agents are administered to colorectal cancer patients with a large tumor burden [10,13]. The current report additionally suggests that oxaliplatin-containing chemotherapy might cause acute TLS in patients with metastatic colon cancer. A large burden of tumors with high sensitivity to treatment, and elevated serum lactate dehydrogenase or uric acid levels, may be considered risk factors for TLS in patients with solid tumors [1-3,15]. The presence of extensive liver metastases may also be a risk factor, as in our patient [1].

In treatment of patients with solid tumors, particularly those with risk factors for TLS, efforts should be made to prevent TLS or to detect it early through careful monitoring using laboratory tests, as well as management of metabolic complications. We report here on the first case of a patient with metastatic colon cancer who developed acute TLS after treatment with FOLFOX chemotherapy.

Conflicts of Interest

Conflict of interest relevant to this article was not reported.

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