Case report

Tumor lysis syndrome in a patient with metastatic colon cancer after treatment with oxaliplatin and 5-Fu

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Abstract

Tumor lysis syndrome in solid tumors is a rare occurrence, with a poor prognosis. We present the case of a patient of recurrent colon cancer who received chemotherapy with FOLFOX regimen (leucovorin, fluorouracil, and oxaliplatin) with subsequent tumor lysis. We present a recurrent rectal cancer patient suffered from tumor lysis syndrome after salvage FOLFOX regimen. After treat with CVVH with improved conscious status. In this case report, we had review the tumor lysis in solid tumor.

1. Introduction

Tumor lysis syndrome is frequently observed in hematologic cancer or in rapidly growing and bulky tumors. The symptoms of this condition include decreased urine output, hyperkalemia, hyperphosphatemia, hypocalcemia and hyperuricemia and may be accompanied by metabolic acidosis, arrhythmia or even seizure. Tumor lysis syndrome rarely occurs in solid tumors but it can frequently be observed in sensitive bulky solid tumors post-treatment with chemotherapy or radiotherapy. Treatment for acute tumor lysis includes renal replacement therapy in patients with severe oliguria or anuria, persistent hyperkalemia, hyperphosphatemia and with a calcium-phosphate product $\geq 70$ mg$^2$/dL.

2. Case report

We herein report on a 65-year-old male with a past history of rectal adenocarcinoma pT3N2M0 in 2002, who had a low anterior resection procedure and received concurrent chemoradiotherapy with a 21-course FOLX regimen (5-FU and leucovorin).

Results from computerized tomography showed tumor recurrence in the pelvic region with fistula formation from the urinary bladder, extending into the presacral space (Figs. 1–4). Thereafter, chemotherapy with FOLFOX (leucovorin, fluorouracil, oxaliplatin) regimen (first cycle chemotherapy after noted recurrent) was initiated. Upon completion of chemotherapy (exact chemotherapy regimen with: oxaliplatin 160 mg (85 mg/m$^2$), 5-FU 2800 mg (1500 mg/m$^2$) for 1 day and leucovorin 200 mg), the patient complained of chest tightness followed by alternating periods of consciousness and ventricular tachycardia requiring cardiopulmonary-cerebral resuscitation and defibrillation. Following his initial resuscitation, the patient was admitted to the intensive care unit and laboratory data showed hyperkalemia, acute kidney injury and oliguria. After 1 day, laboratory data showed persistent hyperammonemia (ammonia 304 ug/dL), which elevated our suspicion that there was complicit drug toxicity due to 5-FU. However, the patient’s high potassium levels persisted, along with ventricular arrhythmia, after which he received defibrillation. Follow-up data on day 4 showed the following: hyperuricemia uric acid: 15.9 mg/DL (normal range: 4.8–8.7 mg/dL) and hypocalcemia Ionized Ca: 1.01 mmol/L (normal range: 1.09–1.30 mmol/L) and serum creatinine increased from 2.14 to 3.14 mg/dL from day 4 to day 5 with normal serum phosphorus level. The patient’s condition was stable before the initiation of chemotherapy. Given the fact that
our patient suffered from 5-FU toxicity first which was complicated with tumor lysis syndrome as evidenced by hyperkalemia with ventricular fibrillation twice, hypocalcemia, hypuricemia, and poor renal function, the typical electrolyte changes may not be as “typical” as suggested. The dose of chemotherapy (FOLFOX) had been adjusted before the initiation of treatment.

Based on these findings, tumor lysis syndrome was strongly suspected. After treatment with rasburicase for hyperuricemia, the patient’s condition improved and increased urine output was noted. When this patient first presented to our facility, we did not consider the possibility of tumor lysis due to the rarity of the disease. Not until the patient twice exhibited ventricular fibrillations with hyperkalemia was tumor lysis confirmed. However, the HD was delayed due to the family’s concern about the patient’s poor condition. He then received renal replacement therapy (continuous veno-venous hemofiltration from day 7 to day 10), regaining consciousness on day 9.

Subsequently, the patient was successfully extubated on day 11. By that point, the final creatinine level was back to 1.41 mg/dL. After this episode, we had shifted chemotherapy to capecitabine 1000 mg–1500 mg daily, to maintain an antitumor effect and diminish poor activity. The patient received another course of chemotherapy Irinotecan 300 mg (180 mg/m²), leucovorin 600 mg (400 mg/m²), 5-FU 2000 mg (1500 mg/m²), after which this treatment scenario concluded. To date, no additional tumor lysis has occurred and the patient is doing well. Our facility did not performed any follow-up imaging arising from the fact that the patient had just received two courses (with one incomplete) of chemotherapy.

3. Discussion

Tumor lysis syndrome can be classified in terms of both clinical and laboratory parameters, according to the Cairo and Bishop grading system. First, at least two or more metabolic abnormalities must be noted simultaneously. Second, a 25% change in the baseline laboratory data should not be considered as a criterion. Third, any symptomatic hypocalcemia should constitute the symptoms of clinical tumor lysis syndrome. Our patient met the criteria of both clinical and laboratory parameters for tumor lysis syndrome (clinically: cardiac dysrhythmia, disturbance in consciousness, and increased serum creatinine level; laboratory: hyperuricemia, hypocalcemia, and hyperkalemia). Tumor lysis syndrome is most frequently observed during treatment of hematologic malignancies, usually leukemia and lymphoma. Most of the hematologic tumors associated with tumor lysis syndrome are poorly differentiated lymphomas, such as Burkitt’s lymphoma, and leukemias such as acute lymphoblastic leukemia and acute myeloid leukemia. Tumor lysis syndrome is rare in solid tumors and more frequently found in bulky tumors and chemotherapy sensitive cancers such as small cell lung cancer, and widespread gastrointestinal tract adenocarcinoma.
or breast cancer. Several studies have reported the occurrence of tumor lysis syndrome in solid tumors post-radiotherapy or even target therapy, such as metastatic gestational trophoblastic neoplasia, renal cell carcinoma, and metastatic transitional cell carcinoma.2-10 The prognosis of tumor lysis syndrome is poor in the case of solid tumors compared to hematologic malignancy, which may be due to the frequent lack of early recognition and prevention.11 One study mentioned tumor lysis syndrome occurring in solid tumor patients typically manifests a later onset than in hematologic malignancies, which may be related to the more synchronous kinetics of lymphomyeloproliferative disorders cells than solid tumor cells.12 The patient had suffered from chemotherapy-associated hyperammonia complicated with tumor lysis syndrome, as indicated by ventricular fibrillation caused by hyperkalemia and hyperuricemia. We do not refer to this scenario as "late onset tumor lysis syndrome". In fact, we believe the tumor lysis probably occurred after the chemotherapy but was masked by the hyperammonia that might be caused by 5-FU. In the very beginning, we did not contemplate the possibility of tumor lysis since it is rare – especially for the FOLFOX regimen. Not until the patient had twice suffered ventricular fibrillations with hyperkalemia did we think the possibility of tumor lysis.

In this case report, we described a rare case of tumor lysis syndrome associated with the FOLFOX regimen and further stress the importance of additional prophylaxis for the huge tumor burden.13-16 Our patient's hyperammonemia may be due to cardiogenic shock, post-cardio-pulmonary-cerebral resuscitation, shock liver or tumor lysis. The causes of hyperammonemia include increased ammonia production (such as infection, GI bleeding, trauma, cancer, or chemotherapy), decreased ammonia excretion (such as acute liver failure, cirrhosis), and drug-induced hyperammonemia.17 Also, a previous case report had mentioned rectovesical and ileal fistula-related hyperammonemia encephalopathy.18 We had repeat ammonia data after this acute episode, which showed the ammonia numbers to be around 90ug/dL. We suggested that the patient with chronic hyperammonemia and worsened by the shock episode and 5-FU was continuous-infusion related.

To the best of our knowledge, this is the second case report in the literature about tumor lysis syndrome occurring in a colon cancer patient treated with FOLFOX regimen.17 However, our case is unique and quite different from the quoted paper. First, our patient suffered from hyperammonia that could be aggravated by 5-FU, which was simultaneously complicated with tumor lysis syndrome and resulted in a change of consciousness and critical condition. In the very beginning, we did not think of the possibility of tumor lysis since it is rare. Not until the patient had ventricular fibrillations twice with hyperkalemia did we think of the possibility of tumor lysis. The delayed use of CVVH can still save a patient's life. However, our patient received only one day of chemotherapy.

Treatment of tumor lysis syndrome includes hydration and control of hyperuricemia, hyperkalemia, and diuresis for a balanced fluid status. Once it is identified, renal replacement therapy is essential for emergency tumor lysis treatment. In this case, we prescribed renal replacement therapy at day 7 after chemotherapy with preserved renal function and corrected metabolic encephalopathy. A earlier study suggested that continuous veno-venous hemodiagnosis is more effective in reducing the phosphate level than conventional hemodialysis.19 The drastic response even after a delay in performing dialysis in our case suggests that there may be chemotherapy related toxicity post chemotherapy, and continuous dialysis for up to 2 weeks may be needed.

Cardiac echography was arranged on day 3 and showed regional wall abnormality with reduced LV systolic function (LVEF: 23%). Regarding differential tumor lysis syndrome and 5-FU related cardiotoxicity, we had reviewed this patient’s risk in conjunction with the chemotherapy regimen. The 5-FU related cardiotoxicity is a rare complication with the incidence around 1.6–3% in the short regimen, and 7.6–18% in the longer regimen.20 We suspected that 5-FU related cardiotoxicity was less likely because the 5-FU dose in our regimen was only a median dose, and the patient had not even completed the 1st day of the 5-FU regimen. The cardiac toxicity on the patient may be due to both chronic kidney disease and suspected congestive heart failure and aggravated on moderate dose 5-fu (but lacking data for baseline heart function).21 Oxaoloplatin sensitivity is related to cytokines and histamine, and often presents with predominantly mild symptoms of flushing, heart rate and blood pressure alternation, dyspnea and chest discomfort. Symptoms usually subsided after discontinuation of drug and administration of steroid and antihistamine.22 For the above reason, we suggested oxaloplatin is less likely in our patient.

4. Conclusions

This is only the second case report of a patient with colon cancer treated with the FOLFOX regimen who suffered from acute tumor lysis syndrome, and the first case in which delayed renal replacement therapy was administered resulting in improved consciousness and renal function, corrected arrhythmia and stable vital signs. Arising from the results of our treatment, we suggest renal replacement therapy be considered by other clinicians for tumor lysis because it is helpful in the delayed stage.

5. Consent

Inform consent was obtained from the patient, who understood the unique clinical course and the possibility of further treatment.

Conflict of interest

There is no conflict of interest in the case report.

References


