Case Report

Tumor lysis syndrome following cabazitaxel administration for metastatic castration-resistant prostate cancer: A case report

Masashi Oshima, Shozaburou Mayumi, Kai Yazaki, Yuuki Nakamura, Tsuzumi Konishi, Kimitoshi Saito, Satoshi Washino and Tomoaki Miyagawa

Department of Urology, Jichi Medical University Saitama Medical Center, Saitama, Japan

Abbreviations & Acronyms
ALP = alkaline phosphatase
ALT = alanine aminotransferase
AST = aspartate aminotransferase
BUN = blood urea nitrogen
CRPC = castration-resistant prostate cancer
CT = computed tomography
Hb = hemoglobin
LDH = lactate dehydrogenase
Plt = platelet
PSA = prostate-specific antigen
TLS = tumor lysis syndrome
UA = uric acid
WBC = white blood cell

Introduction: Tumor lysis syndrome is a rare and potentially fatal complication of oncological treatment. It is characterized by biochemical changes associated with the rapid lysis of malignant cells, usually after chemotherapy. Tumor lysis syndrome is typically noted in patients with hematological malignancies, and it rarely occurs in patients with solid tumors.

Case presentation: We report a case of tumor lysis syndrome after cabazitaxel administration for metastatic castration-resistant prostate cancer. To our knowledge, tumor lysis syndrome after cabazitaxel therapy has not been reported previously. The patient was a 77-year-old man who developed clinical tumor lysis syndrome after a single dose of cabazitaxel for metastatic castration-resistant prostate cancer. He was treated with hydration and the recombinant uricolytic agent rasburicase, and his condition improved.

Conclusion: It is extremely important to assess the risk factors for tumor lysis syndrome and to perform active prevention procedures in order to avoid fatal outcomes. It may be beneficial to use rasburicase in patients with established tumor lysis syndrome.

Key words: cabazitaxel, castration-resistant prostate cancer, chemotherapy, prostate cancer, tumor lysis syndrome.

Correspondence: Masashi Oshima M.D., Department of Urology, Jichi Medical University Saitama Medical Center, 1-847 Amanuma-cho, Omiya-ku, Saitama-shi, Saitama 330-8503, Japan. Email: m_ohshima@jichi.ac.jp

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Keynote message

We report a case of TLS after cabazitaxel administration for metastatic CRPC. To our knowledge, TLS after cabazitaxel therapy has not been reported previously. It is extremely important to assess the risk factors for TLS and to perform active prevention procedures in order to avoid fatal outcomes. It may be beneficial to use rasburicase in patients with established TLS.

Introduction

TLS is one of the major oncological emergencies. TLS is a potentially lethal complication of anticancer treatment, and it occurs when large numbers of neoplastic cells are killed rapidly, leading to the release of large amounts of intracellular ions and metabolic byproducts into systemic circulation.[1,2]

It is typically associated with acute leukemia and high-grade non-Hodgkin lymphoma, and TLS in solid tumors, including prostate cancer, have been rarely reported.[3]

Although occurrences are rare, a literature review revealed 45 case reports of TLS in patients with solid tumors, with a mortality rate of one in three in this patient set.[4]

Clinically, TLS is characterized by hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia, and these metabolic abnormalities can cause renal dysfunction, arrhythmia, and seizures.[5]

Here, we report a case of TLS after cabazitaxel administration for metastatic CRPC. To our knowledge, TLS after cabazitaxel therapy has not been reported previously.

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Case presentation

A 77-year-old man was referred to our department for the treatment of metastatic CRPC. He was diagnosed with metastatic prostate cancer (PSA level >1000 ng/mL, Gleason score 4 + 5, cT4N1M1) at another institution 3 years ago. He received androgen deprivation therapy involving a luteinizing hormone-releasing agonist and nonsteroidal antiandrogen. However, he developed CRPC after 7 months. Thereafter, he received 13 cycles of 3-weekly docetaxel (70 mg/m^2) followed by enzalutamide for 8 months at another institution.

Laboratory test results at presentation to our hospital were as follows: PSA, 12.9 ng/mL; serum creatinine, 1.70 mg/dL; potassium, 5.1 mmol/L; corrected calcium, 9.1 mg/dL; phosphorus, 2.7 mg/dL; LDH, 622 U/L; and UA, 6.7 mg/dL.

CT showed a poorly defined prostate tumor, multiple liver metastases, and pelvic lymphadenopathy, and a bone scan showed multiple bone metastases (Fig. 1a–d).

Enzalutamide was changed to cabazitaxel because of multiple liver metastases. Cabazitaxel (20 mg/m^2) with dexamethasone (1.0 mg once daily) was initiated. He received pegfilgrastim (6 mg) subcutaneously on day 2 after treatment change as the primary prophylaxis for neutropenia. On day 3, he had fever with a temperature of 37.8°C and severe hypotension (systolic blood pressure, 75 mmHg). At this time, laboratory test results were as follows: serum creatinine, 2.85 mg/dL; potassium, 5.7 mmol/L; phosphorus, 2.8 mg/dL; UA, 11.3 mg/dL; calcium, 6.9 mg/dL; LDH, 2911 U/L; AST, 777 IU/L; ALT, 567 IU/L; and Hb, 6.1 g/dL (Table 1).

Based on the laboratory and clinical findings, he was diagnosed with TLS according to the current classification system of Cairo and Bishop.[6] His hypotension was considered to have been caused by hemorrhagic shock from intratumoral hemorrhage of the liver metastases (Fig. 1e).

He was admitted to the intensive care unit and received hydration therapy (3000 mL/day) and red blood cell transfusion. Correction of hyperuricemia was attempted with a recombinant uricolytic agent (rasburicase, 0.2 mg/kg). After treatment, his UA level decreased to 0 mg/dL at 16 h. Additionally, his electrolyte abnormalities almost resolved after 3 days. He was moved out of the intensive care unit on day 6 and was discharged from the hospital on day 14. However, he was readmitted to our hospital for severe pain and dyspnea 8 days after discharge. At that time, he did not want further examination, then he died of respiratory failure on the next day.

Discussion

TLS is considered a rare and potentially fatal complication of oncological treatment.

Eight cases of TLS have been reported in patients with prostate cancer, and the present case is the ninth TLS case (Table 2).[7–14] Of the nine cases, five, including our case, occurred after the administration of either chemotherapy or hormonal therapy.

In two cases, patients developed TLS after the initiation of palliative radiation therapy for bone metastasis, whereas in two other cases, patients developed TLS spontaneously without any treatment. All patients had evidence of metastatic disease, and six of the nine cases had CRPC. TLS is defined as the presence of two or more biochemical variables within 3 days before chemotherapy or 7 days after chemotherapy in the condition of adequate hydration and the use of a UA-lowering agent. Certain tumor and patient characteristics can be used to predict the risk of future TLS (e.g. highly proliferating and bulky malignancy, sensitivity to chemotherapy, and exposure to nephrotoxic substances, such as non-steroidal anti-

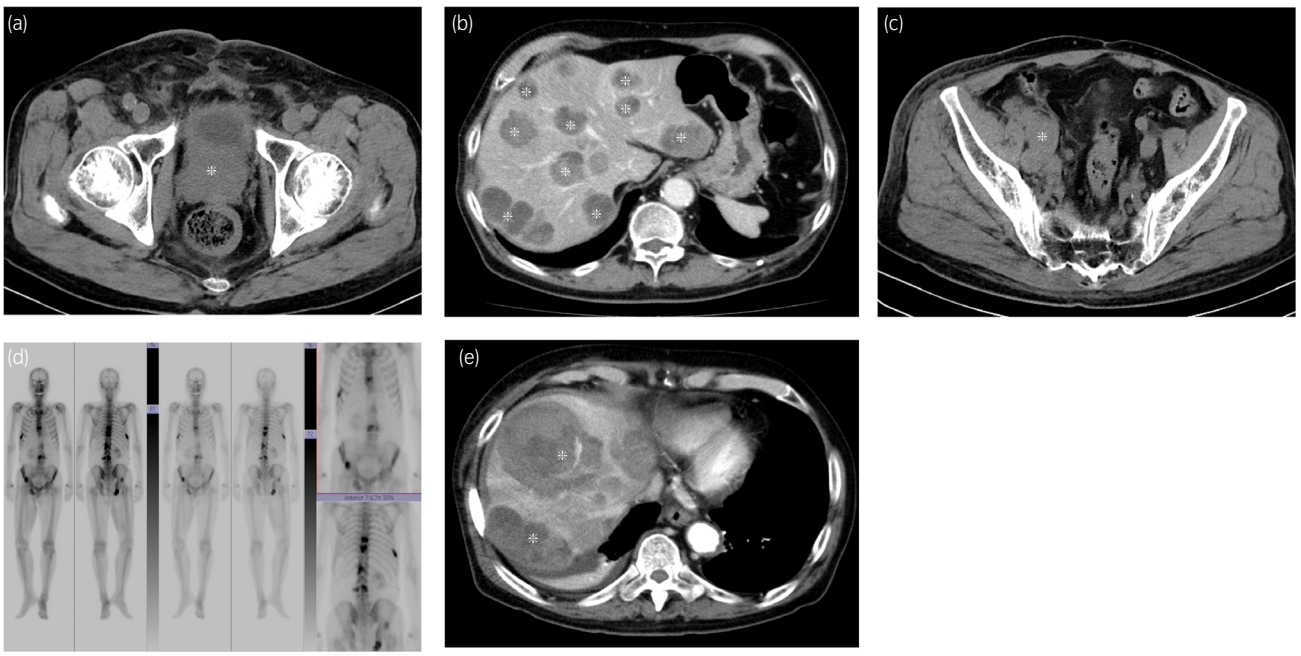

Fig. 1 (a–c,e) CT of the abdomen. (a) Low-defined prostate tumor (*). (b) Multiple tumor burden in the liver (*). (c) Pelvic lymphadenopathy (*). (d) Bone scan. Multiple bone metastases. (e) Hemorrhage from liver metastases (*).

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Table 1 Patient laboratory values

	Admission	Day 3 (pre-rasburicase)	Day 4 (post-rasburicase)	Day 5	Day 9	Day 12 (before discharge)	Day 22 (readmission)	Normal values
WBC	7460	14 140	10 100	8990	7900	18 980	14 360	3900–9800/μL
Hb	9.6	6.1	6.6	7.6	8.1	9.4	9.9	12–17.6 g/dL
Plt	31.4	14.3	7.3	8.7	20.4	28.3	32.2	13–36.9 × 10^4/μL
BUN	28	52	38	34	36	33	21	8–20 mmol/L
Creatinine	1.83	2.85	1.92	1.64	1.63	1.72	1.67	0.65–1.07
Potassium	5.2	5.7	4.9	4.8	4.9	3.9	4.4	3.6–4.8 mmol/L
Calcium	8.2	6.9	6.1	6.7	8	8.4	7.4	8.4–10.1 mmol/L
Phosphorous	2.4	2.8	2.2	2.4	2.2	3.2	1.7	2.7–4.6 mmol/L
LDH	1294	2911	2184	1599	1035	1502	1935	124–222 U/L
AST	34	777	200	78	33	30	46	13–30 U/L
ALT	34	567	256	146	62	30	33	10–42 U/L
ALP	366	473	338	315	344	376	773	106–322 U/L
UA	7.6	11.3	0	0.1	2.9	8.1	8.9	3.7–7.8 mg/dL

Table 2 Summary of existing case reports of TLS in patients with prostate cancer

Author	Year	Patient age	Gleason score	Disease burden	Treatment preceding TLS	Treatment	Outcome	References
Tanvetyanon and Choudhury	2004	77	Not reported	Bone, liver	Fultamide, goserelin	Vigorous supportive measures	Died 8 days following treatment	7
Sorcher	2004	80	3 + 3	Bone, bone marrow	Docetaxel, daxamethasone	Furosemide	Died 40 h after treatment	8
Wright *et al.*	2005	60	3 + 4	Bone, bone marrow	Paclitaxel	Hemodialysis	Died 8 days following treatment	9
Lin *et al.*	2007	72	Not reported	Bone, liver	Fultamide, leuprolide, dexamethasone, medroxy progesterone	Hemodialysis, furosemide, allopurinol	Died 2 weeks following treatment	10
Kaplan *et al.*	2012	60	5 + 4	Bone, bone marrow	Radiation therapy to shoulder	Sodium bicarbonate	Died 11 days following treatment	11
Mazzoni	2016	62	Not reported	Bone, lymph node, bladder invasion	Palliative radiation therapy, leuprolide, bicartamide	Hemodialysis, rasburicase, sodium bicarbonate	Dialysis dependent, transitioned to hospice	12
Serling-Boyd *et al.*	2017	56	5 + 4	Bone, lymph node	None	Allopurinol, sodium bicarbonate, rasburicase	Transitioned to hospice 20 days following treatment	13
Ignaszewski and Kohlitz	2017	69	Not reported	Bone, liver	None	Sodium bicarbonate, rasburicase, hemodialysis	Died shortly thereafter	14
Oshima	2019	77	5 + 4	Bone, liver, lymph node	Cabazitaxel	Sodium bicarbonate, rasburicase, hemodialysis	Died 23 days following treatment	

inflammatory agents and certain antihypertensive medications).[6,15] Other potential risk factors include presence of decreased renal function and elevated LDH, phosphorus, potassium, and UA levels.[3]

Additionally, in solid cancer, the presence of liver metastasis is a risk factor for the development of TLS, and this trend was also seen in prostate cancer (Table 2).[16]

In patients having risk factors for TLS, active prevention procedures are of utmost importance to avoid fatal outcomes. Mirrakhimov *et al.* proposed a risk stratification approach for TLS prevention among patients with solid cancer (Fig. 2).[3]

Our patient had abnormal LDH and potassium levels and renal function before cabazitaxel administration; thus, we believe that it might be better to perform TLS prevention procedures.

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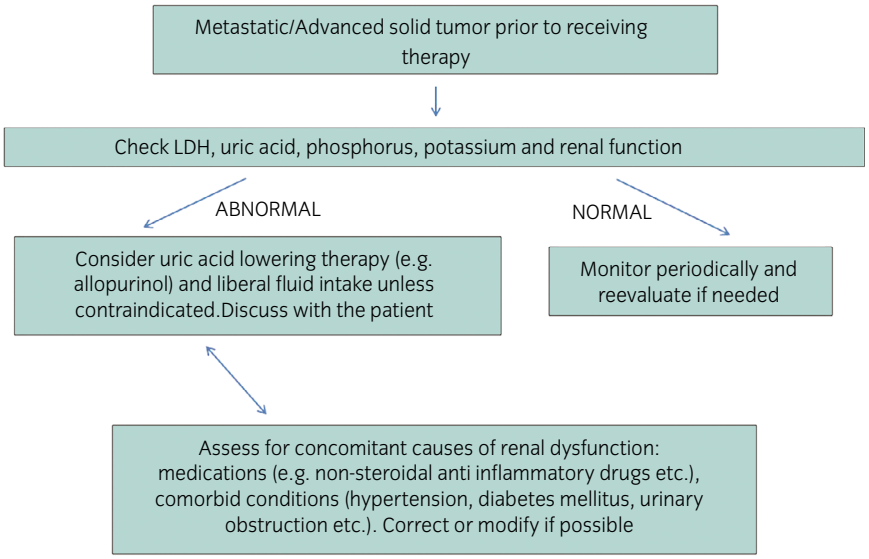

Fig. 2 Proposed evaluation for the risk of TLS and its prevention among patients with solid tumors.

All patients at risk for TLS should receive hydration to improve renal perfusion and glomerular filtration and to minimize acidosis and oliguria. Hydration is the preferred method of increasing urine output, but diuretics may also be necessary.[17] Reducing the UA level with allopurinol and, particularly, with rasburicase can preserve or improve renal function and reduce serum phosphorus levels as secondary beneficial effects.[18] Although allopurinol prevents the formation of UA, existing UA should be excreted. The UA level may take 2 days or more to decrease, and this delay may allow the development of urate nephropathy. Moreover, despite treatment with allopurinol, xanthine may accumulate, resulting in xanthine nephropathy.[19] Rasburicase is considered more effective than allopurinol for the prevention and treatment of TLS because it prevents xanthine accumulation and directly breaks down UA. In our case, after treatment with hydration and rasburicase, the UA level decreased to 0 mg/dL immediately and renal function improved. We believe that it is better to use rasburicase rather than allopurinol for the treatment of established TLS.

In conclusion, we experienced a rare case of TLS after a single dose of cabazitaxel for metastatic CRPC. The use of rasburicase for established TLS is beneficial to decrease the UA level, leading to renal function improvement. However, it is extremely important to assess the risk factors for TLS and to perform active prevention procedures to avoid fatal outcomes.

Conflict of interest

The authors declare no conflict of interest.

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