Tumor lysis syndrome during radiotherapy for prostate cancer with bone and bone marrow metastases without visceral metastasis

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A 60-year-old male patient presented to our clinic with metastatic (bone and bone marrow) prostate cancer. Radiotherapy (RT) with a total of 30 Gy was planned in 10 fractions for the painful left shoulder region. On the 6th day of RT, urinary output decreased suddenly and dyspnea developed. Laboratory findings suggested tumor lysis syndrome (TLS). The patient, who showed improvement in overall status and had no requirement for hemodialysis up to this time, developed sudden impairment in overall status, dyspnea, and hypotension on the 11th day of follow-up. Thirty minutes after the development of these symptoms, the patient had a cardiopulmonary arrest and died. At the time of writing this was the fourth case of TLS during RT for solid tumors in adults, the first case of TLS during RT for prostate cancer and the fifth among total cases of prostate cancer in published reports.

Tumor lysis syndrome (TLS) is a well-described, potentially fatal clinical entity involving hyperkalemia, hyperuricemia, hypocalcemia, hyperphosphatemia, and renal failure that typically occurs in patients with rapidly growing neoplastic disease such as non-Hodgkin lymphoma, leukemia, and, rarely, solid tumors following cytotoxic chemotherapy. It is less frequently described after radiotherapy (RT) for lymphoid and hematological malignancies. TLS following RT for solid tumors is a very rare complication. In published reports, only three cases of TLS following RT for solid tumors have been reported to occur among adults. The occurrence of TLS in prostate carcinoma is also extremely rare. Only four cases of TLS in prostate carcinoma have been reported in the published reports. We report an extremely rare case of TLS during RT for prostate cancer with bone and bone marrow metastases without visceral metastasis. In the published reports, this is the fourth case of TLS during RT for solid tumors in adults and the first case of TLS during RT for prostate cancer.

CASE
A 60-year-old male patient had presented to the urologist with complaints of dysuria 2 years previously, and the tests led to a decision to carry out a biopsy, on the basis of which the patient was diagnosed with adenocarcinoma (Gleason 5+4). Following diagnosis, bone scintigraphy performed for the purpose of staging revealed the presence of bone metastasis. Total prostate specific antigen (PSA) was 53 ng/mL. The following medications were initiated: goserelin acetate 10.8 mg (once every 3 months), ciproteron acetate 100 mg (daily), and zoledronic acid 4 mg (once every 3 weeks). PSA measured at the third month of treatment was 19.3 ng/mL, and the PSA value measured at the sixth month was 35.5 ng/mL. Six months after the diagnosis, the patient had lumbosacral pain, for which he received palliative RT in 10 fractions for a total of 30 Gy. After this, the patient, who did not make his follow-up visits regularly, presented to the physician 18 months after the diagnosis upon occurrence of right femoral pain. An increase in the PSA value (153 ng/mL) was recorded. Bone scintigraphy performed at that time revealed an increase in bone metastases. A total of 20 Gy palliative RT was administered to the right femur in 5 fractions. Following RT, administration of docetaxel (75 mg/m², day 1), estramustine (280 mg, 5 doses, every 6 hours), and zolendronic acid (4 mg, every 21 days) was planned at the clinic where the patient was being monitored. The
case report

patient, who received 6 cycles of therapy, had a PSA value of 34 ng/mL at the end of treatment. The PSA value was found to be 300 ng/mL 2 months after the end of treatment (the highest value that could be measured by the laboratory). Bone scintigraphy, and thorax and abdominal computed tomography (CT) were planned for staging in the patient, who exhibited rapid progression and an increase in bone pain. While no metastasis was detected on thorax and abdominal CT, bone scintigraphy detected prevalent bone metastases that were increased compared to previous scintigraphies (Figure 1).

The hematologic examination revealed mild anemia and thrombocytopenia. Hemogram findings were as follows: hemoglobin 6 g/dL, white blood cells 6.1 × 10^9/L, and platelets 89 × 10^9/L. Peripheral blood smear revealed a leukoerythroblastic blood picture. Platelets were found to be reduced on blood smear. In the differential leukocyte count, neutrophils showed a mild shift to the left. Therefore, an overall picture of leukoerythroblastosis was considered. A bone marrow aspirate revealed that the marrow was infiltrated by tumors composed of nests of poorly differentiated cells. A total of 30 Gy RT was planned in 10 fractions for the painful left shoulder region. On the 6th day of RT, the urinary output decreased suddenly and dyspnea developed. Biochemical analysis revealed the values shown in Table 1.

The patient had previous coronary bypass anamnesis and an ejection fraction of 50% on echocardiography. The central venous pressure catheter was opened. Central venous pressure levels were measured, and the patient was administered a control fluid. Sodium bicarbonate was added to treat for urinary alkalinization. Daily biochemical follow-up was planned. On the 9th day of follow-up, LDH, urea, creatinine, and uric acid regressed (Table 1). The patient, who improved in overall status and had no requirement for hemodialysis up to this time, developed sudden impairment in overall status; dyspnea and hypotension developed on the 11th day of follow-up. Thirty minutes after the development of these symptoms, the patient had a cardiopulmonary arrest and died.

**DISCUSSION**

Tumor lysis syndrome is seen in patients with hematologic malignancies sensitive to chemotherapy, within days of receiving chemotherapy. TLS following RT for solid tumors is a very rare complication. In the published reports, only 3 cases of TLS following RT for solid tumors have been reported to occur among adults. The first case was described by Tomlinson in a patient with medulloblastoma; the second was described by Rostom in a patient with metastatic breast cancer;
and, finally, the third case was described by Noh in a patient with non-small cell lung cancer. In the published reports, this is the fourth case of TLS during RT for solid tumors in adults.

RT is generally used in the treatment of localized targets, which includes cancer. Recent studies indicate that RT recruits biological effectors outside the treatment field and has systemic effects. Investigations suggest that systemic effects are associated with the immune system and cytokines. TLS in our patient may be explained by the systemic effects of local RT.

The occurrence of TLS in prostate carcinoma is also extremely rare. Sorscher reported the first case of TLS associated with docetaxel chemotherapy for metastatic prostate cancer. Another case of TLS was reported by Wright in a patient with metastatic prostate cancer, after treatment with paclitaxel chemotherapy. Only one case of prostate cancer complicated by TLS after 6 days of combined androgen blockage has been reported, and one case of spontaneous TLS in metastatic prostate cancer has been reported. In the published reports, this is the first case of TLS during RT for prostate cancer and the fifth among total cases of prostate cancer. In all of these cases, there was evidence for solid organ metastasis together with prevalent bone metastases (one had pulmonary metastasis and the other had hepatic metastasis). Our patient is the first one to develop TLS without solid organ metastasis among all patients with prostate cancer. This case demonstrates that TLS may develop with RT in solid tumors and prostate cancers, even if rare. As is the case in our patient, one should note that prophylaxis may be required in high-risk patients, even in the absence of solid organ metastasis, primarily in those with a very short PSA half-life.

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