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**Case Report**

# A Case of Tumor Lysis Syndrome during Palliative Radiotherapy for Breast Cancer Metastases

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**Keywords**
Tumor lysis syndrome · Solid tumor · Palliative radiotherapy

**Abstract**
Tumor lysis syndrome (TLS) is the rapid disintegration of a malignant tumor treated with anticancer drugs or radiation, causing electrolyte abnormalities such as elevated uric acid levels, elevated potassium and phosphorus levels, and decreased calcium levels. These abnormalities can lead to hypotension, renal dysfunction, consciousness disorders, and even death in some cases. The current patient was a 65-year-old woman who had breast cancer with local invasion, lung metastasis, and bone metastasis from the time of the initial disease onset. Despite the administration of various chemotherapy and hormone therapy regimens, the tumor increased gradually, and at 2 years and 5 months after the initial onset, pain and bleeding from metastatic infiltration of the cervical lymph nodes were noted. Therefore, radiotherapy was indicated for palliation of pain and bleeding caused by metastatic invasion of the cervical lymph nodes. Irradiation (30 Gy/10fr) was planned with a 3-field technique using 4MVX and 10MVX. Approximately 11 h after the initial irradiation, symptoms such as respiratory distress, tachycardia, and hypotension were observed. Blood tests revealed hyperuricemia and hyperkalemia, leading to a diagnosis of TLS. Dialysis and electrolyte correction were immediately initiated resulting in normalization of electrolytes and stabilization of the blood pressure. It is crucial to understand that TLS is relatively rare but can occur after radiation therapy or in solid tumors, and warrants a prompt response if suspected based on symptoms or blood findings.



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## Introduction

Tumor lysis syndrome (TLS) is caused by the rapid destruction of malignant tumors after treatment with anticancer drugs or radiation. Laboratory data typically show abnormalities such as elevated uric acid levels, elevated potassium/phosphorus levels, and decreased calcium levels. Clinically, hypotension, nausea, and renal dysfunction can lead to impaired consciousness and even death in some cases [1, 2].

In previous reports, most of the cases of TLS occurred after chemotherapy; however, the occurrence of TLS after radiotherapy has also been reported. Moreover, TLS after chemotherapy and radiotherapy often occurs in hematological diseases, such as lymphoma and leukemia, and is rarely observed in solid tumors [1–5]. We report a rare case of TLS that occurred during palliative radiotherapy for breast cancer metastases.

## Case Report

A 65-year-old woman visited a local doctor with the primary complaint of a mass in her left breast. Biopsy revealed invasive ductal carcinoma (ER+, PR+, HER2−, MIB-1 Index: 60%). Because local infiltration and lung and bone metastases were confirmed by imaging diagnosis at the first visit, she subsequently underwent chemotherapy, including doxorubicin, cyclophosphamide, paclitaxel, eribulin, and bevacizumab; and hormone therapy, including anastrozole and letrozole. However, the disease progressed gradually and she was referred to our hospital for palliative radiotherapy for pain relief and hemostasis because of exacerbation of pain from a metastatic lesion located on the right neck and bleeding from an ulcer caused by the skin infiltration of lymph node metastasis. CRP before radiation therapy was 2.02. No hormones or anticancer drugs were taken at the time of irradiation. Two years and 5 months after the initial diagnosis and after 3 months since the last chemotherapy administration, her current medical history included neurofibromatosis type 1 and uterine fibroids. She had no previous history of radiation therapy.

A CT scan revealed a large soft tissue mass and sclerotic destruction of the right scapula. Numerous neurofibromas were also observed in Figure 1. Therefore, as palliative treatment, 3-field irradiation using 4MVX and 10MVX, 30 Gy/10 fr/2 weeks was planned as shown in Figure 2. We used a combination of 4 and 10MVX at the same angle from the ventral side and 10MVX from the dorsal side. The radiation field was mainly the soft tissue mass, and the right scapula was included as far as possible, without inclusion of the lung field. The gross tumor volume calculated using CT was 333.8 $cm^3$. The patient's general condition at the time of treatment planning was an Eastern Cooperative Oncology Group Performance Status score of 3.

After the first irradiation, no particular abnormalities were observed. Approximately 11 h after irradiation session, the patient complained of respiratory distress in the hospital ward and exhibited an $SpO_2$ of approximately 83%, indicating grade 3 hypoxia (CTCAE v 5.0). As SpO2 was low, oxygen administration was started with 2l by cannula and later with 12L by reservoir mask to reach 100% $SpO_2$. Peripheral chilliness, facial pallor, tachycardia, and decreased blood pressure (approximately 80/60 mm Hg; normally approximately 130/80 mm Hg) were observed.

Data obtained immediately after symptom onset revealed marked increases in uric acid, from 4.9 to 8.5 mg/dL, and potassium, from 4.6 to 7.7 mEq/L, compared with the values recorded on the previous day, which met the criteria for grade 4 hyperuricemia and grade 4 hyperkalemia (CTCAE v 5.0). Her creatinine level had also elevated, from 0.45 to 0.76 mg/dL, suggesting acute renal dysfunction. Almost no change was observed in calcium levels. After

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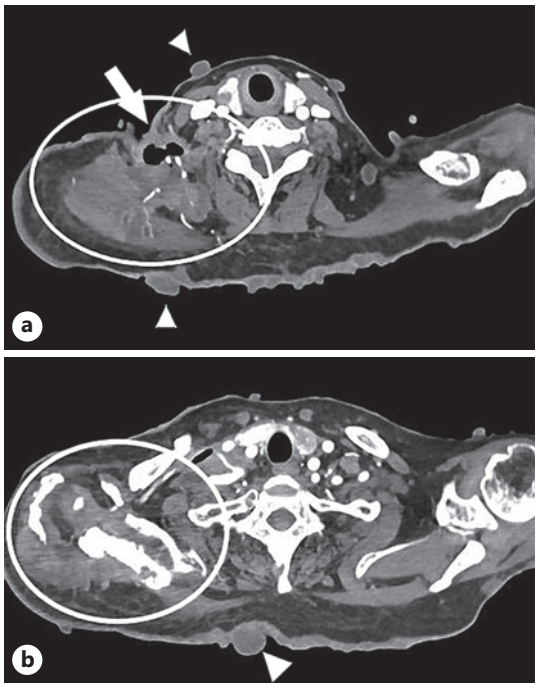


**Fig. 1.** Enhanced CT images before radiotherapy. **a** Soft tissue mass is observed in right clavicular fossa (circle), and skin ulcer is also observed (arrow). Neurofibromas are seen on the skin (arrowhead). **b** Slice is obtained slightly caudal to A. Destruction on the right scapula and surrounding soft tissue mass is observed (circle).

artificial dialysis, the uric acid level was normalized to 6.2 mg/dL, the potassium level to 3.2 mEq/L, and the creatinine level to 0.56 mg/dL. Phosphorus was not measured (with the exception of the measurements performed at admission).

The patient was moved to the intensive care unit with a diagnosis of TLS. Subsequently, artificial dialysis and acidosis correction were performed, which led to improvements in the laboratory data and stabilization of the blood pressure. His respiratory status gradually stabilized and he was turned off oxygen the next day. It was determined that it would be difficult to continue radiotherapy, and the patient was transferred to the referral hospital. After transfer, the pain remained unchanged, the bleeding remained almost unchanged, and no abnormalities in laboratory data were observed. Although image evaluations, such as CT/MRI/PET, were not performed after radiotherapy, there was no significant change in tumor size in appearance. However, her general condition gradually deteriorated because of cachexia, and she passed away about a month and a half later.

## Discussion

TLS occurs when malignant tumors are treated with anticancer drugs or radiation, leading to rapid tumor destruction and causing electrolyte imbalance leading to hyperuricemia, hyperkalemia, hyperphosphatemia, and hypocalcemia. Potassium is typically elevated within 6 h after treatment, followed by abnormal phosphorus, calcium, and uric acid levels, and creatinine elevation. Clinically, hypotension, arrhythmia, nausea, and in worse cases, acute renal failure, decreased level of consciousness, and death have been reported in less than half of the cases [1, 2].

TLS is divided into laboratory TLS and clinical TLS, and the criteria are defined based on the levels of uric acid, phosphorus, potassium, etc. [1, 2]. Laboratory TLS refers to the presence of two abnormalities among hyperuricemia, hyperkalemia, and hyperphosphatemia from 3 days before to 7 days after the start of chemotherapy or radiotherapy. Clinical TLS is

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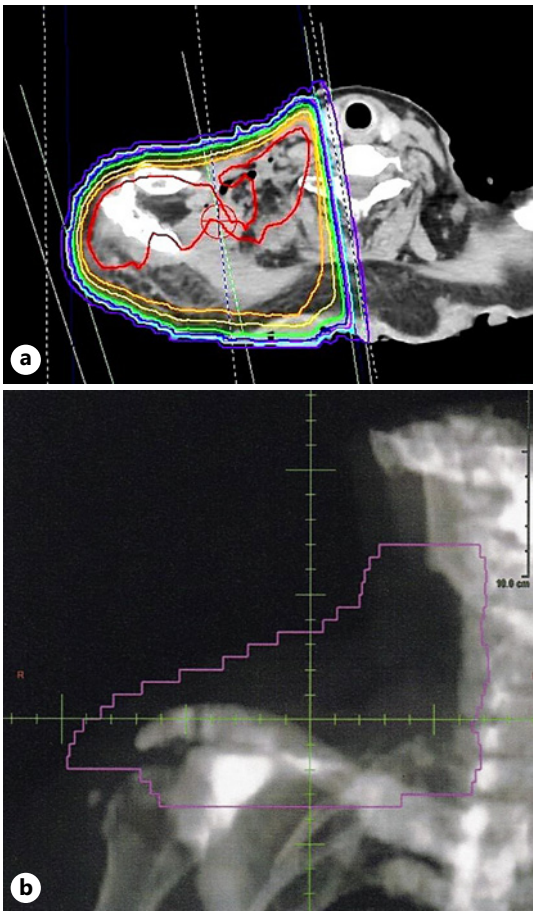


**Fig. 2.** Radiotherapy planning. **a** 3-field irradiation using 4MVX and 10MVX, 30 Gy/10fr/2 weeks was planned (red line at 100% dose, orange line at 95% dose). **b** The DRR image shows that the irradiation field includes the right clavicular fossa to the neck.

defined as a combination of renal dysfunction, arrhythmia, convulsion, or sudden death. As hyperuricemia and hyperkalemia were observed in the present case, it can be classified as laboratory TLS. Moreover, because arrhythmia and an increase in creatinine of more than 0.3 mg/dL from admission were observed, corresponding to renal dysfunction, this case met the criteria for clinical TLS.

Molecular-targeted drugs, such as imatinib mesylate, sorafenib, rituximab, cetuximab, and bevacizumab, as well as docetaxel and gemcitabine hydrochloride, have been reported as causative drugs of chemotherapy-induced TLS [6]. Water load, diuresis, allopurinol, febuxostat, dialysis, and blood purification therapy are used to treat this condition [2]. TLS is common among blood cancers (leukemia, lymphoma, etc.), which usually respond well to treatment, and is rare in solid tumors, being observed at a frequency of about 1–5% [2–5]. TLS after treatment for small cell lung cancer and breast cancer metastases is relatively common among the cases of TLS of solid tumors reported in the literature [3, 7, 8]. Furthermore, most of the reported cases of TLS are caused by chemotherapy, with radiation-therapy-induced TLS being relatively rare. To the best of our knowledge, this case is the eighth reported case of TLS after radiotherapy for solid tumors in adults [Table 1]. None of the patients used concurrent chemotherapy during radiotherapy. Among solid cancers, there are many reports of TLS after chemotherapy for breast cancer, followed by small cell lung cancer; however, this was the second case of TLS after radiotherapy [4, 7, 8]. The first case occurred after wide-area, high-dose, hemi-body irradiation [8]. It has been reported that the cause of TLS in solid tumors may be that some breast cancers are particularly sensitive to chemotherapy and radiotherapy [4]. Although in the present case treatment was also administered to manage breast cancer

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**Table 1.** Reported cases of TLS after radiotherapy for solid tumors in adults

| Author | Year | Primary disease | Age/gender | Onset of TLS | Radiation dose | Outcome of TLS |
|---|---|---|---|---|---|---|
| Tomlinson et al. [9] | 1984 | Medulloblastoma | 34F | 3d | 3 Gy/3fr | Resolved |
| Rostom et al. [8] | 2000 | Breast ca | 73M | 2d | 8.5 Gy + 3.5 Gy | Died |
| Noh et al. [11] | 2008 | NSCLC | 52M | 2d | 6 Gy/2fr | Died |
| Kaplan et al. [10] | 2012 | Prostate ca | 60M | 8d | 18 Gy/6fr | Died |
| Dar et al. [13] | 2014 | Melanoma | 65M | 7d | Not reported | Died |
| Stuart S, [5] | 2017 | NSCLC | Middle M | 3d | Not reported | Resolved |
| Moiseff et al. [12] | 2020 | Gastric ca | 43M | 6d | 20 Gy/5fr | Died |
| Index case | 2023 | Breast ca | 65F | 1d | 3 Gy/1fr | Resolved |

metastasis, the tumor pathology was unremarkable. TLS after radiation therapy for solid tumors has been reported for prostate cancer metastases, non-small lung cancer, gastric cancer metastases, and melanoma metastases [9–13].

Regarding neurofibromatosis type 1, although there is a risk of radiation-induced angiosarcoma and malignant neurofibroma, there are no reports of an association between these conditions and TLS. Noh et al. [11] considered that TLS caused by radiotherapy often occurs relatively early when the dose is low. This case also occurred after one fraction of irradiation; therefore, it was thought that caution is required, especially after the onset of irradiation.

## Conclusion

A case of TLS caused by palliative radiotherapy for breast cancer metastasis is reported. This was the second case of TLS during radiotherapy for breast cancer metastasis in the literature. Although TLS occurs rarely in the case of solid tumors and radiation therapy, it is important to be aware that it can occur. When TLS is suspected based on symptoms and blood examination, an appropriate response is necessary. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material.

## Acknowledgments

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## Statement of Ethics

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images prior to her passing away. Ethical approval is not required for this study in accordance with local or national guidelines.

## Conflict of Interest Statement

The authors have no conflicts of interest to disclose.

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## Author Contributions

Mitsuhiro Furusawa, Kozue Matsuishi, Kei Horino, Hideki Inoue, and Michio Abe treated the patient. Mitsuhiro Furusawa wrote the main text of the manuscript and collected photographs. Natsuo Oya did final revision of the text. All authors approved the final version of the manuscript.

## Data Availability Statement

All data supporting the findings of this case report was included in this article. Further inquiries can be directed to the corresponding author.

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