Docetaxel induces radiation recall myositis: A case report

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Abstract. The present study described a radiation recall (RR) myositis case following docetaxel chemotherapy in a 26-year-old female with metastatic breast cancer. The left pubis and left femur head and neck were treated with palliative radiotherapy to a dose of 20 Gy in 5 daily fractions. After 2 months, a whole-body positron emission tomography scan revealed new lesions, and systemic treatment was initiated with docetaxel chemotherapy (75 mg/m^2, every 3 weeks). After the second dose, the patient started to feel pain in her left femur with erythema on her skin on the lumbar and gluteal region, in addition to swelling. On magnetic resonance imaging, edematous changes, increased signal enhancement on T2 and increased contrast uptake of muscles were observed, suggesting myositis on the irradiated field. The present study is the second case report published on the literature on RR myositis following docetaxel treatment, which emphasizes the importance of awareness about this phenomenon when considering differential diagnosis of pain.

Introduction

Radiation recall (RR) is a rare phenomenon that involves an inflammatory tissue reaction on the previously irradiated site upon systemic administration of an initiating agent within days (>7 days), months or years (1). Since it was first described in 1959, dermatitis has been the most frequently reported and clinically observed RR reaction (2). After skin, muscles, mucous membranes in the upper respiratory tract, lung, gastrointestinal tract and central nervous system are other recognised sites of this inflammatory reaction (3). RR myositis (RRM) is the second most commonly reported RR toxicity after dermatitis in the literature. A literature search using PubMed was performed, and 'radiation recall myositis' was used as a search term to review previous cases related to docetaxel and other chemotherapy agents. RRM has been associated with various chemotherapies, and gemcitabine was responsible for ~2/3 of these cases; however, only 1 case of RRM was found following docetaxel and carboplatin combination chemotherapy (4).

The present study describes a patient with RRM and dermatitis, and constitutes the second reported RRM case after docetaxel chemotherapy in the literature. The difference between the present case and the previously reported case is that the present study reported on RRM after only docetaxel treatment, whereas the previous case reported on RRM after treatment with a combination of carboplatin and docetaxel. The present case highlighted an important but rare phenomenon in a patient with breast cancer receiving docetaxel chemotherapy.

Case report

A 26-year-old woman who was diagnosed with breast cancer was admitted to the Kocaeli University Medical Oncology Clinic (Kocaeli, Turkey) in March 2020, after undergoing a right breast lumpectomy and axillary lymph node dissection. The patient was diagnosed with multifocal invasive breast carcinoma and axillary lymph node metastasis, and the tumor was positive for estrogen and progesterone receptors, negative for human epidermal growth receptor 2 and 80% positive for Ki-67. A post-operative positron emission tomography (PET) scan carried out in March 2020 demonstrated multiple hypermetabolic lymph nodes in the mediastinum, metastasis in the liver and multiple bone metastasis. Her initial treatment involved an aromatase inhibitor combined with a luteinizing hormone-releasing hormone agonist and zoledronic acid. The patient was referred to the Kocaeli University Radiotherapy Clinic (Kocaeli, Turkey) in April 2020 for palliative treatment of the bone metastases, which caused severe pain.

The left pubis and left femur head and neck were treated with palliative 3D-conformal radiotherapy at a dose of 20 Gy in 5 daily fractions (Fig. 1), while the lumbar spine (from L2 to S1) was treated with a dose of 30 Gy sequentially. The treatment ended on 12th May 2020. After 2 months, in July 2020, a PET/computed tomography scan revealed new lesions, and the medical oncologist of the patient initiated systemic treatment with docetaxel (75 mg/m^2 every 3 weeks) as a single agent, while a new bone lesion on T8 was treated with sterotactic body radiotherapy (SBRT) at a dose of 24 Gy in 3 daily fractions. After 3 months of palliative radiotherapy and a second dose of chemotherapy, the patient described a gradually increasing pain in her left femur with erythema on her skin in the lumbar and gluteal region, in addition to

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swelling on the gluteal muscles. Magnetic resonance imaging (MRI) of the pelvis revealed asymmetrical swelling of her left proximal thigh with signal enhancement on T2 and increased contrast uptake on T1 (Fig. 2) on muscles. In the differential diagnosis, autoimmune and inflammatory etiologies (polymyositis, dermatomyositis and vasculitis) were considered, and rheumatoid workup with serologies, including anti-nuclear and anti-double stranded DNA antibodies against nuclear antigens (Euroimmun) was performed. The results were within the normal limits (Table I). In physical examination, the muscle strength was normal.

The diagnosis was myositis and dermatitis associated with an RR reaction induced by docetaxel based on the association with radiation treatment volume and the radiographic evidence of myositis (Figs. 1 and 2). The time period from the final treatment with radiation to the development of myositis was 3 months. The patient was treated with an oral non-steroidal analgesic (etodolac, 400 mg b.i.d), and chemotherapy (docetaxel 75 mg/m^2 every 3 weeks) continued. The patient's pain decreased gradually in 1 month; however, after nine cycles of chemotherapy, extensive liver metastasis appeared and the patient died.

Table I. Laboratory findings of the patient.

Laboratory test	Variable, value (normal range)
Anti-nuclear antibodies	Negative
Anti-double stranded DNA antibodies	Negative
Serum creatine kinase, U/l	47 (0-145)
RF, IU/ml	1.99 (<14.0)
C3, g/l	1.42 (0.90-1.80)
C4, g/l	0.40 (0.10-0.40)

RF, rheumatoid factor; C3, complement 3; C4, complement 4.

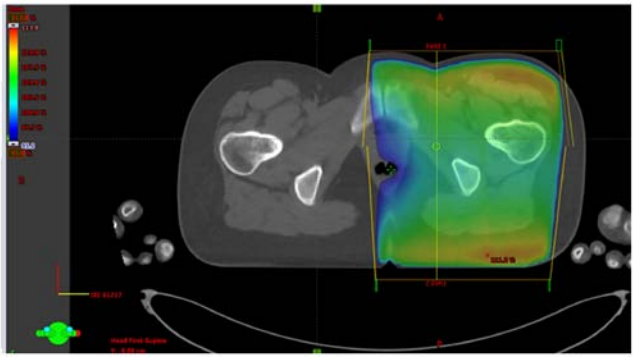

Figure 1. Axial computed tomography section of the patient demonstrating the anteroposterior-posteroanterior radiotherapy treatment field showing the dose-color wash of the irradiated left hip. R, right.

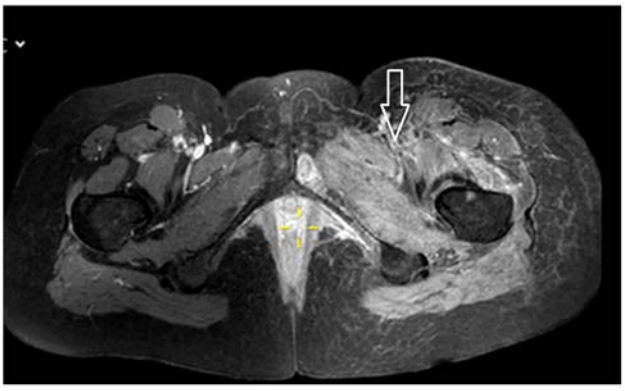

Figure 2. Axial T1-weighted magnetic resonance image showing increased enhancement (indicated by the arrow) and asymmetrical swelling on the left-sided hip muscles and subcutaneous tissue corresponding to the radiotherapy treatment field.

Discussion

Docetaxel is an important agent used to treat breast cancer in all settings (neoadjuvant, adjuvant and metastatic). The most common treatment-related side effects are infusion reactions, febrile neutropenia, fatigue, fluid retention and peripheral neuropathy (5). It can also lead to side effects in muscle, such as myalgia-arthralgia syndrome, which is oftenly associated with moderate or severe generalized musculoskeletal pain during the first hours or days after taxane administration (6). Myositis by itself is an uncommon side effect, and has been reported only in 5 cases (7).

Docetaxel-induced RR reactions have been reported as dermatitis and mucositis since 1994 (8). In 2006, Mizumoto *et al* (9) documented the incidence of a RR reaction following treatment with docetaxel as 1.8% in their series. Chemotherapy-related RRM cases have been reported in the literature to be commonly associated to gemcitabine chemotherapy (10,11). To the best of our knowledge, the present case together with a previous case are the only 2 RRM cases upon docetaxel chemotherapy described in the literature. In the case reported by Chao *et al* (4) a 55-year-old man with metastatic prostate cancer was treated with palliative RT for his right hip at a dose of 30 Gy in 10 daily fractions by anteroposterior and posteroanterior fields. Carboplatin and docetaxel chemotherapy was initiated 2 months after the completion of RT. After 6 months of RT, recurrent and persistent pain, and swelling complaints of the patient emerged in the right hip and thigh, which were resolved temporarily following pretreatment with dexamethasone. His MRI revealed asymmetrical swelling of the right thigh musculature, which was irradiated.

In the present case, docetaxel was the single agent and the triggering cause of RRM, and both dermatitis and myositis were observed. Naranjo *et al* (12) assessed the correlation between adverse effects and docetaxel with a score of 5, and the correlation was defined as 'probable'.

The pathophysiology of RRM is unknown, and the current hypothesis suggests that cytotoxic treatment following radiotherapy causes memory reaction in the remaining surviving cells within the previously irradiated field. The other commonly suggested hypotheses include depletion of stem cells, changes in the local vasculature and drug-induced hypersensitivity reactions (13). There are suggestions about the implication of radiation dose threshold and fraction size in recall reactions, but there is no clear evidence to support such hypotheses. In

addition, they can occur at any time varying from days to years after completing radiotherapy.

In the present case, RRM symptoms started 3 months after radiotherapy and 6 weeks after docetaxel chemotherapy. Myositis, except dermatitis, was not observed in the lumbar region although this area was treated with a higher dose than the one used for the hip. The patient did not complain about any pain in the T8 region, which was treated with SBRT.

In conclusion, pain, swelling, edema and enhanced contrast in the underlying musculature of previously irradiated areas following treatment with a chemotherapy agent are characteristics of RRM, and should be considered in the differential diagnosis of localized pain. Cessation of the treatment is not needed always, and it depends on the severity of the reaction. Since it usually resolves after 1-2 weeks of administration of corticosteroids and nonsteroidal anti-inflammatory drugs, patients can continue treatment without rechallenge.

Despite the most common cause of RRM is gemcitabine, docetaxel should be also acknowledged as a cause of RRM.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

AÜK collected patient data and designed the study. BA participated in the analysis and interpretation of data. AÜK and BA both contributed to manuscript drafting, writing and final correction of the manuscript. All authors read and approved the final version of the manuscript, and confirm the authencity of all the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

The patient provided written informed consent for the publication of the present article, including any associated data and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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