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Teaching Case

Irinotecan-induced radiation-recall myositis in a patient with metastatic breast cancer: A case report

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Introduction

Radiation-recall is an inflammatory reaction in a previously irradiated area following a systemic agent.[1] A hypothesis for radiation-recall development includes radiation-induced local exacerbation of a chronic inflammatory response followed by initiation of chemotherapy at a later time, causing recurrent cytokine up-regulation.[2] A distinction between radiosensitization versus radiation-recall should be made. A reaction occurring within a time interval <7 days from radiation completion and chemotherapy initiation is defined as radiosensitization. Radiation-recall is defined as an inflammatory reaction that occurs weeks to years after radiation therapy.[3,4]

Skin, the most common site of radiation-recall, is hypothesized to undergo cytokine-induced oxidative stress contributing to keratinocyte necrosis, resulting in a skin reaction[5]; however, 33% of radiation-recall cases are in nonskin sites.[3] In particular, radiation-recall myositis has been linked to various chemotherapies. Table 1 summarizes reported incidences of radiation-recall and the inciting chemotherapies.

Although the pathophysiology of radiation myositis is less well-known than radiation dermatitis, endothelial damage may cause intimal proliferation and subsequent subintimal deposition of collagen, with muscle fibrosis and myositis. Radiation myositis imaging can show enhancement on postcontrast scans and is an important diagnostic component.[6]

To our knowledge, radiation-recall myositis has not previously been associated with irinotecan. We describe a case of radiation-recall myositis incited by irinotecan that developed 7 months after palliative radiation therapy for a bone metastasis.

Case report

A 45-year-old premenopausal woman was diagnosed in January 2008 with clinical T1N1M0 high-risk primary breast cancer. She underwent lumpectomy and axillary dissection, showing a 1.2 cm infiltrating ductal, ER+, PR+, HER2/Neu negative carcinoma with a Ki67 >80%. She received adjuvant cyclophosphamide, methotrexate, 5-fluorouracil chemotherapy until October 2008 followed by whole breast radiation therapy. She then underwent a bilateral oophorectomy in mid-2009.

Unfortunately, positron emission tomography/computed tomography scans in 2011 showed metastatic disease. She had rapid disease progression while on weekly Taxol and bavituximab and then on capecitabine. After starting doxorubicin, she developed right hip pain, resulting in its discontinuation. Magnetic resonance imaging of the pelvis demonstrated a 5 cm right acetabular metastasis with a nondisplaced pathologic fracture. She received palliative

Conflicts of interest: None.

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Table 1 Summary of published radiation-recall cases

Author, y	Tumor	Age, sex	Radiation dose (Gy)/fractionation	Chemotherapy	Time interval (chemotherapy to reaction)	Recall reaction treatment	Radiation-recall outcome
Patel, 2016[8]	Nasopharyngeal cancer	16, F	70.2/NR	Gemcitabine, oxaliplatin	Concurrent	Steroids	CR
Florczynski, 2016[9]	Rectal cancer	65, M	50/25	Capecitabine	2 mo	Steroids	CR
Grover, 2015[10]	Cervical cancer	63, M	30/10	Gemcitabine, carboplatin	2 wk	Narcotics	Continued chemo, CR
Maeng, 2014[11]	Adenocarcinoma (unknown primary)	57, F	60/42	Carboplatin, paclitaxel	4 mo	Analgesics	CR
Delavan, 2015[12]	Breast cancer	54, F	8/1, 39/13	Gemcitabine	1 mo	Steroids	CR in 1 wk
Graf, 2014[13]	Lung cancer, anal cancer	44,F	NR	Carboplatin, Gemcitabine	2 mo	Steroids, narcotics	CR in 1 mo
Eckardt, 2013[14]	Forearm sarcoma	14, F	48/18	Gemcitabine, docetaxel	7 d	Steroids	CR in 1 y
Hattangadi, 2012[15]	Ewing sarcoma	11, F	57.6/32	VDC-IE	8 d	NSAID + narcotics	CR in 3 wk
	Ewing sarcoma	16, M	55.8/31	VDC-IE	7 d	NSAID + steroids	CR
Lock, 2011[16]	Poorly differentiated adenocarcinoma	50, F	44.1/15	Gemcitabine	12.5 wk	NSAID + vitamin C/E	Continued chemo, CR
Heirwegh, 2010[17]	Ewing Sarcoma	16, M	64/40	VIDE	NR	None	CR
Squire, 2006[18]	Lung cancer	54, F	30/10	Gemcitabine	2 mo	Steroids	Continued chemotherapy, CR
Fakih, 2006[19]	Pancreatic cancer	52, M	50.4/28	Gemcitabine	4 mo	None	CR
Borroni, 2004[20]	Multiple myeloma	55, M	36/12, 35/10	Cyclophosphamide	Immediate	NR	NR
Friedlander, 2004[1]	Pancreatic cancer	62, M	50.4/28	Gemcitabine	Concurrent	Steroids	CR
Jeter, 2002[21]	Pancreatic cancer	52, F	50.4/28	Gemcitabine	9 wk	NSAID	CR
Fogarty, 2001[22]	Lung cancer	65, F	36/12	Gemcitabine, carboplatin	6 wk	Steroids	CR

CR, complete resolution; F, female; M, male; NSAID, nonsteroidal anti-inflammatory drug; NR, not recorded; VDC-IE, vincristine, doxorubicin, and cyclophosphamide alternating with ifosfamide and etoposide; VIDE, vincristine, ifosfamide, doxorubicin, etoposide.

radiation therapy in October 2012 with 20 Gy in 5 fractions to the right acetabulum. She had improvement in her hip pain.

One month after radiation, her chemotherapy was changed to gemcitabine and cyclophosphamide for 5 months until she developed pulmonary metastases. Her chemotherapy was adjusted to irinotecan. After 2 cycles of irinotecan, she reported increasing pain in her right buttock and anterior groin, prompting imaging scans.

Positron emission tomography/computed tomography scans demonstrated increased uptake in the soft tissues surrounding the right acetabulum, and magnetic resonance imaging of the pelvis demonstrated edema and enhancement throughout the right buttock and pelvic musculature (Fig 1). The inflammatory changes on imaging sharply demarcated her right acetabular radiation fields (Fig 2). The previously treated right acetabular lesion remained stable, and she was diagnosed with irinotecan-induced radiation-recall reaction.

The patient was treated with ibuprofen and, after 1 month, she had reduced hip pain and was able to discontinue all pain medication.

Discussion

Radiation-recall diagnosis requires evaluation of a patient's treatment history, symptoms, physical examination, and radiologic studies. The hallmark is development of symptoms and radiographic changes corresponding to previously irradiated fields.[4] Radiation-recall is unpredictable