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Case Study

A case of thigh swelling in a patient with metastatic breast cancer receiving combination chemotherapy

A. F. Schott

Department of Internal Medicine, University of Michigan Medical School, University of Michigan Comprehensive Cancer Center, MI, USA.

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Presentation and diagnosis

The patient is a 69-year-old woman with metastatic breast cancer. She was initially diagnosed with Stage II breast cancer 13 years previously. The tumor was estrogen receptor (ER) and progesterone receptor (PR) positive, and Her-2 neu negative. Her initial adjuvant therapy was with tamoxifen, but she progressed 5 years after the original diagnosis with liver and bone metastases. Over the subsequent 7 years she received intravenous bisphosphonates in addition to multiple chemotherapy regimens, including docetaxel, doxorubicin, vinorelbine, capecitabine, paclitaxel, and carboplatinum. She responded well to each cytotoxic chemotherapy regimen, and during times of disease stability she was treated with endocrine therapy, although the periods of disease stability became progressively shorter throughout her course.

During the latest of her chemotherapy 'holidays' she developed progressive pain in her left leg, and a lytic lesion in her proximal femur was radiated. Toward the end of radiation treatment, she developed progressive right upper quadrant abdominal pain, nausea, and elevated liver transaminases. She was found to have significant progression of her liver metastases, although it had been only 7 weeks from her last systemic therapy. Combination chemotherapy with 5-fluorouracil, leucovorin, gemcitabine, and cyclophosphamide was initiated 2 days prior to the completion of her radiotherapy.

With chemotherapy, there was prompt improvement in transaminases and reduction in her right upper quadrant pain, in association with an improvement in Karnofsky Performance Status from 60% to 80% within 6 weeks. However, 10 weeks after chemotherapy was started, she began to note mild swelling and pain in the left thigh. On examination, there was no redness of the skin, but there was diffuse brawny edema of the left thigh and significant tenderness on palpation. Doppler examination was negative for deep vein thrombosis (DVT), and X-ray showed no change in the known sclerotic femur lesion. Physical therapy for presumed lymphedema was initiated, along with analgesics, and her chemotherapy was continued. The pain and swelling worsened significantly over the subsequent 3 weeks and required escalation of the dose of narcotic analgesic, though these symptoms were noted by the patient to wax and wane without appreciable pattern.

A magnetic resonance imaging (MRI) of the thigh was performed. This showed, consistent with the clinical examination, diffuse circumferential subcutaneous edema, and skin thickening. The rectus muscle was diffusely swollen and edematous, with surrounding fluid. In addition, there was the impression of a 1.0 cm $\times$ 3.5 cm mass in the muscle, demonstrating rim enhancement with central hypointensity, worrisome for necrotic metastasis or abscess. An ultrasound was done to rule out abscess and to aid in a tissue diagnosis. However, this revealed only

Correspondence to: Anne F. Schott, MD, Department of Internal Medicine, University of Michigan Medical School, University of Michigan Comprehensive Cancer Center, MI, USA. E-mail: aschott@umich.edu; Tel: +1 734 615 4762; Fax: +1 734 647 8792

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hyperechogenicity of the entire central portion of the rectus femoris, and therefore no biopsy was attempted.

A review of the MRI findings in relation to her prior radiation ports showed that the visualized inflammation reproduced very closely the irradiated field. The clinical diagnosis was established as panniculitis and myositis due to radiation recall.

Treatment and outcome

With discontinuation of the chemotherapy, continued analgesics, and physical therapy to prevent developing contractures and treat edema, her condition partially improved over the subsequent weeks. Steroids were initiated but were not associated with appreciable change in symptoms.

Discussion

Radiation recall has been most often described as dermatitis [1], although there have been case reports of panniculitis, colitis, and myositis attributed to this phenomenon. A large number of chemotherapy agents have been implicated in its development [2]. Each drug in this patient's three-drug chemotherapy regimen has been reported to cause radiation recall, though a case very similar to this one has been ascribed to gemcitabine [2], and we favor this as the most likely culprit. A recent review of the literature has suggested that gemcitabine-related radiation recall is more likely to affect internal tissue or organs, as opposed to cutaneous inflammation, though any site that has been previously irradiated could be at risk [3].

Due to the rapid progression of hepatic metastatic disease during radiation therapy in this case, the systemic chemotherapy was initiated concurrently with the last two fractions of radiotherapy. Therefore, one could postulate chemotherapy radiosensitization, since 5-FU and gemcitabine are known to be potent radiosensitizers, as well as having been implicated in the phenomenon of radiation recall. As in this case the symptoms of pain and swelling did not begin until over 2 months after the completion of radiation therapy, we favor the diagnosis of radiation recall.

With the rising popularity of partial breast irradiation performed prior to adjuvant systemic chemotherapy, radiation recall may also become a more common phenomenon within the irradiated breast. The diagnosis of radiation recall should be considered in the case of symptoms of inflammatory tissue damage in areas of previous irradiation, both the early stage and metastatic breast cancer patient.

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