CLINICAL VIGNETTE

Radiation Recall Syndrome After Administration of Vinorelbine Monotherapy

Joshua D. Rosenberg, M.D., and Mahshid Mosallaei-Benjamin, M.D.

Case Report

A 67-year-old woman was originally diagnosed with a stage IIA, T2 N0 M0, right breast invasive ductal carcinoma in April 2014. The molecular signature of her tumor indicated estrogen receptor 25% positive, progesterone receptor and HER-2 expression negative, Ki-67 of 85%, and a tumor grade of 3. She had a markedly elevated Oncotype Recurrence Score of 68, confirming a biologically aggressive breast cancer. She underwent a right mastectomy and sentinel lymph node biopsy followed by 6 cycles of adjuvant docetaxel/cyclophosphamide chemotherapy, which was completed in September 2014 at which time she was placed on adjuvant letrozole.

In June 2015, the patient was diagnosed with biopsy-proven right chest wall disease recurrence. At this time, her disease was triple negative with an elevated Ki-67 to 93%. Her BRCA status is unknown to date. She was initiated on capecitabine but quickly progressed. Since that time, she has failed multiple systemic, cytotoxic agents including pegylated-liposomal doxorubicin, carboplatin, nab-paclitaxel, ixabepilone, and eribulin. While the patient's disease has continuously progressed throughout systemic therapy, essentially declaring itself refractory to each successive line, she has not suffered from visceral involvement. The metastatic lesions have progressed along the bilateral chest wall and skin alone. She has suffered from painful, cutaneous tumor nodules throughout her disease course. Radiation oncology treated the patient with 6,400 cGy to the bilateral chest wall from January 15, 2016 through April 8, 2016. Upon more severe, symptomatic cutaneous progression, she was treated with an additional 3,750 cGy of radiation to the bilateral chest wall, including some overlapping tissue from her prior radiotherapy treatments. This course was provided between July 5-27, 2016.

The patient presented to the infusion clinic in October 2016 to begin palliative vinorelbine chemotherapy. Her most recent systemic therapy had been eribulin, which was last delivered early September 2016. After approximately 45 minutes of vinorelbine infusion, she began to suffer extreme, debilitating, burning pain limited to sites of prior radiation. There were no acute skin color changes. She had no signs or symptoms consistent with anaphylaxis, and she was hemodynamically stable. The patient was provided methylprednisolone 60 mg IV, diphenhydramine 25 mg IV, and lorazepam 1 mg IV. She had minimal improved in pain crisis and was subsequent transferred to the local emergency room for more aggressive pain control measures.

Discussion

Radiation recall, also referred to as radiation recall dermatitis (RRD), was originally described in 1959 by Dr. D'Angio and colleagues[1] who described patients at the Children's Medical Center in Boston developing cutaneous reactions upon exposure to actinomycin D in only those areas of previously irradiated skin. The concept and clinical diagnosis of RRD is clearly recognized; however, the pathophysiology and incidence of this relatively uncommon syndrome is poorly understood. RRD is characterized by an acute inflammatory reaction confined to previously irradiated areas felt to be triggered by administration of precipitating systemic agents following radiotherapy.[2] Clinically, the cutaneous reaction occurs in a previously normal appearing focus of skin that has previously been exposed to radiotherapy. The recall can range from a mild rash and dry desquamation and/or pruritis to symptoms that are increasingly painful and may include swelling, vesicles, maculopapular eruptions, and papules.[3] Since D'Angio's original report, many other systemic agents have been implicated, most commonly including the anthracyclines, taxanes, and anti-metabolites such as gemcitabine and capecitabine.[3] Importantly, not all cases have been associated with traditional, cytotoxic agents. The practicing oncologist must also be aware that several RRD cases have been reported following tamoxifen endocrine therapy,[4] simvastatin, and antibiotics.[5]

Multiple hypotheses have been raised in an attempt to explain the etiology and mechanism of RRD including radiation changes such as local vascular insult, epithelial stem cell inadequacy, epithelial stem cell hypersensitivity, and potentially drug hypersensitivity reactions.[2] There has also been commentary in the literature regarding the temporal association between radiation and RRD in addition to the inciting systemic agent and RRD. Camidge et al[2] suggest that cutaneous reactions truly secondary to RRD are reactions occurring more than 7 days following last radiation exposure. Any cutaneous reaction defined before this period of time should be thought of as radio-sensitization. The speed of onset of RRD reactions following systemic therapy ranges from a few minutes out to 14 days later.[6-7]

Therapeutically, most practitioners hold the offending drug and provide supportive care until the symptoms resolve. Depending on the severity of RRD, patients will often be provided systemic and/or topical corticosteroids or nonsteroidal anti-inflammatory drugs given the postulate that the clinical manifestation is due to an acute inflammatory reaction. There are no definitive studies suggesting the precise risk of recurrent RRD should one

re-challenge a patient with the offending drug whether or not they are aggressively pre-medicated.

In summary, RRD may be encountered by oncologic practitioners, and it is important to recognize the clinical aspects of this syndrome, the associated risk factors, and potential interventions to mitigate the severity of this reaction.

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