

1-1-2018

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Recommended Citation

McClelland, Shearwood; Cooper, Paul H; Acheson, Anupama K; Ciporen, Jeremy N; Jaboin, Jerry J; and Mitin, Timur, "Radiation recall myelitis following paclitaxel chemotherapy: The first reported case." (2018). *Journal Articles and Abstracts*. 928.
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LETTER

Radiation recall myelitis following paclitaxel chemotherapy: The first reported case

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(Received: June 7, 2018; Accepted: June 26, 2018)

ABSTRACT

Introduction: Stereotactic body radiotherapy (SBRT) of the spine has become an increasingly utilized modality in the United States, most commonly for metastatic disease (McClelland et al., 2017). Spinal SBRT in patients with spinal instrumentation has been sparsely examined. We report a patient who developed myelitis following spinal SBRT to a region with existing hardware.

Methods: A 55-year-old woman with Stage IV breast cancer developed a T4 vertebral body metastasis and underwent tumor debulking with posteriorly instrumented T3-T5 fusion. Postoperatively she proceeded with SBRT to the T3-T5 vertebral bodies, receiving 30 Gy in 6 Gy/fraction. Seven months later, she required paclitaxel chemotherapy (80 mg/m² per cycle) for new liver metastases.

Results: Eight months following spine SBRT, four weeks after having started chemotherapy she developed intractable back pain and right lower extremity numbness which improved upon receiving steroids for weekly chemotherapy; the numbness subsequently spread to her left leg. Thoracic spine MRI revealed a 1.7 cm ovoid focus of T4-T5 spinal cord enhancement with extensive surrounding cord edema extending superiorly to C6-C7, consistent with radiation myelitis. Hyperbaric oxygen moderately improved her symptoms; fortunately, she never developed motor symptomatology or bowel/bladder dysfunction. Thorough re-evaluation of the original thoracic spine SBRT plan revealed no deviations from the standard of care, nor did re-planning with alternate treatment planning software demonstrate any significant difference in maximum cord dosage than the original plan.

Conclusions: The timing of symptomatology related to chemotherapy administration is consistent with radiation recall myelitis, which has yet to be reported following SBRT. Given the potentially disastrous consequences of myelitis, patients with metastatic disease previously treated with spine SBRT may be susceptible to developing myelitis if treated with paclitaxel chemotherapy.

Keywords: radiation recall myelitis, paclitaxel, spine SBRT, metastatic breast cancer

INTRODUCTION

Stereotactic body radiotherapy (SBRT) of the spine has become an increasingly utilized modality in the United States, most commonly for metastatic disease (1). The safety and efficacy of spine SBRT has been validated from studies with short-term and multi-year follow-up (2-3). The phenomenon of radiation recall myelitis has been reported only once in the literature, in a metastatic melanoma patient receiving dabrafenib after having previously received stereotactic radiotherapy for a lung metastasis (4). We present the first report of radiation recall myelitis following spinal SBRT in a patient after receiving chemotherapy.

CASE REPORT

A 55-year-old woman with Stage IV breast cancer developed a T4 vertebral body mass despite optimal treatment, which extended into the neural foramina at T3-T4 and T4-T5 in close proximity to the exiting T3 and T4 nerve roots as well as epidural space involvement. She elected to undergo T4 tumor debulking with posterior decompressive laminectomies at T3 and T4 with posterior instrumented T3-T5 fusion (four threaded TI Matrix screws with two TI curved rods, Depuy Synthes, Raynham, MA); histopathology revealed this mass to be metastatic breast cancer. After postoperative discussion in our RADIANS (RADIation oncology And NeuroSurgery) multidisciplinary clinic, the patient elected to proceed with SBRT to the T3-T5 spine, receiving 30 Gy in 6 Gy per fraction; this plan was

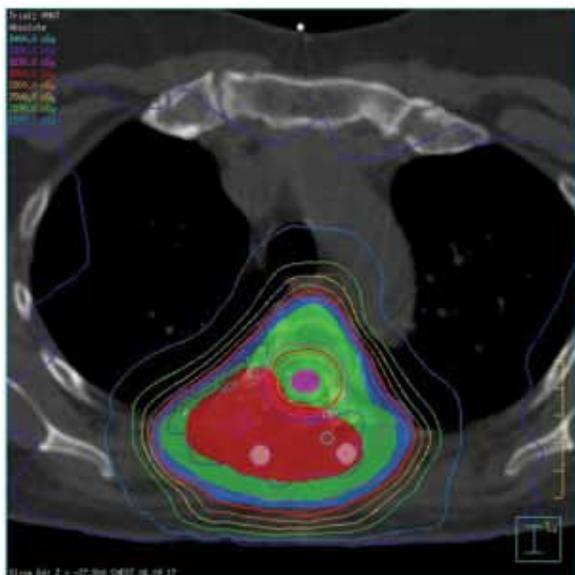


Figure 1. Axial isodose plan of original T3-T5 vertebral body SBRT plan

performed using the Pinnacle treatment planning system (Philips Radiation Oncology; Fitchburg, WI) (Figure 1) (5).

Unfortunately, seven months after SBRT she required chemotherapy for new liver metastases. Four weeks after starting intravenous paclitaxel (80 mg/m² weekly for a five-week course) for chemotherapy (eight months following her spine SBRT), she developed intractable back pain with right lower extremity numbness which improved upon receiving steroids for weekly chemotherapy only to return within each week; this numbness subsequently spread to her left leg. The persistence of these symptoms prompted a thoracic spine MRI eight days after initial symptom onset which revealed a 1.7 cm ovoid focus of spinal cord enhancement at T4-T5 with extensive surrounding cord edema extending superiorly to C6-C7, consistent with radiation myelitis (Figure 2). She was treated with a six-week course of steroids which unfortunately failed to alleviate her symptoms; how-



Figure 2. Sagittal T1-weighted thoracic spine MRI demonstrating spinal cord myelitis at the T4-T5 level consistent with radiation recall myelitis.

ever, she never developed motor symptomatology or any bowel/bladder dysfunction secondary to the myelitis; by this time her fifth and final cycle of paclitaxel chemotherapy had concluded. Subsequently, she elected to undergo hyperbaric oxygen treatment (nine weeks after initial symptom onset), during which her symptoms moderately improved.

Due to the rarity of radiation-induced myelitis, a thorough re-evaluation of the original thoracic spine SBRT plan was performed, revealing no deviations from the standard of care (5). Subsequently, a re-planning exercise was performed using the Monaco treatment planning software (Elekta; Stockholm, Sweden), which revealed a maximum spinal cord dosage within 2% of the original Pinnacle plan, both well in accordance to the spinal cord dose constraints established by Folkert and Timmerman (6).

DISCUSSION

The proximity of metastatic bony spine disease to the spinal cord itself has been a theoretical cause for hesitation when large radiation doses have been proposed for treatment. However, several studies have established the safety and efficacy of spinal SBRT for metastatic disease, as well as appropriate parameters to minimize the morbidity of radiation therapy (2-3, 6).

Given that our center has safely treated patients with indwelling hardware with spinal SBRT in the past without morbidity and that previous series involving instrumented patients demonstrated no increased spine SBRT short or long-morbidity, it is highly unlikely that the spinal instrumentation precipitated the myelopathy in our patient (3, 5). Our re-planning session using a different software system did not indicate a significant difference between the Monaco and Pinnacle treatment planning systems, both of which yielded a maximum spinal cord dose well within the established standard of care (6).

Having ruled out these potential causes of this patient's myelopathy, the most logical explanation is a radiation recall phenomenon, which commonly manifests as myositis, but has only been reported manifesting as myelitis once before (4). In that case, the radiation recall occurred at a similar time frame following completion of radiation after the start of chemotherapy – seven months in that case and eight months in our patient. The recall in the previously reported case occurred after the patient received dabrafenib, a BRAF inhibitor demonstrated to improve overall survival in metastatic melanoma (7). In our case, radiation recall myelitis manifested after our patient was exposed to paclitaxel. Fortunately, hyperbaric oxygen was able to provide her with some symptom relief for her radiation

myelitis, as has been previously reported (8).

First described in 1959, radiation recall manifests as an acute inflammatory reaction confined to previously irradiated areas triggered by administration of precipitating systemic agents after radiation treatment (9-10). Approximately 2/3 of radiation recall cases manifest as skin toxicity, with the remaining 1/3 manifesting as toxicity in previously irradiated internal organs (10). Paclitaxel has demonstrated radiosensitization properties in the central nervous system related to its induction of G2-M cell cycle arrest, and been previously associated with radiation recall (10-11). This is the first report of radiation recall myelitis secondary to paclitaxel administration. As weekly paclitaxel is a standard regimen for metastatic breast cancer, it is imperative for medical oncologists to be aware of previously irradiated regions and proactively be on the lookout for radiation recall. Such action requires frequent communication with radiation oncologists to ensure timely identification and treatment of radiation recall symptoms.

CONCLUSION

This report of radiation-induced myelitis following spine SBRT manifesting within weeks after paclitaxel chemotherapy administration for metastatic breast cancer is consistent with radiation recall myelitis, which has yet to be reported following SBRT. Given the potentially disastrous consequences of myelitis, patients with metastatic disease previously treated with spine SBRT may be susceptible to developing myelitis if treated with paclitaxel chemotherapy. Further study is needed to better understand the pathophysiology of this phenomenon.

ACKNOWLEDGEMENTS

Authors' disclosure of potential conflicts of interest

Dr. Mitin receives research funding from Novocure. Other authors have nothing to disclose.

Author contributions

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Final approval of manuscript: Shearwood McClelland, Paul H Cooper, Jeremy N Ciporen, Jerry J Jaboin, Timur Mitin

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