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Breast Cancer Therapy and Huntington Disease: A case report

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Conflicts of Interest

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ABSTRACT:
Postmastectomy radiotherapy (PMRT) for node-positive breast cancer improves locoregional control and disease-free survival.[1] Accurate daily delivery is a crucial tenet of radiotherapy to achieve superior results.

Huntington disease (HD) is an autosomal dominant incurable neurodegenerative disorder characterized by progressive motor dysfunction, psychiatric disturbances and cognitive decline. Patients commonly develop chorea, an involuntary, dance-like movement that affects the whole body. Typical age of onset for HD is around 35 to 44 years [2,3]. The median survival time after motor symptom onset is around 15 to 18 years[2].

Here we report a woman diagnosed with node-positive breast carcinoma in the setting of HD.

CASE PRESENTATION:
A 42-year-old premenopausal female self-palpated a left breast mass. Her medical history was significant for HD, which was diagnosed 3 years prior after a family member tested positive. At first, she was asymptomatic, but eventually established care with Neurology at the onset of mild choreiform movements and difficulty with daily activities. She was initially not started on any medication for symptomatic management for her chorea given her personal aversion to taking medication and concern about potential side effects.

Diagnostic imaging revealed multicentric abnormal masses with suspicious axillary lymphadenopathy. Core needle biopsy of the breast mass and node confirmed Nottingham grade 2, ER/PR positive and HER2/neu negative invasive ductal carcinoma metastatic to an axillary node. Staging studies were negative for distant metastasis. The clinical prognostic stage was IIA (cT3 N1 M0).

The breast cancer multidisciplinary team recommended primary surgery with the final pathology guiding decision-making for adjuvant chemotherapy. PMRT was recommended given the size of the breast mass and axillary metastasis. Genetic testing was performed and was negative for deleterious mutations. After discussion regarding surgical options, including reconstruction, the patient decided she would like to minimize recovery time and risk of complications. The team also felt radiation planning would be optimized without immediate reconstruction.

A modified radical mastectomy was performed without complication, and the patient discharged on post-operative day one. Pathology demonstrated multiple foci of invasive carcinoma and ductal carcinoma in situ spanning 70mm. One of 8 axillary lymph nodes was positive with a 16mm tumor deposit and extracapsular extension. Final staging was pathologic stage IIB (pT2 N1 M0).

The OncotypeDx recurrence score was 20 indicating a 17% risk of a distant recurrence in 9 years with endocrine therapy alone. Given the patient's concerns for chemotherapy related neurotoxicity and exacerbating her neurocognitive issues, chemotherapy was omitted.

Post-operatively, in a multidisciplinary fashion, with radiation oncology and neurology leading, we discussed options including daily anesthesia, medications, non-medical methods. Discussions also included assessing competing risks of breast cancer recurrence and treatment toxicities in the setting of HD. Furthermore, considering her young age and her pathologic features, the treatment team felt she was likely to experience a breast cancer event of some type during her lifespan.
With these factors in mind, PMRT was recommended using a combination of medications and non-medical approaches to reduce her locoregional risk of recurrence followed by ovarian suppression and endocrine therapy.

DISCUSSION:
The benefits of PMRT in those with nodal disease is well established[1]. The Early Breast Cancer Trialists Group meta-analysis of individual patient data compared the risk of recurrence and breast cancer mortality among women who underwent mastectomy with or without adjuvant post-mastectomy radiation. All women had some type of axillary surgery with axillary dissection defined as ≥10 lymph nodes removed, and axillary sampling defined as <10 lymph nodes removed. All patients were enrolled in trials that included chest wall, supraclavicular or axillary fossa (or both) and internal mammary nodes. Among women with node-positive disease, 19% of unirradiated axillary dissection patients, and 29% of those unirradiated with axillary sampling experienced a locoregional recurrence prior to a distant metastatic event. The relative risk reduction for overall recurrence was greater for the axillary sampling group (RR 0.59, 95% CI 0.53-0.66) compared to the axillary dissection group (RR 0.75, 95% CI 0.67-0.83). Given that our patient had 8 lymph nodes removed, she would presumably derive a significant benefit from PMRT. In the same study, a smaller number of women (n=318) underwent axillary dissection resulting in a single positive node and some type of adjuvant systemic therapy (chemotherapy, endocrine therapy or both). Locoregional recurrence was significantly higher in the unirradiated group (17.8% versus 2.3%, p<0.00001.).[4]

The challenge we faced in this case was the inability to immobilize the patient for daily radiotherapy due to her choreiform movements. Furthermore, during subsequent visits with the patient, it became clear as she became more anxious the choreiform movements became more erratic and more difficult to control.

Therefore, the patient was initially started on very low dose Olanzapine, at 1.25mg at bedtime. The dose was gradually titrated up over the course of 4 months to 5mg daily. During this time, there were concerns raised regarding the protracted delay to starting radiotherapy. She was thus started on monthly Lupron injections while her Olanzapine was being titrated. The patient started to exhibit acceptable movement regulation at 5mg daily dose.

To make up for the treatment delay, minimize the logistical challenge of daily radiation therapy, and encourage adherence to daily therapy, hypofractionated radiotherapy was recommended. We have more than two decades of data solidifying the role of hypofractionated radiotherapy in the treatment of early-stage breast cancer patients. [5,6] This accelerated course has shown not only to yield less acute and chronic toxicities to normal tissues, but it has also shown excellent equivalent locoregional control compared to a standard protracted regimen. The total dose was recommended for 4256cGy over 16 daily treatments.

Radiotherapy was planned to target the left chest wall and low axillary nodes utilizing high tangential fields to encompass the level 1-2 axillary nodes. Pathology confirmed one positive sentinel lymph node without extracapsular extension and seven additional negative sentinel nodes. Several studies have suggested omitting regional nodal irradiation for low burden nodal disease as regional recurrences were extremely rare events in this cohort.[7] Furthermore, data have shown higher rates of upper extremity lymphedema with the use of comprehensive nodal irradiation, which led to more restrictive range of motion.[8] These toxicities would inevitably worsen the patient's already compromised quality of life.

As this was a left-sided lesion, it was imperative that we achieve precise daily positioning to optimally target the high-risk tissues with minimal exposure to the underlying organs including the heart and left lung. Several studies have shown increased cardiac toxicities from breast cancer radiotherapy. The increase is proportional to the mean dose to the heart starting within a few years after exposure.[9]

For simulation we used an alpha cradle and a breast board for immobilization. We also employed relaxation techniques, guided imagery, and music during her radiotherapy to attenuate anxiety during daily treatments.[10]

The radiotherapy utilized a 3D-conformal technique with a daily 5 mm chest wall bolus. Treatment was delivered using 6 MV photons with segments to improve dose homogeneity. Given the patient's inability to perform deep inspiration breath hold the fields were designed with a 5 mm margin around the heart. V90 coverage for the level 1 and 2 axillae were 100% and 90.5%, respectively. The mean heart dose was 111.1cGy. The ipsilateral lung V20 was 14.8%, V10 was 21.0% and V5 was 30.8%. QUANTEC[11] data was used as a guideline for heart and ipsilateral lung tolerances.

For patient positioning and monitoring we utilized surface-guided radiotherapy (SGRT), which uses non-ionizing near-visible light to image the patient's external contour. SGRT has been shown to significantly reduce overall setup errors for breast when compared to setup with subcutaneous tattoos[12] and improves patient safety[13]. SGRT is a non-ionizing image-guidance technology that acts as a 'virtual immobilization' device without having to physically constrain the patient in the treatment position. It is particularly useful for this case as it generally speeds up patient set up and has the capability to monitor the patient's position and movements in real-time during treatment and can

automatically shut off the treatment beam if a pre-determined positional threshold is reached.[14] Additionally, the patient was provided visual biofeedback capability during her daily radiotherapy delivery, which allowed the patient to tolerate the daily treatments and reproduce her treatment position accurately. Daily post-treatment SGRT documents were generated and reviewed to confirm accurate positioning (See Fig. 1). The patient completed radiotherapy without breaks and developed only grade 1 skin toxicity.

CONCLUSION:

Pre-existing comorbidities contribute additional challenges when effectively treating malignancies. Huntington disease uniquely adds an additional layer of complexity to daily radiotherapy as immobilization and accuracy of daily treatment delivery become problematic. This case highlights the benefits of thoughtful and considerate discussion amongst the multi-disciplinary oncology team including neurology as well as state of the art radiation techniques to deliver effective breast cancer treatment in the setting of symptomatic HD.

Declaration of interests

☒The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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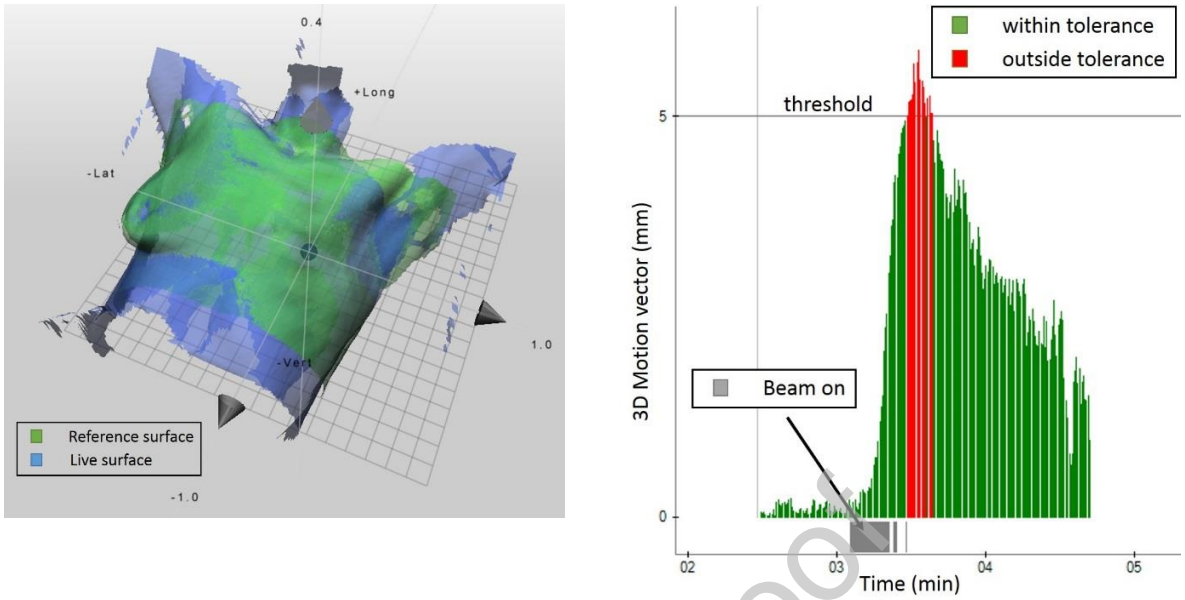

Figure 1: Left: Patient setup with SGRT. Right: Snippet from monitoring report. Shortly after the beam comes on at t≈3 min, sudden patient movement takes place. Once the pre-determined motion threshold of 5 mm was reached the motion vector turns red and the beam automatically shuts off.