


Hypofractionated radiation in secretory breast cancer: A case report

Rare Tumors
Volume 13: 1–4
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DOI: 10.1177/20363613211045252
journals.sagepub.com/home/rtu


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Abstract

Secretory carcinoma is a rare and indolent breast cancer with a lack of established treatment paradigms. We describe a case of a woman who underwent breast conservative therapy in the modern era. A 48 year old woman with a screen-detected left breast cancer was found to have early-stage secretory carcinoma after definitive breast conservation surgery. Further management with adjuvant radiation was recommended. After definitive breast conservative surgery, final pathology was notable for secretory breast carcinoma due to the immunohistologic characteristics of the tumor, ETV6-NTRK3 gene fusion, and histologic findings. After multi-disciplinary discussion, it was recommended that the patient proceed with adjuvant radiation. She was treated using a modestly hypofractionated regimen of 4256 cGy in 16 fractions. She tolerated the treatment well, developing only grade I radiation dermatitis. At 1 year follow-up she was clinically and radiographically free of disease. With a shift in management toward breast conservative therapy, defining the role of adjuvant radiation for secretory carcinomas in the modern era is of increasing importance. Modestly hypofractionated radiation is well-tolerated. Oncologic outcomes will be assessed with continued long-term follow-up.

Keywords

Breast cancer, secretory breast cancer, radiation, breast conservation, hypofractionation

Date received: 24 December 2019; accepted: 21 August 2020

Introduction

Secretory breast carcinomas are rare but biologically favorable tumors that represent <0.01% of all breast cancer cases.¹ Initially thought to primarily afflict children, these cancers were so named “juvenile secretory carcinoma.” Further research has established that adults too are affected by the disease. While these tumors are typically triple negative, they are often slow growing and as such tend to present at an early stage.²

With the publication of NSABP B-06, breast conservative therapy was established as the standard for women with early-stage breast cancer.³ Rather than treat small breast cancers with mastectomy, women could now undergo limited surgery followed by breast irradiation. Conventionally, whole breast irradiation has been delivered over 5–7 weeks. In the modern era shorter schemas have been adopted. With

the publication of long-term results of modest breast hypofractionation showing similar efficacy and cosmetic outcomes, this has now become the standard.^{4–6}

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Interestingly, a SEER analysis was notable for nearly 50% of women 30 years and above and 80% of women less than 30 years with secretory breast cancer underwent mastectomy as their definitive treatment.¹ In our case report, we explore a modern approach to treating this rare tumor with breast conservative surgery followed by adjuvant radiation using a modestly hypofractionated regimen.

Case presentation

Our patient is a 48 year old woman with a screen-detected left breast cancer. She was found to have an abnormal bilateral screening mammogram which demonstrated a suspicious area of architectural distortion in the right breast and an obscured nodule in the left breast. This prompted further imaging with diagnostic mammogram and ultrasound. This was especially concerning for a solid microlobulated nodule in the left breast measuring 7 mm in size at 3:00 and a persistent suspicious area of architectural distortion in the right breast with two adjacent simple cysts. Bilateral breast biopsy was performed. Ultrasound guided core biopsy of the suspicious right breast lesion was consistent with sclerosing adenosis with usual ductal hyperplasia. No atypia or malignancy was noted. Ultrasound guided core biopsy of the left breast lesion was consistent with grade 2 invasive ductal carcinoma, ER 10%, PR 0%, Her2/neu negative (1+), Ki 67 1%. Bilateral breast MRI was performed which showed no suspicious lesions in the right breast and a 2–3 mm ovoid rapidly enhancing nodule with plateau kinetics reflecting a portion of the originally biopsied cancer. No other suspicious lesions were noted within the left breast, left axilla, or internal mammary chain. Her case was reviewed, and the multi-disciplinary decision was to proceed with breast conservative surgery first. She was taken for right partial mastectomy and left partial mastectomy with sentinel node biopsy. Final pathology of the right breast did not show any evidence of malignancy. Initial pathology of the left breast was initially concerning for a biologically unfavorable invasive ductal carcinoma, NOS type. However, further pathologic review revealed that the patient had a grade 2, 8 mm secretory carcinoma. The diagnosis of secretory carcinoma was suspected based on histologic findings which included a microcystic and tubular growth pattern with luminal secretions. The tumor cells were polygonal with eosinophilic to foamy cytoplasm, round nuclei with inconspicuous nucleoli. Mitotic activity was minimal. The morphologic findings of a likely secretory carcinoma were confirmed by FISH studies demonstrating a ETV6-NTRK3 translocation. A healing biopsy site was noted within the specimen. There was no associated DCIS. No LVSI was noted. The margins were widely negative (closest margin was 7 mm from the posterior margin). Five sentinel nodes were sampled of which none contained metastatic disease. The tumor was ER 5%, PR 0%, HER2/neu negative (1+), Ki 67 <10%. She was staged as a pT1bN0(sn).

Treatment

Given the initial concern for biologically unfavorable breast cancer, she was considered for cytotoxic chemotherapy. However, this was not pursued once a final diagnosis of secretory carcinoma was determined, and this diagnosis was subsequently applied to the core biopsy pathology as well. As such, the patient was evaluated for adjuvant radiation. After review of her case and the published literature, we proceeded with an informed discussion of the risks, benefits, and side effects of radiation. She underwent adjuvant radiation to her whole left breast using a modestly hypofractionated regimen using DIBH. She was treated to 4256 cGy in 16 fractions. Treatment planning was performed per ASTRO guidelines and RTOG 1005. Her ipsilateral lung V20 was 12% and her mean heart dose was 61.8 cGy. While she underwent radiation therapy, she used an unscented moisturizing cream and mometasone cream for skin care. She developed grade 1 radiation dermatitis with skin erythema but no dry or moist desquamation. She did not complain of breast pain or fatigue while under treatment.

Outcome and follow-up

She was seen in follow-up about 1 month after completing her radiation. She denied developing any dry or moist desquamation after completing her radiation therapy. She noted she had stopped her mometasone cream on her last day of treatment. Despite this, clinical exam showed improvement in her radiation toxicity with only very mild skin hyperpigmentation and erythema. She denied having any fatigue or breast pain. At approximately 1 year follow up, she was clinically and radiographically without evidence of disease. Breast imaging with diagnostic mammogram and ultrasound was notable for indeterminate calcifications in the subareolar right breast. The left breast was normal and showed post treatment changes. She underwent right subareolar biopsy which showed benign breast tissue. As the patient is perimenopausal, she is planned for initiation of Tamoxifen. An endometrial polyp was noted on imaging and this is followed. At that point she was slated to see medical oncology to review the role of anti-endocrine therapy in her case due to her low ER positivity.

Discussion

Management of rare tumors is often controversial given the limited available data. Similarly, disparate management of secretory breast cancer exists due to lack of established treatment paradigms.

Management of breast secretory carcinoma has evolved over time. Initially managed definitively with mastectomy, there has been a shift toward management with breast conservative therapy. While the role of radiation has not been clearly defined, its use has increased over time.¹ However,

there is concern that the rate of mastectomy is high for such an indolent tumor that often presents at an early stage (80% of women <30 years old undergo mastectomy and 50% of women \geq 30 years).¹ One potential reason for such a high mastectomy rate is that the role of radiation is unclear. Additionally, until recently, patients were often required to undergo 5–7 weeks of radiation. This placed a large burden on patients, and those who could not undergo treatment with such a protracted schedule experienced inferior outcomes.⁷ SEER analysis showed that about one-third of patients undergoing breast conservative surgery for secretory carcinoma do not receive adjuvant radiation. Reports show that when radiation is performed, it is often delivered using a conventionally fractionated regimen.³ Extrapolating from data on invasive breast cancer, there is belief that radiation may improve oncologic outcomes.³

In this case, our patient was managed with breast conservative surgery first. The morphologic features of the tumor were highly suggestive of a secretory carcinoma, which was confirmed by FISH with the presence of a balanced translocation, t(12;15), of the ETV6 variant gene 6 and neurotrophic tyrosine kinase receptor type3, ETV6-NTRK3.⁸ Secretory carcinomas are typically triple negative in terms of ER, PR, and Her-2/neu receptor status. In this case, there was a low ER positivity, which is not typical of secretory carcinoma,⁹ however ER expression in the presence of ETV6-NTRK3 fusion has been documented in prior reports.¹⁰ As such, this patient will be maintained on anti-endocrine therapy. Recent reports have also demonstrated secretory carcinoma having basal-cell markers such as CK5/6, CK14, and CK17, as well as c-Kit, epidermal growth factor receptor (EGFR), and vimentin.¹¹

It has been suggested that secretory carcinoma is the same disease process as acinic cell carcinoma (ACC),^{12,13} based on morphology and immunohistochemistry. These features include a prosecretory phenotype as well as S-100 positivity. Others have disputed this based on the lack of ETV6-NTRK3 translocation in ACC.¹⁴ Regardless, the similarity and often low-grade features of both typify a slow growth rate characteristic of the indolent clinical behavior of these tumors,⁹ suggesting a low alpha/beta ratio. In these circumstances, hypofractionation may be beneficial, or at least not detrimental. This is in keeping with the hypofractionation literature for breast in the setting of breast conservation,⁵ although grade does not appear to strongly determine the efficacy of hypofractionation in breast cancer.¹⁵ Long-term results of modestly hypofractionated radiation therapy over 3–4 weeks from the UK and Canada show equivalent oncologic and cosmetic outcomes.^{4,5} As such, this has been adopted as the standard for treatment of early stage breast cancer in the US.⁶

In this report, we show that breast conservative therapy using modestly hypofractionated radiation treatment regimen is safe and feasible. Such treatment provides a more palatable option compared to mastectomy or a protracted radiation schedule over 5–7 weeks. We recommend that

patients with early stage secretory breast cancer be reviewed in a multi-disciplinary fashion and that such a treatment paradigm should be considered in appropriate patients due to its lower morbidity.

Contributorship

Author (writing the manuscript).

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: ACRO New Practitioner grant funding for evaluation of barriers to promotion for women in radiation oncology. Elsevier pathways consultant.

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