

The Role of Radiation Therapy in Locally Advanced Breast Cancer in a Patient with Li-Fraumeni Syndrome

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Introduction

- Li-Fraumeni syndrome (LFS): Autosomal dominant mutation in TP53 protein leading to increased risk of developing cancer, with 7-20% of patients having de novo germline variants
- Affected individuals have 80-90% lifetime risk of developing cancer and 50% of affected females have breast cancer diagnosis <70 years old
- Historically, radiation therapy (RT) has been avoided due to increased risk of radiation induced malignancy

Case Presentation

- 38 y/o female presented with 2-month history of self-detected left breast mass. She underwent bilateral mastectomy and final pathology was consistent with bilateral invasive ductal carcinoma
- Oncologic PMHx: juvenile granulosa cell tumor of ovary s/p unilateral oophorectomy at age 6, malignant phyllodes tumor of right breast s/p wide local excision and whole right breast radiation at age 27 (negative for BRCA1/2 at that time)
 - Genetic testing positive for one pathogenic variant in TP53 following 2nd breast cancer diagnosis
- Oncologic FMHx: breast cancer in a paternal aunt (55 y/o), gastrointestinal stromal tumor in a maternal aunt (age of diagnosis unknown)

Surgical Intervention

Bilateral skin sparing mastectomies, bilateral sentinel lymph node biopsy, left completion axillary dissection & placement of tissue expanders

Post-op Pathology

Left	Right
Stage pT3N1a	Stage pT1bN0(sn)
Invasive ductal carcinoma measuring 6.5 cm, with 2/19 lymph nodes positive	Two areas of invasive ductal carcinoma, measuring 1.0 cm, 0/2 lymph nodes positive
ER+, PR+, HER2-	ER+, PR-, HER2-

Treatment plan

Four cycles of dose-dense doxorubicin and cyclophosphamide with Neulasta support followed by 12 cycles of weekly paclitaxel

Ovarian suppression with aromatase inhibitor awaiting surgical hysterectomy with right salpingo-oophorectomy

Ultimately decided against RT

Future malignancy surveillance: annual whole-body MRI and brain MRI, routine colonoscopy, annual full skin exams, and abdominal US for adrenal adenoma

Discussion

- Post-mastectomy radiation therapy (PMRT) is indicated in the general population for high-risk cases, including cases with tumor size >5cm, positive lymph nodes, or positive margins/local invasion
- PMRT has historically been avoided in patients with LFS due to malignancy risk
- Without history of LFS, PMRT would be recommended for this patient
- Recent studies have shown that in high-risk cases such as these, PMRT should be considered
 - Hendrickson et al : 0/14 patients receiving curative-intent RT developed radiation induced malignancy
 - Le et al: concluded that there was an upward trend in rates of radiation-induced sarcoma and thyroid cancer in patients with LFS, but the results showed inconsistent statistical significance
 - Also showed lower risk of developing RT-induced malignancy (12%) compared to previous studies (30%)

Conclusion

- Patients with history of LFS are at increased risk of developing radiation induced malignancy, but PMRT should not be ruled out in high-risk cases
- In these situations, a multidisciplinary analysis should occur and should include shared decision making, considering patient comorbidities and goals of care

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