CLINICAL VIGNETTE

Squamous Cell Cancer of the Breast

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An 88-year-old female presented to her primary care physician with a left-sided breast mass. Left breast ultrasound showed a 5.2 centimeter hypoechoic, complex mass with irregular margins and central fluid. There was also a large, irregular, left axillary lymph node measuring 1.7 centimeters. Given the suspicion for malignancy, she had a biopsy of the mass with pathology consistent with a high grade invasive keratinizing squamous cell cancer. Biopsy of the left axillary lymph node and fluid aspirated from the area both demonstrated the same pathology. Approximately 50% of the tumor cells were positive for the estrogen receptor (ER), but all were negative for the progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2). Given her age, her last mammogram had been 6 years prior with no history of abnormalities.

She had several comorbidities including atrial fibrillation requiring amiodarone, pulmonary hypertension, right ventricular enlargement, hypothyroidism, and bronchiectasis/COPD for which she was prescribed oxygen but refused its use. Despite her multiple medical issues and age, she still lived alone in a duplex and remained relatively active with a performance score of 1-2.

Her exam was unremarkable beyond the 5 centimeter left breast mass in the left upper, outer quadrant. Laboratories were also within normal limits.

A PET/CT revealed no evidence of metastatic disease. The only hypermetabolic disease noted was the left breast mass and a left axillary lymph node. She was seen by a breast surgeon who recommended immediate surgery and considerations for adjuvant therapy. As preparations were being made for surgery, her tumor increased in size by about 3 centimeters in 10 days. Given the ER-positivity, she was started on anastrozole in hopes of slowing down the growth of the cancer while she awaited medical optimization prior to planned mastectomy and axillary lymph node dissection. Final pathology demonstrated a 6.5 centimeter high grade, invasive keratinizing squamous cell carcinoma with lymphovascular invasion. Four of nineteen lymph nodes were positive for metastatic disease (T3N2a). Prognostic markers were similar to her prior biopsy. Adjuvant therapy was discussed with the patient and her family.

Squamous cell cancers of the breast are very rare, accounting for <0.1% of all breast cancer diagnoses.[1] Given the rarity of this pathology in the breast, it is imperative that other primary cancers (i.e., head and neck, lung, and skin) that may have metastasized to the breast be ruled out as was done above with the PET/CT scan. Pathology must also demonstrate that the majority of the cells (>90%) are of squamous cell differentiation and not simply a mixed tumor with a small squamous cell component.[2] Some reports suggest this tumor type is more common in the elderly.[3] Breast squamous cell cancers are frequently large (>4 centimeters) and seem to have less lymphatic spread than adenocarcinomas.[2,3]

While many reports suggest these tumors are aggressive and prognosis is poor, controversy still exists in this regard.[2] Thus, whether there is a role for adjuvant treatment is still unknown.[1,2] One case series of 31 patients with localized disease demonstrated a median relapse-free survival of 20 months and median overall survival of 37 months.[2] Squamous cell cancers of the breast tend to be ER-negative and HER2-negative.[1] However, it is possible to have receptor positivity as noted in this case and in previously reported case series.[2] They appear to be fairly chemotherapy- and radiotherapy-insensitive as well.[1] Multiple chemotherapy drugs have been utilized with no support for any specific regimen.[2] Regardless of these facts, due to the paucity of good data, they are often treated in a similar fashion to adenocarcinomas.

A large proportion of these tumors appear to be epidermal growth factor receptor (EGFR)-positive.[1,2] Thus, this may be a pathway to exploit in future studies. The rarity of these tumors makes it difficult to fully understand their biology and to develop appropriate treatment, but further research is necessary.

The patient's case above was complicated by a post-operative seroma and chest wall infection. After surgical excision of the infected tissue, treatment with antibiotics, seroma drainage, and lymphedema management, she did well for about three months at which point she developed an approximately 1 centimeter mass along the scar line. Ultrasound showed benign features, but repeat physical exam 3 weeks later confirmed continued growth. Repeat biopsy was consistent with recurrent squamous cell cancer. She had another wide excision of the area for palliation. Unfortunately, radiation treatment was not a viable option for the patient given her poor pulmonary function. The patient's age, poor performance status, and lack of good evidence for benefit, prohibited chemotherapy as well. A couple months later, the patient's local disease along the chest wall and axilla again recurred.

Imaging now confirmed more widely metastatic disease. At this point, she agreed to comfort care and hospice at home.

REFERENCES

1. **Murialdo R, Boy D, Musizzano Y, Tixi L, Murelli F, Ballestrero A**. Squamous cell carcinoma of the breast: a case report. *Cases J*. 2009 Jul 10;2:7336. doi: 10.4076/1757-1627-2-7336. PubMed PMID: 19829944; PubMed Central PMCID:PMC2740227.
2. **Hennessy BT, Krishnamurthy S, Giordano S, Buchholz TA, Kau SW, Duan Z, Valero V, Hortobagyi GN**. Squamous cell carcinoma of the breast. *J Clin Oncol*. 2005 Nov 1;23(31):7827-35. PubMed PMID: 16258085.
3. **Bhosale SJ, Kshirsagar AY, Deshmukh SJ, Jagtap SV, Langade YB**. Squamous cell carcinoma of the breast. *Am J Case Rep*. 2013 Jun 5;14:188-190. Print 2013. PubMed PMID: 23826464; PubMed Central PMCID: PMC3700481.

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