Two Cases of Plasma Cell Dyscrasias With Systemic Involvement of Breast

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Seminars in Oncology

At times we encounter clinical problems for which there are no directly applicable evidence-based solutions, but we are compelled by circumstances to act. When doing so we rely on related evidence, general principles of best medical practice, and our experience. Each "Current Clinical Practice" feature article in *Seminars in Oncology* describes such a challenging presentation and offers treatment approaches from selected specialists. We invite readers' comments and questions, which, with your approval, will be published in subsequent issues of the Journal. It is hoped that sharing our views and experiences will better inform our management decisions when we next encounter similar challenging patients. Please send your comments on the articles, your challenging cases, and your treatment successes to me at dr.gjmorris@gmail.com. I look forward to a lively discussion.

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The American Cancer Society estimates 235, 030 new cases of breast cancer diagnoses in America in 2014, with 40,430 deaths due to breast cancer, as the second most common malignancy behind lung cancer.[1]

Classic risk factors for the development of breast cancer include increased age, early menarche, late menopause, older age at first live childbirth, prolonged hormone replacement therapy, previous exposure to therapeutic chest wall irradiation, benign proliferative breast disease, increase mammographic breast density, and genetic mutations specifically in the *BRCA1* and *2* genes.[2] Another genetic predisposing factor is mutations of *p53* in Li-Fraumeni syndrome, for which leukemias may run in families also at high risk for breast cancer.[3] However, there have been no other known hematologic malignancies associated with breast cancer, including lack of a link of breast cancer to multiple myeloma.[4]

Multiple myeloma occurs less frequently in the general population, with the American Cancer Society estimating 24,050 new cases in the United States in 2014, and an approximately 10,090 deaths.[1,5] The classification of plasma cell dyscrasias according to the International Myeloma Working Group (IMWG) includes monoclonal gammopathy of undetermined significance, solitary plasmacytoma, smoldering myeloma, active/symptomatic myeloma, and immunoglobulin light chain amyloidosis[5]; patients are risk-stratified according to bone marrow burden, karyotypic abnormalities,[6] and immunoglobulin levels,[7] with a paucity of data thus far showing a link to a proven hereditary risk.[8–11]

Primary systemic light chain amyloidosis is also a clonal malignancy of plasma cells in bone marrow; however, it can produce additional AL or AA proteins, which can infiltrate visceral organs, most commonly renal, cardiac, hepatic, and splenic tissues.[12] Primary treatment for AL amyloidosis is usually derived from systemic treatment for multiple myeloma, and jointly includes proteasome inhibitors, immunomodulatory drugs, corticosteroids, alkylating agents, and conditioning for high-dose therapy followed by peripheral blood stem cell transplantation.[12]

We describe two cases of women diagnosed with plasma cell dyscrasias in two very disparate situations presenting as different entities. In case 1, multiple myeloma was found after workup for an incidental finding of plasma cells in an axillary lymph node after primary breast surgery was performed in a standard fashion for a postmenopausal woman. Unexpectedly, the second case is that of systemic amyloidosis with unique behavior of infiltrating extramedullary breast tissue, thus invoking the need for evaluation by a breast surgical oncologist for symptomatic control.

CASE REPORTS

Case 1

A 75-year-old woman with history of stage I invasive ductal carcinoma of the left breast

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(T1cN0, estrogen receptor [ER]-positive, HER-2–negative) had undergone mastectomy in September 2005. Sentinel lymph nodes removed showed no evidence of breast cancer but did show a plasma cell neoplasm, kappa light chain–restricted. Hematologic workup then took precedence, and showed elevated serum free kappa light chains at 2,070 mg/L, with very low immunoglobulin levels, and urine total protein of 370 mg/d. Bone marrow biopsy showed 50%–60% involvement with plasma cells resembling plasmablasts, and they were also kappa light chain–restricted. The patient was diagnosed with multiple myeloma, International Staging System stage III, Durie-Salmon stage III, and cytogenetics showed a complex karyotype. Over the next year, the patient received induction therapy for myeloma, which included thalidomide, clarithromycin, and dexamethasone, followed by bortezomib, cyclophosphamide, liposomal adriamycin, and dexamethasone, and induced a very good partial remission. She then underwent high-dose chemotherapy with melphalan and autologous peripheral stem cell transplantation in July 2006, achieving a remission, which was maintained for 2 years.

In the fall of 2006, however, she was diagnosed with a contralateral right invasive breast cancer also of T1cN0, ER-positive infiltrating ductal carcinoma with lymphovascular invasion, also HER-2/neu-negative. She underwent right mastectomy, and was started on an aromatase inhibitor, which resulted in severe arthralgias. She was eventually placed on tamoxifen beginning in May 2008, which was more tolerable. She had no previous or subsequent history of thromboembolism. Family history was positive for lung and bladder cancers in both her father and sister, but there was no family history of breast or ovarian cancers.

She had evidence of first relapse of multiple myeloma in 2008, and was treated with lenalidomide and bortezomib. She experienced progressive disease with extramedullary soft tissue plasmacytomas developing, and positron emission tomography (PET)-positive rib lesion, which was biopsied in November 2010 and showed a plasma cell dyscrasia; breast cancer–specific tumor markers remained within normal range. The patient received bortezomib, cyclophosphamide, and dexamethasone followed by bortezomib and bendamustine, which resulted in a partial response. She received lenalidomide maintenance for 2 years. Upon evidence of further progressive disease, she has was given carfilzomib.

Case 2

A 51-year-old premenopausal woman presented to her primary care physician having noted palpable lumps in both breasts increasing over a period of 7 months to be the size of a "bean". She had no family history of breast cancer but a history of thyroid cancer in her mother. She underwent a bilateral diagnostic mammogram with spot magnification views in May 2009, which was compared with previous mammograms and showed no suspicious masses, areas of architectural distortion, or cluster of microcalcifications; dedicated sonography of both breasts identified no solid or cystic lesions or areas of abnormal shadowing but noted extremely dense breast tissue. However, bilateral breast magnetic resonance imaging (MRI) was pursued, and showed focal enhancing lesions bilaterally in the upper inner quadrants corresponding to

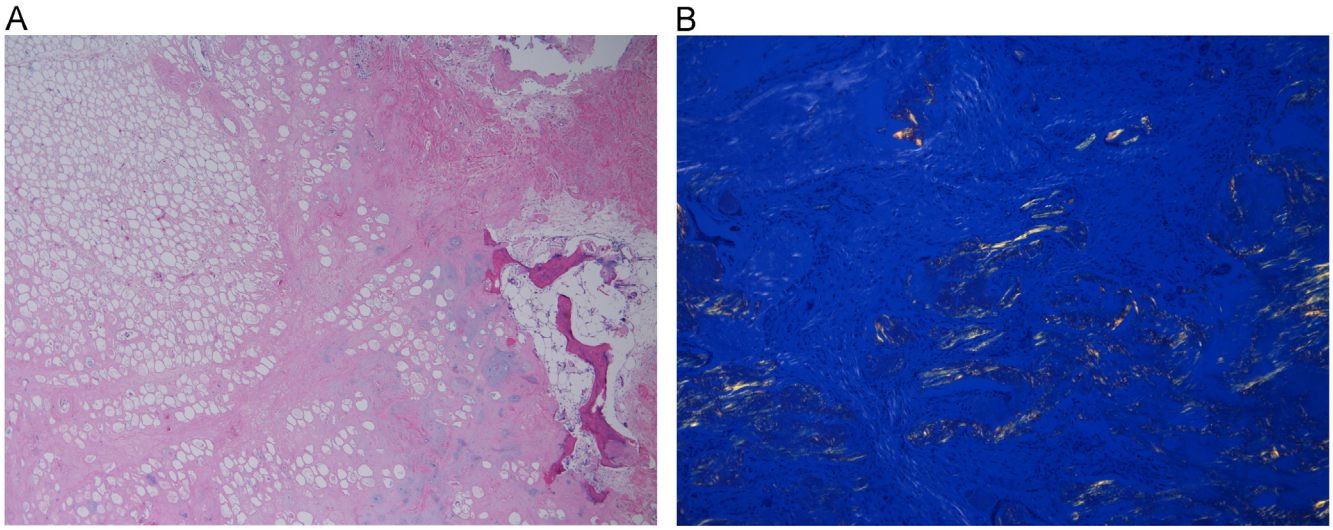

Figure 1. (A) Mastectomy specimen showing breast tissue infiltrated by amyloid deposits with associated calcifications and ossification. Hematoxylin and eosin stain, 40x magnification. (B) Congo red stain is positive under polarized light, confirming the presence of amyloid.