

CHICAGO PATHOLOGY SOCIETY

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BREAST PATHOLOGY

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Case 1

Breast Cancer presenting as an axillary mass: Metaplastic Carcinoma of Breast with Osteoclastic Giant Cells

X% of breast cancers present with lymph node metastases that are far larger than the primary tumor. In most instances there is no palpable mass and frequently routine imaging studies are negative. (MRI, ultrasound can find lesions that are not distinguishable on mammogram).

Metaplastic carcinoma of the breast is less than 5% of all breast cancers. Like carcinosarcoma of the uterus, metaplastic carcinoma of the breast may have homologous elements such as squamous and tumor giant cells, myoepithelium or heterologous elements such as chondroid matrix, osteoid or bone formation, liposarcoma, and osteoclastic giant cells analogous to giant cell tumor of bone. Tumors with heterologous elements constitute about 0.2% of all breast carcinoma. Metaplastic carcinoma must also be distinguished from primary and metastatic soft tissue sarcomas and metastatic carcinomas with sarcomatous elements. Metaplastic carcinoma is more common than either primary or metastatic carcinoma; it behooves the pathologist to suggest work up for breast cancer whenever a woman presents with an axillary mass that is not clearly linked to a previously diagnosed tumor of identical morphology.

This case was originally diagnosed as giant cell sarcoma of soft parts on a large excisional biopsy. However, margins were positive and the patient sought a second opinion. Review confirmed an osteoclastic giant cell tumor, but we suggested that metaplastic breast cancer be considered. Imaging showed tumor extensively involving the upper outer quadrant.

Rosen separates mammary carcinoma with osteoclastic giant cells from metaplastic carcinoma. However, in his series of tumors, the osteoclast giant cells are part of the tumor and frequently intermingled with typical carcinoma. In this case, the bulk of the tumor resemble giant cell tumor of bone with only focal components of infiltrating duct carcinoma with spindle cell morphology and lymph node metastases of the same.

0.2% of all breast cancers, present as firm masses, fixation to skin and fascia common. Sarcomatous elements may be single or mixed: bone, cartilage, myxoid stroma, loose spindle and fibromyxoid stroma, dense spindle and fibrosarcomatoid stroma, anaplastic stroma with osteoclastic giant cells (either

benign or malignant appearing). Sarcomatoid elements range from 10 to 95% of mass. Underlying carcinoma is poorly differentiated duct, NST.

Molecular profile: Triple negative carcinomas many with basal features (138, 169). Young age, risk of BRCA1 mutation, P63, ck5/6, ck17 (121), EGFR positive, p53 mutations. Metastases to LN tend to be epithelial. Distant mets tend to be sarcomatous. Patients with predominantly sarcomatous elements have worse prognosis if untreated 62% vs 38% 5 year survival. 1/3 of case series DOD within 11 month (66). Masses may be circumscribed or infiltrative (200). Grade 3 tumors do better with prolonged chemo (173). Triple negative carcinomas are more frequently higher stage, higher grade, lower % LN mets and decrease OS at six years, but not thereafter (a79). Triple neg carcinoma heterologous group of tumors with variable expression of ck5/6, EGFR, C-kit, p63, pcdherin, do not predict behavior or morphology.

P53 mut predict poor response to chemo (113). CK5, ck 14, and CK 17 markers of poor outcome 148, . Brain mets more common (148) . Alpha B crystalline more commonly expressed (163). In the few tumors with Her2 amplification, IHC expression reported to differ with sarcomatous elements being negative and epithelial positive, even though both elements show gene amplification (a89).

Case 2

Well Differentiated Fibromatosis Like Carcinoma of the Breast with Myoepithelial Differentiation Associated with Lobular Neoplasia

The differential diagnosis of this tumor includes three rare breast carcinomas: myoepithelial carcinoma, fibromatosis like breast carcinoma and well differentiated adenosquamous carcinoma.

Myoepithelial carcinoma may have glandular elements, surrounded by spindle cells, often with nodules of pure spindle cells. The neoplastic myoepithelial elements resemble smooth muscle tumors with bundles of interlacing spindled cells or salivary gland tumors with a mixture of ductal and spindle elements with actin, CD10, high molecular weight cytokeratin and/or p63 positivity. Considered a form of basal type breast carcinoma. (a96)

Fibromatosis like carcinomas of the breast are extremely rare lesions and are classified as low grade metaplastic carcinomas. One of the largest series published by the MD Anderson group consisted of 24 cases. FLBC forms a mass which resemble scar tissue or fibromatosis. Most fibromatosis like tumors are thought to arise from ductal carcinomas. The tumors are ER/PR and Her2 negative. (201)

Rosen includes a group of well differentiated adenosquamous carcinomas which also have FLBC has been shown to have a low rate of lymph node metastases and

or to be a form of well differentiated adenosquamous carcinoma. Analogous tumors in the skin are the syringoma, desmoplastic syringoma and syringoepithelioma. RNA studies show that the stroma associated with these tumors have similar profiles to fibromatosis.

This particular carcinoma differs from this standard in that the in-situ disease and transitional areas are that of lobular neoplasia. Rosen illustrates a metaplastic spindle cell carcinoma arising in lobular carcinoma and cites the loss of e-cadherin in breast cancer cell cultures as causing a spindle cell phenotype. Search of pub med for metaplastic carcinoma and lobular

Case 3

Mass lesion consisting of proliferative fibrocystic change in all its variations

Risk of carcinoma in younger women and African American women. Higher incidence of basal like tumors (triple negative).

Lobular cycling and lobular involution and risk of carcinoma. (find bartow paper)

Case 4 Duct carcinoma NST

By molecular biology, the vast majority of breast carcinomas are luminal types with most expressing ER and negative for Her2/neu. Case

The inflammatory response profiled by Villonodular synovitis is expressed by basal type carcinomas (CSF-1, CD32, CD16, athepsin L) (a90). FOXP3, marker for CD25+/CD4+ Tcells (iimmunosuppressive). Most frequently found associated with ER neg, Grade III carcinomas (A95).

For Duct carcinoma NST:

Age matters. Younger patients tend to have higher grade, more often triple negative carcinomas, increased risk of BRCA1 (24). BRCA1, increased parity, decreased Ca. Brca2, increased parity, increased ca (67)

Metastases: Bone marrow aspirates can identify node neg patients needing chemo. Consider in grade 3 node neg any size, T2-3 node neg grade 2. (28)

Markers: ER/Pr+ in 60% of BC (39). In Grade 3, drops to 40%. PR status in postmenopausal better at predicting response to hormone therapy (69). Excellent concordance between central and local labs in ER determination (a78).

MIB-1. Can divide grade 2 tumors into High and low risk. (74) MIB-1, p53, LN+, high grade all independent predictors of survival in luminal type BC

Her2 expression. Have more gene mutations than ER+ BC (a745). RNA splice variants may account for disparity between amplification and protein expression in discordant cases (a76).

Case 5 DCIS and what to expect when it is encountered in a core biopsy and on wire loc.

Cumulative experience at NMH 1995-2005, 25% of all cases of DCIS dx on CNBx had invasive carcinoma on excision.

Large lesions of DCIS: risk increases with size and with grade. Large excisions for diffuse calcifications. Gross examination critical in coming to correct diagnosis. Pressure to reduce number of cassettes examined.

Case 6

Tubulolobular carcinoma –luminal type carcinoma, well differentiated. (Not as well as either pure tubular or pure lobular)

Hybrid that shows a mixed morphology on routine histology. Retains e-cadherin, unlike pure lobular. Shared mutations with low grade DCIS, lobular neoplasia, well diff lobular invasive (classic) and low grade ductal

Invasive lobular arises in setting of both lobular neoplasia and low grade DCIS. Lobular neoplasia give rise to both invasive lobular and low grade ductal.

In the setting of lobular neoplasia, look carefully for invasion, but do not obsess about a few cells. Instead be wary of missing larger lesions either because of failure to submit enough sections...careful palpation of thinly sliced wet tissue finds more invasive tumors than multiple levels of sections with lobular neoplasia. Also be careful not to overlook subtle alterations in stroma on H&E that turn out to be infiltrating lobular

Concurrent carcinoma in the setting of lobular neoplasia is a major risk. Also be wary of lobular arising in setting of low grade ductal lesions.

Fibromatosis signal (SPARC and CSPG2 proteins) found in low grade ER+, luminal A associated with increase OS and DFS and decrease LN mets.