Medullary Cancer of Breast with Atypical Features - A Case Study

Dr. Asma Erum
Medical Officer, Al Baraha Hospital, Dubai, UAE

ABSTRACT

Invasive ductal carcinoma is the most common form of breast cancer, attributing to about 70 to 80 percent of all breast cancers; the medullary variety constitutes 1 to 10 percent of this carcinoma. A case review of the medullary carcinoma with atypical features is presented with regards to clinical and pathological characteristics.

Key words: Breast, Medullary Carcinoma, Atypical

BRIEF HISTORY

A 58-year-old postmenopausal woman presented with swelling and redness of left breast for 9 months. The swelling gradually increased in size and was associated with yellow discharge from the nipple. History of mastalgia was present. There was no associated fever or weight loss. She denied any other ailment or family history of breast disease. She was multiparous but did not breastfeed her children. She was not sure about age at menarche and menopause was at the age of 55 years.

On physical examination, skin of the left breast showed a peau d’orange appearance. The nipple was retracted. A lump was palpable beneath the areola. The lump was firm and irregular. It measured about 6.0 x 5.0 cm. A lymph node was palpable in the left axilla.

Mammography showed multiple asymmetric densities involving most of the left breast. The margins were ill-defined. The overlying skin was thickened. The nipple was retracted. There was no evidence of micro or macro calcification. There was an enlarged lymph node in the left axilla (not shown).

Ultrasonography of breast revealed thickened edematous skin and subcutaneous tissue of whole of the left breast. Multiple non-compressible hypoechoic lesions with irregular margins and posterior acoustic enhancements were present in all quadrants of the left breast. The largest one in the upper quadrant measured 2.7 x 1.6 cm. A large lymph node in the left axilla measuring 4.7 x 2.6 cm was noted. On A CT scan of the chest, abdomen and pelvis with Doppler color mapping, increased vascularity was noted. The lymph node showed thickened cortex and convex hilum contrast was performed. It revealed irregular soft tissue density mass in the left breast measuring 7.5 x 6.8 x 3.8 cm, with ipsilateral lymph node enlargement in the axilla. There was no evidence of local or distant metastasis either in the chest, abdomen or pelvis.

On the basis of the above findings, the lesion in the left breast was placed in BI-RADS category 5. The carcinoembryogenic antigen was 51.6ng/ml (normal range < 2.5ng/ml) and cancer antigen 15-3 (CA 15-3) was 7.7 (reference range < 31U/ml). Fine needle aspiration revealed malignant sheet of cells containing bizarre nucleoli with chronic inflammatory cells.

The patient underwent modified radical mastectomy with axillary clearance. Gross appearance of the breast specimen revealed a large firm mass 8 x 7 x 4 cm, gray in color with white areas. Microscopic picture revealed breast fibrous tissue stroma that was invaded by large sheets of pleomorphic malignant ductal cells. The tumor cells were not forming glands but formed sheets so that clear boundaries between cells could not be seen. Diffuse areas of necrosis and chronic inflammation were also present. Sections of nipple and areola revealed focal ulcers with superficial spread in near keratinous layers. Out of the 10 axillary lymph nodes which were dissected, 4 showed metastasis.

Immunohistochemistry showed that the mass was estrogen receptor (ER) and progesterone receptor (PR) negative, while HER2 and E-cadherin were positive.
**Figure 1:** Bilateral craniocaudal mammograms reveal asymmetric densities with architectural distortion in the left breast; right breast is normal

**Figure 2-3:** Ultrasound reveals hypoechoic lesions with lobulated margin and posterior acoustic enhancement in all quadrants of the left breast

**DISCUSSION**

According to the World Health Organization, over 1.2 million women are diagnosed with breast cancer annually worldwide[1]. Infiltrating ductal carcinoma is a broad entity which comprises of tumors that exhibit one or more characteristics of specific types of breast cancers. There is evidence of tubular, papillary, medullary or mucinous differentiation microscopically[2]. The etiology is still unknown. Marcus et al have suggested that BRCA1-associated tumors were more likely to be of medullary or atypical medullary type.[3]

For the diagnosis of medullary carcinoma to be made, strict histopathologic criteria should be completed. Traditionally, there has been no clear consensus among pathologists of the best diagnostic parameters for classifying medullary carcinoma. Since the histopathological grouping of breast cancer is subjective, this
results in high interobserver variability.[4] Ridolfi and his colleagues set up criteria for the diagnosis of medullary carcinoma in 1977 which included presence of five elements, namely syncytial growth pattern in at least 75% of the areas examined, microscopic circumscription, high nuclear grade, lymphoplasmacytic infiltrate and absence of tubular differentiation and/or an intraductal component.[2,5] Here it is worth noting that a cancer can be termed as classic medullary only if all of the five features mentioned above are present. "Atypical" medullary carcinoma is a term often used if one or two of the above mentioned features are absent, whereas if there is poor correspondence within the five categories, then the.

Appearance of lymph node on ultrasound also provides important clues. Normal lymph node has a reniform shape with thin hyperechoic cortex (1-2 mm) and a central fatty hilum. An abnormal outward contour and round shape of lymph node should be considered with suspicion. The most predictive signs of axillary metastasis in lymph nodes are maximum cortex thickness greater than 2.3 mm and appearance of the cortex.[7] Markedly hypoechoic cortex with eccentric, bulbous cortical thickening are features which suggest abnormality.[8] Since medullary carcinoma is a subtype of infiltrating ductal carcinoma, it is difficult to differentiate it on the basis of radiological features from other tumors in the same subgroup.

**Figure 4:** Enlarged lymph node with increased thickness of cortex, as seen on ultrasound

Though this is essentially a histopathologic diagnosis, certain features on the imaging modalities are described which underline the malignant nature of the lesion. On mammogram, these features include irregular shape, spiculated or irregular margins, or high density of the lesion. The density of the lesion can be described as low, intermediate or high by comparing it with an area of normal breast tissue on mammogram. Generally, benign masses tend to be of lower density than carcinomas; however, it is not reliable as a distinguishing mammographic sign. Sonographic findings suspicious for cancer include spiculation or thick echogenic halo, microlobulations, hypoechoegenecity, calcification, acoustic shadowing, duct extension. Histopathology plays an important role in this regard. Structural variations that characterize atypical medullary carcinoma include invasive growth at periphery of tumor, well-differentiated nuclear cytology, diminished lymphoplasmacytic reaction, low frequency of mitoses and glandular, trabecular or papillary growth with fibrosis.[17] In my patient, the histopathology fulfilled the criteria; hence, it was placed in the atypical variety.
There are recent publications of classification of breast cancer on the basis of gene expression profile analysis which have proposed that medullary carcinoma can be part of basal-like carcinoma spectrum made up of ER-negative, PR-negative and HER2-negative phenotype.[9] However, there are number of reports in literature that it can be ER, PR and/or HER2 positive, indicating the heterogeneity of this type of breast carcinoma.[9,10,11,12] My patient was ER and PR negative while HER2 was positive. According to a study conducted by Yilmaz, E. et al, comparison between typical and atypical medullary carcinomas on the basis of imaging features concluded that the typical variety tend to be a well-circumscribed mass on both mammography and sonography, and a posterior acoustic shadow was not found on sonography.[13] However, the imaging findings in these two subcategories often resembled each other and histopathology will always be mandatory to confirm the diagnosis.[13]

The prognosis of medullary carcinoma, whether typical or atypical, is better than that of high grade infiltrating ductal carcinoma.[14] It has been proposed that extensive presence of plasma cells and lymphocytes helps to keep the medullary carcinoma in check, preventing it from growing and spreading quickly.[15] The overall 10-year survival rate is 74% and more than 90% in patients with negative lymph nodes.[16] It is interesting to note that pure medullary carcinoma has better prognosis as compared to the one with atypical features.[16] Hence, strict adherence to diagnostic criteria is critical to provide a more accurate prognosis.

The treatment for medullary carcinoma, whether typical or atypical, is similar to invasive ductal carcinoma.[17] The division into typical and atypical subtypes has prognostic significance and does not modify treatment options. The treatment includes modified or radical mastectomy along with radiation or chemotherapy depending on the stage or histologic grade.

Figure 5: CT scan revealing a soft tissue density mass in the left breast with large lymph node in the left axilla

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REFERENCES


