



MEDULLARY CARCINOMA OF BREAST—A RARE VARIANT OF INVASIVE DUCT CARCINOMA

Pathology

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ABSTRACT

Medullary carcinoma, rare variant of invasive duct carcinoma of breast, generally forms 1% to 7% of all histomorphological variants of breast carcinoma. Medullary carcinoma is often classified into two categories, Medullary Breast Carcinoma (MBC) and atypical medullary breast carcinoma (AMBC) based on certain criteria which include total circumscription and absence of glandular structures and presence of diffuse lympho-plasmacytic infiltrate. Any medullary breast carcinoma not conforming to above mentioned criteria strictly is categorized as atypical medullary carcinoma (AMBC). The present case report is of 43-year-old woman who presented with two well-circumscribed nodules with the histomorphological features conforming to all the criteria of pure medullary breast carcinoma (MBC) with its unique morphological and relatively better prognostic implications, a quintessential combination of uncommon occurrence and histopathological features along with relatively better prognostic outcome that makes it find its place as an interesting case to be presented here.

KEYWORDS

Medullary, carcinoma, lympho-plasmacytic infiltrate.

INTRODUCTION

The normal resting (nonlactating, nonpregnant) breast is composed of a relatively small component fraction of ducts radiating from the nipple and glandular parenchymal tissue ("lobules"). The terminal duct lobular unit (TDLU) is part of a terminal duct continuing with a lobule of acinar cells at the most distal or terminal part [1]. Breast is one of the commonest sites of many pathological lesions including benign and malignant tumours, the malignant tumours being classified as ductal and lobular carcinomas depending on the preponderant histomorphological features, which are further subclassified into in situ or intraductal carcinoma and invasive duct carcinoma; in situ and invasive lobular carcinomas mainly based on non-invasiveness or invasiveness of the epithelial malignancies occurring in ductal and lobular tissue components respectively [2]. Invasive duct carcinoma of breast is the most common type of breast carcinoma which is diagnosed by default as invasive duct carcinoma without any specific or special features and often the diagnostic term of *infiltrating duct carcinoma, not otherwise specified* (NOS) or *infiltrating duct carcinoma of no special type* (NST) [3]. Invasive duct carcinoma has many cytoarchitectural variants, some of which are often categorized as special types as they are associated with particular kind of biological behavior. Medullary carcinoma of breast (MBC), one such type of invasive duct carcinoma with characteristic histomorphological features and growth pattern which are used as criteria for its diagnosis, is one of the rare variants of invasive duct carcinoma of breast that forms less than 1-7 percent of invasive duct carcinomas and has highly favourable outcome despite its aggressive growth pattern and marked cellularity [4].

CASE REPORT

The case being presented here is that of a 43-year-old female who presented with history of lump in her right breast since 6 months. On local examination, two discrete nodular masses were noted, which measured 5x4 cm and 2x2 cm respectively in descending order of their size. The nodular masses were painless and varying soft to firm in consistency, and were relatively mobile with the overlying skin, nipple and areola being unremarkable. All routine clinical investigations were within normal limits and radiological findings of chest, pelvis and abdomen revealed no evidence of metastases. The patient had recent history of undergoing fine needle aspiration examination (FNAC) of the nodules and FNAC report was positive for malignant cells. Following surgical exploration, histopathology laboratory received two gray-white soft to firm nodular masses with attached fibrofatty tissue. The nodular masses were fairly circumscribed, soft to firm in consistency and measured 5x4x2 cm and 2x1x0.5 cm respectively in descending order of their size. Microscopically, the variably circumscribed lesions showed marked loss of lobular architecture of breast parenchyma characterized by the presence of solid sheets and nests of round to ovoid cells. At places, cells are arranged in tight clusters reminiscent of syncytial pattern. The cells are predominantly

round to ovoid, with few spindled seen at places, which contain ample pale eosinophilic cytoplasm and pleomorphic nuclei containing prominent nucleoli. Rare focal areas of sheets and nests of cells show poorly formed tubular structures surrounded by irregular fibrosis and dense infiltration by predominantly lymphocytes and plasma cells. Also noted are focal areas of confluent necrosis resembling geographic necrosis and angiolymphatic invasion. The final histological diagnosis was Medullary carcinoma of breast—Grade II (Nottingham Modification of Bloom-Richardson grading system of Breast carcinoma).

DISCUSSION

Breast carcinoma is one of the most common malignancies among females. According to the World Health Organization, 1.5 million women suffer from breast carcinoma every year across the world with breast carcinoma forming almost one-fourth of cancers in females [5]. In India, breast cancer is the leading cancer among females with 145,000 cases detected in 2014 [5, 6]. Invasive breast carcinoma has been conventionally divided into invasive duct carcinoma and invasive lobular carcinoma [2, 3] with the former comprising various histological subtypes of invasive duct carcinoma. Medullary breast carcinoma is one of those rare subtypes of invasive breast carcinoma with an incidence ranging from 1 to 7 percent of all invasive carcinomas of breast. It was described for the first time by Moore and Foote [7], though they described it as a well-circumscribed carcinoma of breast with lymphoid stroma having a better prognosis as the term medullary carcinoma was apparently not well-defined with characteristic diagnostic criteria then. It was Ren L. Ridolfi et al [8] who proposed diagnostic criteria for typical medullary breast carcinoma (MBC). The diagnostic criteria proposed for defining medullary breast carcinoma included the following: 1. More than 75 percent syncytial growth pattern of tumour cells in 'interanastomosing sheets of cells with indistinct cell borders'; 2. Complete microscopic circumscription; 3. No intraductal component; 4. Moderate to marked mononuclear stromal infiltrate; 5. High nuclear grade; 6. Absence of microglandular features. Any deviation from these criteria was considered for any invasive duct carcinoma to be categorized as atypical medullary breast carcinoma (AMBC) or nonmedullary breast carcinoma. Any medullary carcinoma with no more than two atypical features such as tumour margins showing focal or prominent mononuclear inflammatory cell infiltration, presence of intraductal component, mild or negligible mononuclear infiltrate or infiltrate present only at the margins, mild nuclear atypia and presence of microglandular features is categorized as atypical medullary breast carcinoma (AMBC). Various studies carried out by different authors have demonstrated that typical medullary carcinoma of breast has got better clinical outcome than most other histological variants of invasive breast carcinoma [9-11]. Various comparative studies including some population-based studies were conducted to compare histomorphological and prognostic features of medullary carcinoma

with non-medullary variants of breast carcinoma by Park I. et al [12], Zangouri V. et al [13] and Steve R. Martinez et al [14] to endorse the findings of Ridolfi et al [8]. Maria Vittoria Dieci et al [15] described medullary carcinoma as a rare tumour of breast which is having relatively better prognosis, while Fisher E.R. et al [16] who reviewed 6404 cases of breast carcinoma found no significant difference in overall survival rate of medullary carcinoma and other non-medullary variants of invasive breast carcinoma. Wargotz and Silverberg [10] and Pederson L. et al [9] published reports of their extensive studies and found that not all the diagnostic criteria influence the clinical outcome of Medullary carcinoma, and both of them independently described different criteria based founded on prognostic outcome based on individual diagnostic criteria. Celina Kleer [17] described a medullary-like breast carcinoma associated with germline mutation of BRCA1 based on histological and immunohistochemical features. Andrzej Stelmach et al [18] from Poland studied histomorphological features and clinical outcome of 120 cases of typical medullary carcinoma of breast and claimed that typical medullary carcinoma has got very good clinical outcome among most other variants of invasive breast carcinoma.

CONCLUSION

Medullary breast carcinoma is a unique rare breast tumour. More the 75 percent of syncytial growth, microcircumscription, moderate to marked lymphocytic or lymphoplasmacytic or mononuclear inflammatory cell infiltrate, absence of microglandular formation and moderate to marked nuclear pleomorphism and absence of intraductal component are the diagnostic criteria which are strictly followed in diagnosis of Medullary breast carcinoma (MBC).

Medullary breast carcinoma stands out as a distinct variant of invasive breast carcinoma the prognosis of which is certainly better than other variants of invasive breast carcinoma if strict criteria are applied in its diagnosis. This fact makes it incumbent on the Pathologist to use his conventional skills and precise discretion in diagnosing it, which could spare undesirable consequences of elaborate surgical, chemotherapeutic and even radiotherapeutic management of invasive breast carcinoma.

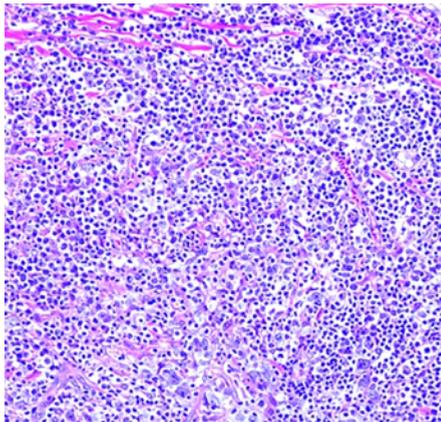


Fig 1. There is marked loss of lobular architecture of breast parenchyma characterized by the presence of solid sheets and nests of round to ovoid cells with infiltration of lymphocytes and plasma cells.

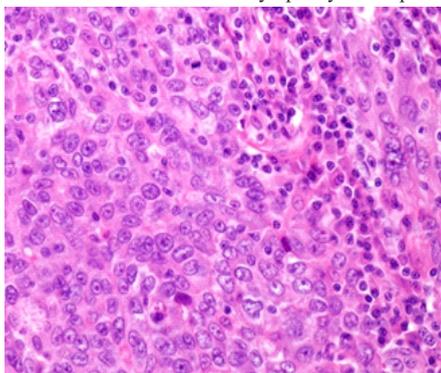


Fig 2. Few spindled cells seen which contain ample pale eosinophilic cytoplasm and pleomorphic nuclei containing prominent nucleoli with infiltration of predominantly lymphocytes and plasma cells.

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