

Osteoclast-like Multinucleated Giant Cells: A Clue to Invasive Mammary Carcinoma

Prachi B. Nichat¹, Kirti Chadha Kazi², Prem Punjabi³ and Vikas S. Kavishwar⁴

¹Department of Surgical Pathology, Metropolis Healthcare Ltd., Mumbai, India

²Department of Surgical Pathology, Metropolis Healthcare Ltd., Mumbai, India

³Consultant Pathologist, Mumbai, India

⁴Department of Surgical Pathology, Metropolis Healthcare Ltd., Mumbai, India

ABSTRACT

Mammary carcinoma with osteoclast-like giant cells is a rare variant of infiltrating breast carcinoma, first described by Rosen in 1979. Clinically and on sonomammography, the well-circumscribed margin of these tumors may suggest a benign lesion such as fibroadenoma and lead to a false negative diagnosis, as in this case of a 46 year old female with right breast lump. Fine needle aspiration cytology showed cohesive clusters with minimal cellular atypia mimicking fibroadenoma. But, presence of osteoclast-like multinucleated giant cells in the background was puzzling. So, lumpectomy was performed. Histopathology showed well differentiated invasive duct carcinoma, confirmed as luminal A type on immunohistochemistry. Till date, over 200 cases have been reported worldwide but we describe probably the only case from India, with complete work-up. The purpose of sharing this experience is to avoid missing malignancy on cytology in lesions which radiographically mimic fibroadenoma, osteoclast-like giant cells being a clue. Immunohistochemistry plays a diagnostic and predictive role. This low grade, rare but unique breast carcinomas must be documented for optimal patient management.

Keywords: Mammary Carcinoma, Osteoclast-Like, Giant Cells, Low Grade

Introduction

Mammary carcinoma with osteoclast-like giant cells is a rare and distinctive variant of infiltrating breast carcinoma. The first series was described by Rosen in 1979.^[1] Till date, approximately 200 cases of this unusual variant have been reported worldwide. We describe probably, the first such case with complete clinical, cytological, histological and immunohistochemistry findings, from India.

Case Report

A 46-year-old woman presented with a month old history of a lump in the upper outer quadrant of her right breast. There were no systemic symptoms, appetite or weight loss. Physical examination revealed a firm, freely mobile lump. Ultrasonography was suggestive of fibroadenoma. However, mammography was not done.

Fine needle aspiration was performed and was reported as fibroadenoma. However, background showed numerous multinucleated giant cells, which could not be explained (Fig. 1). So, the patient underwent lumpectomy. Due to the unusual histology and cyto-histological discordance, the primary pathologist referred the case to our Centre for opinion.

Grossly, the tumor was a fairly circumscribed nodular mass measuring 4.5 x 4 x 3 cms. The cut surface was dark brownish in appearance with a central tan white area (Fig. 2). There was no adjacent breast tissue included, so the margin status could not be commented upon.

Microscopically, the tumour was composed of predominant cribriform pattern (Fig.3) of malignant ductal epithelial cells with islands of cells showing cyst-like spaces containing eosinophilic secretions. The nuclear grade was low and mitoses were infrequent. The stroma was desmoplastic, extensively haemorrhagic and harboured numerous osteoclast-like multinucleated giant cells (OMGCs) along with mononuclear histiocytes (Fig. 4). The multinucleated giant cells contained variable number of small uniform nuclei. The nuclei were round to ovoid in shape and few had conspicuous nucleoli. No granulomas, necrosis or inflammatory infiltrate were observed. Axillary lymph nodes were not available for histopathological examination.

Immunohistochemically, the OMGCs were positive for CD68, a histiocytic marker, while the tumour cells were negative for CD68. The tumour cells were positive for Estrogen Receptor (ER, 1:800, Labvision) - Quick score 8/8, Progesterone Receptor (PR, 1:32, Labvision) - Quick score 8/8 and negative for Human Epidermal Growth Factor Receptor type 2 (Her2/neu, 1:800, Labvision), while the OMGCs were negative for ER, PR and Her2/neu. There was uniform loss of p63 and calponin, confirming the absence of myoepithelial cell layer. Following the WHO classification,^[2] the diagnosis was Mammary carcinoma with osteoclast like giant cells, Grade I.

Subsequently, second opinion was sought by the patient and was reported as Invasive cribriform carcinoma, Grade II. Considering the rarity of tumour and the discrepancy, the case was presented to the breast expert. It was confirmed as Mammary carcinoma with osteoclast like giant cells, Grade I.

The patient's socioeconomic status was poor and is consequently lost to follow-up.

Discussion

Carcinoma with osteoclastic giant cells has been described in various organs such as pancreas, thyroid, stomach, liver and soft tissue.^[3,4,5] Mammary carcinoma with osteoclast-like giant cells constitutes only 0.5-1.2% of breast carcinoma.^[6,7]

Clinically, it can present as a palpable lump in any quadrant of breast, in women aged 28 to 88 years with average age of 50 years. On mammography and ultrasonography, the well-circumscribed margin of most tumors may suggest a benign lesion such as a cyst or fibroadenoma.

The cytologic examination shows abundant giant cells and mononuclear cells in association with cohesive clusters with mild to moderate cellular pleomorphism. The cytologic atypia being minimal and the predominant cohesive nature of the clusters often create an ambiguous picture, which necessitates tissue diagnosis. The presence of giant cells without inflammation in the background must raise a suspicion for this variant and avoid a false negative diagnosis.

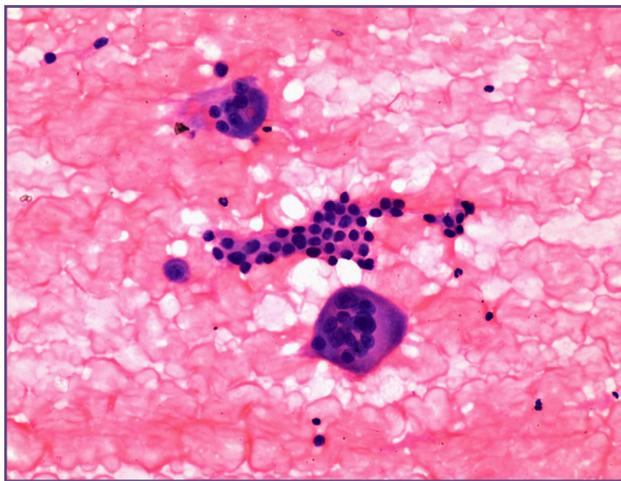


Fig. 1: Cytology smears showing a cohesive cluster of duct epithelial cells and mononuclear cells as well as multinucleated giant cells in the background (H&E, 40X).



Fig. 2: Gross examination: well circumscribed mass, brownish with tan-white areas.

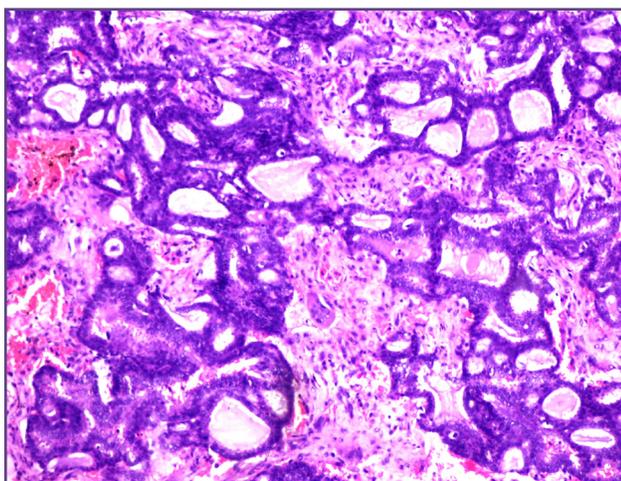


Fig. 3: Predominant cribriform pattern of tumour cells within a haemorrhagic and desmoplastic stroma (H&E, 40X).

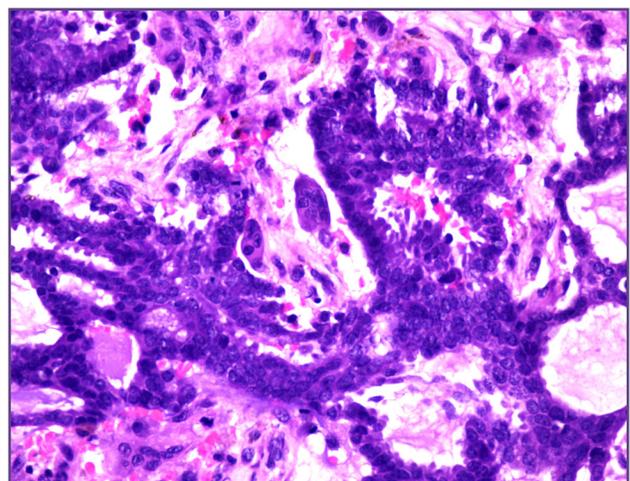


Fig. 4: Stroma shows numerous multinucleated giant cells and mononuclear cells with uniform round to ovoid nuclei, some with conspicuous nucleoli (H&E, 100X).

The gross appearance of this tumour is that of a well defined lump with characteristic dark brown appearance. This appearance is unique but hardly specific as it may also be seen in carcinoma with medullary features, malignant melanoma, haemangioma or angiosarcoma.

The multinucleated giant cells in the stroma can be seen along with various histological types of breast carcinoma including infiltrating duct carcinoma, lobular carcinoma, tubular, papillary, mucinous, apocrine, squamous and metaplastic carcinomas.^[8] Very rarely, they are associated with intraductal carcinomas.^[9]

Majority of the cases in literature have reported predominance of cribriform pattern of the carcinoma. Holland et al^[6] have described the 'adenocystic' pattern of the invasive tumour growth. The invasive tumour can be well to moderately differentiated. Zhou et al^[10] have revealed that invasive carcinoma with OMGCs commonly exhibit a luminal phenotype with luminal A subtype as the major group. Our case is consistent with this finding.

The OMGCs are present near the tumour islands in the lumina and especially in the regions where luminal contents are seen spilling in the stroma. The mechanism of formation of the giant cells is unknown; however, it may be a result of some unusual stromal reaction to cancer cells and their secretions. Considering that the stroma is extensively vascular, the role of vascular endothelial growth factor has also been considered.^[9]

The stromal multinucleated giant cells with overlapping nuclei and scant cytoplasm, in fibroadenoma and phyllodes tumour are Vimentin positive while bizarre tumour giant cells with pleomorphic and atypical nuclei are cytokeratin positive. OMGCs in the background of mammary carcinoma are cytokeratin negative and CD68 positive. Thus, OMGCs probably best represent a reactive macrophage polykaryon and are not neoplastic in nature.

The influence of the presence of osteoclast like giant cells on the prognosis is yet to be understood. Agnantis et al^[11] suggested that the prognosis is less favorable as compared to the more ordinary infiltrating lesions. But, nearly two thirds of patients have been reported to be alive and well with follow-up rarely reaching beyond 5 years.^[8]

Conclusion

The purpose of sharing this experience is to avoid missing malignancy on cytology in lesions which radiographically mimic fibroadenoma, osteoclast-like giant cells being a clue. Immunohistochemistry plays a diagnostic and predictive role. These low grades, rare but unique breast carcinomas must be documented for optimal patient management.

Acknowledgements

Metropolis Healthcare Ltd has supported the processing and compilation of the article for publication.

References

1. Rosen PP. Multinucleated mammary stromal giant cells: a benign lesion that simulates invasive carcinoma. *Cancer* 1979; 44: 1305-1308.
2. Ellis IO, Collins L, Ichihara S, MacGrogan G. Invasive carcinoma of no special type. In: World Health Organization Classification of Tumors of the Breast, Lakhani SR, Ellis IO, Schnitt SJ, Tan PH et al. 4th edition, IARC Press, Lyon, France, 2012:36-37.
3. Bauditz J., Rudolph B., Wermke W. Osteoclast-like giant cell tumors of the pancreas and liver. *World Journal of Gastroenterology*. 2006; 12:7878-7883.
4. Baschinsky DY, Frankel WL, Niemann TH. Gastric carcinoma with osteoclast-like giant cells. *American Journal of Gastroenterology* 1999; 94:1678-1681.
5. Kobayashi S, Yamadori I, Ohmori M, Kurokawa T, Umeda M. Anaplastic carcinoma of the thyroid with osteoclast-like giant cells. An ultrastructural and immunohistochemical study. *Acta Pathol Jpn*. 1987 May; 37(5):807-15.
6. Holland R, van Haelst UJ. Mammary carcinoma with osteoclast-like giant cells. Additional observations on six cases. *Cancer* 1984; 53: 1963-1973.
7. Cai N, Koizumi J, Vazquez M. Mammary carcinoma with osteoclast-like giant cells: a study of four cases and a review of literature. *Diagn Cytopathol* 2005; 33: 246-251.
8. Chapter 23 - Mammary Carcinoma with Osteoclast-Like Giant Cells. In: Rosen's Breast Pathology. Rosen PP. 3rd Edition, Lippincott Williams & Wilkins 2009: 571-580.
9. Krishnan C, Longacre TA. Ductal carcinoma in situ of the breast with osteoclast-like giant cells. *Human pathology* 2006; 37: 39-372.
10. Zhou, S., Yu, L., Zhou, R. et al. *Virchows Arch* 2014; 464: 681. doi: 10.1007/s00428-014-1573-y
11. Agnantis NT, Rosen PP. Mammary carcinoma with osteoclast-like giant cells: A study of eight cases with follow up data. *Am J Clin Pathol* 1979; 72:383-389.

*Corresponding author:

Dr Prachi Nichat, 4th floor, Commercial building, 1A Kohinoor mall, Vidyavihar West, Mumbai, Maharashtra 400070 India

Phone: +91 9987519304

Email: prachibnichat@gmail.com

Financial or other Competing Interests: None.