

## Case Report

# Pleomorphic Lobular Carcinoma of the Breast – A Diagnostic Dilemma

Kini H\*, Pai R\*, Rau AR\*, Lobo FD\*, Augustine AJ#, Ramesh BS#

### Abstract

*Pleomorphic lobular carcinoma of the breast has been identified as a histological variant of infiltrating lobular carcinoma (ILC) with poor prognosis. Thus, cytological recognition of this tumour is important. It is characterized by pleomorphism to a degree that contrasts with the cytologic uniformity of classic ILC. Due to this feature it is often misinterpreted as infiltrating ductal carcinoma and diagnosed only on appreciating the Indian file and targetoid pattern of lobular carcinomas on histology. We report three cases with this unusual tumour that can present a diagnostic dilemma on cytology.*

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**Key Words :** Aspiration cytology, lobular carcinoma, pleomorphic lobular carcinoma.

### Introduction

Pleomorphic lobular carcinoma (PLC) of the breast, a variant of infiltrating lobular carcinoma (ILC),<sup>1-4</sup> is an aggressive tumour accounting for 0.67% of all breast carcinomas and not more than 5% of lobular carcinomas. It is associated with short recurrence free survival.

The tumour cells in PLC show similar dissociated, linear and single file growth pattern together with targetoid distribution around benign ducts as seen in ILC. However, the cells are pleomorphic to a degree that contrasts with the cytological uniformity of classic ILC. Hence there is a need to differentiate it from infiltrating ductal carcinoma (IDC).

With the increasing use of fine needle aspiration cytology (FNAC) in the diagnosis of breast lumps, the scope for cytology has been gradually shifting from the mere identification of malignancy to accurate cytological categorization of various lesions.<sup>5</sup> Diagnosis of PLC by FNAC though challenging, is important due to the associated clinical implications. We report the cyto-histomorphological features of three cases of PLC with apocrine / histiocytoid

features. However, histopathology was available in only two cases.

### Case Reports

The clinical details are shown in Table 1. All three cases had highly cellular smears with moderate to large sized tumour cells, predominantly arranged as dispersed cells with focal small, loosely cohesive clusters. The cells had distinct cell borders, moderate to abundant, pale to dense, granular cytoplasm, pleomorphic, hyperchromatic nuclei and prominent nucleoli. Case 1 was originally reported as consistent with IDC. In Case 2, air-dried Romanowsky stained slides were received for review from another laboratory. The cellular smears predominantly showed dissociated, medium to large sized, plasmacytoid cells with moderately dense cyanophilic, granular to vacuolated cytoplasm and occasional signet-ring cells. The eccentrically placed hyperchromatic nuclei with prominent nucleoli combined with cytoplasmic basophilia, binucleation and cellular dissociation led to the mistaken diagnosis of a plasmacytoma (Fig.1). A trucut biopsy, histologically and immunohistochemically (cytokeratin positivity), confirmed PLC. Case 3 showed identical features as Case 1, along with a few cells with intracytoplasmic lumina (ICL) and occasional large cells with bizarre multilobated nuclei. However, a diagnosis of lobular carcinoma was made in this case. Mastectomy with axillary clearance was performed in the first two cases. The third patient refused surgery and was lost to follow-up. Histopathology reflected the cytological features. The cells were arranged in Indian file (Fig.2) and targetoid pattern with periparenchymal streaming as well as singly dispersed cells separated by desmoplastic stroma. In both cases, focal in-situ

\*Associate Professor, \*Additional Professor; Department of Pathology; #Associate Professor; Department of General Surgery; Kasturba Medical College Light House Hill Road, Mangalore- 575001.

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**Corresponding Author:** Dr. Hema Kini, Associate Professor, Department of Pathology, Kasturba Medical College, Light House Hill Road, Mangalore - 575001. Karnataka.

**E-mail:** hemakini@hotmail.com

**Table 1: Clinical details of the three cases of PLC**

Case No.	Age/Sex	Clinical features	FNAC diagnosis	Surgery	Stage
1	30 /F	Lump left breast, 4cm for 10 months	Infiltrating ductal carcinoma	Simple mastectomy with axillary clearance	T <sub>2</sub> N <sub>1</sub> M <sub>0</sub>
2	28 /F	Lump left breast, 10cm for 4 months	Plasmacytoma	Modified radical mastectomy with axillary clearance	T <sub>3</sub> N <sub>1</sub> M <sub>0</sub>
3	70 /F	Bleeding per vagina, mass left breast for 2 months	Infiltrating lobular carcinoma	-	-

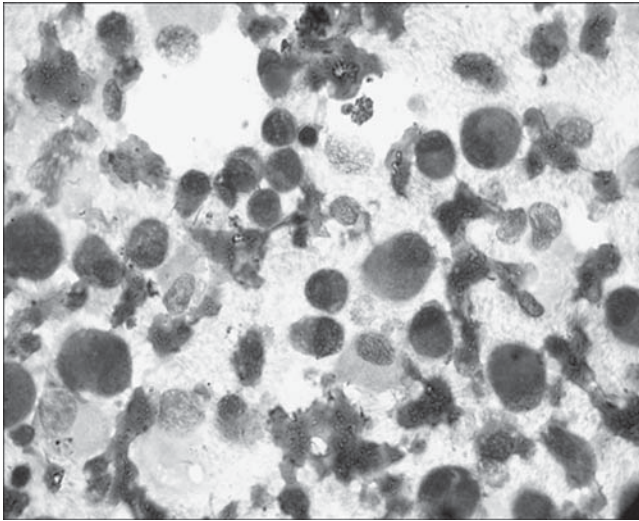


Fig. 1 : FNAC smear showing a dissociated population of medium to large plasmacytoid cells (MGG, x1000).

lobular carcinoma was seen. In Case 2, focal alveolar and tubulolobular pattern of ILC as well as minor foci of atypical ductal hyperplasia, in-situ and invasive ductal carcinoma were also present. In both cases, the lymph nodes showed metastatic deposits either in a sinusoidal pattern or with complete nodal effacement.

### Discussion

Pleomorphic lobular carcinoma most often occurs in postmenopausal women,<sup>1,4</sup> the mean age being 58.9 years (age range 24-94 years). Reported tumour size is from 1.2 to 25 cm.<sup>4</sup> Middleton et al<sup>4</sup> observed that the largest tumour they encountered (25 cm) was in a young 24 year old woman. Interestingly, the tumour in our youngest patient was also the largest (10cm).

The histopathological diagnosis of classic ILC is seldom difficult and experienced pathologists concur in the vast majority of cases.<sup>2</sup> However, variant forms of ILC have more diverse appearance.<sup>1</sup> The distinguishing features of PLC from ILC is the presence of a significant proportion of the tumour cell nuclei showing grade 2 to 3 features by the Scarf-Bloom-Richardson grading system combined with the single file growth pattern that is typical of the latter.

Traditionally, the cytological preparations in classic ILC are known to be an important cause of false

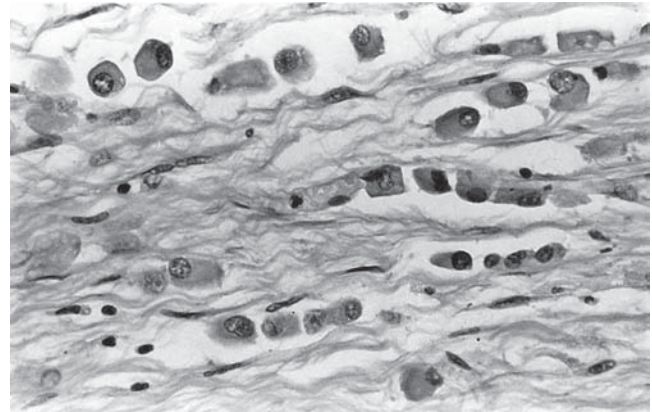


Fig. 2 : Histopathology showing plasmacytoid cells arranged in Indian file pattern in a bed of desmoplastic stroma (H&E, x 400).

negative diagnosis due to hypocellularity, small cell size and bland cellular features.<sup>5-8</sup> A high index of suspicion and experience is required to overcome this pitfall. The features which favour ILC include low cellularity, dissociated, homogenous, small malignant cells with scanty cytoplasm, nuclei which are regular in size but irregular in shape and inconspicuous nucleoli. Short single files, intracytoplasmic lumina and signet-ring cells are characteristic features though not pathognomonic of ILC.<sup>5-8</sup>

The cytologic features of PLC are a hybrid between the appearances of lobular and ductal carcinoma.<sup>7-10</sup> Invariably, cellular smears show individual tumour cells that are 2 to 3 times the size of cells in classic ILC, with moderate nuclear pleomorphism, prominent nucleoli and moderate to abundant eosinophilic, granular (apocrine/myoid) to finely vacuolated (histiocytoid) cytoplasm.<sup>6-10</sup> PLC is consistently immunoreactive for gross cystic disease fluid protein-15 (GCDFF-15), a marker of apocrine differentiation and hence, the term -"Pleomorphic lobular apocrine carcinoma".

The lobular carcinoma cell has been reported to have a 'plasmacytoid' appearance due to the eccentric nuclear location.<sup>7, 10</sup> The differential diagnosis for plasmacytoid cells in breast cytology includes ILC and its pleomorphic variant, IDC including the apocrine

type, plasmacytoma, carcinoma with endocrine differentiation, and the rare granular cell tumour.<sup>1,5,7-13</sup> In IDC, irregular, angular, loosely cohesive cell groups are seen along with single cells. Higher nucleocytoplasmic ratio, absence of cytoplasmic granularity and negative GCDFP-15 staining are distinguishing features in favour of IDC. Apocrine change is sometimes focally seen in ductal and lobular carcinomas but pure apocrine carcinomas are rare (<1%). As with PLC these tumours are also GCDFP-15 positive. Eosinophilic macronucleoli, lack of intracytoplasmic lumina and the solid/comedo growth pattern on histopathology are distinguishing features of apocrine carcinoma.

Plasmacytic tumours of the breast may arise as part of disseminated multiple myeloma or as the isolated initial manifestation of systemic disease or as an isolated plasmacytoma limited to the breast. In these tumours the cells show the presence of paranuclear hof, cartwheel chromatin and lack intracytoplasmic mucin, features which were not present on review of the slides in Case 2. Mitosis, pleomorphism and multinucleated cells may be seen. In histological sections, presence of sheets of neoplastic plasma cells with the absence of intervening stromal response, effacement of glandular structures in the region of the lesion and the absence of in-situ lobular carcinoma are helpful features in favour of plasmacytoma. Immunohistochemically, the absence of cytokeratin and GCDFP-15 and presence of cytoplasmic immunoglobulins is diagnostic of plasmacytoma. Availability of a preceding diagnosis of myeloma usually makes the interpretation of these lumps easier,<sup>11</sup> but in cases presenting initially with a breast lump, misinterpretation as lobular carcinoma or poorly differentiated carcinoma is known.<sup>12</sup>

Endocrine carcinomas of the breast may show plasmacytoid cells. However, in these lesions the smears show smaller cells of low nuclear grade, typical salt and pepper chromatin, small nucleoli, accentuation of staining in the paranuclear region due to aggregation of dense core granules detected by electron microscopy and positivity for neuroendocrine markers (neuron specific enolase, synaptophysin, chromogranin). Histology shows an organoid growth pattern, festoons or cords, with or without peripheral palisading.

The rare granular cell tumours of the breast also possess granular cytoplasm due to intracytoplasmic

lysosomes.<sup>14</sup> The tumour cells are of schwannian differentiation and express S-100 protein.

In conclusion, though for an experienced pathologist with regular exposure to breast FNACs, it is usually not difficult to distinguish classic ILC from IDC, an awareness of the cytohistomorphological features and a high degree of suspicion is required to diagnose PLC. In cases where typing presents a dilemma, a diagnosis of "carcinoma breast, type unclear, i.e. ductal vs lobular" can be offered and histopathology examination asked for confirmation.

It is important to diagnose PLC, as ILCs in general, are more often multifocal and bilateral. PLC has a prognosis worse than either IDC or classic ILC and hence, is described as the lethal variant.<sup>5</sup>

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