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Pleomorphic lobular carcinoma of breast – cytological characteristics and differentials

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Abstract

Pleomorphic lobular carcinoma of breast (IPLC) is a very rare and distinct morphological variant of invasive lobular carcinoma (ILC), characterized by nuclear atypia and pleomorphism contrasted with the cytologic uniformity of ILC. Also it is associated with poor prognosis. Thus, cytological recognition of this tumour is important. We report a case with this unusual tumour in a fifty eight year old female that presented as a diagnostic dilemma on cytology.

Keywords

aspiration cytology; breast carcinoma; pleomorphic lobular carcinoma

Introduction

Pleomorphic lobular carcinoma(PLC) of breast is a distinct histological variant of invasive lobular carcinoma(ILC) [1,2,3,4,5]. Cytological recognition is important as the degree of pleomorphism exhibited in this specific subtype may lead to misinterpretation of this particular subtype of lobular carcinoma as infiltrating ductal carcinoma. Also, it is associated with aggressive clinical course in having larger size, marked cytologic atypia, more prone to distant metastasis, higher chance of lymphovascular invasion and presentation at a higher stage [6,7,8,9,10]. The cytological literature on this entity is very little. We present a case of Pleomorphic Lobular Carcinoma diagnosed retrospectively, discuss the cytologic features that are useful in the recognition of this entity and the diagnostic pitfalls.

Case Presentation

A fifty eight year old female presented with a three month history of a self-discovered, progressively increasing, painless palpable lump in the left breast. She had no significant medical history. There was no family history of breast disease. On physical examination, a relatively ill-defined firm mass measuring 7x6 cm was palpable in the outer quadrant. The overlying skin appeared normal. There was evidence of palpable lymphadenopathy in the ipsilateral axilla. Mammography reported well-defined asymmetric density in the left breast (BIRADS-4). Fine Needle Aspiration Cytology (FNAC) was done and the smears showed scanty cellularity with occasional cells showing large nuclei. As the number of these large cells were very few and no conclusion could be drawn a repeat aspiration was performed which was highly cellular with large dyscohesive cells (Figure 1a). These cells were plasmacytoid, had coarse chromatin, inconspicuous to prominent nucleoli and variable amount of cytoplasm. Few binucleated cells were also noted. Mitotic figures were also seen (Figure 1b). The dissociated pleomorphic cell population

along with binucleation and mitotic figures led to the diagnosis of malignancy. Based on this report, wide excision lumpectomy with guided wire was performed as the patient was unwilling for a radical excision. This specimen showed multiple dilated vessels with tumour emboli showing aggregates of malignant cells (Figure 2a). These cells were similar to those seen in cytology smears showing large sized plasmacytoid cells with moderate to abundant cytoplasm and eccentrically placed large round nuclei (Figure 2b). Many binucleated cells were also noted. Adjacent stroma showed multiple calcific spherules and periductal lymphocytic infiltrate. Adenosis, cystically dilated ducts and focal epithelial hyperplasia was also noted. No primary foci of tumour were seen. Immunohistochemistry (IHC) workup was performed on this specimen. Tumour cells were positive for Pan CK (Figure 3a), CK7 and GCDFP-15 (Figure 3b) and were negative for E-cadherin(Figure 3c), ER and PR. CD138 and LCA were also negative. The tumour cells also showed 3+ positivity for Her 2-neu (Figure 3d). A diagnosis of Pleomorphic Lobular carcinoma was given. The patient underwent Modified Radical Mastectomy (MRM) with axillary clearance, MRM specimen was received which after careful grossing and sectioning showed two small foci of around 1cm each which on microscopy showed tumour cells with similar morphology as in the lumpectomy specimen. Nine out of twelve lymph nodes also showed tumour metastasis.

Discussion

The origin of PLC has been a matter of controversy because of the morphology and immunophenotypic characteristics that overlap between ILC and invasive ductal carcinoma. The histological architecture and pattern of tissue invasion closely resembles ILC; however the cellular pleomorphism and nuclear atypia are more consistent with IDC. In fact, some authors have suggested that PLC is a high grade IDC that has lost E-cadherin expression.

It predominantly affects postmenopausal women between the ages of 60-80 years. [8, 11, 12] But those associated with BRCA may present at a younger age [13,14]. This may explain the data that which says that PLC may occur over a wide age range, varying from 35 to 80 years of age [8].

Importance of diagnosing PLC lies in the fact that patient with PLC are more likely to develop distant metastasis and recurrence than those with classical for of ILC thus associated with a poorer outcome [6]. However, it remains to be determined, whether the pleomorphic histology independently predicts a worse outcome or other known associated negative prognostic factors such as larger tumor size, increased metastatic disease, and associated worse molecular subtypes commonly present in pleomorphic carcinoma account for the poor prognosis [23,24].

The clinical and histopathological features of the cases of pleomorphic lobular carcinoma of breast described so far, have been summarized in Table 1.

The cytology of PLC is hybrid between lobular and ductal carcinoma [18,19,20,21]. The smears are cellular with individual cell being 2-3 times the size of cells in classical ILC, with moderate nuclear pleomorphism, prominent nucleoli and moderate to abundant eosinophilic, granular to finely vacuolated cytoplasm. Multinucleated malignant cells may be seen and mitosis is frequent [10,15]. Because of the degree of pleomorphism and tendency to form occasional aggregates in small groups , distinguishing it from high grade ductal carcinoma can be challenging at times[16]. Our case demonstrated plasmacytoid cells due to eccentric nuclear location. The differential for plasmacytoid cells in the breast cytology

includes ILC and its pleomorphic variant, IDC including its apocrine type, plasmacytoma , carcinoma with endocrine differentiation and rarely granular cell tumours [17,18,19,20,21,22]. A higher nucleo-cytoplasmic 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 carcinoma but pure apocrine carcinomas are rare (<1%). Like PLC they are GCDFP positive but are E-cadherin positive and may be distinguished from PLC by the eosinophilic macronucleoli, lack of intracytoplasmic lumina and the solid/ comedogrowth pattern on histopathology. Plasmacytoma show a perinuclear hof, cartwheel chromatin and lack of intracytoplasmic mucin that may help to differentiate them from PLC. Although, multinucleation, mitosis and pleomorphism may be seen similar to PLC. Endocrine carcinoma of breast may also show plasmacytoid cells. However these cells are smaller, of low nuclear grade, have the typical salt and pepper chromatin, accentuation of staining in paranuclear region due to aggregation of dense core granules detected by EM and positivity for neuroendocrine markers. The rare granular cell tumours of the breast possess granular cytoplasm due to intarcytoplasmic lysosomes. The tumour cells are of schwannian differentiation and express S100. The histology of PLC retains the distinctive growth pattern of ILC but shows marked cellular atypia, nuclear pleomorhpism with an increased mitotic rate and may show signet ring cells and /or show apocrine or histiocytoid differentiation.

Conclusion

In conclusion, PLC may be a challenging diagnostic dilemma in cytology and require experience and regular exposure to breast FNAC. Suboptimal yield, as in our case, may be a compounding factor. Its behavioral differences like increased recurrence, multifocality and bilaterality mark the importance of its recognition and differentiation from IDC as well as ILC. A thorough knowledge of the cytohistomorphological features and a high degree of suspicion is required to diagnose PLC. In cases presenting as dilemma, histopathology and immunohistochemistry comes in handy.

Figures

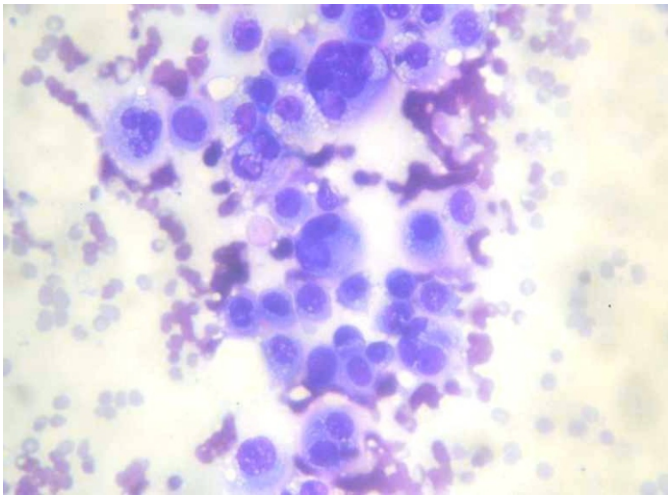

Figure 1a: On fine-needle aspiration biopsy, smears are cellular with predominantly dyshesive malignant cells. Tumor cells are plasmacytoid, eccentric nucleus with prominent nucleoli and abundant cytoplasm. (MGG, x400)

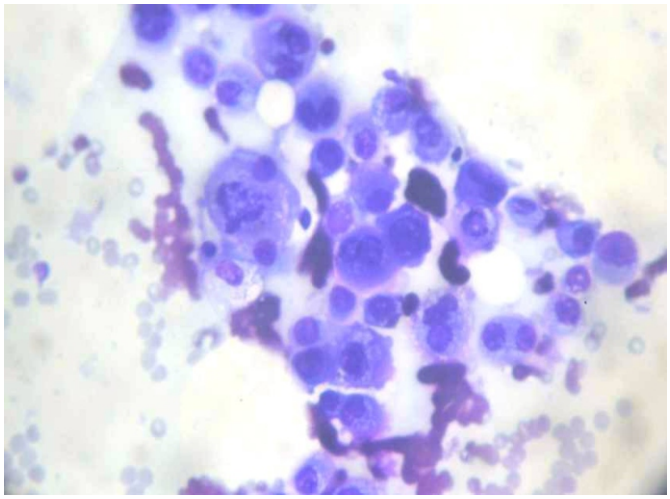

Figure 1b: Multinucleation and atypical mitotic figure noted. (MGG, x400)

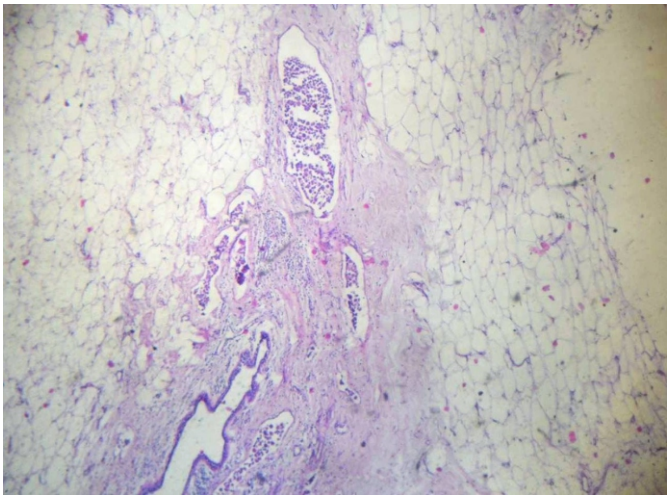

Figure 2a: Tumour emboli seen in multiple dilated vessels. (H&E, x400)

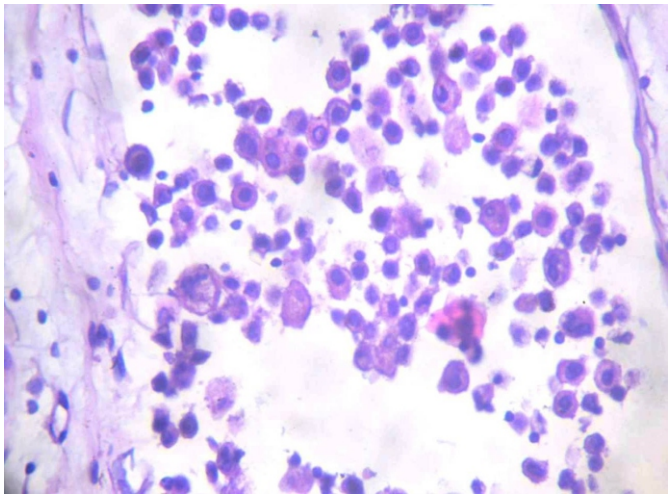

Figure 2b: Tumour cells are large sized plasmacytoid with moderate to abundant cytoplasm and eccentrically placed large round nuclei. (H&E, x100)

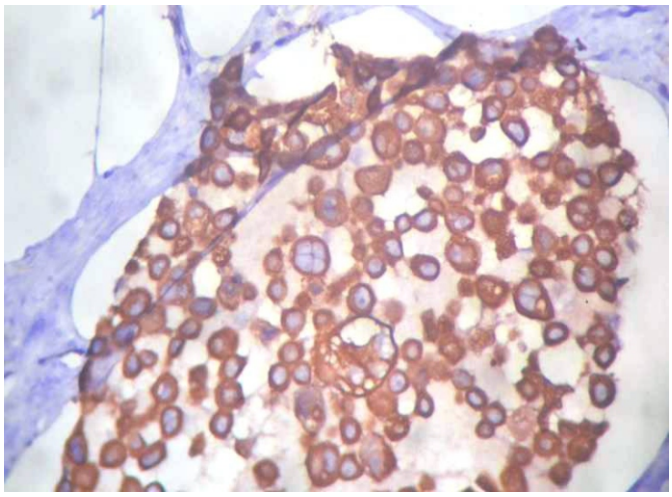

Figure 3a: PanCK: Immunostain shows positive cystoplasmic membrane staining.(x400)

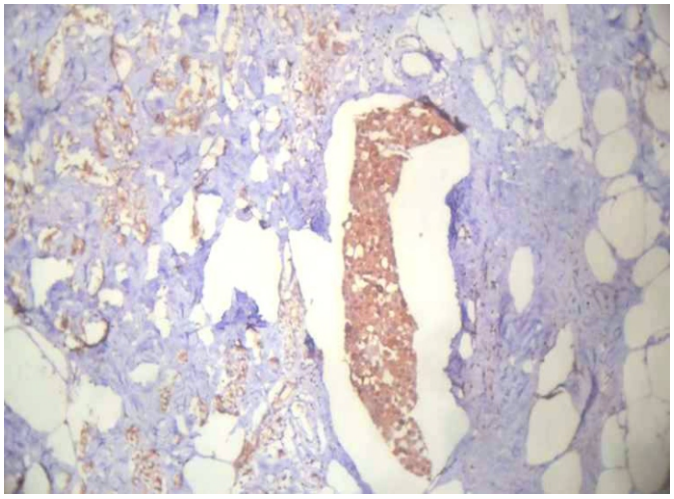

Figure 3b: GCDFP-15: Immunostain shows positive cytoplasmic staining.(x100)

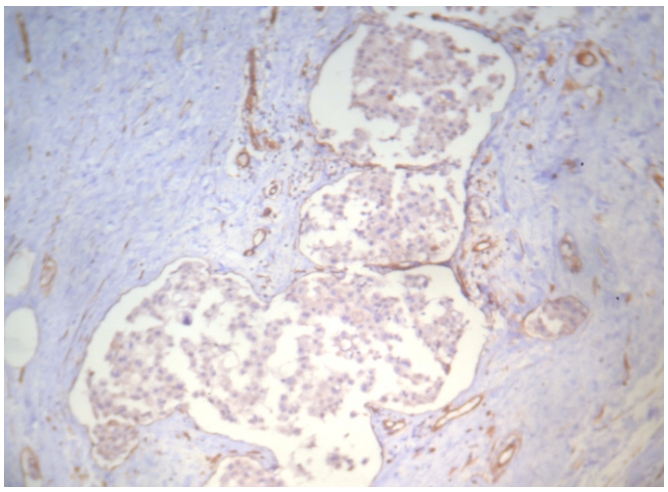

Figure 3c: E-cadherin: Immunostain for E-cadherin shows absence of membranous staining.(x100)

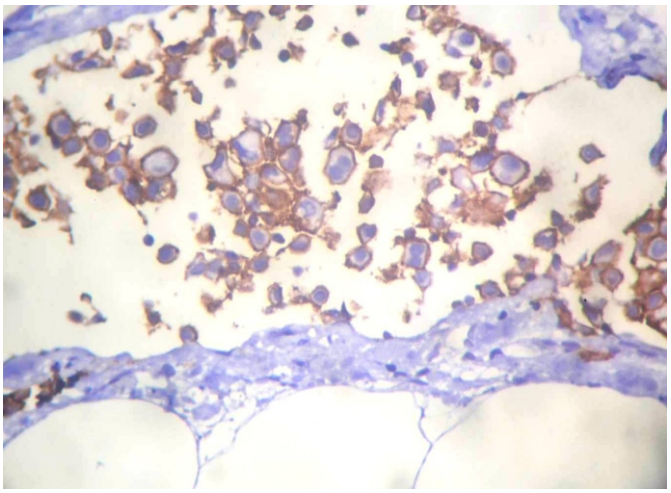

Figure 3d: Her 2-neu: Immunostain shows 3+positive staining.(x400)

Table

Table 1: Clinical and histopathological features of pleomorphic lobular carcinoma of the breast reported so far:

	Age	Sex	Lateralization	Size	ER/PR/ Her2neu	E-Cadherin	Lymph node status
Zahir et al (2013)	68	M	Left	2.8x2.5cm	+/+/+	-	+
Ishida et al (2013)	76	M	Right	3x2.5cm	+/-/-	-	-
Gupta et al (2012)	34	F	Left	2x1.5cm	-/-/-	Not mentioned	-
Manucha et al (2011)	67	F	Left	Two foci: 1.1.7cm 2.1.5cm	-/-/-	-	-
Rohini et al (2010)	55	M	Left	3x2.5cm	Not mentioned	-	-
Augustine et al(2007) (Three cases)	1.30	F	Left	4cm	Not mentioned	Not mentioned	+
	2.28	F	Left	10cm	Not mentioned	Not mentioned	+
	3.70	F	Left	Biopsy specimen	Not mentioned	Not mentioned	Not assessed
Maly et al (2005)	44	M	Left	2.5x2cm	+/+/-	-	-
Present case	58	F	Left	7x6cm	-/-/+	-	+

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