

Pitfalls in diagnosing specific subtypes of carcinoma breast on fine needle aspiration cytology: A report of two cases with review of literature

ABSTRACT

Fine needle aspiration cytology (FNAC) is a useful procedure that can be conveniently performed in the outpatient department (OPD) and can be used in the subtyping of breast carcinomas. However, some specific subtypes can cause a hindrance to that. We present two such cases, one of tubulolobular carcinoma breast and the other of squamous cell carcinoma breast that were missed on FNAC, and subsequently diagnosed on histopathology and by immunohistochemistry. A thorough knowledge of the cytological features of the subtypes and the use of immunocytochemistry can appropriately make FNAC a standard, accurate, and simple OPD procedure, thus helping us in arriving at specific diagnosis.

KEY WORDS: Fine needle aspiration cytology, immunohistochemistry, squamous cell carcinoma, tubulo-lobular carcinoma

INTRODUCTION

Fine needle aspiration cytology (FNAC) is a basic investigative tool used in diagnosing breast lesions, and based on the results, the treatment modality is decided. Surgeons insist upon knowing the grade and subtype of cytology to decide the mode of treatment. In few variants of breast carcinoma, histological subtype is often missed on FNAC. In our case report, we have presented two distinct variants of carcinoma breast where FNAC failed to identify the subtype correctly.

CASE REPORTS

Case 1

- A 50 year old female came to our department with the complaint of a lump in the left breast of 6 months duration measuring 3 × 3 cm. FNAC aspirates from tumour were cellular, consisting of malignant ductal epithelial cells, with increased nuclear cytoplasmic ratio, bland nuclear chromatin, and irregular nuclear borders with scant to moderate amount of cytoplasm arranged in cohesive clusters and tubular patterns in a hemorrhagic background. [Figure 1a]
- Provisional Diagnosis** of Ductal carcinoma- low grade was made. Subsequently, mastectomy was done and the specimen collected was

subjected to histopathological examination.

- Gross findings:** Left mastectomy specimen measures 25 × 19 × 11 cm was obtained. Cut section revealed a tumour-measuring 4 × 3 × 2 cm.
- Microscopy:** The tumour proper showed cells arranged in tubular pattern surrounded by few tumour cells were seen arranged in singles and small clusters. These tumour cells had scant cytoplasm, mildly increased N:C ratio, and round to oval nucleus with bland chromatin [Figure 1b]. Histopathological diagnosis of Tubulo-lobular carcinoma was made.
- Immunohistochemical examination** with E-Cadherin showed a positive membranous staining of tumour cells in the tubular areas [Figure 1c].
- Final Diagnosis** of Tubulo-lobular carcinoma was made after immunohistochemistry (IHC).

Case 2

- A 52 year old female presented with a hard lump in the right breast. FNAC showed a high cell yield with cells arranged in discrete and loose irregular clusters. Cells were round to polygonal in shape with moderate to dense eosinophilic cytoplasm, nuclei were round to oval with dense chromatin and with a single prominent nucleoli. Few cells showed mitotic figures.

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Access this article online

Website: www.cancerjournal.net

DOI: 10.4103/0973-1482.103534

Quick Response Code:



- **Provisional Diagnosis** of Ductal carcinoma - intermediate grade was made [Figure 2a]. Subsequently, mastectomy was performed and the specimen collected was subjected to histopathological examination
- **Gross findings:** Mastectomy specimen measured 22 × 10 × 10 cm. Cut section revealed a grey white ill-defined infiltrating tumour measuring 3 × 2 × 1.5 cm.
- **Microscopy:** Tumour cells were arranged in sheets, few in a glandular pattern and few in small nests. Cells were large, round to polygonal in shape with hyperchromatic nucleus and abundant eosinophilic cytoplasm. Tumour cells were seen infiltrating the stroma and adipose tissue. Some cells showed abundant individual keratinisation [Figure 2b].
- **Histopathological diagnosis** of metaplastic carcinoma – Adenosquamous variant of the carcinoma was identified,
- **Immunohistochemistry report** – Tumour cells were positive for antibodies against high molecular weight cytokeratin [Figure 2c]. Tumour cells were negative for antibodies against Estrogen Receptor (ER) and Progesterone receptor (PR).
- **Final diagnosis** of metaplastic carcinoma - Squamous cell (SCC) variant was made. No lesions were found in the cervix, oral cavity, lungs, esophagus or skin.

DISCUSSION

FNAC of the breast lesions have a wide range of accuracy (72-99%) in diagnosis of the malignancy and in its subtyping. Histologically, 25-30% of epithelial malignancies fall into the specialized breast cancer groups such as the lobular, papillary, apocrine, tubular, cribriform, medullary, mixed and others.^[1] However exact subtyping of tumour is always not feasible on FNAC. Tubulolobular carcinoma is a rare tumour that accounts for about 1% of all breast cancers. It is a hybrid tumour sharing features of both infiltrating lobular and infiltrating ductal (tubular) variants.^[2] This tumour was first described by Fisher *et al.* as a variant of the invasive lobular carcinoma.^[3] On FNAC, this tumour is composed of tightly knit, angulated clusters of uniform, bland epithelial cells forming tubular structures containing occasional lumen at the center. Rarely are the tumor cells present singly. Nucleus is round to oval in shape with a bland nuclear chromatin, minute nucleoli and intracytoplasmic vacuoles. These cells are present in a littered background. Sometimes, an "Indian file pattern" similar to the infiltrative lobular carcinoma can be seen on both the FNAC and histopathology.^[3] However, our case was misdiagnosed as Infiltrating ductal carcinoma due to the absence of angulation of ducts and the presence of mild nucleomegaly. A similar,

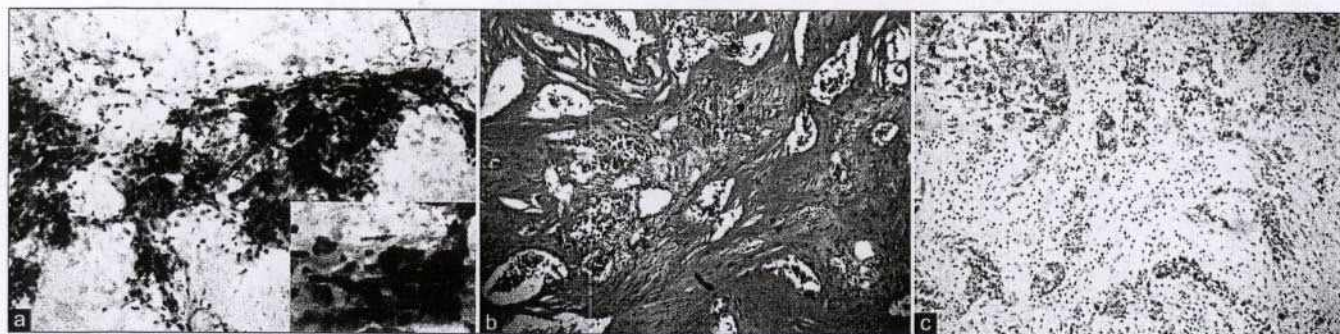


Figure 1: (a) Smear stained with May-Grünwald-Giesea stain showing tumor cells in sheets. Note the lumen at some places. (100x), Inset shows bland nuclear chromatin of tumor cells. (MGG stain 400x), (b) Section stained with Hematoxylin and eosin stain (H and E) showing tumor cells in tubular pattern. Note the dense sclerotic stroma in background. (H & E stain 100x), (c) Immunohistochemistry (IHC) with E cadherin shows positive staining in tumour cells lining the tubules (Dab stain 100x), Inset shows membranous positivity of tumour cells. (DAB stain 400x)

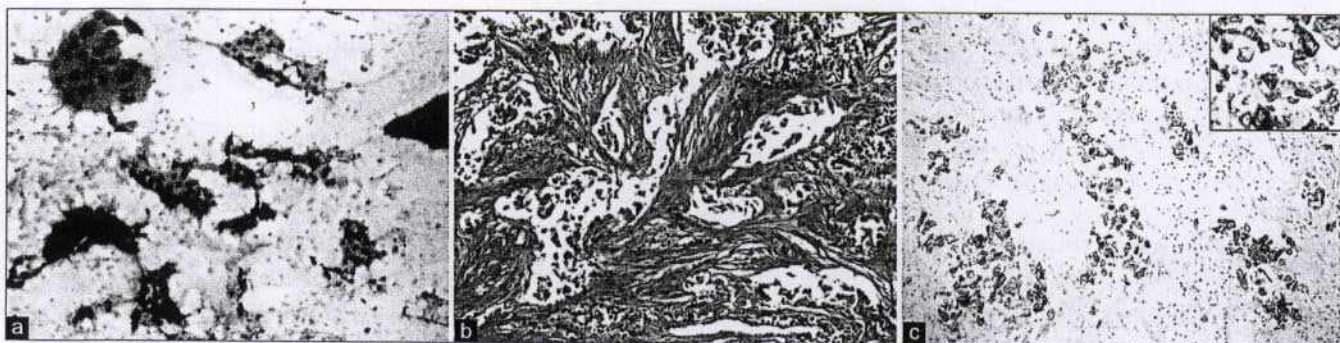


Figure 2: (a) Hematoxylin and eosin stain (H and E) stained smear shows high grade tumor cells in sheets. (H&E stain 100x), Inset shows H and E stained smear with tumor cells showing absence of individual cell keratinisation. (H & E stain 400x), (b) H and E stained section studied shows tumor cells in singles and few in glandular pattern. (H & E stain, 100x), (c) Immunohistochemistry (IHC) with High molecular weight cytokeratin shows positive staining in tumour cells. (DAB stain 100x). Inset shows Cytoplasmic positivity of tumour cells. (DAB stain 400x)

misdiagnosis was also described by Das *et al.*^[4] However, subsequent histopathology and immunohistochemistry were helpful in reaching the final diagnosis. Recent studies are of the opinion that these tumours must be termed as Ductal Carcinoma – tubulo-lobular subtype or ductal carcinoma with a tubulo-lobular pattern. This change in the nomenclature is because of membranous E – cadherin-Catenin, staining positivity in these tumours.^[2] Diagnosis is important as conservative breast surgery is the mode of treatment.

SCC of the breast is a rare variant, which accounts for about 0.04 to 0.075% of all breast malignancies. The first case was reported in 1908, and till now only about 100 cases of SCC has been reported.^[1] The criteria to define pure squamous cell carcinoma of breast include: a) no other neoplastic elements such as ductal or mesenchymal elements should be present; b) tumour should be independent of adjacent cutaneous structures; c) and, no distant epidermoid tumour should exist in the patient.^[1,5] Controversy exists whether a pure form of SCC exists, or these cases actually represent extreme squamous metaplasia within an adenocarcinoma. Variations range from minute areas of squamous differentiation in a predominant adenocarcinoma to pure squamous cell carcinoma where no glandular elements can be identified. Some are even of the opinion that SCC arise from dermoid cyst, chronic abscess and/or metaplasia of the glandular breast tissue.^[6]

SCC of the breast are usually ER and PR negative (our case too was ER, PR negative), and are usually associated with lower rate of lymph node metastasis at presentation (22% vs 40 to 60% for Invasive Ductal Carcinoma - IDC). This feature is in contradiction to SCC at the other parts of body.^[1] Differentiation of breast carcinoma carries great prognostic significance as squamous cell carcinomas behaves more aggressively with higher locoregional and distant relapses as compared to other metaplastic carcinomas.^[5,6] Also, these patients require adjuvant chemotherapy in the premenopausal period, and radiotherapy in case of small tumors. In our

case, we missed the diagnosis of SCC on FNAC due to lack of individual cell keratinisation on Papanicolaou stain (PAP) stain. Histopathology and subsequent IHC (HMW CK) confirmed the diagnosis of SCC.

CONCLUSION

Histological variants such as tubular carcinoma, medullary carcinoma, and mucinous carcinoma have a better prognosis than squamous cell carcinoma and metaplastic carcinoma. This study highlights the pitfalls of FNAC in diagnosis of the subtypes of carcinoma breast. Thorough knowledge of the cytological features of the subtypes, and immunocytochemistry as an adjunct to FNAC, help us to arrive at specific diagnosis.

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Cite this article as: Anantharamaiah H, Raju K, Suresh SP, Manikyam UK. Pitfalls in diagnosing specific subtypes of carcinoma breast on fine needle aspiration cytology: A report of two cases with review of literature. *J Can Res Ther* 2012;8:454-6.

Source of Support: Nil, **Conflict of Interest:** None declared.

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