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A Rare Case of Breast Carcinoma: An Entity Posing Cytological Challenge

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Abstract: Fine needle aspiration cytology (FNAC) is an important and primary screening tool for all breast lumps with high level of sensitivity and specificity. Diagnosing the rare breast carcinoma on FNAC is very challenging on account of various mimickers of the same. We hereby describe a rare case of breast carcinoma diagnosed on FNAC in a 34-year-old female confirmed on histopathology and immunohistochemistry (IHC). Preoperative diagnosis of apocrine carcinoma on FNAC and later confirmation on histopathology along with IHC study gives better insight to the cytopathologist and helps in better management protocol of the patient.

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Introduction

Fine needle aspiration cytology (FNAC) is an important and primary screening tool for all breast lumps with high level of sensitivity and specificity. Diagnosing the rare breast carcinoma on FNAC is very challenging on account of various mimickers of the same.

Case report

We report a case of 34-year-old female who presented with a hard painful well-defined 5×3 cm lump in the upper inner quadrant of left breast in the last one month. Nipple areola complex was normal with no discharge. Axillary lymph nodes were not palpable. The other breast was unremarkable. FNAC smears showed high cellularity comprising of tumour cells arranged in sheets, clusters and singly scattered (Figure 1A). Cells showed moderate to marked pleomorphism with high nucleo-cytoplasmic (N:C) ratio, large nuclei with coarse chromatin, prominent nucleoli and moderate amount of vacuolated cytoplasm (Figure 1B and inset, Figure 1C). Many binucleated, multinucleated, and bizarre cells along with few tumour giant cells and mitotic figures were also noted (Figure 1D). Background showed few hemosiderin

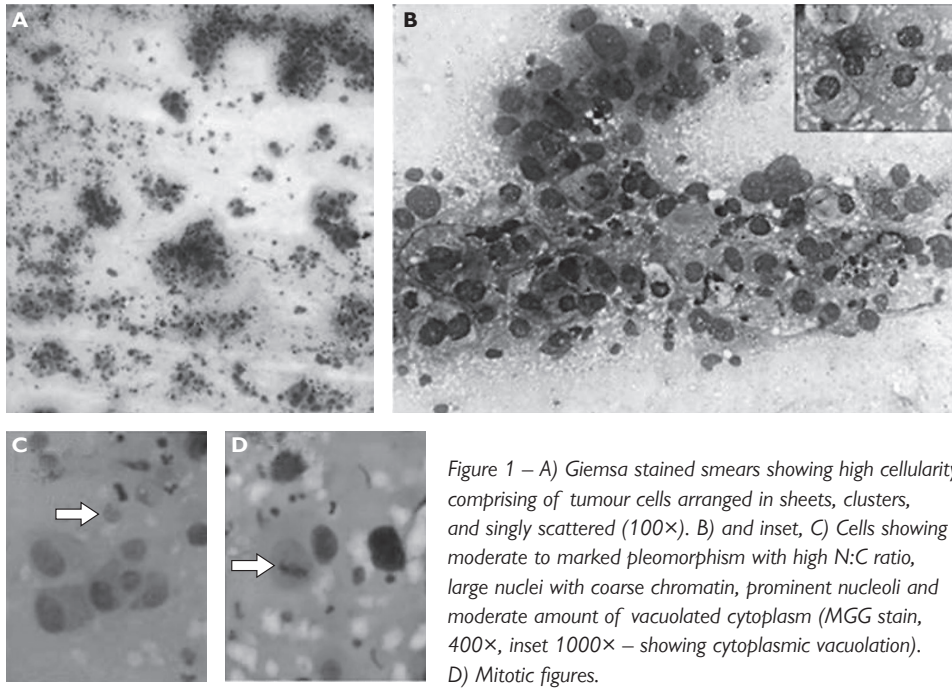

Figure 1 – A) Giemsa stained smears showing high cellularity comprising of tumour cells arranged in sheets, clusters, and singly scattered (100×). B) and inset, C) Cells showing moderate to marked pleomorphism with high N:C ratio, large nuclei with coarse chromatin, prominent nucleoli and moderate amount of vacuolated cytoplasm (MGG stain, 400×, inset 1000× – showing cytoplasmic vacuolation). D) Mitotic figures.

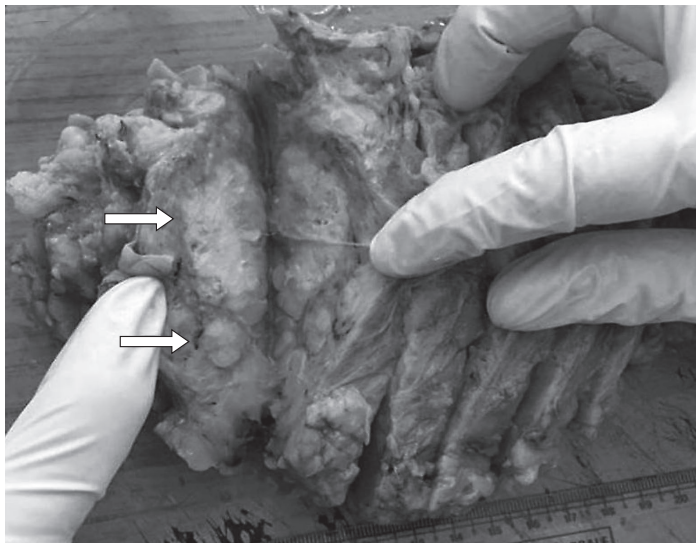

Figure 2 – Two foci of tumour measuring 3×3×2.8 cm in upper outer quadrant and 1.5×1.4×1.0 cm in lower inner quadrant.

laden macrophages. An impression of duct carcinoma of breast with the possibility of apocrine carcinoma was suggested. Mastectomy with axillary dissection was performed. On serial sectioning, a greyish white tumour measuring 3×3×2.8 cm was seen in upper outer quadrant. Another focus measuring 1.5×1.4×1.0 cm was observed in lower inner quadrant (Figure 2). Hematoxylin and eosin stained sections showed tumour cells predominantly arranged in a tubular pattern (10–75% of the tumour area, score 2 according to Elston Ellis modification of Scarff-Bloom-Richardson grading system) with hobnailing and apical snouting at places. These cells show marked nuclear pleomorphism, vesicular chromatin, prominent single to multiple nucleoli (score 3) and cytoplasmic vacuolization and clearing. High mitotic activity of 11–12/10 HPF was seen (score 3) (Figure 3A–C). Tumour was associated with atypical apocrine proliferations. All the resected margins and lymph nodes were free of tumour. There was no lymphovascular invasion. Immunohistochemistry (IHC) for estrogen receptor (ER) and progesterone receptor (PR) and Her2neu came out to be negative. Cytoplasmic positivity for GCDFP15 and focal nuclear positivity for androgen receptor (AR) was seen (Figure 3D). A final diagnosis of apocrine carcinoma (AC), Modified Bloom Richardson's Grade 3 was given (total score: 2 + 3 + 3 = 8). Patient was put on hormonal therapy including androgen analogue along with supportive care and was responding to the treatment.

Discussion

Breast apocrine cells have large vesicular nuclei, prominent nucleoli, abundant eosinophilic cytoplasm with apical snouting at places which shed into the lumen

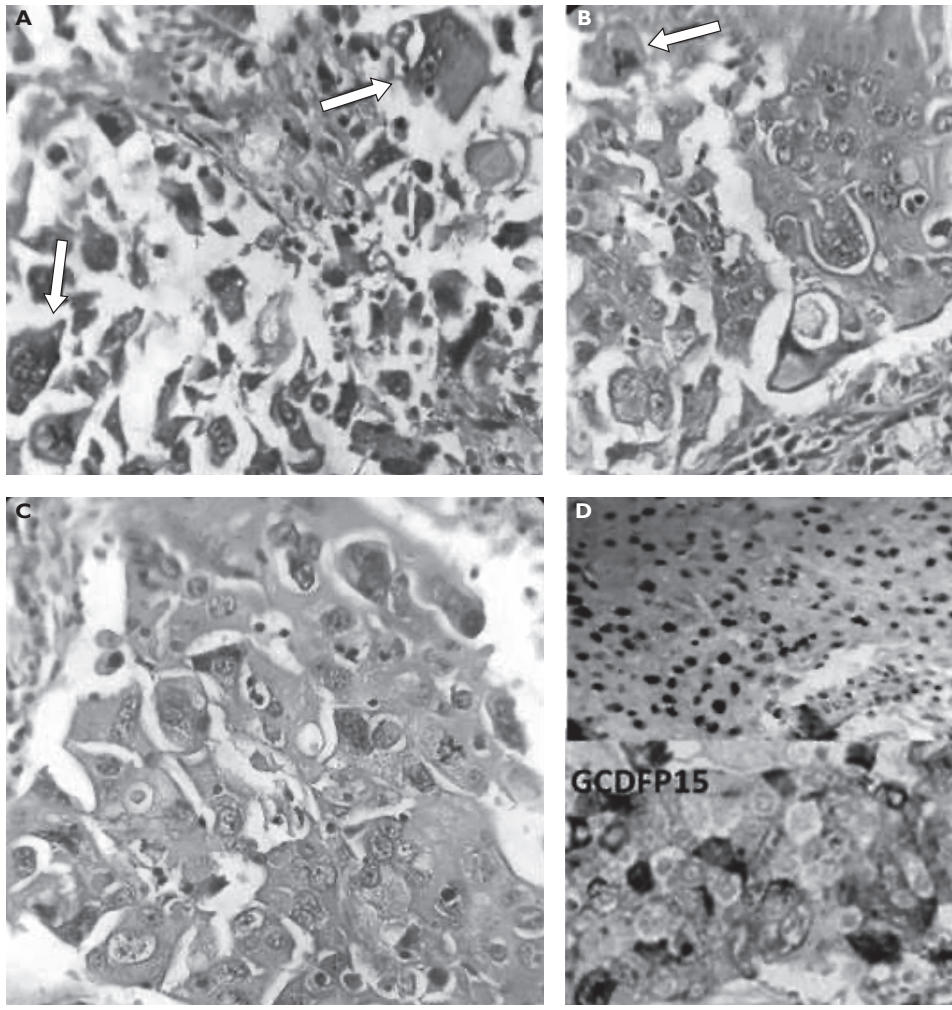

Figure 3 – A) Hematoxylin and eosin (H and E) stained section, 20×, showing singly scattered tumour cells showing nuclear pleomorphism, prominent nucleoli and multinucleated tumour giant cells (arrow). B) H and E stained section, 40×, showing mitotic figure (arrow). C) H and E stained section, 40×, showing tumour cells arranged in tubular pattern with marked nuclear pleomorphism, vesicular chromatin, prominent single to multiple nucleoli and cytoplasmic vacuolization and clearing. D) Photomicrograph showing nuclear androgen receptor (AR) positivity in >10% of tumour cells (above) and cytoplasmic GCDFP-15 positivity (below).

of the ducts. Microscopic cysts to invasive carcinomas fall within the purview of apocrine changes (Khandeparkar et al., 2014). Malignant transformation of apocrine epithelium was first described in 1916 by Krompecher (Wader et al., 2013). Pure AC of the breast is a rare entity accounting for <1% of primary breast carcinoma (Mills et al., 2016) and has predilection for women in their 60s and 70s (Kulkarni, 2012). The presentation varies from asymptomatic to the presence of a hard unilateral

breast lump with irregular borders with or without skin or nipple retraction (Bedford et al., 2014).

AC needs to be differentiated from its benign mimickers on cytology. FNAC smears in benign apocrine lesions, such as atypical apocrine adenosis, apocrine adenoma, granular apocrine metaplasia and degenerative cysts, show low cellularity comprising of cells arranged in flat and regular sheets with round to oval, bland and monotonous nucleus, centrally located nucleoli and abundant granular cytoplasm. Whereas, FNAC smears in invasive AC are moderately to highly cellular, show predominantly loosely cohesive pleomorphic tumour cells with round to oval to eccentrically placed nuclei, high N:C ratio, prominent macronucleoli and dense to vacuolated cytoplasm in a granular background (Kulkarni, 2012; Khandeparkar et al., 2014). It is difficult to reach to the correct diagnosis only on the basis of cytological features (Tavassoli and Devilee, 2003).

On histopathology, tumour cells have enlarged nuclei with prominent nucleoli and either abundant granular, eosinophilic cytoplasm that shows diastase-resistant periodic-acid-Schiff (PAS) positivity (type A cells), or abundant foamy cytoplasm (type B cells), or a combination of both (Iwa et al., 2015). Morphologically, our case belonged to type B. Many other tumours simulate AC due to the presence of cytological granules or vesicles in the cytoplasm such as glycogen rich carcinoma, lipid rich carcinoma, oncocytic carcinoma, and sclerosing adenosis (Tavassoli and Devilee, 2003). However, breast tumours of these entities are rarely encountered and do not express AR and GCDFP-15. However, these markers are positive in most of the cases of apocrine carcinoma. AR and GCDFP-15 were positive in our case. Vranic et al. in 2010 described strict morphological and IHC criteria to classify a tumour as pure apocrine carcinoma: >90% of the tumour must show apocrine morphology and the tumour must be negative for ER and PR and positive for AR in at least 10% of tumour cell nuclei on IHC. Tumours fulfilling either morphological or IHC criteria but not both were best classified as “apocrine like”. In our case >90% of the cells had apocrine morphology, were negative for ER, PR and exhibited positivity for AR. Hence the impression of pure apocrine carcinoma was rendered.

IHC has great utility in stratifying apocrine lesions of the breast. Apocrine epithelium; whether benign, atypical or malignant; are ER/PR negative and AR positive (in at least 10% of cell nuclei). GCDFP-15, used as a marker for apocrine differentiation, has varying rates of positivity in ACs. It is positive (cytoplasmic, diffuse, or apical) in up to 75% of ACs defined solely on morphologic grounds and in up to 71% of cases when defined solely by IHC. However, expression may be lost in higher stage tumours. Rate of positivity of HER2 also varies with the grade of tumour, higher rate in high versus low-grade apocrine ductal carcinoma *in situ* and invasive pure AC. Ki-67 and p53 show increase expression in malignant when compared with benign or borderline apocrine lesions (D’Arcy and Quinn, 2019).

Recent advances in the molecular classification have described apocrine tumours as a subset of breast tumours which are associated with high expression of androgen

receptor mRNA including the so-called "luminal androgen receptor (LAR) tumours" and "molecular apocrine tumours" (MATs) (D'Arcy and Quinn, 2019). Pure apocrine carcinoma when diagnosed using strict morphologic and IHC criteria, appears to have a worse disease-free survival rate than apocrine-like and invasive carcinoma not otherwise specified (D'Arcy and Quinn, 2019). Studies have shown that androgen blockade may offer a potential therapeutic benefit for a subset of AR expressing triple negative breast carcinomas (D'Arcy and Quinn, 2019). Our patient was put on hormonal therapy including androgen analogue along with supportive care. Hence, it is important to diagnose these tumours as a separate entity as they have different clinical behaviour and management protocol.

Conclusion

Preoperative diagnosis of apocrine carcinoma on FNAC and later confirmation on histopathology along with IHC study gives better insight to the cytopathologist and helps in better management protocol of the patient. Our case highlights the diagnostic challenge on cytology for this rare entity.

References

Bedford, T., Alperstein, A., Nathani, Y., Marx, R., DeVito, P. (2014) A rare presentation of triple-negative apocrine breast carcinoma with metastases. *J. Surg. Case Rep.* **2014(5)**, rju045.

D'Arcy, C., Quinn, C. M. (2019) Apocrine lesions of the breast: Part 2 of a two-part review. Invasive apocrine carcinoma, the molecular apocrine signature and utility of immunohistochemistry in the diagnosis of apocrine lesions of the breast. *J. Clin. Pathol.* **72(1)**, 7–11.

Iwa, N., Yutani, C., Hiraoka, K., Ichihara, T., Nakatuka, S. I. (2015) Fine needle aspiration cytology of apocrine carcinoma of the breast: Detection of androgen receptor, gross cystic disease fluid-15 and intranuclear vacuoles. *Ann. Clin. Cytol. Pathol.* **1011**, 1–5.

Khandeparkar, S. G., Deshmukh, S. D., Bhayekar, P. D. (2014) A rare case of apocrine carcinoma of the breast: Cytopathological and immunohistopathological study. *J. Cytol.* **31(2)**, 96–98.

Kulkarni, N. (2012) Fine needle aspiration cytology of apocrine mammary carcinoma: Report of five cases. *Oncocytology* **2**, 6–9.

Mills, A. M., Gottlieb, C. E., Wendroth, S. M., Brenin, C. M., Atkins, K. A. (2016) Pure apocrine carcinomas represent a clinicopathologically distinct androgen receptor-positive subset of triple-negative breast cancers. *Am. J. Surg. Pathol.* **40(8)**, 1109–1116.

Tavassoli, F. A., Devilee, P. (2003) *Pathology and Genetics of Tumours of the Breast and Female Genital Organs.* IAPS Press, Lyon.

Vranic, S., Tawfik, O., Palazzo, J., Bilalovic, N., Eyzaguirre, E., Lee, L. M., Adegboyega, P., Hagenkord, J., Gatalica, Z. (2010) EGFR and HER-2/neu expression in invasive apocrine carcinoma of the breast. *Mod. Pathol.* **23(5)**, 644–653.

Wader, J. V., Jain, A., Bhosale, S. J., Chougale, P. G., Kumbhar, S. S. (2013) Apocrine carcinoma of breast: A case report with review of the literature. *Case Rep. Pathol.* **2013**, 170918.