CASE SERIES OPEN ACCESS

Fine needle aspiration cytology of apocrine mammary carcinoma: Report of five cases

Nagarekha Kulkarni

ABSTRACT

Introduction: Apocrine carcinoma (AC) is an uncommon variant of breast carcinoma. The incidence of apocrine carcinoma is approximately 4% of mammary carcinomas. Case Series: In this study five cases of apocrine breast carcinoma were identified. Three cases of apocrine breast carcinoma with infiltrating (IF) AC and two cases with intraductal (ID) AC. The cytologic featuers showed large malignant cells with vesicular, eccentrically placed nucleus, macronuclei and abundant eosinophilic cytoplasm and were diagnosed as apocrine mammary carcinoma. The diagnosis was confirmed by reviewing histopathology slides. Conclusion: Apocrine carcinoma is a distinct morphologic entity with a natural history similar to that of non-apocrine ductal carcinoma. It needs to be distinguished from benign apocrine metaplastic lesions pre-operatively, so that appropriate treatment can be given to the patient.

Keywords: Apocrine carcinoma, Infiltrating duct carcinoma, Intraductal

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INTRODUCTION

Apocrine carcinoma (AC) is an unusual variant of breast carcinoma of possible sweat duct or ductal origin [1, 2]. The biologic behaviour is similar to that of the common invasive ductal carcinoma but in some cases it is difficult to ascertain whether the apocrine carcinoma originates in the breast apocrine cells (breast-primary), or started somewhere else, such as the apocrine cells of the axillary regions. The incidence is approximately 4% of mammary carcinomas and effects women in their 60s and 70s, with an average age of 65 years [3]. The largest series previously described consisted of 72 cases by Andrea et al. and 37 cases by Tavassoli et al. [4, 5]. The prognosis of apocrine carcinoma has been reported to be equal to or more favourable than that of non-apocrine ductal carcinoma but because of the rarity of these tumors, definitive conclusion have not been possible [6].

CASE SERIES

Case 1: A 62-years-old woman had a firm to hard, mobile, well defined mass measuring 4x3x2 cms in the upper outer quadrant of the left breast since three months. There were no papable axillary lymph nodes and systemic examination revealed no abnormalities. Past and family history was unremarkable.

Mammography findings showed microcalcifications. Fine needle aspiration cytology revealed atypical cell clusters with abundant, finely granular or vesicular cytoplasm and oval nuclei with prominent nucleoli. A cytological diagnosis of apocrine carcinoma was made. Histopathological examination showed features of papillary intraductal apocrine carcinoma. Patient was treated by radical mastectomy and mass reccured after one year.

Case 2: A 58-years-old woman had a painless, firm to hard, well defined mass measuring 3x2x2 cms in the upper outer quadrant of the right breast since one month. Mobility of the mass was restricted. There were no palpable axillary lymph nodes and systemic examination revealed no abnormalities. Past and family history was unremarkable. Mammography findings showed well defined tumor shadow. The cytologic findings revealed moderate to high cellularity, consisting of predominantly dispersed or loosely cohesive tumor cells having abundant, dense to granular cytoplasm, round to oval and sometimes eccentrically located nuclei, a smooth nuclear outline, evenly dispersed chromatin and solitary nucleoli. Nuclear overlapping, frequent nuclear pleomorphism, increased nuclear/cytoplasmic ratios and occasional mitotic figures were noted. Histologic exaaminaton showed solid intraductal apocrine carcinoma. Patient

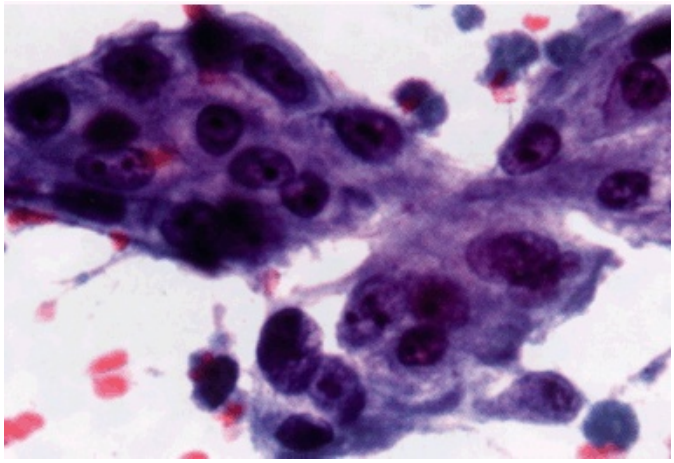

Figure 1: Highly cellular smear shows malignant epithelial cells with abundant eosinophilic cytoplasm and prominent nucleoli (MGG x200).

was treated with modified radical mastectomy and the mass reccured after 18 months.

Case 3: A 70-year-old woman had a firm to hard, well defined mass measuring 6x4x3 cms in the upper outer quadrant of the left breast since nine months. Mobility was restricted. Axillary lymphadenopathy was present and systemic examination revealed no abnormalities. Past and family history was unremarkable. Mammography findings showed tumor shadow. Fine needle aspiration cytology revealed large amount of eosinpohilic, finely granular or vesicular

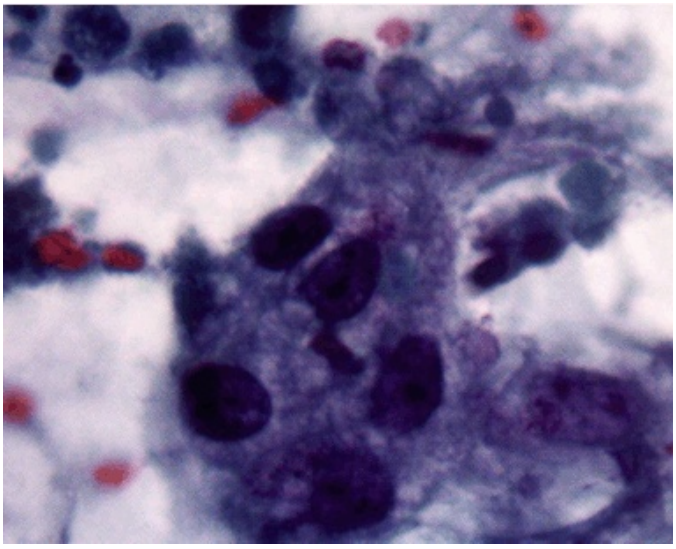

Figure 2: Large malignant epithelial cells showing multinucleation and prominent nucleoli (PAP 40x).

cytoplasm, oval nuclei with prominent nucleoli and tumor cells with well-defined margins. Nucleus to cytoplasm ratio was about 1:2. The cytological diagnosis of apocrine carcinoma was made. Histopathological examination showed features of poorly diffentiated infiltrating duct apocrine carcinoma. Patient was treated by radical mastectomy and radiotherapy, but died after one year.

Case 4: A 65-year-old woman had a firm to hard, well defined mass measuring 5x3x3 cms in the upper outer quadrant of the left breast since four months. Mobility of the mass was restricted. There were no palpable axillary lymph nodes and systemic examination revealed no abnormalities. Past and family history was unremarkable. Mammography findings showed multifocal calcification. Fine needle aspiration cytology smears were cellular, composed of large polygonal cell clusters with abundant, finely granular or vesicular cytoplasm and oval nuclei with prominent nucleoli. The nuclei showed atypia. Occasional binucleate nuclei were seen. The cytological diagnosis of apocrine carcinoma was made. Histopathological examination showed features of infiltrating duct apocrine carcinoma. Patient was treated by radical mastectomy, radiotherapy and chemotherapy. Recurrence was absent even after follow up of 20 months.

Case 5: A 60-years-old woman had a firm to hard, well defined mass measuring 7x5x3 cms in the upper outer quadrant of the right breast since seven months. Mobility of the mass was restricted. There were no palpable axillary lymph nodes and systemic examination revealed no abnormalities. Past and family history was unremarkable. Mammography findings showed well defined tumor shadow. Fine needle aspiration cytology revealed atypical cell clusters with apocrine features, abundant, finely granular or vesicular cytoplasm and pleomorhic nuclei with prominent nucleoli. The cytological diagnosis of apocrine carcinoma was made.

Histopathological examination showed features of infiltrating duct apocrine carcinoma. Patient was treated by radical mastectomy, radiotherapy and chemotherapy. Recurrence was absent even after follow up of 20 months.

Cytology findings: Five cases of apocrine carcinoma were identified between 2005 to 2010. The cytology slides which were stained with MGG and PAP were reviewed. Smears were cellular and composed of clusters of large polygonal cells with abundant cytoplasm that stained basophilic with MGG stain. Nuclei were round or oval and vesicular with prominent mostly single inclusion like, large nucleoli. Cell clusters showed irregular margins and cellular overlapping and mild to moderate nuclear atypia were present occasional binucleate nuclei and multinucleate nuclei were seen.

Histopathology findings: The histopathology slides were also reviewed to confirm the diagnosis. Three cases showed infiltrating apocrine carcinoma (IF-AC) and two cases showed intraductal apocrine carcinoma (ID-AC). Clinical features of all these five cases are summarized in table 1. There was a left–sided predominance among IF-AC. The age ranges for both groups were similar, but the mean age was 65 years in IF-AC and 60 years in ID-AC. These differences in age distribution were not statistically significant. All tumors were located in the upper outer quadrant. Mammography detected calcification in 34% and 50% cases of ID-AC and IF-AC respectively. Patients with IF-AC lesions had a higher proportion of palpable tumors (53%) and those with ID-AC (44%). The size range was 6–8 cm in IF-AC than 2–4 cm in ID-AC.

All five patients were treated by radical mastectomy. Three of them received local radiotherapy. Recurrences in the breast occurred in two ID-AC patients who were treated by mastectomy alone. One patient with IF-AC had axillary metastases at the time of mastectomy and died after one year. Recurrence was absent in other two IF-AC even after a follow up of 20 months.

Table 1: Major clinical features of patients with apocrine carcinoma (present study).

Sl. No.	Clinical features	Infiltrating apocrine carcinoma (n = 3)	Intraductal apocrine carcinoma (n = 2)
1	Side		
	Left	2	1
	Right	1	1
2	Mean Age (years)	65	60
3	Size (cm)	6–8	2–4
4	Mammography detected calcification	1 (34%)	1 (50%)
5	Lymphadenopathy	1	none
6	Systemic examination	normal	normal

DISCUSSION

The World Health Organisation classification of mammary tumors describes apocrine carcinoma as a tumor that is composed predominantly of cells with abundant eosinophilic granular cytoplasm. Apocrine carcinoma, whatever their origin, are usually composed of two types of variously intermingled cells. Type A cells have abundant, granular, intensely eosinophilic cytoplasm. The granules are periodic acid–Schiff positive after diastase digestion. Their nuclei vary from globoid with prominent nucleoli to hyperchromatic nuclei. Type B cells show abundant cytoplasm in which fine empty vacuoles are seen. This later feature results in foamy appearance so the cells may resemble histiocytes and sebaceous cells. Nuclei are similar to those in type-A cells. Apocrine carcinoma are negative for estrogen and progesterone receptors. HER-2 is positive in 50% apocrine carcinomas and androgen receptors are positive in 50–100% [7].

Apocrine carcinoma is rare, and mostly effects women in their 60s and 70s, with an average age of 65 years [1]. Andrea et al. studied 72 cases of apocrine carcinoma and observed that the average age of occurance was 55 years [4]. In the present study the average age was 65 years which is similar to other studies. The age distribution of patients with apocrine carcinoma does not appears to differ notably from that of woman with non-apocrine invasive duct carcinoma. In the present study the location of the tumor was in the upper outer quadrant. Apocrine metaplasia and apocrine cysts are found most commonly in lower mammary quadrants, whereas apocrine breast carcinoma is more frequent in upper outer quadrant [8]. The location of the cancer in this study correlates with other studies. Mammography revealed calcification in two cases and shadows in three cases which is similar to reports of other authors [4, 6]. In this study the most common cytologic feature noted were large, polygonal cells with abundant eosinophilic cytoplasm, vesicular eccentrically placed nuclei, macronucleoli, cellular overlapping and binucleate nuclei. These features were similar to the description of apocrine carcinoma made by Andrea et al. [4]. These tumor cells should be differentiated from apocrine cells in benign diseases which are characterized by abundant pink, sometimes granular cytoplasm and their nuclei are usually bland and monotonous. Nucleoli is small and centrally located in the nucleus as shown in Table 2. IF-AC had the same cytologic features as the ID-AC lesions.

The recurrence rate in the present study was 40% which is similar to that reported by others [9–10]. Recurrence in the breast is reduced when ID-AC is treated by radiotherapy after lumpectomy, and a similar phenomenon was observed in the small number of cases in this study [4]. The prognosis of patients with IF-AC

Table 2: Shows the cytological and histological difference between apocrine metaplasia and apocrine carcinoma [4, 10–11].

	Apocrine metaplasia	**Apocrine carcinoma**
Cytology:		
Smears	Low cellularity	Moderate to high cellularity
Cells	Arranged in flat sheets	Loosely cohesive in a granular background
Cytoplasm	Abundant granular cytoplasm	Abundant, dense to granular cytoplasm
Nucleus	Round to oval,bland and monotonous	Round to oval, pleomorphic sometimes eccentrically placed, vesicular nucleus
Nucleoli	Small and centrally located	Prominent eosinophlic macronucleoli
Nuclear /cytoplasmic ratio	Normal	Increased
Mitotic figures	No	Occassionally present
Histology	Benign apocrine cells line the cyst or dilated structures. The apical portion of the cells show apocrine snout	Apocrine carcinoma cells are arranged in sheets, cords, sometimes tubules Cells frequently reveal apocrine snouts

was not significantly different from that of women with non-apocrine invasive duct carcinoma and is consistent with other reports based on smaller series of patients [10].

CONCLUSION

Apocrine carcinoma is a morphologic variant of duct carcinoma that does not have a distinctive clinical course. It needs to be distinguished from benign apocrine metaplastic lesions pre-operatively, so that appropriate treatment can be given to the patients.

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Author Contributions

Nagarekha Kulkarni – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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