

Fine needle aspiration cytology of secretory carcinoma of breast: a case report

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Abstract

A 39-year-old female presented with a mobile 1.5 cm nodule in the right breast. Fine needle aspiration cytology smears stained with May Grunwald Giemsa were highly cellular with a monotonous population of dissociated and clustered tumour cells that showed a bland cytological appearance with cytoplasmic vacuolation and occasional signet ring forms. Intracellular and extracellular mucus was present. Histological study of the excised breast mass showed a secretory carcinoma. This is a rare breast neoplasm in which cytological features are characteristic enough to permit a specific diagnosis on needle aspirates.

Key words: Secretory carcinoma, breast, cancer, fine needle aspiration, cytology.

INTRODUCTION

Secretory carcinoma of the breast was first described in 1966 by McDivitt and Stewart¹ in children and designated by them as "juvenile carcinoma." It is recognised to be an uncommon variant of breast carcinoma that has a less aggressive behaviour and carries a relatively better prognosis. Two distinctive features characterize this neoplasm: the presence of large amounts of intracellular and extracellular secretions and the granular, eosinophilic cytoplasm of the cells.² The characteristic histological features coupled with the observation that such tumours have been encountered in adult and even postmenopausal women, have led to the more acceptable currently used term "secretory carcinoma" for these neoplasms.³

Secretory carcinoma of breast shows certain distinctive cytological features^{2,4,7} knowledge of which could enable planning of optimal surgical therapy in these patients especially in view of the fact that a conservative approach with local excision may often be advocated² as treatment.

This paper reports the cytological and histological features of a case of secretory carcinoma of breast and reviews previous descriptions.

Case report

A 39-year-old female presented with a right breast nodule that she had noted during self-palpation two days previously. Physical examination revealed a 1.5 cm painless mobile nodule in the upper outer quadrant of the right

breast. No skin retraction or nipple discharge were detected and no axillary nodes were palpable. Mammography showed no abnormality and ultrasound of the breast revealed a 1.3 cm well defined echogenic mass with a smooth outline in the upper outer quadrant of the right breast. Fine needle aspiration (FNA) of the nodule performed with a 22 gauge needle attached to a 20 c.c. plastic syringe mounted on a handle yielded mucoid material. The cytological picture was suggestive of carcinoma of the breast. Chest X-ray, abdominal ultrasound and a bone scan did not show any evidence of metastatic disease. Three days after FNA, a wide excision of the breast lump and an axillary dissection were carried out. Post-operative recovery was uneventful and radiotherapy to the remnant breast tissue was given followed by six cycles of chemotherapy with the CMF regime (cyclophosphamide 500 mgm/m², methotrexate 50 mgm/m² and 5-fluorouracil, 500 mgm/m² at three weekly intervals).

Cytologic features

Two smears stained with May-Grunwald Giemsa (MGG) were studied. Cellularity was high with numerous dissociated and clustered tumour cells (Fig. 1) that were medium sized, rounded, oval or polygonal with moderate to abundant basophilic cytoplasm and vesicular round nuclei, many of which showed single small nucleoli. Cytoplasmic margins were indistinct in many of the cells (Fig. 2) and variably sized granular metachromatic mucoid material (Fig. 3) was

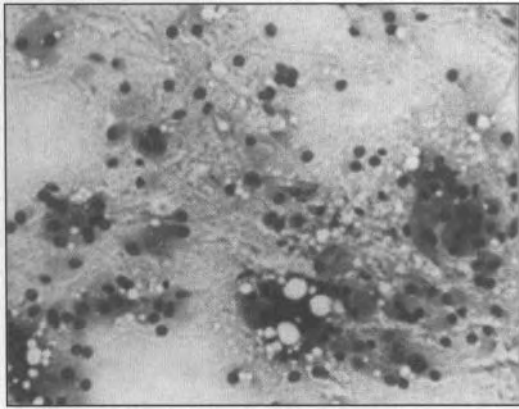


FIG. 1: Clustered and dissociated tumour cells with abundant cytoplasm. Note granular material in the background. MGG X200.

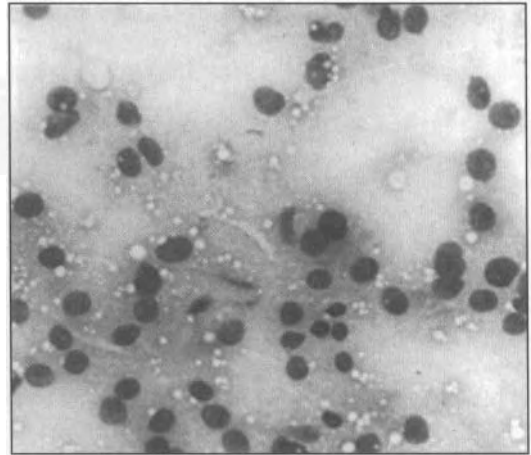


FIG. 2: Dissociated tumour cells with vesicular nuclei, indistinct cell margins and granular material in the background. MGG X400.

present in some cells. Many of the cells showed cytoplasmic vacuolation (Fig. 4) and a few signet ring cells were seen (Fig. 5). The smear background was characterized by abundant metachromatic granular mucoid material (Figs. 1 & 2) in which cells were often seen in a "swirling pattern" reminiscent of chordoma. Globular structures of varying size (staining deep blue with MGG) were seen in proximity to papilliform clusters of monomorphic epithelial cells. These gave an impression of collagenous spherules associated with papillary epithelial hyperplasia. A cytological diagnosis of breast carcinoma was given.

Histologic features

Macroscopically, the excised specimen was yellowish-white, measuring 5 x 4.5 x 3 cm in

size, with an ellipse of skin 2.5 cm long. On cut section, there was a firm, fleshy, spherical, 1.3 cm diameter greyish-white mass in the centre. The axillary dissection specimen measured 11 x 7 x 3.5 cm and contained 7 small lymph nodes.

Microscopy revealed the tumour to be composed of polygonal epithelial cells forming variably sized, solid alveolar nests containing follicular-acinar, honeycombed and microcystic structures with round spaces (Fig. 6). The latter contained eosinophilic secretions mimicking the appearance of thyroid gland. The cells also showed prominent intracytoplasmic vacuoles, large vesicular nuclei and prominent nucleoli. The vacuoles and secretions showed an admixture of diastase-resistant periodic-acid-Schiff (Fig. 7) and alcian blue positive

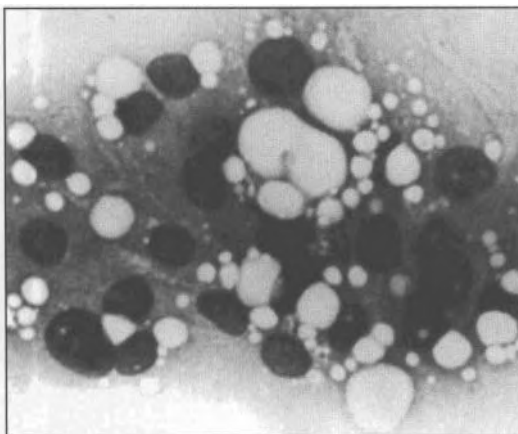


FIG. 3: Cells showing cytoplasmic vacuoles of varying sizes. MGG X600.

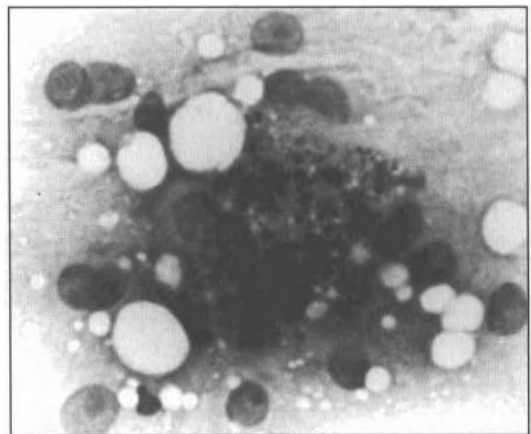


FIG. 4: Granular metachromatic material in the cytoplasm of tumour cells. MGG X600.

mucosubstances (Fig. 8) which also stained with **mucicarmin** (Fig. 9). Nests of tumour cells with honeycombed pattern and irregular margins resembled mucoepidermoid tumour of salivary gland **type** while other foci resembled skin adnexal tumours of the sebaceous or sweat gland type.

The tumour cells were negative for **C-erbB-2**, positive for P53 (20% of cells) and negative for oestrogen receptor (ER) protein, based on immunostaining using commercial DAKO monoclonal antibodies. The surgical margins were not involved by the tumour and all the lymph nodes in the **axillary** dissection were free of tumour.

The **benign** breast tissue surrounding the tumour showed occasional foci of papillary epithelial hyperplasia (papillomatosis) with collagenous spherules of varying sizes showing radiating internal structure which were better brought out on PAS stain.

DISCUSSION

Cytological features recognized previously in secretory carcinoma of the breast include prominent intracytoplasmic vacuolation and numerous signet ring **forms**.⁴ Shinigawa *et al*⁴ in addition described mucoglobular structures resembling bunches of grapes. Electron microscopic examination revealed the cells of secretory carcinoma to show one or more intracytoplasmic lumina, intercellular lumina and abundant secretory **material**.⁴ It was suggested that mucoglobular structures, which consisted of a small amount of mucinous material located in the centre and a rim of tumour cells, represented markedly expanded intercellular or extracellular lumina that are continuous with intracytoplasmic lumina.

The dominating cytological feature in the present case was the uniformity of the tumour cells, which showed no evidence of mitotic activity or nuclear atypia. The presence of numerous dissociated cells, however, was highly suggestive of malignancy. Dissociated as well as clustered cells showed **uniform** single nucleoli. **Metachromatic** granular secretory material of varying sizes seen within the cytoplasm of some of the tumour cells in this case, has not been described previously. Although the material aspirated was mucoid and there was extracellular mucus in the smears, distinction from mucinous carcinoma was possible because of the granular background metachromasia that differed markedly from the "sea of mucin" appearance

seen in mucinous carcinoma. Shinigawa *et al*⁴ also noted that the background mucus was less in secretory carcinoma than in mucinous carcinoma and attributed this to the fact that secretory carcinoma retains some intracellular mucin whereas the latter shows predominantly extracellular mucin. The granular background material with dissociated and clustered cells in swirling pattern somewhat resembled chordoma but the voluminous cytoplasm and physaliferous appearance of chordoma cells were lacking. The bland appearance and absence of mitotic activity are features shared by mucinous carcinomas but the latter usually do not show so much intracellular mucin. Prominent nucleoli are a feature of apocrine carcinomas which may also show minimal **atypia** and mitotic activity. Cells of apocrine carcinoma however have larger nuclei and a very uniformly polygonal shape that was not a feature of the present case. **Lipid-rich** breast carcinoma, "an aggressive variety of breast carcinoma, can be distinguished from secretory carcinoma by the different **histochemical** properties of its vacuoles, which contain oil red **O** staining lipids, easily demonstrated on air dried **smears**."⁵

Association with ductal papillomatosis as described by Nonomura *et al*⁷ was also seen in our case and interestingly, collagenous spherules (described in association with benign proliferative lesions such as intraductal papillomas, sclerosing adenosis and radial **scars**^{9,10}) were observed in these foci of papillomatosis. These possibly corresponded to the deep staining globular structures and papillary clusters of benign epithelial cells seen in the cytological smears.

This was the first case of secretory carcinoma we have encountered and we could not cytologically categorize this tumour as secretory carcinoma. However, we realised the cytological picture was definitely very different from the normal type of invasive ductal and lobular carcinomas and special types of breast carcinoma most of which we have been able to categorize with ease on cytological **preparations**.¹¹ No doubt awareness of the distinctive cytomorphology of secretory carcinoma will enable recognition of this interesting variant and help in planning of patient management.

The significance of the absence of ER protein expression in this patient's tumour is uncertain. Previous reports have not demonstrated steroid receptor **positivity**.⁶ This may be an important point distinguishing its biological nature from

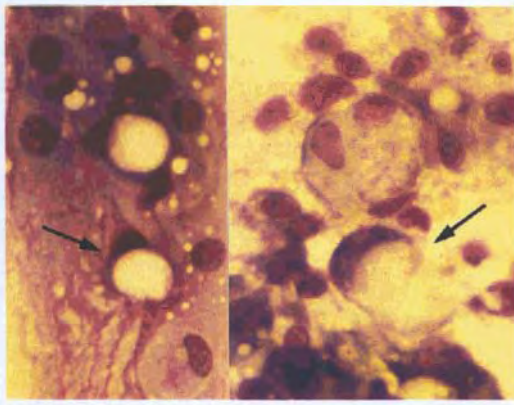


FIG. 5: Tumour cells with signet ring appearance (arrows). MGGX600.



FIG. 6: Follicular-acinar structures and honeycombed spaces containing eosinophilic secretions. H&E X300.

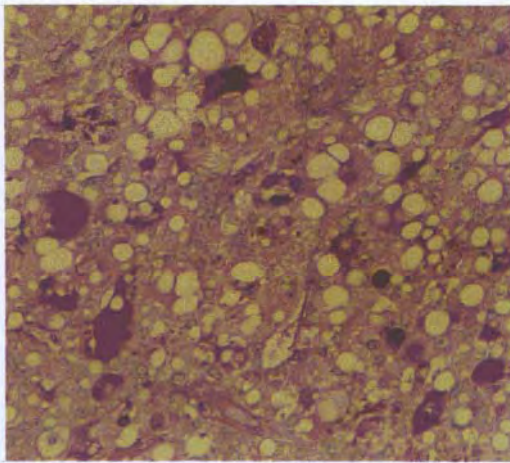


FIG. 7: Secretory carcinoma of breast showing PAS-positive secretions. Periodic acid Schiff-diastase X300.

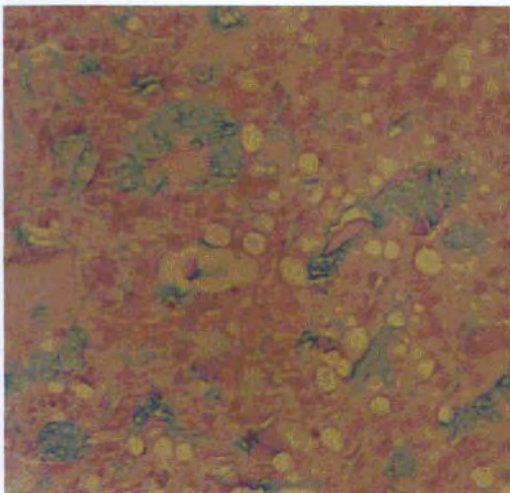


FIG. 8: Secretory carcinoma of breast showing alcian blue positive secretions. Alcian blue X300.

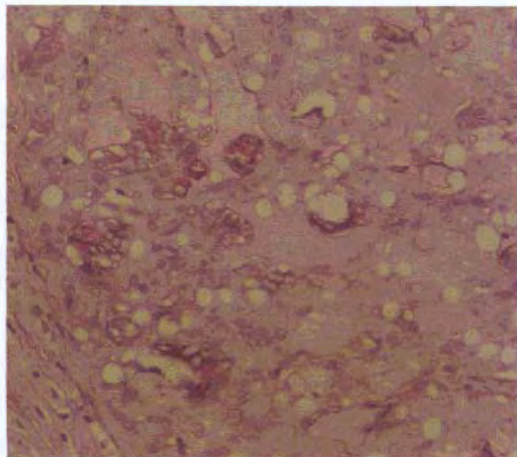


FIG. 9: Secretory carcinoma of breast with mucicarmine positive secretions. Mucicarmine X300

mucinous carcinoma, which is frequently ER positive.¹²

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