Communication - Cytopathology

Cytological features of mucinous carcinoma of breast

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Introduction

Mucinous carcinoma (MC) of the breast is a distinctive, well differentiated type of adenocarcinoma, constituting 2%-5% of breast cancers (1). Pure MC of breast has been reported to have a more favourable prognosis than other well differentiated adenocarcinomas of breast, with a lower frequency of axillary node metastases (2) and excellent short term prognosis, especially when the tumour measures less than 5 cm in diameter. Fine needle aspiration cytology (FNAC) has been described to yield copious amounts of mucinous material in MC with a variable proportion of tumour cells. The tumour cells have been described as being generally small and fairly uniform with minimal atypia (3,4) and this may give a false impression of benignancy. The present report describes the spectrum of cytological features observed in 18 cases of MC of breast with histological correlation.

Materials and methods

This study was conducted both retrospectively and prospectively spanning a 10

year period from 2004 – 2013. A total of 18 cases were analysed of which 14 were retrospective and 4 were prospective. The retrospective cases were collected from the records and slides were reviewed. FNAC was done using a 21 gauge needle and the aspirates were air-dried and stained with MGG. Where-ever possible smears were wet fixed with 95 % ethanol for Papanicolaou and mucin stain.

Histological material obtained from the mastectomy specimens were fixed in formalin and processed routinely. H&E stained sections were studied. Histochemical stains for mucin were done in selected cases. Immunostaining for ER was done in all cases.

Results

Cytological features: In 18 cases the cytological picture was dominated by the presence of ball-like, three-dimensional or loosely cohesive clusters of tumour cells, flat sheets and occasional single cells floating in a "sea of mucin" or surrounded by "whirlpools of mucin" (Fig.1). The mucin was present as homogenous, filmy,

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Fig.1. Sheets of bland tumour cells in a sea of mucin (MGG x100)

Fig.2. Sheets of bland tumour cells surrounded by mucin (H&E x200)

wispy extracellular material, staining variably deep blue or bright pink (metachromatic) with MGG stain. In nine cases the cellularity was mild with proportionately larger amounts of mucin. Two of these cases showed mainly histiocytes (muciphages) and only occasional clusters of tumour cells with a bland appearance. In 16 cases, the ratio of cells to mucin was almost equal. In three cases the cellularity was high. Myxovascular fragments were seen in 12 cases.

Histological features:

Histological study of sections of the tumour showed that all the cases were pure mucinous carcinoma. In 16 cases, the bulk of the lesion was composed of mucin in which groups of tumour cells appeared to be floating (Fig.2). One of these showed only mucin pools with muciphages and very small areas showed tumour. Two cases showed high cellularity with scanty extracellular mucin (Grade III tumour). These

tumours exhibited acinar or papillary formations with a minimal desmoplastic reaction. Fourteen patients had Grade I tumours, while two had Grade II tumours. 16 out of 18 cases were ER-positive. The two negative cases were Grade III tumours.

Discussion

Pure mucinous carcinoma is a rare histologic type of mammary neoplasm, seen in elderly women and has a better prognosis than the usual invasive ductal carcinoma (5). To the inexperienced eye, the relatively bland features of the tumour cells from MC may suggest a benign lesion. However, even while looking through the 4x or 10 x objectives, the "sea of mucin" or "whirlpool" effect of the extracellular mucin bathing these bland cells is a very distinctive clue to the identification of MC. This feature was seen in all cases in the present and earlier series (1,3). The mucin stained variably blue

or metachromatic on MGG stain and appeared as homogenous filmy or wispy extracellular material. Dense linear strands staining variably blue-green, violet, or pink with the Papanicolaou stain and bright pink with Romanovsky stains has also been described (6).

The myxovascular fragments seen in most of our cases probably correspond to the "thin endothelial lined vessels lying in mucin" seen in 50% of Fanning et al's cases of MC. The bland monomorphic features of pure colloid carcinoma (7) may be the cause of false negative cytodiagnoses. In our opinion however, careful examination of these uniform cells in the 40x objective shows these cells to be larger than the cells of fibroadenoma (FA) and other benign lesions with larger nuclei and higher nuclear-cytoplasmic (NC) ratio. Besides, about 40% of cases showed focal mild or moderate nuclear pleomorphism with one or more macronucleoli.

Presence of single cells (variable in number) in most cases of MC and the absence of bipolar naked nuclei (a common feature in FA) further helps in the differential diagnosis. It appears that, although MC is characteristically a low grade malignancy with Grade I nuclear features, (2,6) Grade II nuclear characteristics may be seen in a few cases. In our study, two cases had Grade II and two cases had Grade III nuclear characteristics. Dawson and Mulford (8) found that six of 45 cases showed Grade III nuclear features.

Secretory carcinoma of the breast, another prognostically favourable type of breast carcinoma may (like MC) show uniform tumour cells and abundant metachromatic extracellular mucin. In this variant however, intracellular as well as extracellular mucin, many signet-ring cells, vacuolated cells, and in some cases mucoglobular structures resembling "bunches of grapes (2) may also be seen. Besides, the granular background metachromasia in smears of secretory carcinoma differs markedly from the "sea of mucin" appearance of MC (9).

Mucocele-like lesions of the breast, benign papillomas and FAs containing extracellular mucin have been considered as differential diagnostic problems (2,10,11). FAs with myxoid degeneration have been stated as being able to produce a similar "sea of mucin with islands of cells" effect as seen in MC (11). In a cytology series of 651 benign breast lesions (12) that contained 223 FAs and in a subsequent series of 780 cases that included 178 FAs (4) Jayaramet al did not find any "sea of mucin" or "whirlpools of mucin" appearance in any of the FAs. Besides, in FA, the amount of mucin is usually limited and generally found in one sample or slide, whereas it is abundant and consistently present in all of the smears of colloid carcinoma. Smears from FA generally show stromal fragments and bipolar nuclei that are not seen in MC (4, 11-12) and patients with FA are generally much younger than those with MC (11).

Fanning et al (6) described smears from mucocoele-like lesions showing abundant extracellular mucin and few cohesive flat sheets of epithelial cells with uniform round nuclei, indiscernible nucleoli and fine chromatin. Single cells were absent. They suggested that smears containing abundant extracellular mucin should be diagnosed as MC only when they were cellular and contained numerous single cells (in addition to clustered cells). Mesenora and Tabbara (10) reported an uncommon case of ductal carcinoma in which FNA smears showed features overlapping those of MC, mucocoele-like lesion, lactating adenoma and intraductal papilloma.

Therefore, cytological evaluation of breast lesions containing abundant extracellular mucin should be done carefully to diminish the likelihood of false negatives and false positives. The observation that at least a proportion of MCs may appear clinically and mammographically benign underscores the importance of FNAC in the correct preoperative diagnosis of MC.

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