

## Four quadrant fine needle aspiration cytology for the detection of benign proliferative breast lesions accompanying breast carcinoma

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### Abstract

Forty-eight patients with breast carcinoma were subjected to four quadrant fine needle aspiration (FNA) cytology examination of the ipsilateral and contralateral breast in an attempt to detect any accompanying benign proliferative lesion. Mastectomy of ipsilateral and open biopsy of contralateral breast provided material for histopathological study. Cytological evidence of epithelial proliferation was found in 8 (16.6%) cases which included atypical lobular hyperplasia (ALH), lobular neoplasia *in-situ* (LNIS), atypical ductal hyperplasia (ADH), and proliferative disease without atypia (PDWA). In lobular proliferative lesions, cytological smears showed configurations of cells that resembled filled up or expanded lobular units. The cytology was not distinctive enough to distinguish the sub-types of lobular proliferations. Likewise, the presence of ductal alterations could be suggested by cytological study but the distinction of proliferative disease without atypia (PDWA) from atypical ductal hyperplasia (ADH) was not possible on a cytological basis.

**Key words:** Breast carcinoma, proliferative disease, fibroadenoma, fine needle aspiration cytology.

### INTRODUCTION

Malignant breast lesions are often accompanied or preceded<sup>2,8</sup> by benign proliferative lesions. While the majority of these proliferations are not considered premalignant,<sup>6</sup> atypical ductal hyperplasia (ADH), atypical lobular hyperplasia (ALH) and lobular neoplasia *in-situ* (LNIS) have been found to significantly increase the subsequent risk of invasive breast cancer. Many of these lesions are nonpalpable<sup>9</sup> and mammographic features may not always indicate the benign nature of these proliferations.<sup>8</sup> In an attempt to identify accompanying benign proliferative lesions, we have performed four quadrant fine needle aspiration (FNA) cytology in 48 patients with breast carcinoma.

### MATERIALS AND METHODS

Forty-eight cases of breast carcinoma diagnosed on FNA cytology were cytologically assessed for the presence of accompanying benign proliferative lesions in the ipsilateral and contralateral breasts. These included 47 females and 1 male, whose ages ranged from 43 to 67 years. In all cases, FNA cytology was performed with a 22 gauge needle attached to a 20 cc plastic disposable syringe mounted on a handle for a single hand grip. Smears were air dried, fixed in

methanol and stained with May Grunwald Giemsa. Wet fixation in absolute alcohol and special stains were done as and when required. In all cases, two to four needle passes of the dominant presenting lump was first performed. This was followed by FNA of the quadrants of the ipsilateral breast not involved by the growth and subsequently four quadrant FNA of the contralateral breast. Mastectomy provided material for histopathological study of the ipsilateral breast. The typing of breast carcinomas was done as per the WHO classification.<sup>10</sup> The quadrant of the contralateral breast showing proliferative activity on FNA cytology was roughly mapped out and subjected to open biopsy. The entire biopsied tissue was processed in each case for histopathology.

### RESULTS

The cytological and histological diagnosis of the dominant lesions and the co-existent benign proliferative features observed on cytology and histology are tabulated (Table 1).

Benign alterations were associated with malignancy in 33 out of 48 cases (79%). The ipsilateral breast showed changes in 23 cases (47.9%) and the contralateral breast in 10 cases (20.7%). In 6 cases (12.7%) both breasts were

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affected.

Columnar alteration of the lobule was the most frequent change observed. Smears in these cases were mildly cellular and showed cohesive clusters of monomorphic epithelial cells (Fig. 1). In 5 cases, microcysts with apocrine change were present. In 4 of these cases, cytological smears showed apocrine cells (Fig. 2). In 7 cases, lobular proliferative lesions such as lobular hyperplasia, ALH or LNIS, sometimes in combination with ADH, were seen. Cytological smears in these cases showed cohesive clusters of epithelial cells (Fig. 3) with focal mild nuclear pleomorphism in 2 cases, clusters with cytoplasmic vacuolation in 2 cases (Fig. 4) and cell configurations simulating expanded and filled up lobular units in 2 cases (Fig. 5). In two cases, tiny microscopical fibroadenomas were seen within the dominant lump. In both these cases, FNA cytological smears showed, in addition to malignant ductal cells, monomorphic clusters of epithelial cells with prominent cytoplasmic vacuolation (Fig. 6). Cohesive clusters of monomorphic epithelial cells were also seen in two cases in which there was accompanying PDWA and in the case of gynaecomastia (Fig. 7).

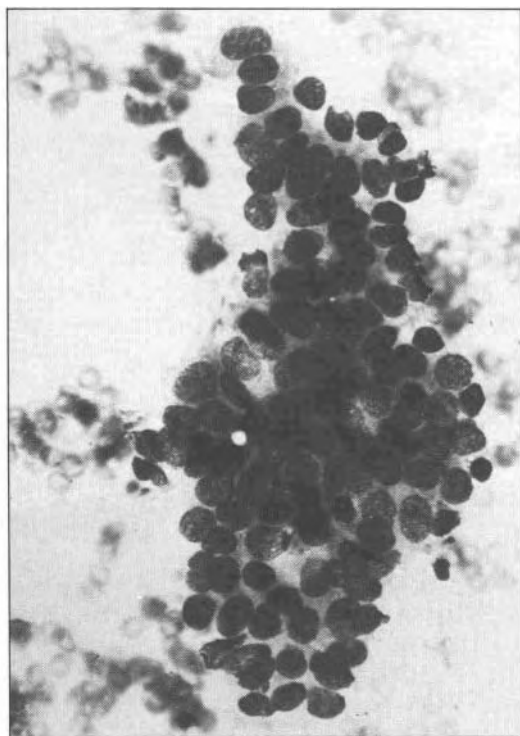


FIG. 1: Cohesive cluster of monomorphic epithelial cells in columnar alteration. MGG X400

## DISCUSSION

Benign proliferations of the breast cover a wide spectrum of lesions, some of which may have a premalignant significance.<sup>2,6,11</sup> Haagensen<sup>2</sup> and Page and Anderson,<sup>6</sup> doing follow up studies of women with biopsy proven benign proliferative lesions, attempted to quantify their subsequent risk of breast cancer. Black and Chabon<sup>1</sup> suggested that invasive breast cancer was associated with a greater degree of proliferative alteration in the breast. They demonstrated that most breast cancers were associated with recognizable progressive changes in multiple portions of the duct system, which ranged from atypical duct proliferations to carcinoma *in-situ*. Numerically grading these proliferative lesions, they concluded that the great majority of invasive breast cancers were associated with atypical ductal changes ranging from grade 3 (atypical hyperplasia) to well defined carcinoma *in-situ* (grade 5) which tended to occur simultaneously in different divisions of the duct system.

Some of the benign proliferations of the breast may not present with palpable lumps.<sup>9</sup> Consequently, cytological descriptions of these lesions are few.<sup>9,12</sup> We had earlier performed four quadrant FNA cytology of the breast in symptomatic women in an attempt to identify such benign proliferations. In this study, four quad-

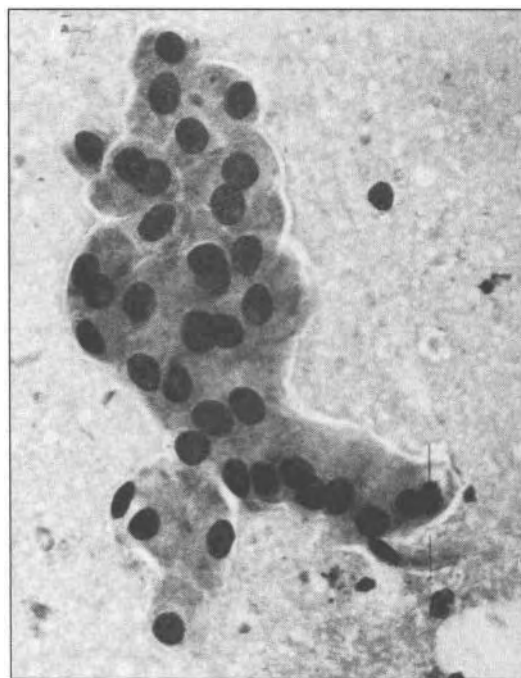


FIG. 2: Cluster of apocrine cells in a case with microcystic change. MGG X400

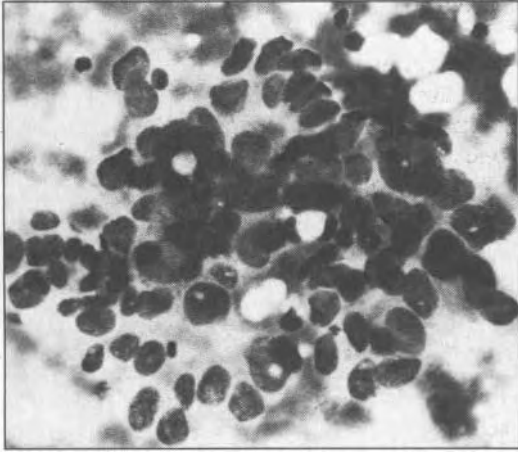


FIG. 3: Cluster of epithelial cells showing focal mild pleomorphism. MGG X400

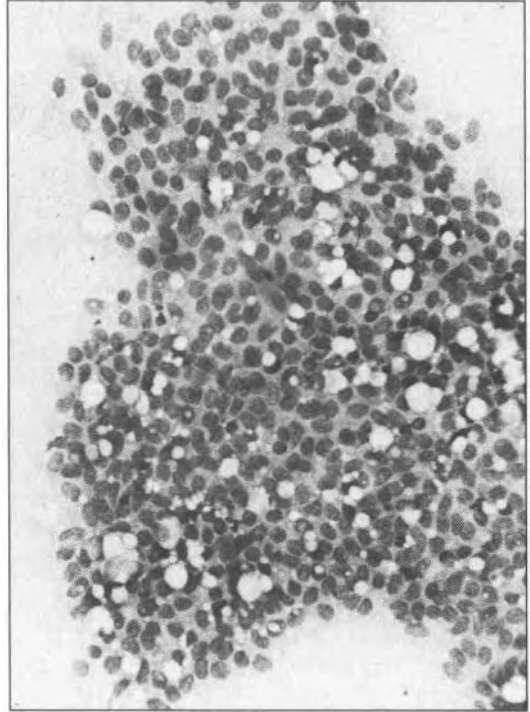


FIG. 6: Cluster of monomorphic epithelial cells with prominent cytoplasmic vacuolation. MGG X350

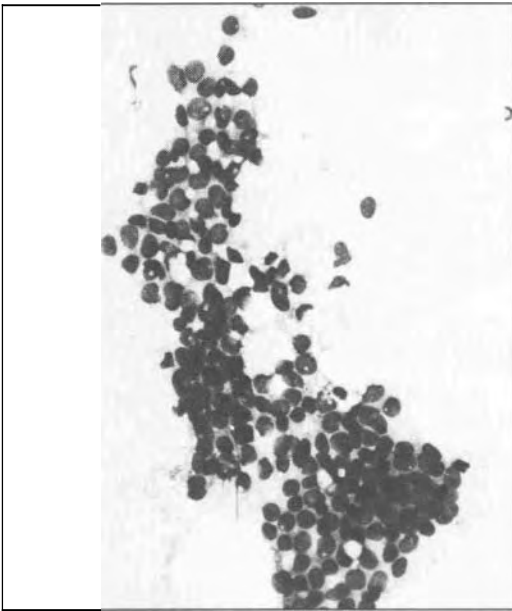


FIG. 4: Cluster of cells with focal cytoplasmic vacuolation. MGG X300

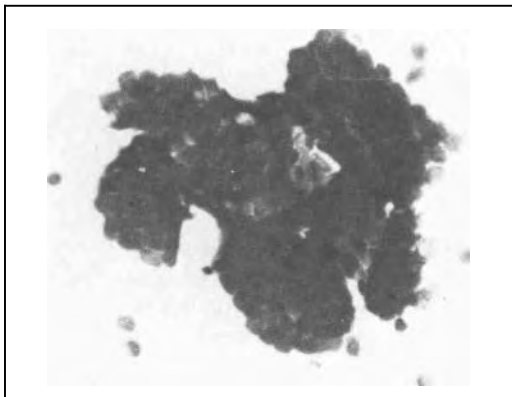


FIG. 5: Cell configuration simulating filled up lobular units. MGG X300

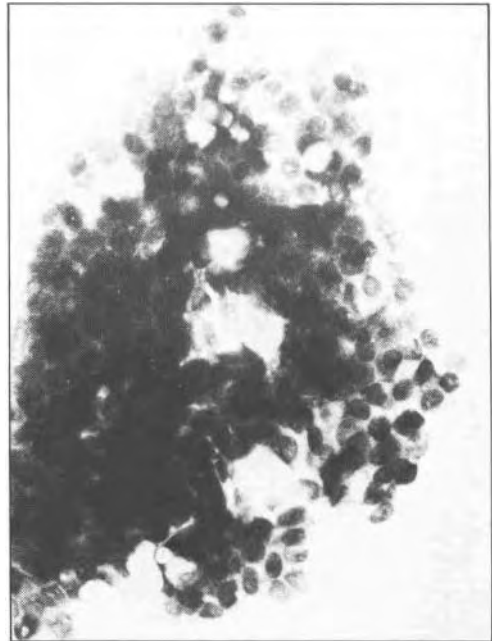


FIG. 7: Cluster of monomorphic epithelial cells in gynaecomastia. MGG X400

**TABLE 1: Cytological diagnosis correlated with histological diagnosis in 48 cases of breast carcinoma**

Cytodiagnosis	Dominant lesion		Coexistent benign features				
	No. of cases	Histodiagnosis	No. of cases	Cytology	No. of cases	Histopathology	No. of cases
Invasive ductal carcinoma	24	Invasive ductal carcinoma	24	Monomorphic epithelial cells	19	Columnar alteration	19
				Monomorphic epithelial cells	2	Lobular neoplasia in-situ	2
Invasive ductal carcinoma with apocrine carcinoma	7	Invasive ductal carcinoma with apocrine carcinoma	5	Monomorphic epithelial cells	1	Proliferative disease without atypia	1
				Benign apocrine cells	2	Microcysts with apocrine change	2
				Monomorphic epithelial cells with prominent vacuoles	1	Fibroadenoma	1
				Monomorphic epithelial cells with lobular filling	1	Lobular hyperplasia with columnar alteration	1
				Nil	1	Nil	1
Invasive ductal carcinoma with apocrine carcinoma	1	Infiltrating papillary carcinoma	1	Nil	1	Nil	1
				Monomorphic epithelial cells with prominent intra cytoplasmic vacuolation and apocrine change	1	Microcysts with apocrine change, atypical ductal hyperplasia, lobular hyperplasia	1
				Nil	1	Nil	1
Invasive ductal carcinoma with invasive lobular carcinoma	1	Invasive ductal carcinoma with invasive lobular carcinoma	1	Monomorphic epithelial cells with lobular units	1	Atypical lobular hyperplasia and lobular neoplasia in-situ	1
Apocrine carcinoma	5	Solid intraductal and infiltrating apocrine carcinoma	4	Nil	4	Nil	4
		Cribriform and micro papillary comedo carcinoma with apocrine component	1	Monomorphic epithelial cells with prominent vacuoles	1	Atypical ductal hyperplasia and atypical lobular hyperplasia	1

Medullary carcinoma	4	Medullary carcinoma	4	Nil	3	Nil	3
				Monomorphic epithelial cells	1	Proliferative disease without atypia, microcysts with apocrine change, atypical lobular hyperplasia and fibroadenoma	1
Papillary carcinoma	4	Papillary carcinoma	4	Nil	3	Nil	3
				Monomorphic epithelial cells with foam cells	1	Gynaecomastia	1
Suspicious of malignancy	2	Intraductal carcinoma	1	Nil		Nil	
		Intraductal and tubular carcinoma	1	Apocrine change	1	Microcysts with apocrine change	1

rant FNA cytology was performed with a view to identify benign proliferations that accompany malignancy of the breast.

**Benign alterations of the breast**, as detected by four quadrant FNA cytology, were frequent accompaniments of breast cancer, occurring in 73.3% of the cases, in ipsilateral, contralateral or both breasts.

Columnar alteration of the lobules, the most frequent change observed, has been found to have no premalignant connotation<sup>13</sup> and manifested in cytological smears as cohesive clusters of monomorphic epithelial cells. The presence of the latter was, however, not specific for columnar alteration as these were seen in other associated benign lesions such as gynaecomastia (GM), fibroadenoma, PDWA and ALI-I. Microcysts are felt to be a normal feature in breasts of modern women<sup>2</sup> and neither cysts nor apocrine change significantly elevate cancer risk.<sup>1</sup> Epithelial proliferative lesions accompanied malignancy in X cases (16.7%). Lobular proliferations, including LH, ALH and LNIS predominated (7 cases) and in 2 of these ADH was also present. PDWA occurred in 2 cases (and in one of them it was associated with ALII). While PDWA carries a slightly increased risk of subsequent invasive carcinoma (1.5-2 times that of the general population), in ADH the risk is four fold.<sup>4</sup> Cytological smears in these cases, although not distinctive for ADH, nevertheless indicated the presence of proliferative changes and helped choose the site for open biopsy, which enabled distinction of ADH from PDWA.

Atypical lobular proliferations including LNIS were found in 6 cases. In one of these the invasive carcinoma was both of the ductal and lobular type. Smears in ALH and LNIS showed clusters of monomorphic epithelial cells with prominent vacuolation of some and configurations of cells that simulated filled up lobular units with or without expansion in four cases. We, however, found vacuolated epithelial cells in fibroadenoma also. Salhani and Page<sup>12</sup> described prominent intracytoplasmic vacuolation and intracytoplasmic lumina in smears from ALH and LNIS. Like Shu *et al.*,<sup>14</sup> we are of the opinion that this feature is only an indicator for the lobular origin of cells. Expanded lobular units seen by us in LH, ALH and LNIS have been described by Finely *et al.*<sup>15</sup> in breast masses in pregnant and lactating women. We believe that this is a feature of all physiological and pathological conditions in which the terminal ductular lobular unit fills up with cells. This is aptly brought out by the illustration of smears in LNTS by Sneige<sup>16</sup> which resembles the illustration of lactating adenoma by Novotny *et al.*<sup>17</sup>

Since in-situ lobular proliferations do not show cytological atypia, ALH cannot be distinguished from LNIS on cytological preparations. Microscopical fibroadenoma accompanied invasive carcinoma in two cases and in both cases the fibroadenoma was included in the dominant presenting lump. In spite of the presence of cohesive clusters of monomorphic benign epithelial cells in both cases, the presence of fibroadenoma was not identified. Some recent data suggest that there may be an increased

risk of invasive carcinoma in patients with fibroadenoma.<sup>7,8</sup> Unilateral gynecomastia which occurred in a case of intracystic papillary carcinoma has been reported to exist in up to 20% of cancerous male breasts.<sup>9</sup>

Four quadrant FNA cytology appears to be useful in the identification of benign proliferations that may occur in women with breast cancer. Their identification by cytology made it possible to roughly map out the area for open biopsy which then enabled the distinction of the non atypical from the atypical proliferative lesions. The presence of ADH and ALH significantly increases the risk of subsequent invasive cancer which may occur in the contralateral or the ipsilateral breast? One serious limitation of this study was the relative inaccuracy of mapping out the proliferating area without radiographic needle localization (a facility unavailable to us). The other disadvantage was the inherent scope of false negative cytodiagnosis. Therefore, some of the cases in which 4 quadrant FNA of contralateral breast was cytologically normal could be the result of inadequate cytologic sampling. It is at present unlikely that our procedure will be tried in developed countries where sophisticated radiological localizing procedures are feasible. We have shown, however, that cytological identification of benign proliferations in cases of carcinoma breast, especially in the contralateral breast helps in choosing the site for open biopsy, which will then correctly categorize the lesion. We are living in an era of conservative surgery and it is possible that, with increasing experience, distinctive cytologic patterns may emerge which could enable prospective long term cytologic population screening studies of benign proliferations, whose natural history need not be disturbed by diagnostic biopsies.

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