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Research Article

Important Parameters in the Discrimination of Benign and Malign in Fine Needle Aspiration Biopsy in Solid Breast Lesions

Ozlem Turelik,[1] Umit Bayol[2]

[1]Department of Pathology, Bilecik Training and Research Hospital, Bilecik, Türkiye
[2]Department of Pathology, Izmir Tepecik Training and Research Hospital, Izmir, Türkiye

Abstract

Objectives: There are many cytologic features defined to distinguish benign-malignant solid breast lesions. This study was conducted to investigate important additional parameters in the cytological differentiation of benign and malignant solid breast lesions.

Methods: We evaluated 99 cases (45 benigni 44 malignant) registered in our laboratory. The cases are investigated in terms of various cytologic parameters.

Results: When the results were examined, it was seen that bare cell had diagnostic value in favor of benign. Bipolar cells and bare epithelial cells were not observed in most of the malignant cases. Benign giant cells were not seen in any of the malignant cases. Malignant giant cells were detected in 31.8% of malignant cases. Cytoplasmic vacuoles were observed at the level of 81.8% in malignant cases and 57.8% in benign cases and were evaluated as significant. Discohesive groups were observed at a higher rate in malignant cases and were evaluated as significant. Macronucleolus was found to be significant in the differentiation of benign and malignant. Nucleocytoplasmic ratio increased in all malignant cases. While mitotic activity was not observed in any of the benign cases, it was seen in 20.5% of the malignant cases and was considered significant.

Conclusion: Besides well-known criteria, parameters such as metaplastic epithelium, benign/malignant giant cells, epithelial cells amongst the lipomatous stroma and even an artificial sign: cytoplasmic vacuolization should be considered in the cytological differential diagnosis of solid mammary masses.

Keywords: Breast FNA, breast lesions, cytologic parameters

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One of the four cancers in women is located in the breast, and breast cancer is the most common cause of death from cancer.[1, 2] An accurate and adequate examination according to age and characteristics of the mass increases the rate of cancer detection, while minimizing unnecessary tests and interventions. Diagnostic steps in the approach to a breast mass are primarily physical examination, then radiological examination and, if necessary, biopsy.[3]

Fine-needle aspiration biopsy (FNAB) is a fast, economical, specific and sensitive, safe diagnostic method used in the evaluation of palpable and nonpalpable lesions in the breast without the need for anesthesia. Diagnostic accuracy ranges from 50-95% depending on sampling quality and experience of the evaluating cytopathologist. The purpose of aspirations is to distinguish between benign and malignant ones. This rate increases as the quality of the material

Address for correspondence: Ozlem Turelik, MD. Bilecik Egitim ve Arastirma Hastanesi Patoloji Bolumu, Izmir, Türkiye
Phone: +90 536 732 88 99 **E-mail:** ozlemturelik@gmail.com

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and the proficiency of the pathologist increase. However, it is not always possible to make a definite conclusion.

Necrosis, calcification, mitosis, nucleocytoplasmic ratio, pleomorphism, macronucleoli, cohesion, myoepithelial/bipolar cells, configuration are well-known differential diagnostic criteria in the cytologic evaluation of solid breast lesions. The existance of metaplastic epithelial cells, benign/malignant giant cells, epithelial cells amongst the lipomatous stroma and cytoplasmic vacuolization as an artifact has not been documented before.

Methods

Fine needle aspiration biopsies (FNABs) of the 45 benign and 44 malignant solid breast lesions were reevaluated semiquantitatively as regards necrosis, calcification, mitosis, nucleocytoplasmic ratio, pleomorphism, macronucleoli, cohesion, myoepithelial/bipolar cells, configuration, cytoplasmic vacuolization, metaplasia, giant cells (benign/malignant) and epithelial cells amongst the lipomatous stroma. We have compared the results statistically with chi-square test.

Results

All of the parameters were statistically significant between the benign and malignant groups. Necrosis, calcification, mitosis, pleomorphism, macronucleoli, high nucleocytoplasmic ratio, discoheziveness, loss of myoepithelial cells, malignant giant cells, cytoplasmic vacuolization and epithelial cells amongst the lipomatous stroma are highly correlated with malignancy. Metaplastic epithelium, benign giant cells are correlated with benign lesions (Figs. 1-6).

Benign stromal elements, Stromal cellularity, stromal elements other than fibrous elements (hyalinized, calcified, rich in vessels), nuclear vacuoles, 3-dimensional cohesive epithelial groups, papillary structures are statistically in-

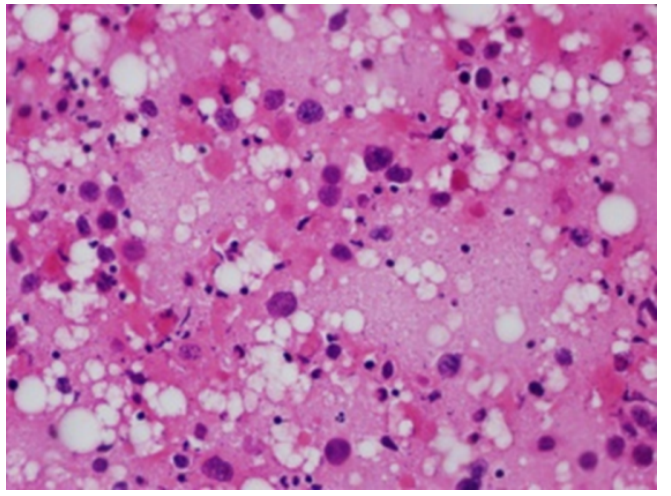

Figure 2. Epitelial cells amongst the lipomatous stroma.

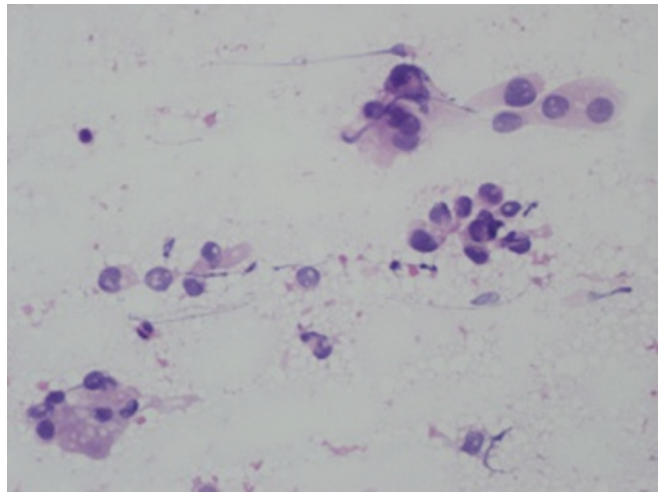

Figure 3. Cytoplasmic vacuolization.

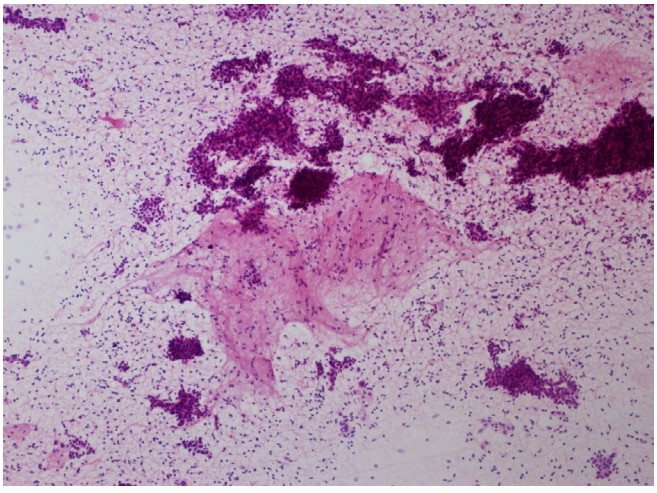

Figure 1. Bipolar and bare cells, cohesive cell groups.

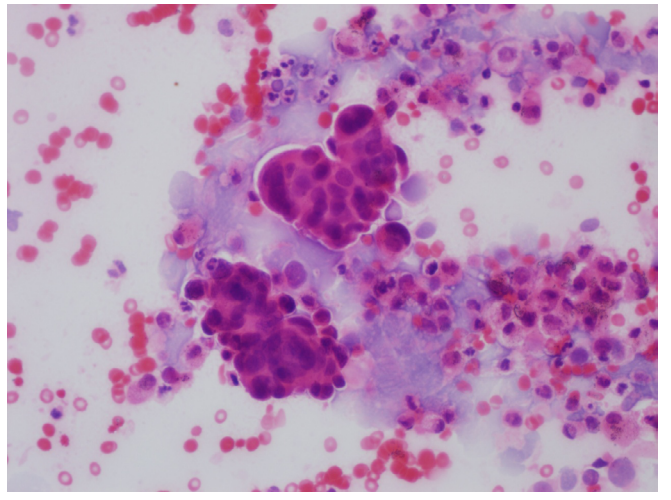

Figure 4. Papillary structures.

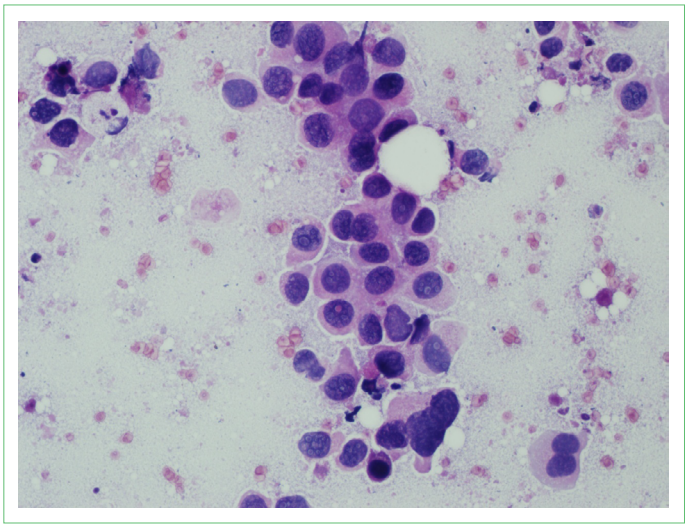

Figure 5. Macronucleolus.

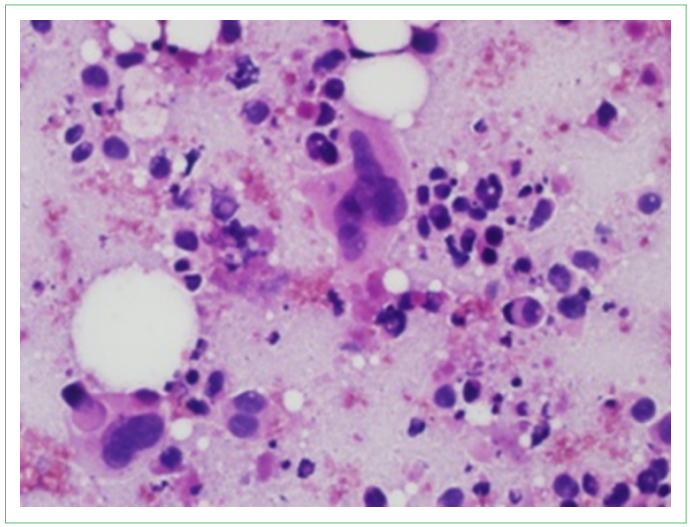

Figure 6. Malignant giant cell.

significant, necrosis/necrobiosis, bare cells (fusiform myoepithelial elements), bipolar cells, nucleocytoplasmic ratio, pleomorphism, macronucleolus, myoepithelial layer in cohesive groups, 3-dimensional discohesive epithelial groups, array in epithelial groups, structuring (except papillary structures), calcification, bare epithelial cells, mitosis, cribriformity in epithelial groups, epithelial metaplasia, benign giant cells, malignant giant cells, epithelial cell between adipose tissue elements, cytoplasmic vacuoles were found statistically significant (Table 1).

Table 1. Distribution of cytological parameters between benign and malignant cases (p<0,05)

	Benign (n=45)		Malignant (n=44)		
	Case	%	Case	%	p
Necrosis	15	33.3	37	84.1	0.00
Calcification	20	44.4	32	72.7	0.01
Mitosis	0	0	35	20.5	0.00
High nucleocytoplasmic ratio	11	24.4	44	100	0.00
Pleomorphism	14	31.1	44	100	0.00
Macronucleoli	3	6.7	39	88.6	0.00
Discoheziveness	9	20	41	93.2	0.00
Myoepithelial cells	43	95.6	16	36.4	0.00
Bipolar cells	29	64.4	0	0	0.00
Configuration	35	77.8	4	9.1	0.00
Cytoplasmic vacuolization	26	57.8	36	81.8	0.02
Metaplasia	28	62.2	11	25	0.00
Benign giant cells	7	15.6	0	0	0.01
Malignant giant cells	0	0	30	31.8	0.00
Epithelial cells amongst the lipomatous stroma	3	6.7	19	43.2	0.00

Discussion

FNAB is a specific and safe method with a high sensivitiy to diagnose the palpable and nonpalpable breast tumors. The FNAB is a minimally invasive method without anesthesia, rapid and cheep. Sampling quality and experience of the pathologist are the important factors that determine the diagnostic accuracy rate of FNAB in solid breast masses.

The main purpose of FNABs is to select the benign and malignant cases. Ductal epithelial cells in benign aspirations are generally uniform in appearance, with rounded smooth nuclei. Occasionally, slightly pleomorphic cells with large and hyperchromatic nuclei may be found. Pleomorphism is rather characteristic of malignant aspirations. An increase in the nucleocytoplasmic ratio (N/S) is considered a sign of malignancy. Although the nucleoli are slightly prominent in constantly regenerating normal tissues, a large, prominent nucleolus is the defining feature for rapidly proliferating cancer cells.[4] However, in some benign lesions, ductal epithelial cells with prominent nucleoli and atypical features can be found among small uniform cells. Necrosis is an important criterion in the differentiation of benign and malignant in both cytology and histology.[5] It is a common finding especially in invasive breast carcinomas. The presence of individual epithelial cells as loosely attached, small groups and single cells is an important feature in the differentiation of benign and malignant lesions. While the relationship between cells is preserved in benign lesions, this feature is lost in malignant tumors. The fact that epithelial cell groups are surrounded by myoepithelial cell line is a feature seen in benign lesions. They are not usually found in malignant tumors. The presence of abundant bipolar bare nuclei on the aspiration floor is one of the diagnostic fea-

tures especially for fibroadenoma. There is no consensus among researchers about the origin of these bare nuclei. There are studies suggesting that it may be of myoepithelial, stromal and ductal epithelial origin.[6-8] Regardless of their origin, if the presence of bare nuclei is consistent with other findings in the aspirate, it suggests that the lesion is benign and especially supports fibroadenoma.[4, 8, 9] However, few researchers have suggested that it can also be seen in other benign and malignant breast lesions.[8, 10] Dystrophic calcification can be observed in aspiration. [11, 12] It is mostly detected in malignant lesions. Apocrine metaplasia is frequently encountered in FNAB. Atypical apocrine metaplastic cells require differential diagnosis between benign and malignant diseases. There are not many publications in the literature on nuclear vacuoles.

Morphological parameters such as microcalcification, necrosis, prominent nucleoli, naked nuclei, three dimentional cell clusters, nucleocytoplasmic ratio, coheziveness, papillary structures, apocrine metaplasia, inflammation, mucus on the backgound are the main parameters discussed in the literature. Sauer et al. in a study of 225 ductal carcinoma in situ (DCIS) cases conducted in 2004, in low-grade DCIS cases comedo necrosis 16%, microcalcification 90%, myoepithelial cell 51%, cribriformity 94%, micropapillary groups 57%, true papillary structures %. 8, in high-grade DCIS cases, comedo necrosis was 61%, microcalcification was 84%, myoepithelial cell was 27%, cribriformity was 76%, micropapillary groups were 20%, and true papillary structures were 2%.[13] In 2003, Simsir et al. conducted a study of 70 cases diagnosed as papillary. In this study, cellularity as mild, moderate, severe cellular atypia, nucleolar prominence, nuclear contour irregularity, nucleocytoplasmic ratio, no chromatin coarsening, mild, moderate, severe, myoepithelial and apocrine cells present or absent, background cystic, hemorrhagic, necrotic evaluated.[14] In a study conducted by Zhao et al. in 2009, 172 cases were evaluated in terms of cellularity, epithelial cell arrangement, cellular composition, pleomorphism, nuclear overlap, cellular dispersion, horn-shaped epithelial layer, fibromyxoid stromal fragments, apocrine metaplasia, and myoepithelial cell presence.[15]

We noted necrosis, calsifications, mitosis, nucleocytoplasmic ratio, pleomorphism, macronucleoli, cohesion, myoepithelial/bipolar cells, configuration, cytoplasmic vacuolization, metaplasia, giant cells (benign/malignant) and epithelial cells amongs the lipomatous stroma for both groups (benign/malignant). Statistical analyses revealed that; necrosis calcification, mitosis, pleomorphism, macronucleoli, high nucleocytoplasmic ratio, discohesiveness, loss of myoepithelial cells, malignant giant cells, cytoplasmic vacuolizations and epithelial cells amongs the lipomatous stroma are highly correlated with malignancy. Metaplastic epithelium, benign giant cells are correlated with benign lesions.

Unlike the other studies in the literature, metaplastic epithelium, benign/malignant giant cells, epithelial cells amongst the lipomatous stroma and cytoplasmic vacuolizations are found to be statistically significant in the differential diagnosis on cytology.

Conclusion

Besides well-known criteria, parameters such as metaplastic epithelium, benign/malignant giant cells, epithelial cells amongst the lipomatous stroma and even an artificial sign: cytoplasmic vacuolization should be considered in the cytological differential diagnosis of solid mammary masses.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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