Fine-Needle Aspiration Cytology of the Breast

12

Chen Zhou, Gang Wang, and Malcolm Hayes

Contents

List of Frequently Asked Questions

1. What are the advantages of FNA of the breast? What are the indications of FNA of the breast?

Breast FNA offers a safe, fast, inexpensive, and minimally invasive diagnostic solution to various breast lesions. It has few complications and is well accepted by patients. It does not require facility for tissue processing. When performed by aspirators trained with FNA technique and interpreted by cytopathologists experienced in reporting breast cytology, breast FNA cytology is highly accurate in diagnosing benign and malignant breast lesions, having a sensitivity and specificity almost similar to the core needle biopsy of the breast. A recent meta-analysis of 46 studies showed that breast FNA has a sensitivity of 92.7% and specificity of 94.8%.

In North America and in most developed countries, breast FNA has been replaced by core needle biopsy for preoperative diagnoses of breast palpable masses and impalpable radiologic abnormalities for the last 20 years. However, in developing countries, breast FNA is still being widely used for preoperative diagnoses of breast palpable mass and for some impalpable radiologic abnormalities. Breast FNA is also used in developed and developing countries for rapid on-site evaluation (ROSE), in "one-stop" diagnostic clinics, and for certain breast lesions (Table 12.1).

References: [1–4].

Table 12.1 Indications of breast FNA cytology

Indications	Purposes	Countries
Cyst of the breast	Diagnostic and therapeutic	Developing and developed
Palpable mass of the breast	Diagnostic	Developing and developed[a]
Impalpable radiologic abnormality	Diagnostic	Developing
Recurrent mass or metastasis after breast surgery	Diagnostic	Developing and developed
Preoperative axillary lymph node aspiration	Diagnostic and triage	Developing and developed
Nipple discharge	Diagnostic	Developing and developed

[a]Breast mass in pregnant and postpartum women or in women with contraindication to core needle biopsy; clinically inoperable or locally advanced breast mass

2. How are FNA techniques used to obtain cytology specimens of the breast?

Breast FNA can be performed with or without an image guidance. For palpable mass, manual aspiration without an image guidance is preferred. The mass can be fixed with one hand and aspirated using another hand. Needles of 23, 25, and 27 gauge are used for aspiration. We routinely use a 25-gauge needle and hold the needle hub in one hand to aspirate the lesion. To generate adequate aspirate material, more than three aspirations are performed with needle passing into the mass in different directions using a rapid back-and-forth oscillating motion. For sclerotic lesion or to make a good cell block, a syringe is attached in conjunction with a syringe holder or aspiration "gun" to provide suction for the aspira-

C. Zhou (✉) · G. Wang · M. Hayes
Department of Pathology, British Columbia Cancer Agency, University of British Columbia, Vancouver, BC, Canada
e-mail: czhou@bccancer.bc.ca

H. Xu et al. (eds.), *Practical Cytopathology*, Practical Anatomic Pathology, https://doi.org/10.1007/978-3-030-24059-2_12

tion. The advantages of holding the needle hub by hand not only are having better control during the aspiration, less fearful to the patients, but also enabling the aspirators to feel the nature of the lesions through the aspiration needle. For example, the aspirator could feel the "gritty" sensation of carcinoma or fat necrosis, or the "sucked in" sensation of a benign fibrous scar. To avoid blood clot formed within the needle, the aspirator should stop aspiration once a small amount blood or aspirating material is accumulated within the needle hub.

In our experience as aspirators, we usually perform first 2–3 aspirations using the needle hub held by hand and last 1–2 aspirations using a syringe holder or aspiration "gun" to obtain adequate materials for cytology smears and cell block without causing excessive bleeding or trauma.

3. What are the preparation methods used to prepare the FNA cytology specimens of the breast?

Several preparation methods can be used to prepare breast cytology specimens, almost similar to FNA from other body parts.

After the aspirate, a syringe filled with air is used to connect the needle hub, and a drop of the aspirate is expressed onto a glass slide to make at least two cytological smears in a way similar to making a blood film. The cytology smear can be air-dried and stained with May-Grünwald Giemsa (MGG) stain or fixed immediate with alcohol spray or in alcohol solution and stained with Papanicolaou's (Pap) stain. For rapid on-site assessment, air-dried cytology smear can be stained with Diff-Quik solutions, and alcohol-fixed cytology smear can be stained with H&E staining.

Cytology aspirate and/or needle rinse can be collected in CytoLyt or other fixative solutions to prepare cytospin slides or monolayer liquid-based cytology slides such as ThinPrep or SurePath slides. The remaining material from the solution is used to prepare a cell block. This preparation method is helpful for facilities with no on-site support or a shortage of cytotechnologists or cytopathologists. As compared to conventional cytology smear, there are several other benefits of liquid-based cytology, including better cellular preservation, less interference from inflammatory cells, and more efficiency in screening cytology slides; however, there are also disadvantages of liquid-based cytology such as alterations in architecture and cell morphology and loss of myoepithelial cells and stromal fragments, which require modification in diagnostic criteria or additional training for interpretation of the liquid-based cytology slides, especially for those borderline lesions of the breast.

In our institution, we routinely prepare two cytology smears, one smear stained with MGG stain and another smear stained with Pap stain. We also use needle rinse or make dedicated passes of FNA to prepare a ThinPrep cytology slide and a cell block. For referral or sent in cytology specimens, we instruct the outside facilities to place FNA material directly into CytoLyt solution to send to our laboratory to prepare a ThinPrep cytology slide and a cell block.

Reference: [5].

4. How are the FNA cytological results of the breast reported? What is the minimal number of cells required for reporting FNA cytology of the breast?

In 1996, the National Cancer Institute Fine-Needle Aspiration of Breast Workshop Subcommittees proposed a uniform approach for reporting breast FNA cytology. A breast FNA cytology report should include (1) exact site of the FNA (side and position of the clock); (2) type of sample (FNA or nipple discharge); (3) a brief description of the cytological features; (4) conclusion of diagnosis using the following five categories (inadequate (C1), benign (C2); atypical, probably benign (C3); suspicious, favor malignancy (C4); and malignant (C5)); and (5) comments or recommendations. However, the NCI-recommended reporting has not been adopted widely and has not been updated after 10 years in its use. Recently, the International Academy of Cytology (IAC) brought together a group of cytopathologists, surgical pathologists, radiologists, surgeons, and oncologists to work on a standardized and comprehensive approach to breast FNA reporting. Because the reporting system was first proposed and discussed in 2016 at the19th IAC meeting in Yokohama, Japan, it is also called "Yokohama" reporting of breast FNA cytology.

The consensus for Yokohama reporting of breast FNA was to use five categories:

- Category 1: Insufficient material
- Category 2: Benign
- Category 3: Atypical, probably benign
- Category 4: Suspicious, probably in situ or invasive carcinoma
- Category 5: Malignant

The minimal cells required for a breast FNA cytology reporting varies according to different criteria proposed. Generally, 6 groups of ductal epithelial cells and at least 5–10 cells in each group are considered adequate. This rule does not apply to breast cystic lesions and inflammatory lesions, breast lipoma, or other stromal lesions. The Yokohama reporting of breast FNA cytology will also recommend the minimal number of cells required for the reporting of breast FNA cytology in its final version.

Reference: [2].

5. What are normal cytology components of FNA cytology of the breast?

Normal breast consists of large ducts (lactiferous, segmental, and subsegmental ducts), terminal duct-lobular units, and

fibroadipose stroma. The ducts and acini of lobules are lined by an inner layer of columnar to cuboidal epithelial cells and an outer layer of myoepithelial cells. In breast FNA specimens, components of normal breast cells and tissues can be seen in the background. The normal ductal or acinar epithelial cells are columnar to polygonal in shape and are arranged in cohesive groups or sheet with a honeycomb pattern. The epithelial cells have regular, oval nuclei, indistinctive or small nuclei, and a small amount of granular or clear cytoplasm. The myoepithelial cells appear in single dispersed pattern or within the groups of ductal epithelial cells. The cells have small, darkly stained, oval, or bipolar nuclei without cytoplasm (naked bipolar nuclei). The stromal components are mainly small fragments of adipose tissue (Figs. 12.1 and 12.2).

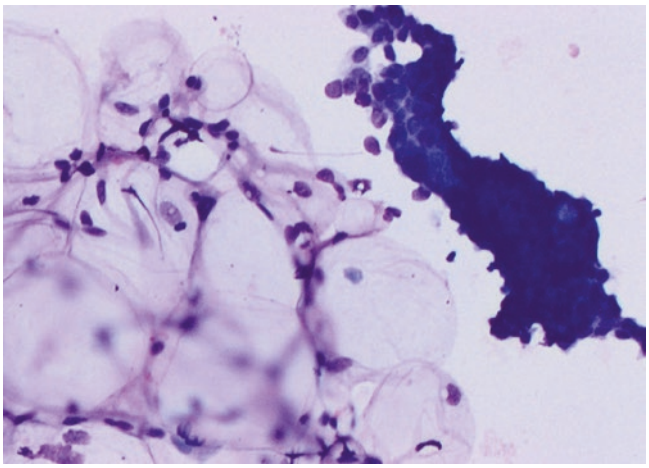

Fig. 12.1 Normal breast. The right upper shows a small duct, containing regular round nuclei of ductal epithelial cells and surrounded by a vague layer of darkly stained myoepithelial cells. The left lower shows a fragment of adipose tissue of normal breast (MGG stain)

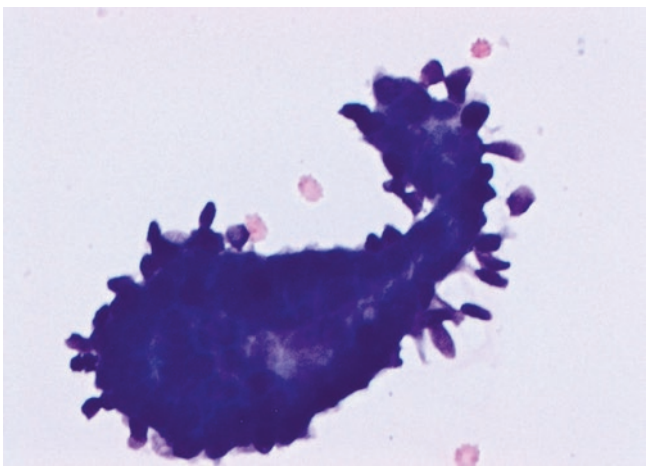

Fig. 12.2 Normal breast. An acinar and duct of terminal lobular unit is arranged in 3-D group, showing the pale nuclei of the inner layer of duct epithelial cells and the dark nuclei of the outer layer of myoepithelial cells (MGG stain)

6. What are the cytological features of a lactating adenoma?

Lactating adenoma is a nodular mass produced from secretory or lactational hyperplasia of lobules of breast during pregnancy or lactation. It is not a true neoplasm but rather nodular aggregates of hyperplastic lobules with lactation change. Clinically, FNA is performed to rule out malignancy that occurs during pregnancy or lactation. The cytological features of a lactating adenoma include (1) a moderately cellular specimen; (2) sheets of ductal epithelial cells with nuclear enlargement, prominent nucleoli, and foamy or vacuolated cytoplasm; and (3) many single epithelial cells and/or stripped round nuclei associated with a background of lipid droplets (Fig. 12.3).

Ductal epithelial cells of lactating adenoma are discohesive and have prominent nucleoli, which to some degree resemble malignant cells of breast carcinoma. However, the cells do not show variation in nuclear sizes and shapes and are present in a background of lipid droplets.

7. What are the cytological features of subareolar abscess? What are the cytological features of fat necrosis?

Subareolar abscess and fat necrosis are the two most common nonneoplastic mass lesions present for breast FNA.

Subareolar abscess is caused by plugging of lactiferous duct by ductal squamous material, resulting in acute inflammation, dilatation, and rupture of the duct with formation of a mass-like abscess. The cytological features of a subareolar abscess include (1) a cellular aspirate; (2) numerous acute inflammatory cells, histiocytes, and cell debris; (3) multinucleated histiocytes or loose formed granulomas; (4) anucleated squamous cells and/or benign squamous cells; and (5) occasional reactive ductal epithelial cells (Figs. 12.4 and 12.5).

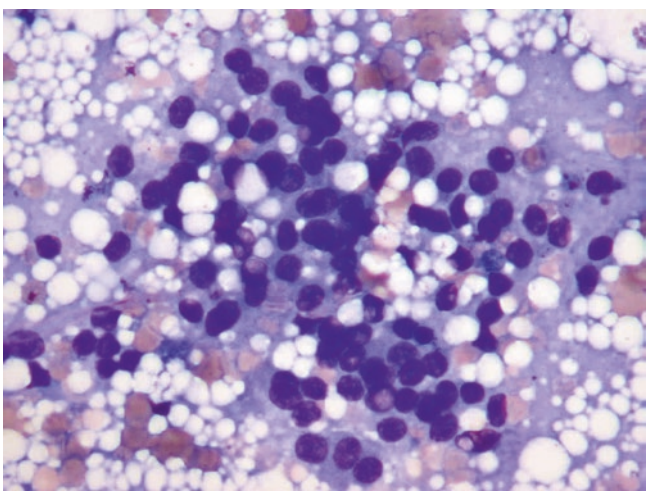

Fig. 12.3 Lactating adenoma. Many single dispersed, discohesive stripped nuclei without variation of nuclear sizes and shapes are present. Some of the nuclei contain prominent nucleoli. The background shows lipid droplets (MGG stain)

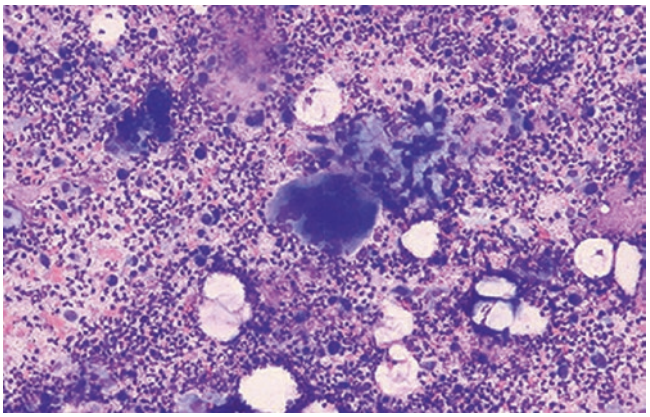

Fig. 12.4 Subareolar abscess. A hypercellular cytology smear shows multinucleated giant cells present in a background of numerous acute inflammatory cells (MGG stain)

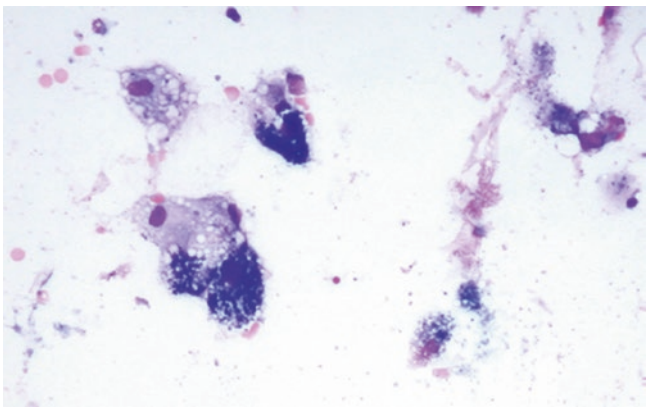

Fig. 12.6 Fat necrosis. Scattered foamy histiocytes; some have cytoplasmic blue-colored granular material present in a background of purple debris (MGG stain)

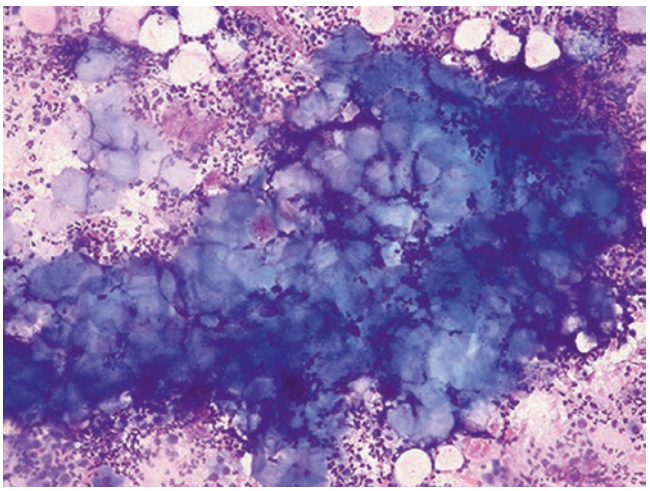

Fig. 12.5 Subareolar abscess. Sheets of anucleated squamous cells with sea blue cytoplasm are present in a background of numerous acute inflammatory cells (MGG stain)

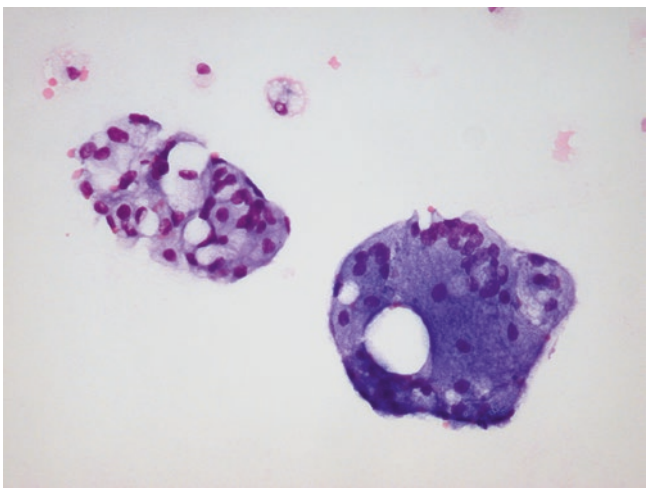

Fig. 12.7 Fat necrosis. One aggregate of foamy histiocyte containing several lipid vacuoles and a multinucleated giant cell containing a large round lipid vacuole are present. Several foamy histiocytes are present in the background (MGG stain)

The differential diagnoses of a subareolar abscess include a breast abscess associated with acute mastitis and an epidermal inclusion cyst. During breastfeeding, bacteria can enter the breast through traumatized nipple, causing an acute mastitis, breast abscess, and a tender mass. The FNA of breast abscess shows numerous acute inflammatory cells but no presence of anucleated squamous cells. An epidermal inclusion cyst of the breast can present as a breast mass and its FNA shows many anucleated squamous cells and a few multinucleated giant cells but does not have numerous acute inflammatory cells in the background.

Fat necrosis is caused by traumatic necrosis of breast or subcutaneous adipose tissue, resulting in a mass lesion. Clinically, fat necrosis is much more commonly caused by surgical trauma than by physical trauma. The cytological features of fat necrosis are as follows: (1) a hypocellular aspirate; (2) lipid debris and fat vacuoles; (3) foamy histiocytes and loose granuloma consisting of histiocytic aggregates; and (4) a few neutrophils, lymphocytes, and plasma cells (Figs. 12.6 and 12.7).

The differential diagnoses of fat necrosis include granulomatous mastitis and silicon granuloma; both of them contain foamy histiocytes and multinucleated giant cells. Besides the difference in clinical history, the FNA of granulomatous mastitis shows much more cellular specimen and contains many inflammatory cells; the FNA of silicon granuloma shows silicon globules within multinucleated giant cells and in the background.

8. What are the cytological features of a breast cyst? What are the cytological features of fibrocystic changes?

Breast cyst is a part of the fibrocystic change, which also typically displays changes of apocrine metaplasia, adenosis,

sclerosing adenosis, stromal fibrosis, and ductal hyperplasia. Large cysts can arise from the expansion of ducts into clinically palpable cystic masses. Clinically, fibrocystic disease presented by breast cysts is commonly seen in middle-aged and elderly women. FNA of breast cysts is not only a diagnostic test, but also a therapeutic procedure. After draining the content of the cyst, the aspirator should make sure that there is no palpable lesion left. Grossly, the cystic fluid is clear and yellow or dark and brown. FNA cytology of breast cysts typically shows (1) apocrine cells in cohesive sheets; (2) foamy histiocytes, some may have brown pigments; (3) cell debris (Figs. 12.8 and 12.9).

A breast cyst is reported as an apocrine cyst when apocrine cells are present, or a simple cyst when apocrine cells are absent and an inflamed cyst when inflammatory cells are present. Some of the inflamed cysts may contain cytological atypical apocrine cells or squamoid cells.

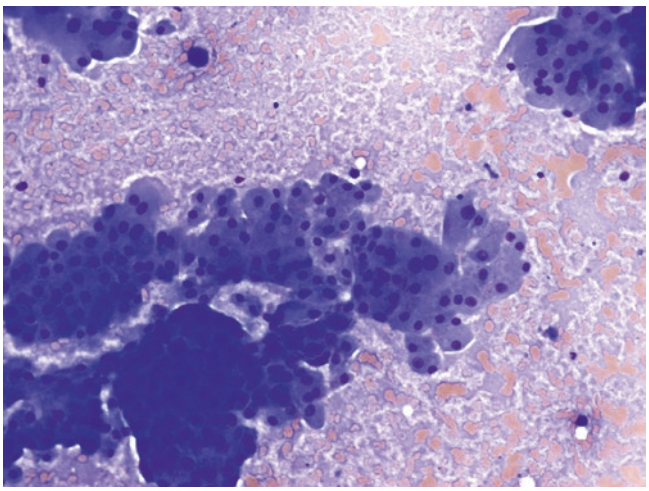

Fig. 12.8 Apocrine cyst. Large sheets and single apocrine cells are present. The cells have round nuclei, prominent nucleoli, abundant dense granular cytoplasm, and low N/C ratio (MGG stain)

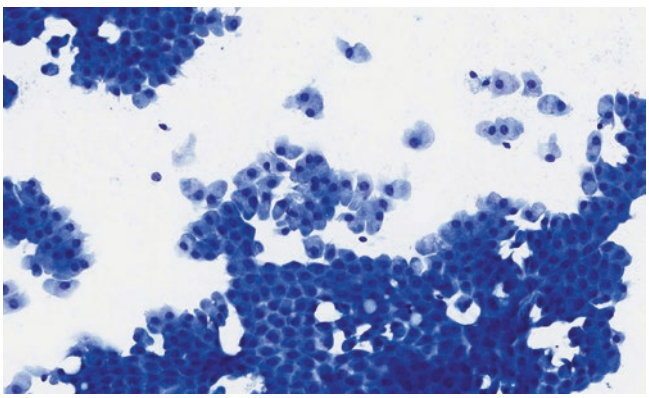

Fig. 12.9 Apocrine cyst. Sheets of benign apocrine cells are arranged in honeycomb pattern. The cells have round nuclei, prominent nucleoli, and abundant dense cytoplasm. The background is clean without necrosis (Pap stain)

9. What are the cytological features of proliferative lesion of the breast?

A proliferative breast lesion is fibrocystic change associated with epithelial hyperplasia, either usual ductal hyperplasia, atypical ductal hyperplasia, or atypical lobular hyperplasia. Fibrocystic change without epithelial hyperplasia is classified as nonproliferative breast lesions.

The cytological features of proliferative breast lesion without atypia are (1) cellular specimen; (2) cohesive sheets and large groups of benign ductal epithelial cells; (3) myoepithelial cells present within groups of epithelial cells or as single stripped nuclei in the background; and (4) no marked nuclear atypia and no dyshesive atypical ductal cells (Figs. 12.10 and 12.11).

The cytological features of proliferative breast lesions with atypia are (1) cellular specimen; (2) large and small

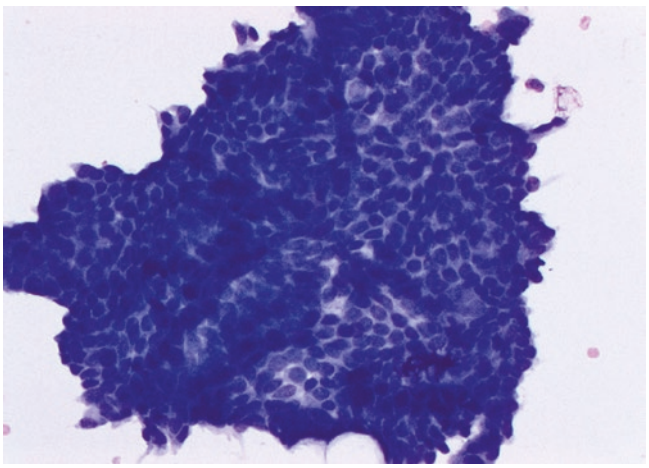

Fig. 12.10 Proliferative disease without cytologic atypia. Large cohesive sheet of ductal epithelial cells is present. The nuclei are regular, round to oval, without overlapping or crowding, and contain fine chromatin and indistinct nucleoli (MGG stain)

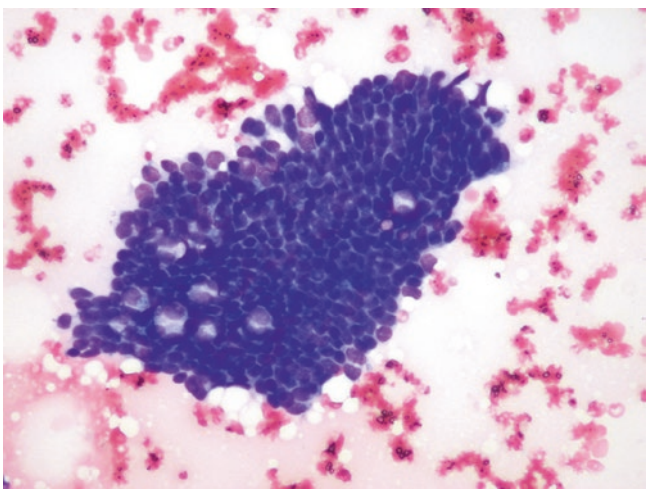

Fig. 12.11 Proliferative disease without cytologic atypia. Large flat sheet of ductal epithelial cells with regular, round to oval nuclei, without nuclear overlapping, and nucleoli are present (MGG stain)

groups of mild to moderately atypical ductal epithelial cells showing nuclear enlargement, nuclear crowding, loss of polarity, and prominent nucleoli; and (3) few myoepithelial cells in the background (Figs. 12.12 and 12.13).

Masood proposed a score index using six cytological features to classify breast lesions into nonproliferative breast disease, proliferative without atypia, proliferative with atypia, and carcinoma. Later, the Modified Masood Score Index was also proposed for such classification. Despite the efforts, it is still difficult to separate atypical proliferative breast lesion from low-grade in situ and invasive carcinoma; therefore, it is recommended that all atypical breast lesion should be excised or further investigated by core needle biopsy (Fig. 12.14).

References: [6, 7].

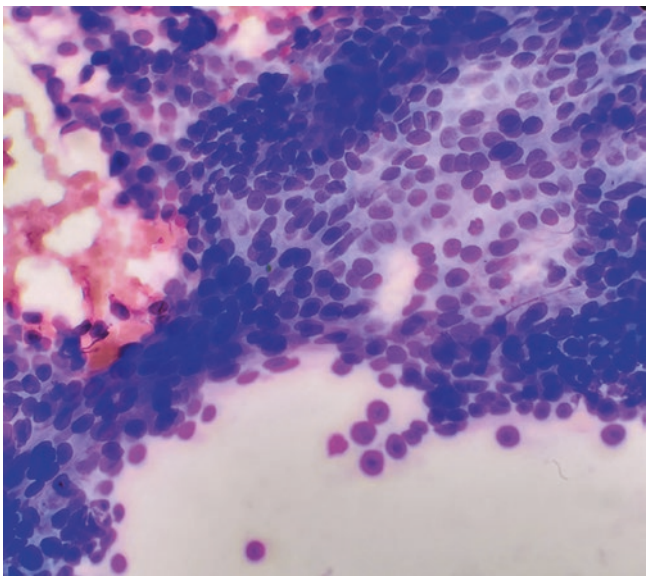

Fig. 12.12 Proliferative disease with cytologic atypia. Large flat sheet of ductal epithelial cells with regular, round to oval nuclei, and also with nuclear crowding and overlapping. Some scatter cells containing naked nuclei and prominent nucleoli are also present (MGG stain)

10. What are the cytological features of a fibroadenoma?

Fibroadenoma is the proliferation of both epithelial and stromal components of the breast. It is the most common type of benign breast nodule that underwent for FNA. Clinically, fibroadenoma typically occurs in young women but can also occur in middle-aged women. On palpation, it is a mobile rubbery nodule and, on imaging study, a round, well-circumscribed hypoechoic mass. The FNA of fibroadenoma typically has (1) a cellular aspirate; (2) cohesive branching sheets of ductal epithelial cells with "antler-horn" shapes; (3) numerous naked nuclei of myoepithelial cells in the background; and (4) fragments of fibromyxoid stroma with cloverleaf-like shape (Figs. 12.15, 12.16, and 12.17).

Because FNA from fibroadenoma is usually cellular, some of them display dispersed small groups of epithelial cells and single ductal epithelial cells with nuclear enlargement and prominent nucleoli, mimicking a low-grade ductal carcinoma. Such "atypical" fibroadenoma is difficult to

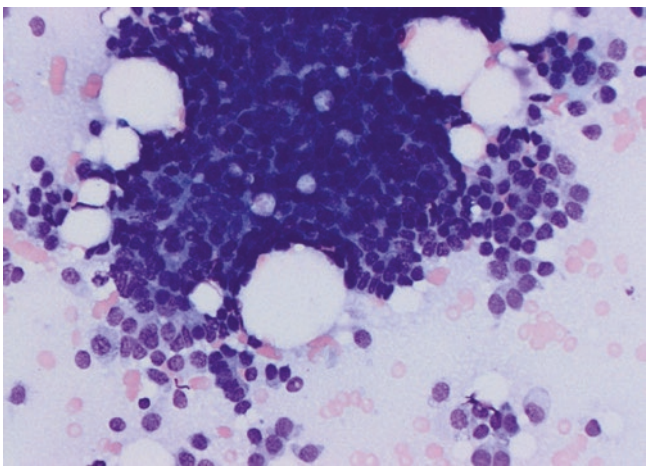

Fig. 12.13 Proliferative disease with cytological atypia. Cellular cytology smear displays large flat discohesive sheet of ductal epithelial cells with regular, round nuclei, and also with nuclear crowding and overlapping. Many scattered single cells containing pale cytoplasm are also present (MGG stain)

Cellular arrangement	Cellular pleomorphism	Myoepithelial cells	Anisonucleosis	Nucleoli	Chromatin clumping	Score
Monolayer	Absent	Many	Absent	Absent	Absent	1
Nuclear overlapping	Mild	Moderate	Mild	Micronucleoli	Rare	2
Clustering	Moderate	Few	Moderate	Micronucleoli and/or rare macro nucleoli	Occasional	3
Loss of cohesion	Conspicuous	Absent	Conspicuous	Predominantly macro nucleoli	Frequent	4
Total score						
Nonproliferative breast disease 6 – 10						
Proliferative breast disease without atypia 11 – 14						
Proliferative breast disease with atypia 15 – 18						
Carcinoma in situ / Carcinoma 19 – 24						

Fig. 12.14 Masood Score Index for assessment of breast FNA and for classification of breast lesions. (Modified from Masood and others)

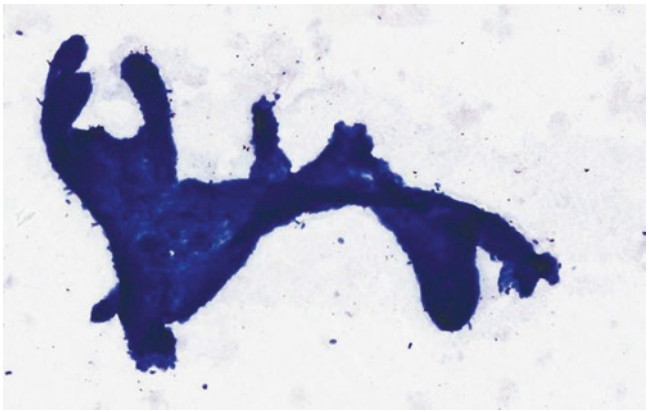

Fig. 12.15 Fibroadenoma. Low-power view of a fibroadenoma showing "antler-horn"-like 3-D structure (MGG stain)

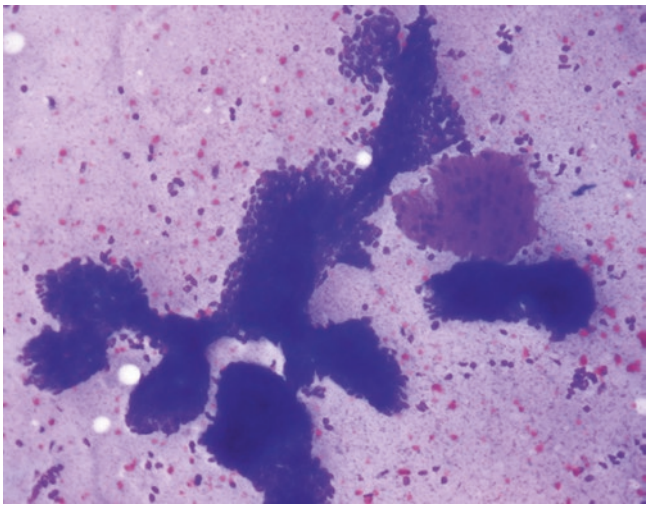

Fig. 12.16 Fibroadenoma. Under the low power, 3-D branching groups of ductal epithelial cells, a fragment of acellular stroma in round shape, and a background of stippled round to oval nuclei of myoepithelial cells are present (MGG stain)

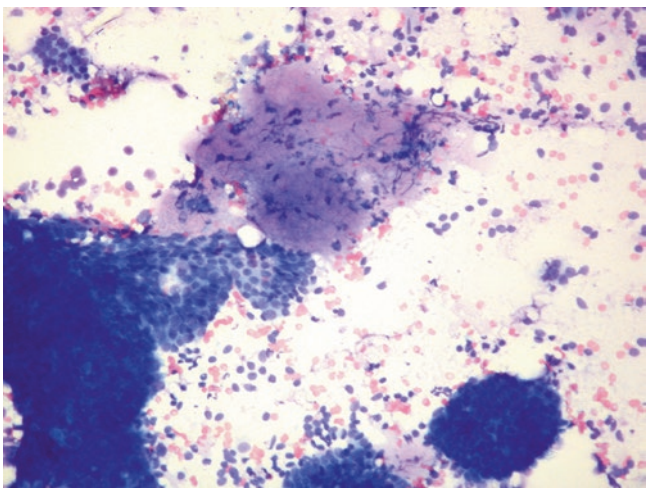

Fig. 12.17 Fibroadenoma. Large group of ductal epithelial cells with regular, round nuclei arranged in honeycomb pattern, round clover-shaped stroma, and a background of stippled round to oval nuclei of myoepithelial cells are present (MGG stain)

distinguish from a low-grade ductal carcinoma and is the most common cause of false-positive diagnosis in breast FNA cytology.

Reference: [8].

11. What are the cytomorphologic features of papillary neoplasm of the breast?

Papillary neoplasm of the breast encompasses a spectrum of benign and malignant papillary lesions: intraductal papilloma, atypical papilloma, papillary carcinoma in situ, encapsulated cystic papillary carcinoma, solid papillary carcinoma, and invasive papillary carcinoma. Clinically, papillary neoplasm presents with either symptom of nipple discharge or a subareolar solid mass. If both nipple discharge and breast mass are present, FNA of the breast mass should be performed because its sensitivity is much higher than those of nipple discharge. The cytomorphologic features of papillary neoplasm are characterized by (1) a cellular aspirate specimen; (2) three-dimensional papillary groups or tissue fragments with fibrovascular core; (3) flat sheets and cluster of epithelial cells surrounded by myoepithelial cells; (4) dispersed single or stripped nuclei of myoepithelial cells; (5) dispersed single or small cluster of uniform columnar cells; and (6) foamy histiocytes and hemosiderin-laden macrophages (Figs. 12.18, 12.19, and 12.20).

Although the presence of background myoepithelial cells and rare dispersed single columnar cells favor a diagnosis of benign papilloma and a lack of background myoepithelial cells and an increase in dispersed single columnar cells favor a diagnosis of a malignant papillary lesion, the cytological distinction of intraductal papilloma from atypical and malignant papillary lesion is unreliable. Tse et al. reported that the diagnostic accuracy was only 59% for papillary neoplasm, and there was no demonstrable quantitative difference between papilloma and papillary carcinoma using four cytological parameters: overall cellularity, epithelial cell ball

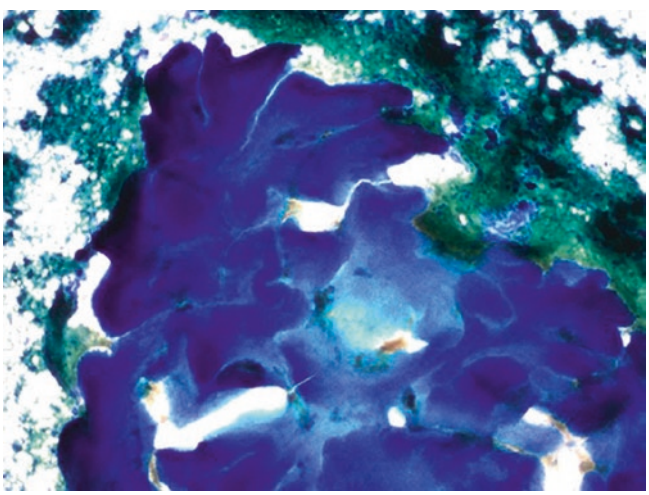

Fig. 12.18 Papillary neoplasm. Under low power, 3-D complex papillary structure is present (MGG stain)

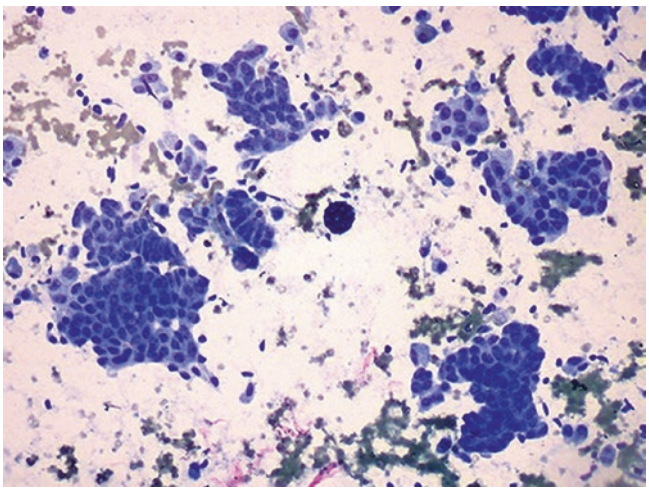

Fig. 12.19 Papillary neoplasm. Scattered small groups and single cells are present. The cells have regular round nuclei and moderate amount of cytoplasm. Occasional pigmented histiocytes are also present (MGG stain)

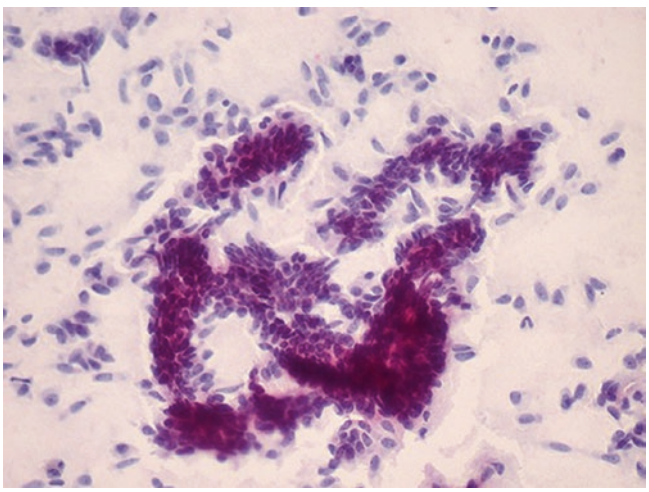

Fig. 12.20 Papillary neoplasm. Discohesive small groups of ductal epithelial cells and scattered single columnar cells are present. The cells have regular round nuclei and moderate amount of cytoplasm (MGG stain)

devoid of fibrovascular cores, background single cells, and papillary fragments and their morphology.

Fortunately, since all papillary neoplasm either papilloma or papillary carcinoma diagnosed on FNA or on core needle biopsy requires an excisional biopsy, a cytological reporting of papillary neoplasm is adequate for breast papillary lesions.

Reference: [9].

12. What are the cytomorphologic features of ductal carcinoma of the breast?

Invasive ductal carcinoma is the most common cause of malignant palpable mass of the breast, accounting for about 80% of invasive breast cancer. Ductal carcinoma in situ (DCIS) sometimes also presents as a mass lesion.

The cytomorphologic features of invasive ductal carcinoma and DCIS are basically the same, and their shared common features include (1) a hypercellular specimen; (2) loss of cohesion of ductal epithelial cells, forming loose small irregular clusters and many single isolated ductal epithelial cells; (3) absence of background myoepithelial cells; and (4) variable cytological atypia by displaying nuclear enlargement, overlapping, crowding, hyperchromatism, and pleomorphism as well as prominent nucleoli.

FNA of low-grade ductal carcinoma shows only mild nuclear atypia, small or distinct nucleoli, and discohesion of epithelial cells. As a result, false negative can occur. A recent study shows that the sensitivity of FNA is 80.9% for grade 1 ductal carcinoma and 57.1% for invasive tubular carcinoma. In contrast, FNA of high-grade ductal carcinoma usually shows marked cytological atypia and contains pleomorphic nuclei and visible mitosis (Figs. 12.21, 12.22, 12.23, and 12.24).

The presence of malignant cells embedded within adipose tissue and stroma on cytology smear was previously suggested to be a sign for invasion, but the claim is no longer accepted because malignant cells embedded in stroma could be produced by displacement from aspiration needle or by smearing artifact.

Reference: [10].

13. What are the cytomorphologic features of invasive lobular carcinoma?

Invasive lobular carcinoma accounts for less than 20% of invasive carcinoma of the breast. It can produce irregular thickening or lump of the breast. A majority of invasive lobular carcinoma is classic type, and its cytomorphologic fea-

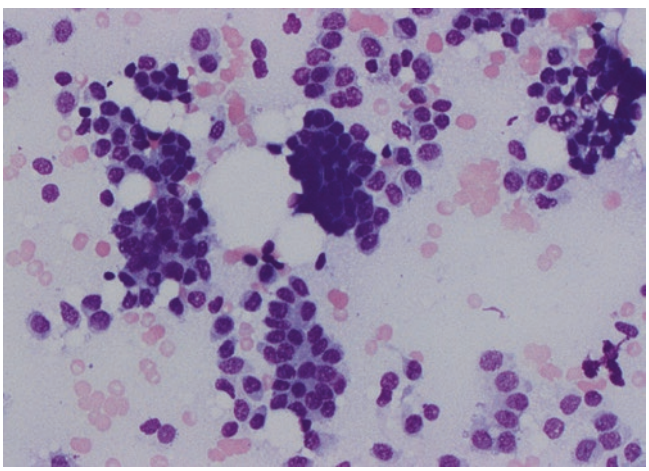

Fig. 12.21 Low-grade ductal carcinoma. A cellular cytology smear contains many discohesive ductal epithelial cells arranged in small groups and in single cell pattern. The cells display minimal cytologic atypia with regular round nuclei and indistinctive small nucleoli and small amount of pale cytoplasm. Occasional cells arranged in tubular glandular pattern are also seen (MGG stain)

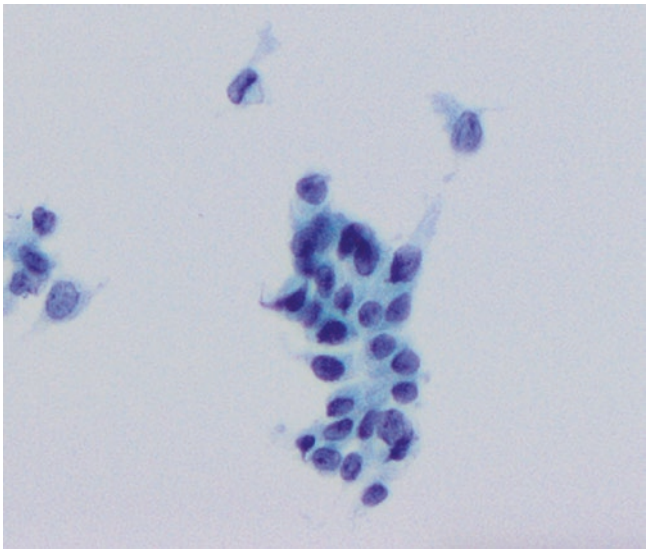

Fig. 12.22 Low-grade ductal carcinoma. ThinPrep slide shows mildly atypical cells with hyperchromatic, irregular nuclei arranged in small tubular pattern (Pap stain)

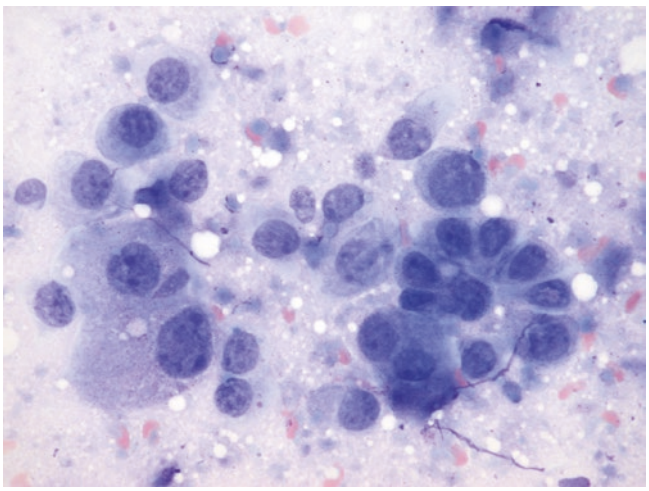

Fig. 12.23 High-grade ductal carcinoma. Discohesive small groups and single malignant cells with marked cytologic atypia are present. The cells show enlarged nuclei, variation of nuclear sizes, and crumped chromatin. Several cells display small glandular pattern (MGG stain)

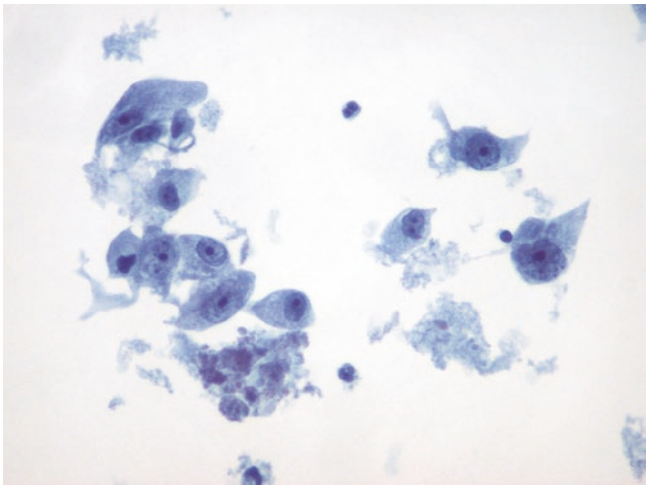

Fig. 12.24 High-grade ductal carcinoma. Markedly atypical large cells with enlarged nuclei, prominent nucleoli, and moderate amount of cytoplasm are present in the background of necrosis (Pap stain)

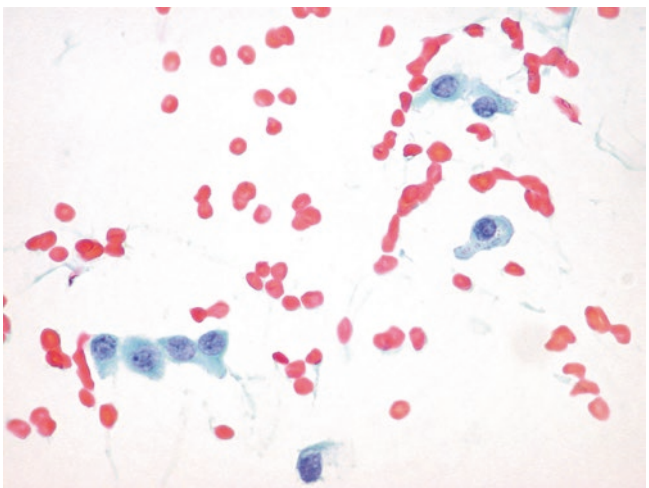

Fig. 12.25 Lobular carcinoma. Cytology smear shows discohesive epithelial cells with slightly enlarged round nuclei and moderate amount of cytoplasm present in a clean background; some of the nuclei are eccentric (Pap stain)

tures are (1) a hypocellular specimen; (2) dispersed non-cohesive single cells or small groups of cells arranged in linear shape; (3) cells with eccentric nuclei and cytoplasmic vacuoles (signet ring) or cytoplasmic vacuoles containing mucin with a central dot (targetoid) pattern; and (4) hyperchromatic nuclei with irregular outline (Figs. 12.25, 12.26, and 12.27).

FNA diagnosis of lobular carcinoma is a difficult task because it has low cellularity and minimal cytological atypia. Recent studies showed that the sensitivity of FNA of invasive lobular carcinoma is only 50% and it is much lower in classic type than in other variants of invasive lobular carcinoma. In contrast, the pleomorphic variant of invasive lobular carcinoma can be easily diagnosed because the tumor cells have significant cytological atypia, showing enlarged hyperchromatic nuclei, prominent nucleoli, nuclear pleomorphism, and moderate amount of cytoplasm with apocrine appearance.

References: [10, 11].

14. What are the cytomorphologic features of mucinous carcinoma of the breast?

Mucinous carcinoma accounts for about 2% of invasive breast carcinoma. It consists of scattered aggregates of malignant ductal epithelial cells floating within mucinous

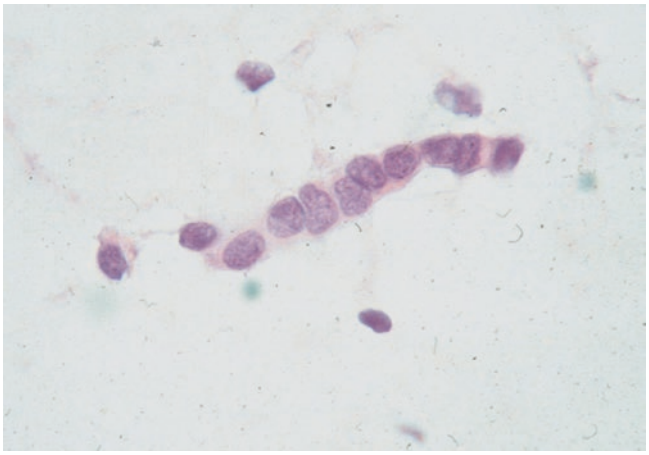

Fig. 12.26 Lobular carcinoma. Mildly atypical cells with slightly irregular nuclear outline are arranged in linear shape. A few discohesive epithelial cells are present in the background (MGG stain)

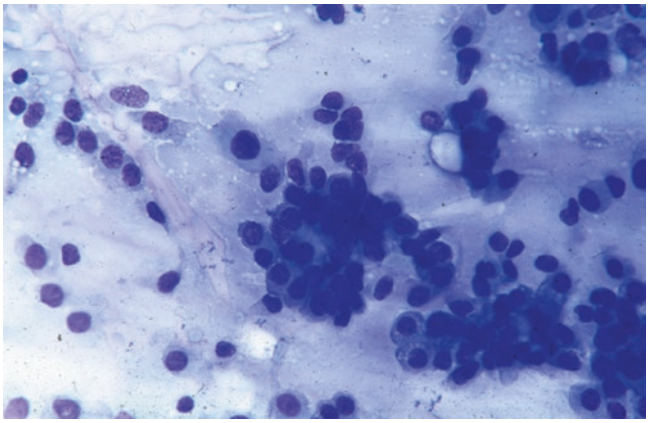

Fig. 12.28 Mucinous carcinoma. Small groups and single epithelial cells with regular round nuclei, small to moderate cytoplasm are present in a mucinous background. Some cells have stripped bare nuclei (MGG stain)

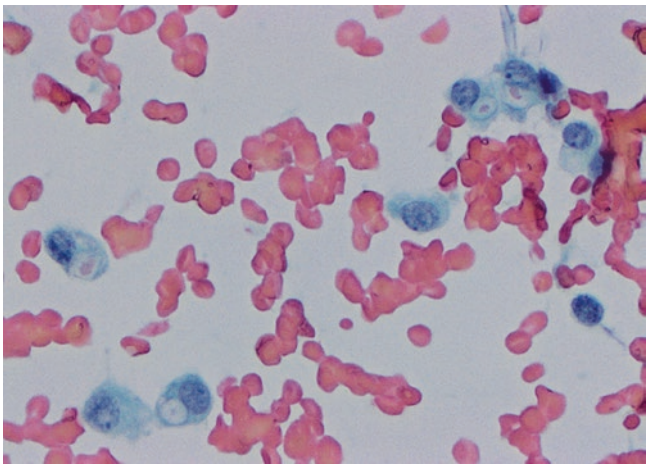

Fig. 12.27 Lobular carcinoma. Discohesive epithelial cells with slightly enlarged round eccentric nuclei and moderate amount of cytoplasm are present. Some cells contain cytoplasmic round vacuolation and have a red dot within it (targetoid pattern) (Pap stain)

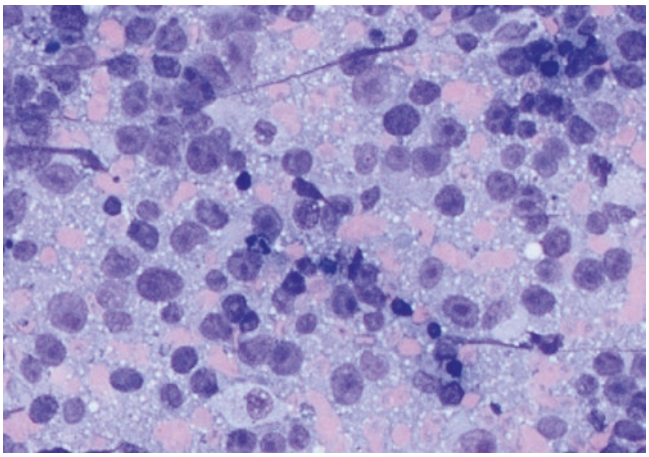

Fig. 12.29 Medullary carcinoma. A cellular cytology smear contains many dispersed stripped malignant nuclei displaying large nuclei and prominent nucleoli. A few lymphocytes are present within malignant cells (MGG stain)

pools. Clinically, the tumor usually presents as a soft, well-circumscribed palpable mass, simulating a fibroadenoma or a cyst. The cytomorphologic features of mucinous carcinoma are (1) three-dimensional clusters of ductal epithelial cells with mild cytological atypia; (2) abundant mucinous materials surrounding ductal epithelial cells; and (3) no high-grade nuclear atypia (Fig. 12.28).

Separation of pure mucinous carcinoma from mixed mucinous carcinoma on cytology specimens is difficult. It was reported that pure mucinous carcinomas have cytological features of abundant mucin, small nuclei, and/or regular nuclear outline, while mixed mucinous carcinomas have sparse mucin, large nuclei with irregular nuclear outline, or presence of nucleoli.

Reference: [12].

15. What are the cytomorphologic features of medullary carcinoma of the breast?

Medullary carcinoma accounts for about 1% of invasive breast carcinoma. It consists of aggregates of high-grade invasive ductal carcinoma surrounded by heavy lymphocytic infiltrate. Clinically, it usually presents as a soft, well-circumscribed mass simulating a fibroadenoma. The cytomorphologic features of medullary carcinoma include (1) a hypercellular aspirate; (2) single and small cluster of large malignant vesicular nuclei, prominent nucleoli, and scanty cytoplasm; (3) bizarre stripped nuclei with prominent nucleoli; and (4) numerous lymphocytes in the background (Fig. 12.29).

Because atypical medullary carcinoma and some poorly differentiated invasive ductal carcinoma of basal cell type

can mimic medullary carcinoma histologically, a cytological diagnosis of medullary carcinoma is often not possible; therefore, a cytological reporting of a "medullary-like carcinoma" is adequate, followed by an explanation note raising the possibility of a medullary carcinoma.

Reference: [13].

16. What are the cytomorphologic features of metaplastic carcinoma of the breast?

Metaplastic carcinoma of the breast accounts for less than 1% of invasive breast carcinoma. It is an invasive carcinoma with squamous cell or mesenchymal differentiation. Histologically, it has low-grade and high-grade types. The low-grade type consists of components of low-grade malignant squamous cells and spindle cells; in contrast the high-grade type consists a mixture of high-grade carcinoma and matrix-producing sarcoma. The cytomorphologic features reflect the spectrum of the metaplastic carcinoma of the breast: (1) hypocellular specimen in low-grade lesion or hypercellular specimen in high-grade lesion; (2) malignant spindle cells and squamous cells; (3) large pleomorphic malignant cells or sarcomatoid cells in high-grade lesion; and (4) malignant cartilage and bone in high-grade lesion (Figs. 12.30 and 12.31).

Reference: [14].

17. What are the cytomorphologic features of the breast implant-associated anaplastic large cell lymphoma?

Breast implant-associated anaplastic large cell lymphoma (BI-ALCL) is a newly described entity of primary breast lymphoma, occurring rarely but more commonly in women with breast implants. Patients usually present with a late-onset seroma or an effusion around implant and infrequently with a breast mass. Because of the risk associated with BI-ALCL, it is now recommended that late seroma of breast implant should be aspirated and investigated.

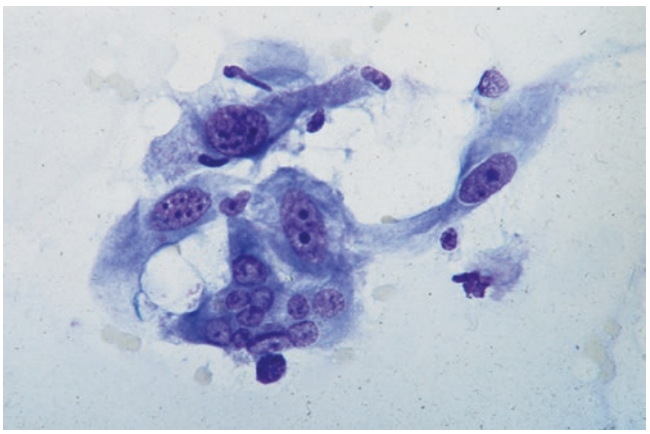

Fig. 12.30 Metaplastic carcinoma. Pleomorphic malignant spindle cells and multinucleated malignant cells are present. The cells have round to elongated nuclei and abundant blue cytoplasm, displaying squamous differentiation or squamoid appearance

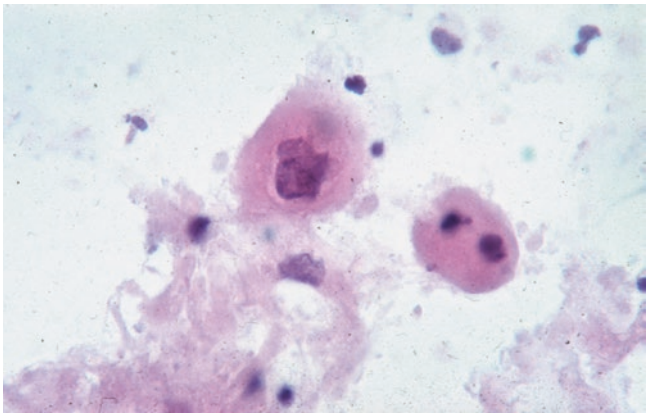

Fig. 12.31 Metaplastic carcinoma. Two cells of atypical chondrocytes are present. The cells have pink dense cytoplasm, sharp cell outline, and dark-stained irregular nuclei

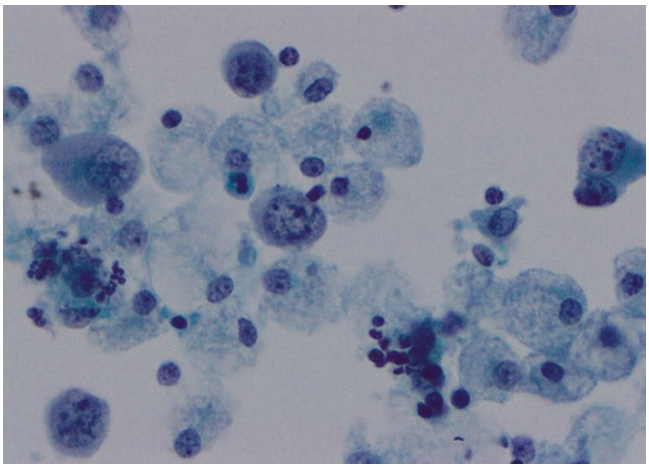

Fig. 12.32 Breast implant-associated anaplastic large cell lymphoma. The ThinPrep cytology slide shows some dispersed large malignant cells containing enlarged hyperchromatic round nuclei and small to moderate amount of basophilic cytoplasm, foamy histiocytes, and other chronic inflammatory cells (Pap stain)

The cytomorphologic features of BI-ALCL are (1) cellular specimens; (2) non-cohesive large pleomorphic cells with irregular, lobulated nuclei, prominent nucleoli, and basophilic cytoplasm; and (3) a background of variable inflammatory cells (Figs. 12.32 and 12.33).

Cell block is useful for the diagnosis and differential diagnoses of BI-ALCL which include chronic inflammation, poorly differentiated carcinoma, and other lymphomas. Tumor cells of BI-ALCL show strongly and diffusely positive staining for CD30 and EMA, variable positive staining for CD4 and CD45 but negative for ALK and cytokeratin. A majority of tumor demonstrate T-cell receptor gene rearrangement.

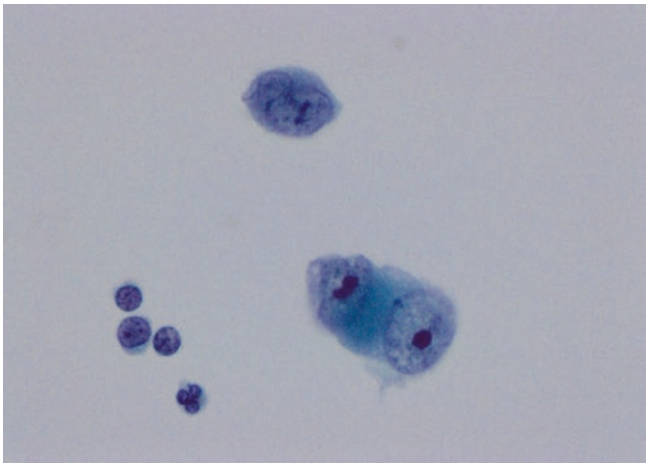

Fig. 12.33 Breast implant-associated anaplastic large cell lymphoma. Two binucleated large cells with abundant cytoplasm are present. One of the large cells has the "Reed-Sternberg" cell or Hodgkin cell-like appearance (Pap stain)

Once ALCL is diagnosed on cytology specimens, systemic ALCL and cutaneous ALCL also need to be ruled out using patient's clinical history and axillary tests.

Patients diagnosed with BI-ALCL in breast effusion/seroma cytology specimens need to have immediate removal of implant and excision of the fibrous capsule around the implant.

References: [15, 16].

18. What are the limitations of FNA cytology of the breast? What is the triple test?

There are three limitations that exist in breast FNA cytology. First, it is the inadequate cytological sample, frequently due to FNA performed by inexperienced or inadequately trained aspirators and infrequently due to sclerotic breast lesions such as sclerotic fibroadenoma, sclerosis adenosis, radial scar, and invasive lobular carcinoma. Second, it is the cytological borderline lesions of the breast, which poses a diagnostic hardship even for the most experienced cytopathologists. The challenges of borderline lesions include "atypical" fibroadenomas, various papillary lesions, atypical ductal hyperplasia, low-grade carcinoma, and others. Third, cytologically it is impossible to separate DCIS from invasive ductal carcinoma.

Because of the limitations of breast FNA cytology, triple test has been applied to improve the diagnostic accuracy. Triple test is the consideration of results from three parameters: clinical, radiologic, and cytological. Besides cytological results, clinical history, and physical examination, imaging results from ultrasound and/or mammography and/or MRI should also be considered before rendering a cytological diagnosis. If any of the three parameters is positive, triple test is positive. If all of the three parameters are negative, triple test is negative. Triple test has a sensitivity of 99.6% and specificity of 93%.

19. What are the common pitfalls of FNA cytology of the breast? When is the "atypical" category used for reporting breast cytology?

Recognizing common pitfalls of FNA cytology of the breast could prevent cytopathologists from making false-negative and false-positive diagnoses. False-negative diagnosis occurs due to inadequate sampling or sampling error, or due to interpretation error. Certain carcinomas (e.g., invasive lobular carcinoma, low-grade metaplastic carcinoma) and low-grade carcinoma (e.g., low-grade ductal carcinoma, invasive tubular carcinoma, and invasive mucinous carcinoma) are the common sources of interpretation error. False-positive diagnosis occurs in "atypical" fibroadenoma, atypical ductal hyperplasia, and lactating adenoma and rarely in fat necrosis.

Atypical category (C3) based on NCI reporting of breast cytology accounts for about 5% of FNA cytology specimens and reveals about 30–40% of malignancy in the follow-up histology. However, there are significant inter-observer and intra-observer variations of atypical cytological diagnosis. Masood and others reported using Masood Score Index (MSI) and Modified Masood Score Index (MMSI) to quantitatively assess six cytological parameters to define cytological atypia. As shown in Fig. 12.14, an MSI score of 15–18 was considered proliferative breast disease with atypia. Recently, IAC Breast Group attempted to define the use of atypia in the following scenarios: (1) epithelial hyperplasia with marked dispersed often columnar cells but minimal nuclear atypia (differential diagnosis is epithelial hyperplasia or low-grade DCIS); (2) intraductal papillomas with diagnostic stellate papillary fragments but again marked dispersal of cells (differential diagnosis is low-grade DCIS); (3) epithelial hyperplasia with more complex possibly cribriform or micropapillary tissue fragments (differential diagnosis is low-grade DCIS); (4) stromal hypercellularity without nuclear atypia or necrosis in the otherwise typical fibroadenoma raising a possibility of a low-grade phyllodes tumor; and (5) low cellularity smears with minute epithelial tissue fragments and single cells showing eccentric cytoplasm that raise a concern for lobular carcinoma.

References: [2, 6, 7, 11, 17–21].

20. How is FNA cytology of axillary lymph node interpreted?

Preoperative FNA of the axillary lymph node is performed for both diagnostic and triage purposes. For women with a suspicious breast mass and suspicious axillary lymph node, aspiration of axillary lymph node at the same time could provide not only a cytological diagnosis but also information for decision on axillary sentinel lymph node biopsy procedure. Because FNA of axillary lymph node has a very low false-positive rate (<1.5%), women with a positive cytology diagnosis of axillary lymph node will bypass the procedure of axillary sentinel lymph node biopsy and directly receive axillary lymph node dissection. In some institutions, rapid

on-site assessment of cytology smear of FNA of axillary lymph node is performed at the time of the breast surgery.

The cytomorphology of a positive axially lymph node is almost similar to adenocarcinoma metastatic to a lymph node: (1) a hypercellular specimen; (2) epithelial groups or single epithelial cells with cytological atypia; and (3) a background of small mature lymphocytes and small lymphohistiocytic aggregate. In cell block, the metastatic carcinoma can be further confirmed by immunostaining using ER, GATA-3, or keratin antibodies.

Reference: [22].

21. What are the cytological diagnoses of nipple discharge?

Cytology of nipple discharge does not involve FNA procedure. The specimen is prepared from touching the droplet of nipple secretion/discharge on to the surface of a glass slide and making cytology smears.

Nipple discharge occurs in physical conditions from hormonal imbalance and also in breast neoplasms, such as intraductal papillary lesions and ductal carcinoma. Bilateral nipple discharge of milky, serous fluid is more commonly associated with hormonal effect, while unilateral nipple discharge of bloody fluid is more likely associated with a neoplastic breast lesion, especially an intraductal papillary lesion.

The cytomorphology of nipple discharge due to hormonal effect includes (1) a hypocellular smear; (2) foamy histiocytes; and (3) background of inflammatory cells and/or red blood cells (Fig. 12.34).

The cytomorphology of nipple discharge due to intraductal papillary lesions includes (1) a hypocellular smear; (2) single and small three-dimensional clusters of ductal epithelial cells with mild cytological atypia; and (3) background of inflammatory cells and/or red blood cells (Fig. 12.35).

A cytological reporting of "suspicious for papillary neoplasm" is warranted for such lesion, which will lead to an excisional biopsy.

The cytomorphology of nipple discharge caused by ductal carcinoma is similar to those of ductal carcinoma: (1) a cellular smear; (2) dispersed single and small clusters of ductal epithelial cells with marked cytological atypia; and (3) necrotic debris and/or red blood cells (Fig. 12.36).

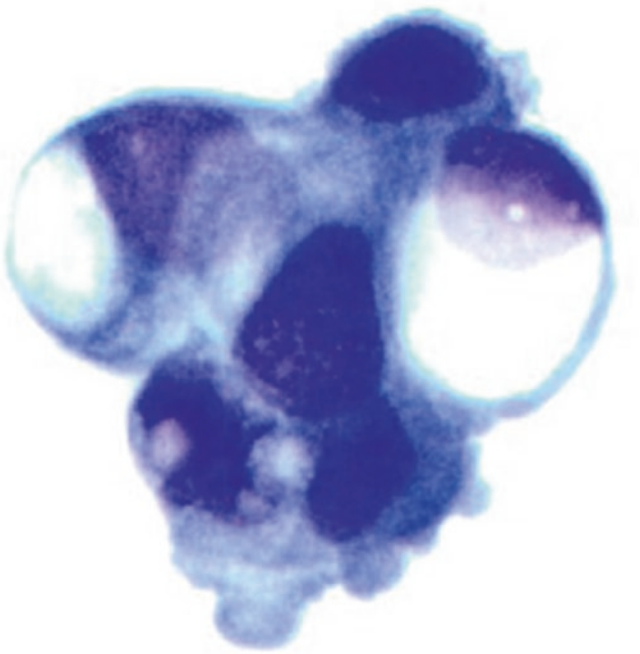

Fig. 12.35 Nipple discharge. A hypocellular specimen contains a small papillary cluster of ductal epithelial cells with mild nuclear atypia and cytoplasmic vacuolation (MGG)

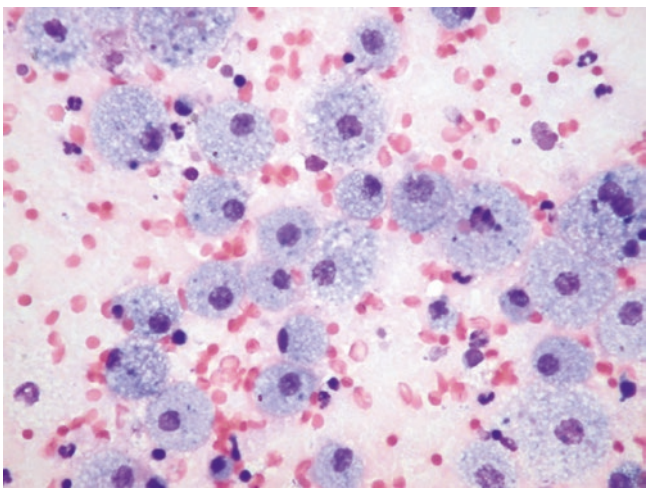

Fig. 12.34 Nipple discharge. Many foamy histiocytes containing small round nuclei and abundant foamy cytoplasm are present in the cytology smear (MGG stain)

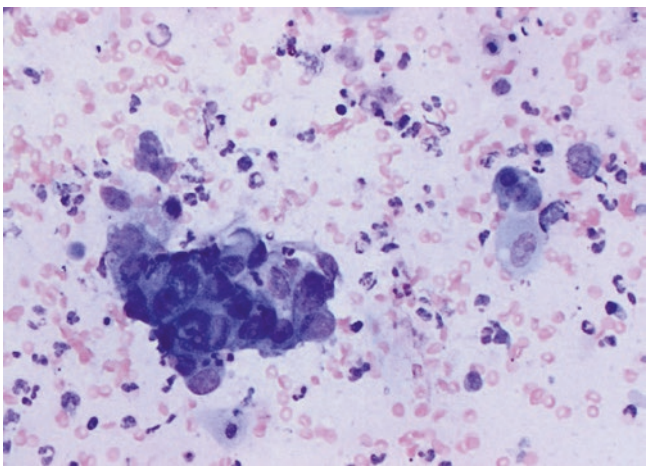

Fig. 12.36 Nipple discharge. A rather cellular cytology smear contains several dispersed single cells and a small 3-D cluster of cells displaying nuclear crowding, overlapping, and variation of nuclei. The background shows necrotic debris and inflammatory cells (MGG)

22. How is the cell block of breast FNA cytology specimens used to assist diagnosis?

A cell block could be applied to assist cytological diagnoses, as it reveals histologic/architectural pattern in borderline lesions and enables immunocytochemistry testing in a way similar to those used for histology specimens.

To differentiate atypical hyperplasia or low-grade DCIS from usual ductal hyperplasia, including differentiating a malignant papillary lesion from intraductal papilloma with usual ductal hyperplasia, cytopathologists could use the cell block to perform immunostain using ER and high molecular weight keratin such as CK5/6 and CK34beta. Cells of atypical hyperplasia or low-grade DCIS show diffusely and strongly positive staining for ER and negative staining for high molecular weight keratin; in contrast cells of usual hyperplasia show patchy positive staining for ER and diffusely and strongly positive staining for high molecular weight keratin.

To differentiate in situ carcinoma from invasive carcinoma including separating papillary carcinoma in situ from invasive papillary carcinoma, cytopathologists could also use the cell block to perform immunostain using p63, heavy-chain smooth muscle actin, and CK5/6 to demonstrate the presence or absence of the myoepithelial cell layer. For example, a papillary lesion with an intact basal layer of myoepithelial cell is considered a benign intraductal papilloma (Figs. 12.37 and 12.38).

Cell block could also be used to differentiate invasive ductal carcinoma from invasive lobular carcinoma by E-cadherin immunostain.

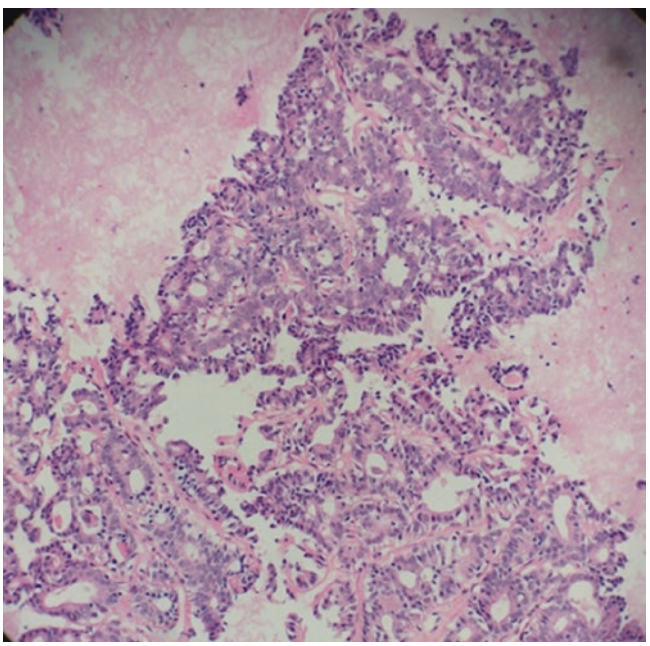

Fig. 12.37 Cell block of an atypical cytology smear was prepared, and the H& E slide shows a cellular lesion, raising a concern for papillary lesions or adenosis or others

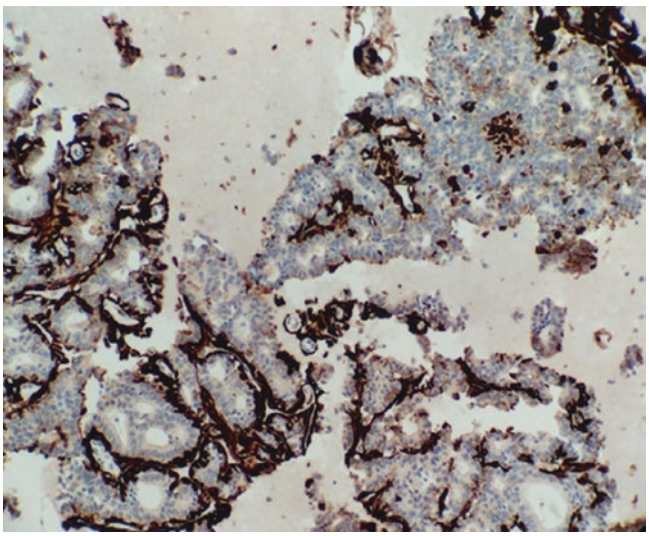

Fig. 12.38 p63 and heavy-chain myosin double staining highlights the basal cell layer of the lesion, indicating that this is a benign tumor

Cell block is frequently used to differentiate primary from metastatic carcinoma. To confirm the breast primary, ER, GATA-3, GCDFP-15, and mammaglobin antibodies have been used. Recent studies showed that GATA-3 is the most sensitive marker for breast carcinoma, being 100% positive in ER-positive breast carcinoma and positive in some triple negative breast carcinoma in cell block cytology specimens. Because GATA-3 is negative in ER-positive gynecologic cancer, a panel of GATA-3 and ER offers the most sensitive and specific conformation test for a primary breast carcinoma.

References: [23, 24].

23. Could we use FNA cytological specimens for ER, PR, and Her2 testing and for other predictive marker testing?

Breast FNA cytology specimen is a good source of material for breast biomarker testing when the specimen is adequately fixed and well prepared. Testing of ER, PR, and Her2 has been reported in a variety of cytology specimens including air-dried cytology smear without fixation, alcohol-fixed cytology smear, alcohol- or formalin-fixed cytospin specimen, alcohol-fixed liquid-based cytology slides, and cell block made from cells fixed in alcohol or formalin. The concordance of ER between immunocytochemistry and immunohistochemistry is highest in cell block specimens followed by cytospin and liquid-based cytology slides and lowest in air-dried cytology smear. Therefore, for biomarker testing especially ER testing, cell block made of cells fixed in formalin is the specimen of choice, offering highest concordance (98%) to the histologic specimens.

Although Her2 testing using immunocytochemistry is not recommended unless it is done using cell block made of

formalin-fixed cells, Her2 FISH testing could be performed using various cytology specimens because the procedure is not fixation dependent.

One of the drawbacks of using cytology specimens for breast biomarker testing is that malignant cells of invasive carcinoma and DCIS cannot be separated in the testing; therefore, breast biomarker testing using cytology specimens is only recommended for metastatic carcinoma or recurrent invasive carcinoma and is not for preoperative primary carcinoma of the breast.

Testing of Ki-67 of breast cancer on cytology specimens is not recommended because of its low concordance to immunohistochemistry, and its clinical value still awaits further confirmation.

Recently, rapid development in targeted therapy and immunotherapy for cancer treatment has called for new genetic testing and new molecular marker testing of breast cancer. FNA from breast is a good source of material for these new genetic and molecular testing.

References: [25, 26].

Case Presentation

Case 1

Clinical History

A 21-year-old college student noticed a lump in her right breast 2 weeks ago. On physical examination, the lump was mobile, firm, and well circumscribed. Mammogram showed a 2 cm well-defined mass and reported a benign BIRAD 2 lesion. Because of her anxiety, the patient was referred to FNA clinic for breast FNA.

Cytomorphologic Findings

Under the low power, the MGG-stained cytology smear displays branching fragments and groups of ductal epithelial cells, stromal fragments with a broad round smooth border surrounded by ductal epithelial cells, and scattered stripped naked nuclei in the background. Under the high power, ductal epithelial cells show mild nuclear crowding, nuclear variation in sizes and shapes, and focal distinct nucleoli. A few small darkly stained nuclei of myoepithelial cell are present with the cell group (Figs. 12.39 and 12.40).

Differential Diagnosis

Fibroadenoma
Phyllodes tumor
Well-differentiated ductal carcinoma
Papilloma

Final Diagnosis: Fibroadenoma

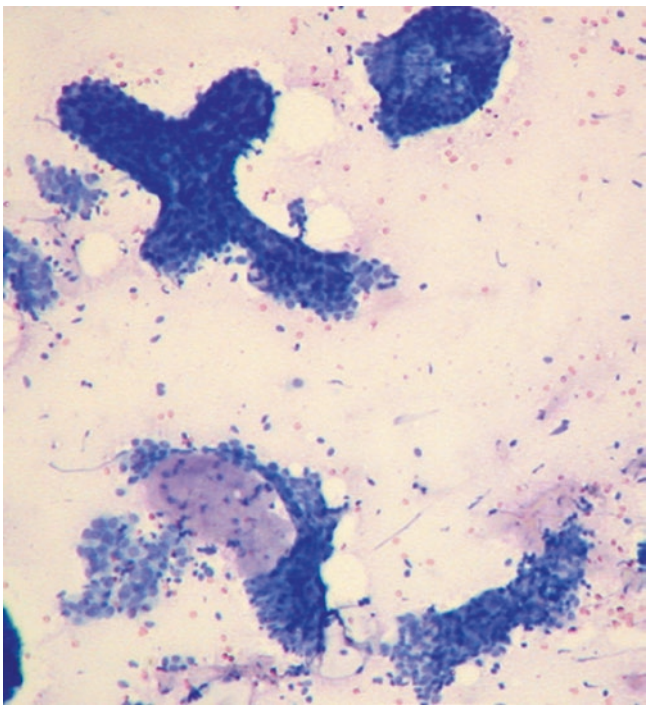

Fig. 12.39 Cytology smear of breast FNA of the 21-year-old college student displays, under the low power, branching fragments and groups of ductal epithelial cells, stromal fragments with a broad round smooth border, and scattered single naked nuclei in the background (Case 1, MGG stain)

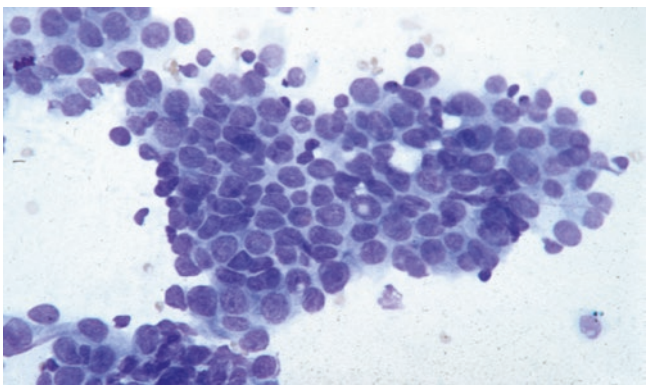

Fig. 12.40 Cytology smear of breast FNA of the 21-year-old college student shows, under the high power, ductal epithelial cells with mild nuclear crowding, mild variation in nuclear sizes and shapes, and focal distinct nucleoli (Case 1, MGG stain)

Case 2

Clinical History

A 45-year-old woman presents with a painless, slow-growing lump in her left breast for 6 months. Physical examination reveals a 3.5 cm well-circumscribed firm mass in left low quatrant of her

breast. There is no axillary lymphadenopathy. Mammogram showed a well-defined mass and suggested a benign tumor. FNA of the breast mass was performed.

Cytomorphologic Findings

Under the low power, the MGG-stained cytology smear reveals a multibranching 3-D structure or group of ductal epithelial cells and scattered single cells in the background. Under high power, both MGG-stained slide and ThinPrep cytology slide contain dispersed small groups or single columnar cells. A few columnar cells are arranged in strips. Occasional hemosiderin-laden macrophages are present in the background. A cell block was prepared which contains small fragments of tissue showing a hyalinized fibrovascular core surrounded by a sheet of monotonous ductal epithelial cells (Figs. 12.41, 12.42, 12.43, and 12.44).

Differential Diagnosis

Fibroadenoma
Invasive lobular carcinoma
Papillary neoplasm

Final Diagnosis: Papillary Neoplasm

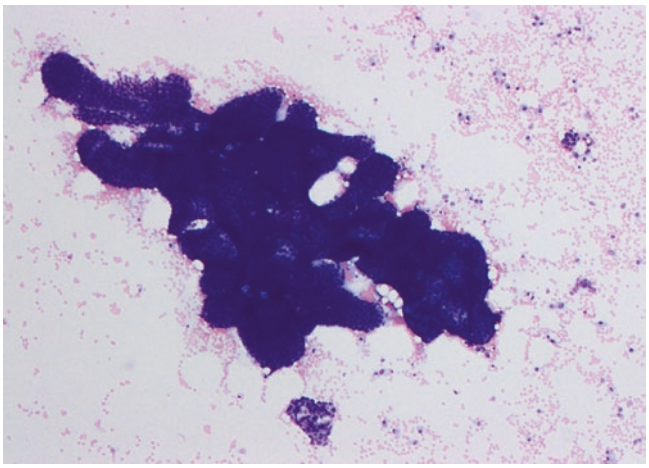

Fig. 12.41 Cytology smear of breast FNA of the 45-year-old woman reveals, under the low power, a multibranching 3-D structure of ductal epithelial cells and scattered single cells in the background (Case 2, MGG stain)

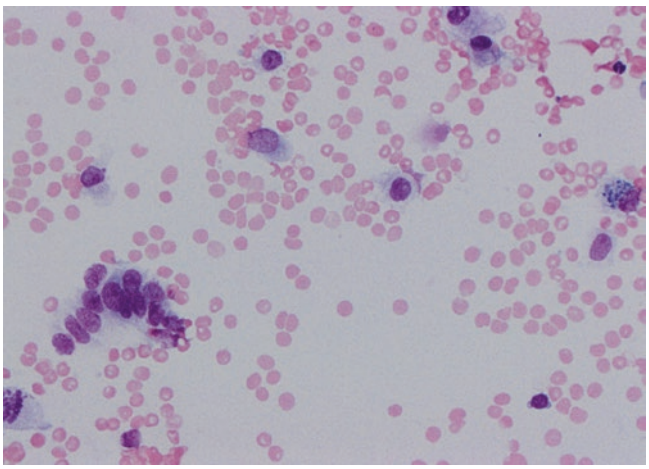

Fig. 12.42 Cytology smear of breast FNA of the 45-year-old woman displays, under the high power, scattered small strips and single columnar cells. Occasional hemosiderin-laden macrophages are present in the background (Case 2, MGG stain)

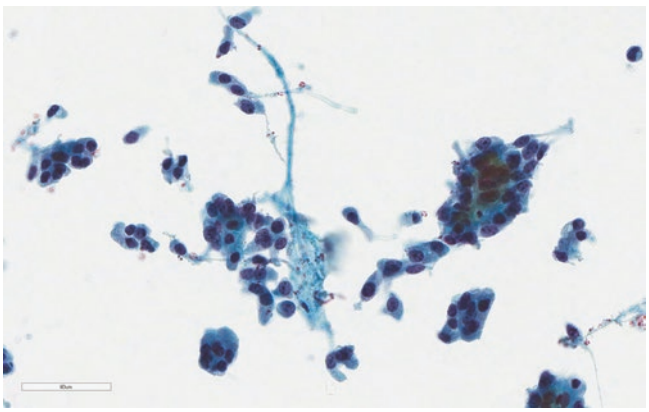

Fig. 12.43 ThinPrep cytology slide of breast FNA of the 45-year-old woman exhibits a cellular specimen containing small groups and single columnar cells. The ductal cells have moderate amount of cytoplasm, round to oval nuclei with mild nuclear crowding, and occasional distinct nucleoli (Case 2, Pap stain)

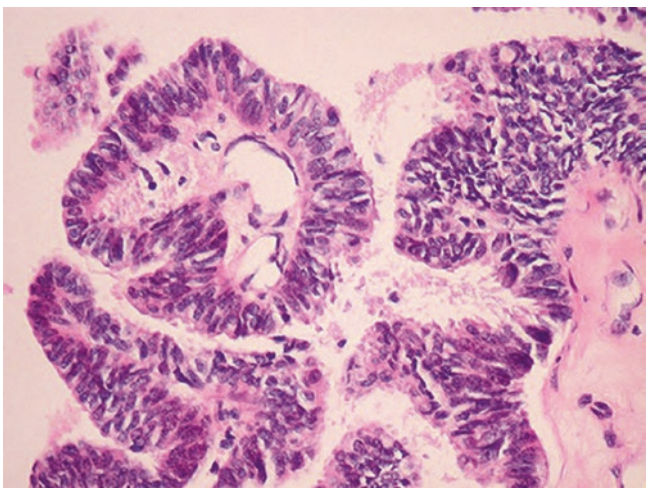

Fig. 12.44 Cell block made from the breast FNA of the 45-year-old woman contains small fragments of tissue showing a hyalinized fibrovascular core surrounded by monotonous stratified columnar ductal epithelial cells (Case 2, H/E stain)

Case 3

Clinical History

A 42-year-old nurse told her family doctor that she might have fibrocystic disease of the breast because she felt a small soft cystic nodule in her right breast for the past 5 months. The nodule was painless and slow growing. Physical examination showed a 1.2 cm soft well-circumscribed mass. Ultrasound showed a hypoechoic lesion. A FNA was performed trying to drain the "cyst."

Cytomorphologic Findings

Under the low power, MGG-stained cytology smear reveals many blue staining pools of mucin. Some groups of ductal epithelial cells are "buried" with the pools of mucin. Under high power, MGG-stained cytology slide reveals small groups of ductal epithelial cells that are closely associated with mucin. The cells have small nuclei, indistinct nucleoli, mild nuclear crowding, and focal irregular nuclear outline (Figs. 12.45 and 12.46).

Differential Diagnosis

Apocrine cyst
Fibroadenoma
Invasive mucinous carcinoma

Final Diagnosis: Invasive Mucinous Adenocarcinoma

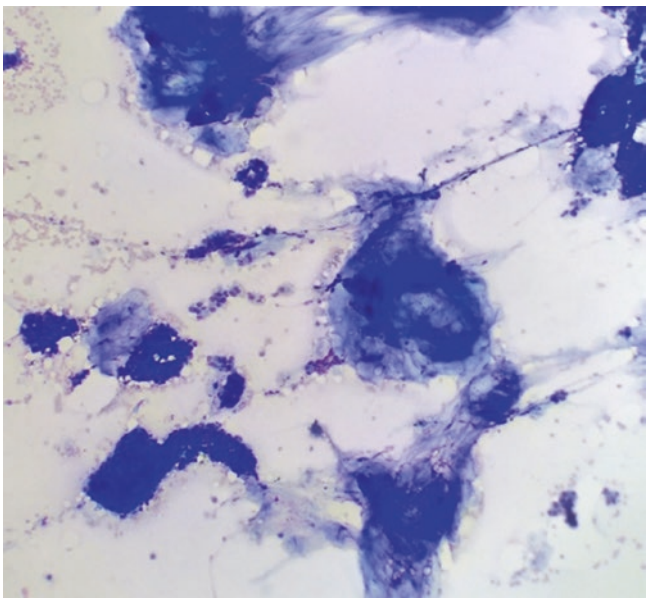

Fig. 12.45 Cytology smear of breast FNA of the 42-year-old nurse exhibits, under the low power, many blue staining pools of mucin; some have groups of ductal epithelial cells "buried" with them (Case 3, MGG stain)

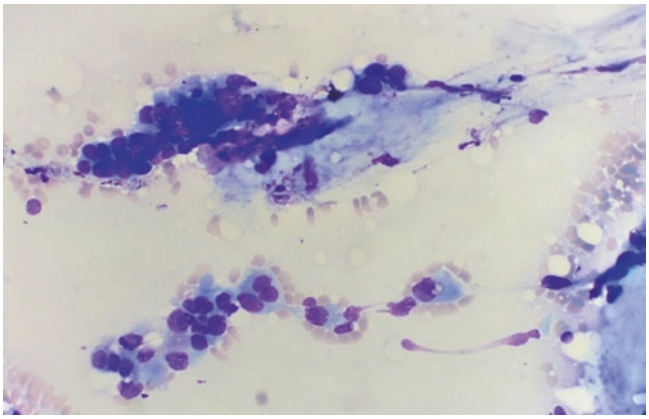

Fig. 12.46 Cytology smear of breast FNA of the 42-year-old nurse displays, under the high power, small groups of ductal epithelial cells closely associated with mucin. The cells have small nuclei, mild nuclear crowding, and focal irregular nuclear outline (Case 3, MGG stain)

Case 4

Clinical History

A 68-year-old woman with a past history of right breast carcinoma treated with surgical excision and chemotherapy 10 years ago now presents with a small subcutaneous nodule in her right upper chest wall. The nodule is 0.5 cm, painless, and firm. The patient also had a history of basal cell carcinoma on her face and melanoma in situ in her left arm diagnosed a year ago. The subcutaneous nodule is aspirated.

Cytomorphologic Findings

ThinPrep cytology slide shows many scattered isolated large atypical cells containing eccentric round nuclei, occasional binucleation, and abundant cytoplasm. The cells have somewhat "plasmacytoid" appearance but do not have prominent nucleoli. The H&E slide of cell block contains similar "plasmacytoid" cells, but a few cells also have signet ring cell appearance. Immunostaining was performed using the cell block, and the tumor cells show positive staining for ER (Figs. 12.47, 12.48, and 12.49).

Differential Diagnosis

Melanoma
Recurrent breast carcinoma
Plasma cell-rich skin lesions

Final Diagnosis: Recurrent Breast Carcinoma

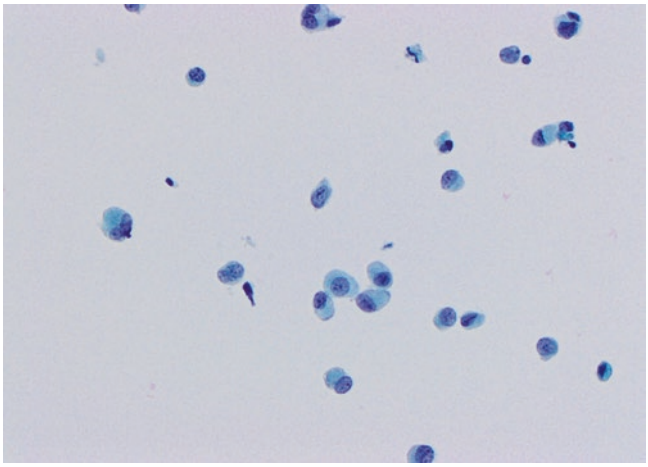

Fig. 12.47 ThinPrep cytology slide of breast FNA of the 68-year-old woman shows many scattered isolated large atypical cells containing eccentric round nuclei, occasional binucleation, and abundant cytoplasm, having somewhat "plasmacytoid" appearance (Case 4, Pap stain)

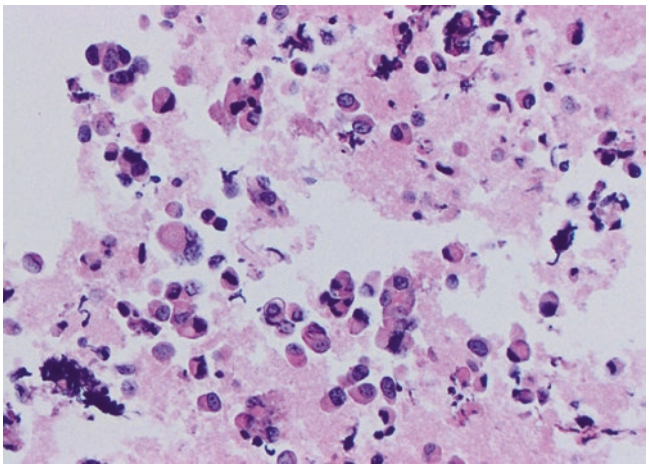

Fig. 12.48 Cell block made from the breast FNA of the 68-year-old woman contains many large atypical "plasmacytoid" cells and a few signet ring-like cells (Case 4, H/E stain)

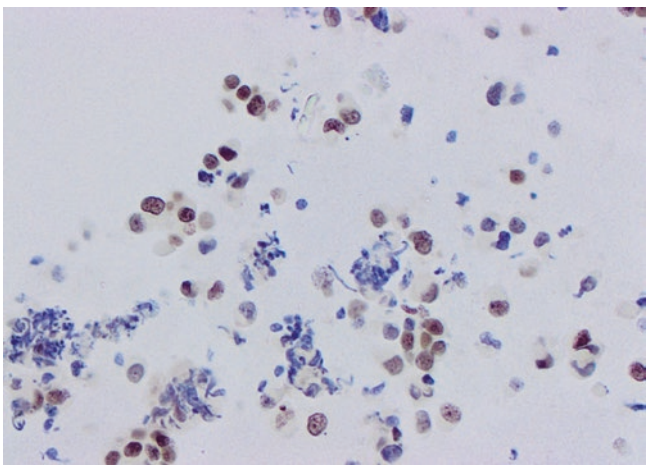

Fig. 12.49 Immunohistochemistry (IHC) performed on the cell block of the breast FNA of the 68-year-old woman shows that the nuclei of the cells are stained positively for ER (Case 4, IHC stain)

Case 5

Clinical History

In follow-up visit, a 60-year-old woman presents with a small solid mass at the site of her previous left breast lumpectomy performed 9 months ago for an invasive ductal carcinoma. Physical examination shows a 1.5 cm hard mass at the edge of previous surgical site. Clinically recurrent breast carcinoma is suspected and a FNA is performed

Cytomorphologic Findings

Both MGG-stained and Pap-stained cytology smears display multinucleated giant cells containing several round to irregular nuclei, distinct nucleoli, and abundant foamy cytoplasm. The Pap cytology smear also contains several small aggregate and isolated cells; some have round nuclei and prominent nucleoli (Figs. 12.50 and 12.51).

Differential Diagnosis

Fibrous scar
Recurrent carcinoma
Fat necrosis

Final Diagnosis: Fat Necrosis

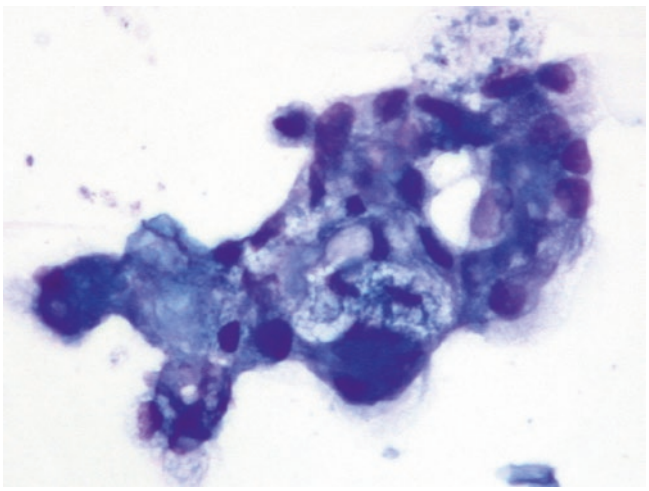

Fig. 12.50 Cytology smear of breast FNA of the 60-year-old woman displays multinucleated giant cells containing multiple round to irregular nuclei, distinct nucleoli, and foamy cytoplasm (Case 5, MGG stain)

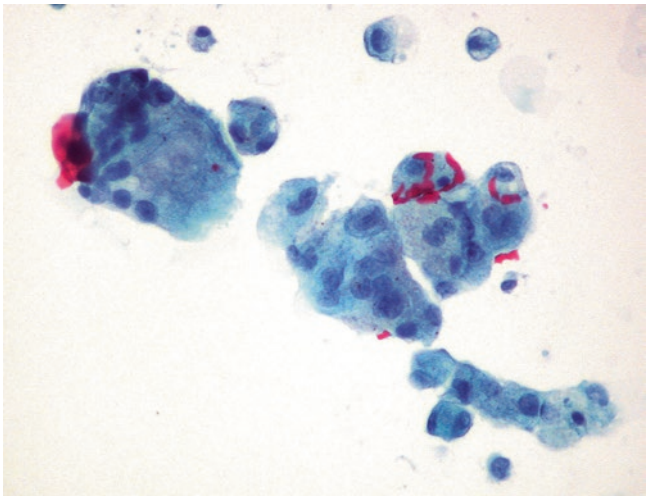

Fig. 12.51 ThinPrep cytology slide of breast FNA of the 60-year-old woman shows some multinucleated giant cells and scattered histiocytes. The giant cells contain multiple round pale stained nuclei with mild nuclear crowding, focal distinct nucleoli, and abundant foamy cytoplasm (Case 4, Pap stain)

References

1. NCI. The uniform approach to breast fine-needle aspiration biopsy. National Cancer Institute Fine-Needle Aspiration of Breast Workshop Subcommittees. Diagn Cytopathol. 1997;16(4):295–311.
2. Field AS, Schmitt F, Vielh P. IAC standardized reporting of breast fine-needle aspiration biopsy cytology. Acta Cytol. 2017;61(1):3–6.
3. Yu YH, Wei W, Liu JL. Diagnostic value of fine-needle aspiration biopsy for breast mass: a systematic review and meta-analysis. BMC Cancer. 2012;12:41.
4. Masood S, Vass L, Ibarra JA Jr, Ljung BM, Stalsberg H, Eniu A, et al. Breast pathology guideline implementation in low- and middle-income countries. Cancer. 2008;113(8 Suppl):2297–304.
5. Gerhard R, Schmitt FC. Liquid-based cytology in fine-needle aspiration of breast lesions: a review. Acta Cytol. 2014;58(6):533–42.
6. Masood S. Cytomorphology of fibrocystic change, high-risk proliferative breast disease, and premalignant breast lesions. Clin Lab Med. 2005;25(4):713–31, vi.
7. Nandini NM, Rekha TS, Manjunath GV. Evaluation of scoring system in cytological diagnosis and management of breast lesion with review of literature. Indian J Cancer. 2011;48(2):240–5.
8. Jing X, Normolle D, Michael CW. Fine-needle aspiration of gray zone lesions of the breast: fibroadenoma versus ductal carcinoma. Diagn Cytopathol. 2013;41(9):806–11.
9. Tse GM, Ma TK, Lui PC, Ng DC, Yu AM, Vong JS, et al. Fine needle aspiration cytology of papillary lesions of the breast: how accurate is the diagnosis? J Clin Pathol. 2008;61(8):945–9.
10. Karimzadeh M, Sauer T. Diagnostic accuracy of fine-needle aspiration cytology in histological grade 1 breast carcinomas: are we good enough? Cytopathology. 2008;19(5):279–86.
11. Madubogwu CI, Ukah CO, Anyanwu S, Chianakwana GU, Onyiaorah IV, Anyiam D. Sub-classification of breast masses by fine needle aspiration cytology. Eur J Breast Health. 2017;13(4):194–9.
12. Cyrta J, Andreiuolo F, Azoulay S, Balleyguier C, Bourgier C, Mazouni C, et al. Pure and mixed mucinous carcinoma of the breast: fine needle aspiration cytology findings and review of the literature. Cytopathology. 2013;24(6):377–84.
13. Racz MM, Pommier RF, Troxell ML. Fine-needle aspiration cytology of medullary breast carcinoma: report of two cases and review of the literature with emphasis on differential diagnosis. Diagn Cytopathol. 2007;35(6):313–8.
14. Sood N, Soin N, Gupta R, Gupta S. Metaplastic carcinoma of the breast: a diagnostic challenge on fine needle aspiration cytology. Cytopathology. 2019;30:253–5.
15. Xu J, Wei S. Breast implant-associated anaplastic large cell lymphoma: review of a distinct clinicopathologic entity. Arch Pathol Lab Med. 2014;138(6):842–6.
16. Di Napoli A, Pepe G, Giarnieri E, Cippitelli C, Bonifacino A, Mattei M, et al. Cytological diagnostic features of late breast implant seromas: from reactive to anaplastic large cell lymphoma. PLoS One. 2017;12(7):e0181097.
17. Scarpa Carniello JV, Pareja F, Santos-Zabala ML, Edelweiss M. Diagnostic dilemmas and pitfalls in ThinPrep((R)) cytology of breast fine needle aspiration biopsy: report of six cases with histological correlates. Diagn Cytopathol. 2017;45(7):655–61.
18. Arul P, Masilamani S. Application of National Cancer Institute recommended terminology in breast cytology. J Cancer Res Ther. 2017;13(1):91–6.
19. Yu SN, Li J, Wong SI, Tsang JYS, Ni YB, Chen J, et al. Atypical aspirates of the breast: a dilemma in current cytology practice. J Clin Pathol. 2017;70(12):1024–32.
20. Weigner J, Zardawi I, Braye S. The true nature of atypical breast cytology. Acta Cytol. 2013;57(5):464–72.
21. Smith MJ, Heffron CC, Rothwell JR, Loftus BM, Jeffers M, Geraghty JG. Fine needle aspiration cytology in symptomatic breast lesions: still an important diagnostic modality? Breast J. 2012;18(2):103–10.
22. Ciatto S, Brancato B, Risso G, Ambrogetti D, Bulgaresi P, Maddau C, et al. Accuracy of fine needle aspiration cytology (FNAC) of axillary lymph nodes as a triage test in breast cancer staging. Breast Cancer Res Treat. 2007;103(1):85–91.
23. Braxton DR, Cohen C, Siddiqui MT. Utility of GATA3 immunohistochemistry for diagnosis of metastatic breast carcinoma in cytology specimens. Diagn Cytopathol. 2015;43(4):271–7.
24. Deftereos G, Sanguino Ramirez AM, Silverman JF, Krishnamurti U. GATA3 immunohistochemistry expression in histologic subtypes of primary breast carcinoma and metastatic breast carcinoma cytology. Am J Surg Pathol. 2015;39(9):1282–9.
25. Schmitt F, Vielh P. Fine-needle aspiration cytology samples: a good source of material for evaluating biomarkers in breast cancer. Histopathology. 2015;66(2):314–5.
26. Acs B, Szekely N, Szasz AM, Lotz G, Szekely T, Istok R, et al. Reliability of immunocytochemistry and fluorescence in situ hybridization on fine-needle aspiration cytology samples of breast cancers: a comparative study. Diagn Cytopathol. 2016;44(6):466–71.