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Breast Fine Needle Aspiration Biopsy: Prevailing Recommendations and Contemporary Practices	631
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In 1996, a National Cancer Institute conference was held in Bethesda, Maryland to define parameters for the practice of breast fine needle aspiration (BFNA). Representatives of the American Society of Cytopathology, Papanicolaou Society of Cytopathology, American College of Radiology, American College of Obstetricians & Gynecologists, Society of Surgical Oncology, American Academy of Family Physicians, College of American Pathologists, National Consortium of Breast Centers, International Academy of Cytology, American Society of Clinical Pathologists, American Cancer Society, American College of Surgeons, and American Society for Cytotechnology developed and reviewed recommendations. These guidelines were referred to as "The Uniform Approach to Breast Fine Needle Aspiration Biopsy." This article reviews these recommendations and the contemporary evolution of the practice of BFNA since their original publication.

Image-Directed Fine Needle Aspiration Biopsy in Nonpalpable Breast Lesions	655
Paula B. Gordon	

Fine needle aspiration biopsy of nonpalpable breast lesions may be performed with imaging guidance. The technique has a potential role, but is underused because of a relative paucity of specialty-trained, enthusiastic breast cytopathologists. This article discusses the strengths and limitations of the technique in the context of the various imaging modalities, and in comparison with needles used for histologic sampling.

**Core Needle Biopsy Versus Fine Needle Aspiration Biopsy:
Are There Similar Sampling and Diagnostic Issues?** 679
Shahla Masood

Evidence suggests that in experienced hands fine needle aspiration biopsy (FNAB) is highly safe and effective for the evaluation of patients who have palpable breast lesions. In most cases, FNAB leads to an appropriate clinical or surgical management. FNAB can also be effectively used in evaluation of cystic lesions under ultrasound guidance. Other nonpalpable lesions can benefit from image-directed core needle biopsy (CNB). Overall, cost should influence the decision to use FNAB or CNB. FNAB may be the only affordable procedure in developing countries. Breast cancer affects significant numbers of women worldwide. Attempts should be made to take all the measures necessary to consider optimal approaches to breast health care for everyone regardless of age, race, ethnicity, or social status.

Cytomorphology of Benign Breast Disease 689
Pascale Hummel Levine and Joan Cangiarella

Fine needle aspiration biopsy is a widely used technique for the initial diagnosis of mammary lesions. The majority of patients undergoing fine needle aspiration biopsy of a breast lesion will have a benign disease of the breast. This article provides a review of the cytomorphologic features in a variety of benign breast lesions, and discusses the commonly encountered differential diagnoses on aspiration biopsy. Topics discussed include inflammatory and reactive conditions, treatment-induced changes, pregnancy-related changes, benign proliferative lesions, and benign neoplasms of the breast.

**Cytomorphology of Fibrocystic Change, High-Risk
Proliferative Breast Disease, and Premalignant Breast Lesions** 713
Shahla Masood

In a prospective study using mammographically guided fine needle aspirates in 100 nonpalpable breast lesions, the author's group assessed the reliability of a cytological grading system to define the cytological features of proliferative and nonproliferative breast disease and to differentiate between benign, premalignant and malignant breast lesions. We developed a cytological grading system evaluating the aspirates for the cellular arrangement, the degrees of cellular pleomorphism and anisonucleosis, presence of myoepithelial cells and nucleoli and the status of the chromatin pattern. This grading system, now recognized as the Masood Cytology Index, is commonly used as a surrogate end point biomarker in chemoprevention trials.

Cytomorphology of Common Malignant Tumors of the Breast

733

Lydia Pleotis Howell and Lynne Lin-Chang

A definitive cytologic diagnosis of breast cancer is usually possible when using the six major criteria of malignancy (cellularity, dys-hesion, monomorphism, anisonucleosis, irregular nuclear membranes, prominent nucleoli) as part of the triple test. Carcinomas of special type have unique clinical and cytologic features that pathologists need to consider, because these may confuse interpretation. Complete subtyping of carcinomas may not always be possible by fine needle aspiration. Diagnostic accuracy for breast carcinoma is excellent. False-negative diagnoses are infrequent and chiefly due to sampling issues. False-positive diagnoses are extremely rare. Uniform report terminology should be used to ensure that diagnostic information is conveyed appropriately and consistently to guide the next diagnostic or treatment step.

Cytomorphology of Rare Malignant Tumors of the Breast

761

Walid E. Khalbuss

This article reviews cytomorphology of rare malignant tumors of the breast: squamous carcinoma, metaplastic carcinoma, adenoid cystic carcinoma, apocrine carcinoma, secretory carcinoma, lipid-rich carcinoma, and carcinoma with choriocarcinomatous features. It is important to bear in mind the cytomorphology and diagnosis of rare malignant tumors of the breast in analysis of breast fine needle aspiration smears. Although rare, these malignant tumors can be diagnosed by the cytomorphological characteristics, and should be included in the differential diagnoses of breast neoplasms.

Medical-Legal Issues Associated with Breast Fine Needle Aspiration Biopsy

777

R. James Brenner

This article discusses medical and legal issues associated with breast fine needle aspiration biopsy and develops risk-management considerations for clinical practice. Basic legal considerations are first discussed, including the law of negligence as it applies to breast fine needle aspiration. The variable concept of duty to patients is reviewed. Communication of diagnosis, both formally and informally, in the medical setting is covered. The claims review process is then discussed. The meaning of misdiagnosis, including overdiagnosis and delay of diagnosis, is discussed in terms of legal harm and expert review.

Nipple Fluid Cytology

787

Shahla Masood and Walid E. Khalbuss

With increasing emphasis on public awareness of breast cancer and screening mammography, more women seek consultation for breast symptoms, including nipple discharge. The presence of

nipple discharge is distressing for the patient; however, its origin is fortunately most often benign. Nipple discharge associated with a recognizable mass requires sampling and surgical excision. Currently, clinical breast examination, cytology, ductography, mammogram, and ultrasound are commonly used to evaluate patients who have nipple discharge. Ductal lavage and ductoscopy, in association with emerging new technology, may be of help in increasing the sensitivity of nipple fluid cytology. In addition, nipple fluid cytology may offer a new way to study the spectrum of premalignant breast lesions, and to identify women at risk for breast cancer.

Intraoperative Imprint Cytology in Assessment of Sentinel Lymph Nodes and Lumpectomy Surgical Margins

795

Ardeshir Hakam and Ni Ni Khin

Intraoperative imprint cytology (IIC) in the assessment of sentinel lymph nodes (SNs) allows immediate, cost-effective axillary lymph node dissection. IIC diagnosis is accurate in up to 100% of grossly abnormal SNs. Despite overall low sensitivity for grossly negative SNs, the benefits of immediate complete axillary lymph node dissection offset the increased risk of missing micrometastases or loss of isolated tumor cells (ITCs) by performing frozen section. IIC of the lumpectomy margins is rapid, accurate, and cost effective. It allows re-excision during initial surgery if needed with better cosmetic result. It is a useful adjunct to, and frequently a replacement for frozen section in many centers. Cytopathologists must familiarize themselves with both advantages and pitfalls of IIC to avoid errors.

Prognostic/Predictive Factors in Breast Cancer

809

Shahla Masood

This can be an exciting time for pathologists and cytopathologists as we refine our knowledge of prognostic/predictive factors in breast cancer. We can become more visible in our role as consultants to the other physicians, and more engaged in our role as researchers. Recent advances in computer science, coupled with the availability of new biological markers, now provide unique opportunities for us to expand our diagnostic abilities and also predict the biologic behavior of a given tumor. Thus, we must become more familiar with emerging concepts and technologies in different disciplines.

Cytomorphology as a Risk Predictor: Experience with Fine Needle Aspiration Biopsy, Nipple Fluid Aspiration, and Ductal Lavage

827

Shahla Masood

Primary prevention of breast cancer requires identification and elimination of cancer-causing agents, which is an incredibly difficult task to follow. Secondary prevention involves screening individuals

who are at increased risk for breast cancer in hopes that early intervention will affect survival. In the 1980s, chemoprevention received serious attention. This approach was aimed at reducing cancer risk by administration of natural or synthetic clinical compounds that prevent, reverse, or suppress carcinogenesis in individuals at increased risk for cancer. It was not until 1998, however, when the first report from the National Surgical Adjunct Breast and Bowel Project (Breast Cancer Prevention Trial BCPT; P-1) randomized clinical trial appeared in the literature supporting the hypothesis that breast cancer can be prevented. This study showed that administration of tamoxifen reduced the risk for invasive and noninvasive breast cancer by almost 50% in all age groups. With the current availability of tamoxifen as a chemopreventive agent and with the increasing emphasis on early breast cancer detection and prevention, more women seek consultation to determine their risk for breast cancer. However, in the absence of any detectable breast lesion, clinically and mammographically, only a few women may volunteer to have their breasts sampled by surgical biopsy for risk assessment. Other non-surgical procedures include fine needle aspiration biopsy (FNAB), nipple aspirate fluid (NAF), and the recently introduced procedure, ductal lavage. These techniques may provide better alternatives. These minimally invasive procedures are capable of recruiting cellular material for cytomorphologic interpretation and biomarker studies.

The Future Prospect: Ductoscopy-Directed Brushing and Biopsy

845

William Chesnut Dooley

The intraductal approach to breast cancer and premalignant lesions has now developed to yield substantial cytologic samples of exfoliated cells. Standard cytology is still inadequate in sensitivity and specificity to accurately interpret the majority of samples. As techniques evolve using ductoscopic biopsy and molecular marker panels to increase accuracy of cytologic interpretation, these tools will be able to unravel the breast carcinogenesis pathways. They will also offer considerable benefit in screening for premalignant changes and developing effective chemoprevention strategies.

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