

FINE NEEDLE ASPIRATION FINDINGS OF SPECIFIED CARCINOMAS OF THE BREAST; 60 CASES WITH CYTO-HISTOPATHOLOGIC CORRELATIONS

MEMENİN ÖZELLEŞMİŞ TİPTEKİ KARSİNOMLARINDA İNCE İĞNE ASPİRASYONU BULGULARI: 60 OLGUNUN SİTO-HİSTOPATOLOJİK KORELASYONLARI

Sevgiye KAÇAR ÖZKARA^{1,*}, Ayşegül TOHUMCU¹

* Corresponding author

¹ Kocaeli University, Medical School, Department of Pathology, Umuttepe, 41380, Kocaeli, TURKIYE
E-posta: emrecaan1999@yahoo.com

ÖZET

Anahtar Kelimeler:

Meme, ince iğne aspirasyonu, spesifikite, karsinom, kanser, sitopatoloji

Amaç: Bu çalışmanın amacı, meme karsinomlarının spesifik subtiplerinin (lobüler, papiller, medüller, müsinoz, tubuler ve diğer), ince iğne aspirasyonu sitopatolojisi (İİAS) ile tanısındaki performansımızı değerlendirmektir.

Yöntem: Bölümümüzde, 2006-2011 yıllarında sitopatolojik ve histopatolojik incelemeleri yapılan, spesifik subtipteki meme karsinomu olgularının İİAS sonuçları histopatolojik tanılarıyla karşılaştırıldı. İİAS tanıları, benign, atipik, kuşkulu, malign ve temsil edici olmayan olarak gruplandı. Kesin ve total sensitivite oranları, atipik (gri-zon) ve yetersiz İİAS sonuçlarının, histopatolojik subtip ile korelasyonu araştırıldı.

Bulgular: Sito-histopatolojik korelasyonu yapılan toplam 60 olgunun, 59 (%98,3)'u kadın, 1(%1,7)'i erkek hasta olup; yaş aralığı 34-83 yıl arasındaydı. Genel ortalama yaş 58,5(±13,3) iken; medüller karsinom olgularında anlamlı derecede (49) düşüktü. Sitopatolojik olarak, olguların 1(%1,7)'i benign (C2) ve 5(%8,3)'i atipik (C3) tanısı alırken; 10(%16,7) olgu malignite kuşkulu (C4) ve 37(%61,7) olgu malign (C5) olarak değerlendirilmiş; 7(%11,7)'si ise tanı için yetersiz bulunmuştu. Histopatolojik spesifik subtiplere göre, 36(%60,0) invaziv lobüler, 8 papiller, 7 medüller, 5 müsinoz, 3 tubuler ve 1 adenoid kistik karsinom bulunmaktaydı. İnvaziv lobüler subtipteki karsinomlar, daha düşük (%52,8 kesin (C5) ve %69,5 total (C5+C4) sensitivite oranlarına sahipti. Total sensitivite oranları, papiller, medüller, müsinoz ve tubuler karsinomlarda %100'dü. Gri-zon olguları (%13,9) ve yanlış negatiflik (%2,8) invaziv lobüler karsinomlarda daha yüksek iken; tubuler karsinomlarda daha yüksek yetersizlik (%33,3) oranı bulundu.

Sonuç: Memenin spesifik subtipteki karsinomlarının İİAS ile preoperatif değerlendirmesinde, invaziv lobüler ve tubuler karsinom subtipleri, İİAS'nin tanısal gücünü sınırlamaktadır. Meme hastalıklarına yaklaşımın üçlü sacayağı (klinik, radyolojik ve patolojik) gerektirmesi nedeniyle, özellikle spesifik subtipteki meme karsinomu olgularını değerlendirirken, İİAS'nin bu konudaki sınırlılıklarının ilgili uzmanlıklar için farkındalığı, yanlış-negatif ve yanlış-pozitif sonuçların azaltılması açısından önemlidir.

ABSTRACT

Keywords:

Breast, fine needle aspirasyonu, specified, carcinoma

Objectives: Fine needle aspiration (FNA) continues to be an acceptable and reliable procedure for the preoperative diagnosis of breast lesions, particularly. The purpose of this study is to evaluate our performance with FNA cytopathology (FNAC) in specific subtypes of (lobular, papillary, medullary, mucinous, tubular and other) breast carcinomas.

Methods: FNAC results of specified carcinomas of breast, cyto-diagnosed and subsequently biopsied in 2006-2011 were compared with final histopathological evaluation. The results of FNAC were interpreted as benign, atypical, suspicious, malignant and non-representative. The absolute and complete sensitivity rates, underestimation of malignancy rate and inadequacy rate of FNAC were correlated with histopathologic subtype.

Results: Of cyto-histopathologically correlated 60 cases, 59 (98.3%) were females and 1(1.7%) was a male. Age range was 34-83 years with a mean value of 58.5(±13.3). Mean age was significantly lower (49) in medullary carcinoma patients. Of cases, 1(1.7%) was diagnosed as benign (C2), 5(8.3%) were atypical (C3), 10(16.7%) were suspicious (C4), 37(61.7%) were malignant (C5) and 7(11.7%) were inadequate (C1) by cytopathology.

Of specified histopathologic subtypes, 36(60.0%) lobular, 8 papillary, 7 medullary, 5 mucinous, 3 tubular and 1 adenoid cystic carcinomas were included.

Invasive lobular-type carcinomas had lower (52.8% absolute (C5)); 69.5% complete (C5+C4) sensitivity rates. The complete sensitivity rate was 100% in papillary, medullary, mucinous and tubular carcinomas. The underestimation of malignancy rate (13.9%) and false negativity (2.8%) was higher in lobular carcinomas while tubular carcinomas showed a higher inadequacy rate (33.3%).

Conclusion: For FNAC of the breast in the preoperative diagnosis of specified breast carcinomas, lobular and tubular carcinoma subtypes limit cytodiagnostic yield of FNAC. As management of breast diseases necessitates triple approach (clinical, radiological, pathological), an awareness of the FNAC limitations by all specialists is important, especially when dealing with specified breast carcinomas to decrease false-negative and false-positive results.

INTRODUCTION

Fine needle aspiration (FNA) continues to be an acceptable and reliable procedure for the preoperative diagnosis of breast lesions, FNA cytopathology (FNAC) has been used as the first-line method to assess symptomatic breast lesions in Kocaeli University Hospital for fifteen years. And when triple assessment is concordant, final treatment may be ensued without open biopsy.

The purpose of this quality control study was to evaluate our performance with FNAC in the cytopathologic diagnoses of specified breast carcinomas in particular, namely invasive lobular, papillary, medullary, mucinous, tubular and others.

METHODS

All cases with histopathologic diagnoses of specified carcinomas of the breast consecutively examined between March 2006 and March 2011 were retrieved. A total of 60 patients had both cytopathologic examination and histopathologic diagnoses of specified carcinomas of the breast and therefore fulfilled the criteria for this study. Informed consent had been signed by the patients before the FNA procedures.

The FNA smears were air dried and stained with May-Grünwald-Giemsa while tissue sections were processed routinely and stained with H&E.

The results of the FNAC interpretations were grouped as inflammatory/benign (C2), atypical (C3), suspicious for malignancy (C4) or malignant (C5). The results of FNAC diagnoses were compared with final histopathologic diagnoses. The absolute and complete sensitivity rates, underestimation of malignancy rate (gray-zone), and inadequacy rates of FNAC were calculated and were correlated with each histopathologic subtype.

The absolute sensitivity rate was calculated as the number of cancers cytodagnosed as malignant (C5) by FNAC; while the complete sensitivity rate was defined as the number of cancers cytodagnosed as malignant (C5) and suspicious for malignancy (C4) by FNAC. The underestimation of malignancy rate was determined as the number of cancers cytodagnosed as atypical (C3) by FNAC; and finally inadequacy rate from cancer means the number of non-representative specimens (C1) on FNAC; and all expressed as a percentage of the total number of cancers sampled¹.

RESULTS

The study group consisted of FNAC material from 60 consecutive breast tumors examined cytopathologically prior to surgical biopsy and/or resection and subtyped finally as lobular, papillary, medullary, mucinous, tubular and adenoid cystic carcinomas on histopathologic examination. Histopathological material was available for cyto-histopathologic correlation in all cases that were included into the study. Informed consents of the patients have been obtained before both FNA and surgery as a routine procedure in our hospital.

The results of original cytopathologic interpretations and cyto-histopathologic correlations and their clinico-pathologic implications are presented on the Tables 1,2 and 3.

Table 1. Frequency distribution of cytopathological diagnoses of specified carcinomas of the breast.

Category	FNAC diagnoses	Number of cases	Percentage (%)
C5	Malignant	37	61.7
C4	Suspicious for malignancy	10	16.7
C3	Atypical	5	8.3
C2	Benign	1	1.7
C1	Non-representative	7	11.7
TOTAL		60	100

C: cytodiagnostic category

Table 2. Overall sensitivity rates of FNAC for specified carcinomas of the breast.

FNA category	Cytopathologic diagnoses	Number and percentage of the cases	Clinico-pathological implication
C5	Carcinoma	19 (52.8%)	Absolute positivity
C4	Suspicious for malignancy	6 (16.7%)	Complete positivity (included into)
C3	Atypical	5 (13.9%)	Underestimation of malignancy
C2	Benign	1 (2.8%)	False negative
C1	Non-representative	5 (13.9%)	Inadequacy
Overall		36 (100%)	

Table 3. Cytopathologic interpretation results and their clinicopathological implications in invasive lobular carcinoma (ILC) cases.

Histopathologic Subtype	Number of cases	Percentage (%)	Complete Sensitivity (%)
Invasive Lobular ca	36	60.0	69.5
Papillary ca	8	13.3	100
Medullary ca	7	11.7	100
Mucinous ca	5	8.3	100
Tubular ca	3	5.0	100
Adenoid cystic ca	1	1.7	100
Overall	60	100	-

ca: carcinoma

Of the cyto-histopathologically correlated 60 cases, 59 (98.3%) were females and 1 (1.7%) was a male. The age range was 34-83 years with a mean value of 58.5 (\pm 13.3) years. Mean age was significantly lower (49 years) in medullary carcinoma patients.

Of the cases, 1 (1.7%) was cyto-diagnosed as benign (C2), 5 were (8.3%) atypical (C3), 10 (16.7%) suspicious for malignancy (C4), 37 (61.7%) malignant (C5) and 7 (11.7%) inadequate (C1) on FNAC (Table 1). Specific cytopathologic diagnoses were given whenever possible.

Of the specified histopathologic subtypes, 36 (60.0%) invasive lobular carcinomas, 8 papillary, 7 medullary, 5 mucinous, 3 tubular and 1 adenoid cystic carcinomas were included (Table 2).

There was one false negative case of cytopathological interpretational error. Lobular type carcinomas had a lower (52.8%) absolute (C5) and 69.5% complete (C5+C4) sensitivity rates. The complete sensitivity rate was 100% in papillary, medullary, mucinous and tubular carcinomas. The underestimation of malignancy rate was higher in lobular carcinomas (13.9%) (Table 3). On the other hand, tubular carcinomas showed a higher inadequacy rate (33.3%).

DISCUSSION

FNA has been used for many years as a diagnostic tool for breast lesions, with high sensitivity and specificity. However, there is controversy as to whether this technique should be replaced by core needle biopsy (CNB). This retrospective analysis aims to re-evaluate the usefulness of breast FNAC in the cytodagnosis of a special group: specified carcinomas of the breast.

A 5-year retrospective study was performed using records of all patients who had both FNAC material and histopathologic results of specified carcinomas of the breast. We aimed to highlight the continuing role of FNAC in the diagnosis of specified breast carcinomas, against a background of its diminishing use in some centers, particularly those involved in breast screening, because of its controversial inadequate rate and suboptimal accuracy.

The issue of optimal sampling to obtain adequate cytologic material in sufficient quantity and quality is of paramount importance when assessing the accuracy of FNAC. The multidisciplinary approach is necessary to amplify FNAC quality and to reduce its diagnostic limits. Only when this model of activity is not available, the role of FNAC is less effective and the addition of CNB to FNAC should be considered as an alternative diagnostic modality and should be used advisedly, in situations where it is more likely to yield diagnostic information, e.g.: in the diagnosis of impalpable masses, microcalcifications or a clinically apparent malignancy where also preoperative chemotherapy is planned. In microcalcifications, suspicious FNAC findings and in malignancies where radiology cannot guarantee stromal invasion, CNB is recommended².

A clear reporting system ensures that an unequivocal cytopathological diagnosis of malignancy is reliable, and in cases where mammography/ultrasonography and clinical examination are in agreement with FNAC, frozen section examination is not mandatory. Suggested thresholds for breast FNAC performance according to the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis are the following: absolute sensitivity (C5 only) >60%, complete sensitivity (C4 + C5) >80%, specificity >55%, positive predictive value >99%, false negative <4%, false positive <0.5%, inadequacy rate <15%, inadequacy rate from cancers <5% and suspicious rate <15%^{1,3}. We use, as the majority of European countries, similar reporting system for breast FNAC (C1-C5), in keeping with the guidelines.

Among the specified carcinoma subtypes, FNAC of invasive lobular carcinoma (ILC) is associated with notoriously high rates of false negative and equivocal diagnoses. Classical ILC, in which single neoplastic cells are embedded in fibrous stroma, is more likely to yield a paucicellular smear with subtle atypia and rare single intact epithelial cells. As such, an inconclusive diagnosis in a certain percentage of classical ILC cases may be unavoidable^{1,4}.

Present study showed that in cases of histopathologically proven ILCs (n=36); the initial cytopathologic diagnoses were carcinoma in 52.8%, suspicious for carcinoma in 16.7% and atypical in 13.9%; and 2.8% of the cases were misinterpreted as benign. Thus, the ILC group failed the European Guidelines standard in absolute (52.8%) and complete sensitivity rates (69.5%). In addition, the underestimation of malignancy rate was higher (13.9%). We concluded that although ILC displays some cytomorphologic features of malignancy, however they may not be recognized or at least suggested by FNA even if evaluated carefully in conjunction with clinical and radiological findings.

In the study by *Cariaggi M.P. et al* (n=1609), among the misdiagnoses, false negatives (overall 2.9%) were more frequent among invasive lobular subtypes (5.4%); suggesting that in most cases, cytopathological faults were due to the absence of cytological atypia in cells sampled from well differentiated tumors, rather than to misinterpretation or sampling from adjacent normal tissues⁵.

The best FNAC results were observed in special histopathological subtypes of papillary, medullary and mucinous, confirming the data reported in the literature^{1,6}.

Regarding papillary carcinomas, there is an overlap in cytomorphologic features between papillary and nonpapillary benign lesions as well as between benign and malignant papillary neoplasia. Overlap of cytopathologic features in nonneoplastic and neoplastic benign papillary lesions and between benign and malignant papillary neoplasia necessitates histopathologic evaluation in all cases diagnosed as papillary on cytopathology. According to *Jayaram G et al*, since 49.2% of lesions showing papillary features on cytopathology prove to be malignant, all cases reported as papillary on cytopathology should be excised urgently for histopathologic assessment⁷. In the present study, the complete sensitivity for malignancy was quite high in papillary carcinomas but it may not be repeated in other circumstances.

Medullary carcinoma (MC) is a rare variant of breast carcinoma with a relatively good clinical prognosis as strictly defined. Characteristic features on FNAC allow MC to be considered in the cytopathologic differential diagnosis⁸. The cytopathologic picture is characterized by cellular smears composed of highly atypical epithelial tumor cells in loosely cohesive sheets and lying singly, admixed with polymorphous lymphocytes, plasma cells and neutrophils. Tumor cells have predominantly abundant finely granular, eosinophilic cytoplasm and moderate to marked nuclear pleomorphism with prominent nucleoli⁹.

Familiarity with the cell components is a prerequisite in cytopathologic accuracy¹⁰. The complete sensitivity rate for malignancy was also quite high in the medullary carcinomas in the present study. This is due to fact that nuclear atypia of MC cell is quite remarkable to facilitate the diagnosis.

Mucinous carcinomas generally display high cellularity, mild to severe nuclear atypia. FNAC material contains abundant single, intact cells along with; three-dimensional cellular clusters in most cases; Excisional biopsy is advised for all hypocellular cases for further separation into benign and malignant MLL and to rule out the possibility of hypocellular mucinous carcinoma¹¹. In the present study, the complete sensitivity for malignancy was again quite high in mucinous carcinomas.

On the other hand, tubular carcinoma of the breast is another problematic subtype in FNAC. In the study by *Dawson et al*, the aspirates from 24 cases of biopsy-confirmed tubular carcinoma were studied and the majority of these carcinomas were nonpalpable masses detected by mammography. The cytopathologic diagnoses were atypical in 12, and malignant in only 3. When the FNAC in all cases were reviewed, the authors concluded that the presence of angular epithelial groups and single epithelial cells, along with nuclear atypia, should warrant consideration of the diagnosis of tubular carcinoma¹².

In another study by *Fischler et al*, twenty cases of FNAs of histopathologically proven tubular carcinoma of the breast were reviewed, and the staining distribution of alpha-smooth muscle actin (SMA) was evaluated to see if this improved FNA sensitivity. They concluded that alpha-SMA staining might help in selected cases in

FNAC¹³. Although tubular carcinomas had high complete sensitivity rate in the present study, they also showed the highest inadequacy rate (33.3%).

CONCLUSIONS

Lobular and tubular carcinoma subtypes limit the cytodiagnostic yield by FNAC. As management of breast diseases necessitates the triple approach (clinical, radiological and pathological), an awareness of the limitations of FNAC by all specialists is important, especially when dealing with these specific subtypes of breast carcinomas to decrease false-negative and false-positive results. We recommend biopsy for suspected lobular carcinomas given the low sensitivity of FNAC for these tumors.

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