

Fine Needle Aspiration Of Breast Lesions: Ten Years Experience Ali Hassan Al-Timimi

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Summary :

330 fine needle aspiration cytologies (FNA) of breast lesions performed during a ten year period , from 1992 to 2002 , at the Pathology Department and Surgical Teaching Hospital were studied . The cytological diagnosis were compared with the results of the histological examination of the same lesions and statistically evaluated . Most of cytologically false negative (22%) and inadequate cases (6%) were found in clinical stage VI, while most of suspicious cases were found in clinical stage I (50%) . The sensitivity of the present study was 93% . while specificity was 100% . The overall accuracy rate was 70% in the whole study . Positive predictive value for carcinomas was 100% , negative predictive value for absence of carcinoma was 86% and efficiency of the test was 95% . The agreement between cytological and histological typing of malignant tumors was 95% in infiltrating , 35% in medullary carcinoma and 100% in cytosarcoma phyllodes . While in benign lesions , it was 100% in granulomatous mastitis 86% in fibrocystic disease , 90% in breast abscess and 95% in fibroadenoma . The agreement between cytological and histological grading of infiltrating duct carcinoma cases was 78%.

الخلاصة :

تم دراسة 330 حالة بالشفط بالإبر الدقيقة لإصابات الثدي المرضية خلال الأعوام 1992-2002 في قسم الأمراض والمستشفى الجراحي - كلية الطب - جامعة بابل. النتائج الخلوية تم مقارنتها بالنتائج النسجية المرضية وتم تقييمها احصائياً. وجدت معظم النتائج الخلوية المخطوئة السالبة (22%) والحالات غير الكافية (6%) في المرحلة السريرية الرابعة بينما معظم الحالات المشتبه بها وجدت في المرحلة السريرية الأولى (50%). حساسية الدراسة الحالية كانت (93%) بينما الخصوصية (100%). مجمل معدل الصحة هو (70%) في عموم الدراسة. القيمة التكنية الموجبة لوجود السرطان (100%). بينما القيمة التكنية السالبة لعدم وجود السرطان هي (86%) وكفاءة الفحص هي 95%. التوافق بين النتائج النسجية والخلوية كانت بنسبة 95% في السرطان المنتشرة، (35%) في السرطان الليفي، (100%) في غرن فلويديز. بينما في الإصابات المرضية الحميدة للثدي وجدت في (100%) لالتهاب الثدي التبرعمي. (86%) في مرض الثدي الكيسي التليفي، (90%) في خراج الثدي، (95%) في ورم التليف الغددي الحميد. كان التوافق بين النتائج النسجية والخلوية لدرجة الخباثة في سرطانة الثدي المنتشرة هي (78%).

Introduction :

Breast cancer is the most frequent malignant disease in Iraqi females . There has been no decrease in the death rate due to breast cancer since 1930[1] . the only hope in reducing rate deaths is early detection of the disease.

The FNA procedure is easily performed in outpatient clinics it is a diagnostic tool that contributes to the early diagnosis of breast carcinoma [2] . The procedure has been demonstrated to be simple , safe accurate and cost-effective [3-4] . FNA cytology can prevent unnecessary surgery for benign disease in women of any age , especially in women below the age of 30 [5] . It also enables us to make the diagnosis of breast carcinoma with certainty , allowing clinicians to

approach therapy differently , depending on the patients clinical stage . The present study was undertaken to evaluate our experience in FNA cytology of breast lesions in terms of accuracy , sensitivity , especially positive and negative predictive values .

Materials and methods :

Cytological diagnosis of 330 breast fine needle aspirations performed at the Department of Pathology and Surgical Teaching Hospital , Babylon University, Babylon, IRAQ, were analyzed through comparison with their histopathological diagnosis . Following detection of breast abnormality by palpation and/or by mammography, a tumor sample can be obtained by a procedure called "fine needle aspiration" or FNA. The FNA procedure will be guided by a thin needle (using 10 ml syringe with an attached 23 gauge needle), under local anesthetic, into the breast to the location of the breast abnormality. Then, cells are aspirated into the needle with several passes through the abnormal area. The cells are placed on glass slides ,fixed in 100% ethyl alcohol and stained by the modified papincoleau stain, to highlight the cells, and then examined. We tries to determine if malignant cells are present. In general, false positive diagnoses (a lesion is called cancer, but in reality is not) are rare. However, with this technique, false negative diagnoses (in which a cancer may be missed) are possible some of the time, because of sampling error or the small number of cells examined or the nature of the lesion. Breast biopsy is performed to remove a lesion and make a definitive diagnosis, if a malignancy has not been demonstrated by FNA but is still suspected, or if a lump is likely to be malignant. The biopsy is processed routinely, and a histopathological diagnosis is made.

The cytopathological reports were classified into four diagnostic classes :

1- Benign : characterized by sheets of regular ductal cells with nuclear features of benign cells often admixed with a large number of stripped nuclei. 2- Malignant : hypercellular specimen composed of cells with equivocal cytological features of malignancy . 3-Suspicious : hypercellular specimen with an admixture of regular cells and others with abnormal nuclear and cytoplasmic features falling short of a firm diagnosis of malignancy. 4-Inadequate : either extremely hypocellular or bloody aspirates obscuring cellular elements .

The data were analyzed and sensitivity (true positive diagnosis) , specificity (true negative diagnosis) , positive predictive value (PPV) and negative predictive value (NPV) were calculated [6-7] .

The nuclear grading (NG) was assigned according to Fisher's modification of Black's nuclear grading scheme [8] .The histopathologic grading was assigned according to the modified scarff-Bloom-Richardson grading system [9] that evaluates the nuclear pleomorphism, mitotic count and ductoglandular formation .

Results:

During the ten years a total of 330 fine needle aspirations of various lesions of the breast were obtained . the cytological diagnosis were : negative in 111 cases (34%) , suspicious in 17 (5%) , positive in (198) (Fig 1). (60%) and inadequate in 4 (1.2%) (table -1) .Carcinomas were diagnosed by histology in 231 cases and benign lesions in 99 instances. The results of histological typing and grading are given in tables (2&3)(Fig 2).

Of the cytologically negative aspirates , 95 (85.6%) were found to be negative by histological examination (true negatives) , whereas 16 (14.4%) were histologically malignant (false negatives) . Histological examination of the cytologically suspicious cases revealed malignancy in 15 cases (88.4%) and fibroadenoma in 6 cases (11.6%) (table -1) .

Sensitivity of the present study for the presence of carcinoma was 92.4% and specificity for the absence of malignancy was 100%. The overall accuracy rate was 70% in the whole study, including benign lesions. Positive predictive value for carcinoma was 100%. Negative predictive value for absence of carcinoma was 85.6% and efficiency of the test was 94.7%.

The results of the comparison of histological types of carcinomas and cytology are presented in table (2). The rate of false negative was higher in invasive lobular carcinoma (26.7%) than in invasive ductal carcinoma (5.3%). When considering only carcinomas with adequate smears (n=226), the rate of false negative cases was 7%.

The results of FNA in 99 histologically examined benign lesions were 95 (96.2%) true negatives. Another 6 cases (2%) were classified by cytology as suspicious while histological examination revealed fibroadenoma. Five (1.7%) of the smears were inadequate, three of them were fibrocystic and the other two were benign phyllodes tumor by histological examination (table 3).

TNM clinical staging was done in all malignant cases (table 4). The highest true positive diagnosis was in stage II (94%) and lowest in stage I (28.54%).

Cytological nuclear grades are shown in table (5). Agreement between cytological and histological grading was observed in 127 of the 168 invasive ductal cases studied (75.6%). Of 125 cytologically grade II, 101 (80%) had the same grade histologically, while 26 (60%) of cytologically grade III had the same grade histologically (table 5).

Discussion :

Fine needle aspiration (FNA) cytology of palpable breast lesions has been shown to be a diagnostically accurate procedure that has many advantages for the patients as well as the physician [10].

Inadequate cellular sampling has been found to be a major cause for failure of accurate cytological diagnosis [11]. Adequacy of cytological sampling could be related in part to the efficiency of the sampler himself or due to histological composition of the aspirated lesion [12]. The range of inadequate cellular sampling of breast lesions was reported to be between 1.7% and 34.5% [13]. The inadequate sampling was relatively infrequent in the present study, 1.2%.

Failure of cellular sampling in the present study was essentially related either to target miss or to the presence of densely fibrous lobular tumor that was hard to aspirate. Target miss was commonly observed in stage IV disease associated with pronounced breast edema that made tumor palpation impossible. In such cases, as well as in the presence of small masses in large breasts, sonar guided cellular sampling may enhance the accuracy of the procedure.

As recorded in the present work, the sensitivity, accuracy, false positive and false negative rates were comparable to those reported in the literature [14-17]. The lowest sensitivity was found with cases with lobular carcinoma (62.2%). Failure of aspirating representative cells or else aspiration of relatively uniform unremarkable elements has led to a relative low sensitivity. In ductal lesions, it was mainly the target miss and less commonly the presence of scirrhous hard to aspirate lesions that led to false negative diagnoses. Similar explanations were reported in the literature [17-20].

Some investigators consider suspicious cases to be positive [16], while others considered them to be negative for malignancy [18]. Our approach was to use the suspicious classification as infrequently as possible. The rate of malignancy among suspicious cases was high, while cellular fibroadenoma was the most common benign lesion interpreted as suspicious for malignancy. The same observation was recorded by other authors of interpreting cellular fibroadenoma as suspicious for malignancy [17-21].

In the present work, positive correlation between cytological and histological typing of benign and malignant tumors was higher than other authors [22]. In malignant lesions, it was high in cystosarcoma phyllodes (100%) and infiltrating ductal carcinoma (95%), but it was low in infiltrating lobular carcinoma (30%) and medullary carcinoma (33%). The cytological differential diagnosis of ductal versus lobular carcinoma was difficult in few cases. The same difficulty reported by other authors who recommended the use of the noncommittal term breast carcinoma leaving the final typing for histology [23-28].

In the current study, we reported tumor grade in FNA smears and analyzed their reproducibility as compared with the histological grade in their respective biopsies or surgical specimens. The agreement between the cytological and histological grading was high (75%) as other reports. The lack of correlation (24.3%) may have been due to tumor heterogeneity and observer subjectivity when assigning nuclear grade.

Conclusion :

fine needle aspiration is an effective modality for the diagnosis of breast lesions. Lower rates of false positive and false negative diagnosis are achieved if the cytopathologist has personally performed the FNA, prepared the smear and performed the microscopic interpretation.

References :

- 1- Boring C.C., Squires T.S. and Tong T.: Cancer statistics . Cancer J. Clin. , 42:19-38,1992.
- 2- Griffen M.M. and Welling R.E. : Surg . Gynecol . Obstet ., 170:145-148, 1990 .
- 3- Lannin R.R. , Silverman J.F., Ann. Surg. 203:474-480, 1986.
- 4- Smith T.J. Safaii H., Foster E.A. and Reinhold R.B. : Am. J. surg., 149:540-545, 1985.
- 5- Ciato S., Cecchini S., Grazzini G., Jossa A., Bartoli D., Cariaggi M.P. and Bulgaresi P: Acta . Cytol., 33:894-898, 1989.
- 6- Feichter G.E., Haberthur F., Gobat S. and Dalquen P. : Acta Cytol. , 41:327-332, 1997.
- 7- Rocha P.D.S., Nadkarni N.S. and Menezes S.: Acta . Cytol ., 41:705-412, 1997 .
- 8- Fisher E., Fisher B. and Redmond C. Pathol . Annu., 15:239-251,1980.
- 9- Le Doussal V., Tubiana – Huiln M., Cancer , 1914-1921, 1989.
- 10-Hammond S., Keyhani – Rofagha S. and O'Tool R.V. : Acta . Cytol ., 31:276-280, 1987 .
- 11-Layfield L.J. : Am. J. Clin. Pathol., 480:145-147, 1992.
- 12- Wollenberg N.J., Caya J.G. and Clowry L.j.: Acta. Cytol., 29:425-429 , 1985.
- 13-Abele J.S., Miller T.R. , Goodson W.H. , Hunt T.K. and Hohn D.C.: Arch . Surg. , 118:859-863, 1983.
- 14-Antonio de las M., Pedro C., Krzstof M. and Margare M.D. : Acta . Cytol., 39:865-869, 1995.
- 15-Costa M.J., Tadros T. , Hilton G. and Bridsong G: Cytol., 37:461-471 , 1993.
- 16-Costa M.J., Tadros T., Hilton G. and Bridsong G. : Cytol ., 37:461-471 , 1993 .
- 17-Dominguez F., Riera J.R., Tojo and Junco P. : Acta . Cytol ., 41:341-347, 1997 .
- 18-Eisenberg A.J., Hajdu S.I., Wilhelmus J., Melamed M.R. and Kinne D . : Acta . Cytol ., 30:135-146, 1986 .

- 19-Kline T.S. : Handbook of fine needle aspiration biopsy cytology . Second edition .
New York . Churchill Livingstone , 1988.
- 20-Frable W.J., : Hum. Pathol., 14:9-28 , 1983 .
- 21-Taxin a., Tartter P.I. and Zappetti D. : Acta . Cytol ., 41:302-306 , 1997 .
- 22-Kline T.S., : Handbook of fine needle aspiration biopsy cytology . Second edition .
New York , Chirchill Livingstone , 1988.
- 23-Kline T.S. : Acta cytol. , 25:263-266 , 1981.
- 24-Shabb N.S.: Phyllodes tumor , Acta. Cytol., 41: 321-326, 1997 .
- 25-Taxin A., tatter P.I. and Zappetti D. : Acta . Cytol., 41:302-306, 1997.
- 26-Wollenberg N.J. Caya J.G. and Clowry L.J. : Acta . Cytol .m 29: 425-429, 1985.
- 27-Zarbo R.J., Howanitz P.J. and Bachner P. : Arch . Pathol. Lab. Med., 115: 743-750 ,
1991.
- 28- Hitchcock A, Hunt CM, Locker A, et al. Cytopathology. 1991;2:167-176

Table (1) : cytological categories of 330 fine needle aspirations corresponding results of histological examinations and results of statistical analysis.

Cytology	Histological (No.of cases)		
	No. of cases	Malignanat	Benign
Benign	111 (100%)	16= (14.4%)	95=TN• (85.6%)
Suspicious	17 (100%)	15(88%)	2 (12%)
Malignant	198 (100%)	198=TP• (100%)	FP• =0%
Inadequate	4 (100%)	3(75%)	1 (25%)
Total	330 (100%)	232 (70%)	98 (30%)

• TP= True positive, FP= False positive, TN =True negative, FN= False negative

Table (2) results of cytological examination in relation to histological type of carcinomas

Histological type of carcinoma	No. of cases	True positive	False negative	Suspicious	inadequate
Invasive ductal	208	179	12	13	4
Invasive lobular	14	9	3	1	1
Medullary	4	4	0	0	0
Mucinous	1	1	0	0	0
Tubular	1	0	1	0	0
Papillary	1	1	0	0	0
Ductal in situ	1	1	0	0	0
Cystosarcoma phyllodes	2	1	1	0	0
Total	232	196	17	14	5

Table (3) : Diagnostic accuracy of cytologic typing of breast lesions .

Histological diagnosis	No. of cases	% correct cytological typing
Malignant cases:	179	95%
Infiltrating duct carcinoma		
Infiltrating lobular carcinoma	9	30%
Medullary carcinoma	4	33%
Malignant cytosarcoma	1	100%
Benign cases :		85%
Fibrocystic disease	15	
Benign phyllodes	2	100%
Chronic abscess	21	90%
Ductectasia (figure 8)	14	100%
Fibroadenoma	41	95%
Tuberculous	1	100%

Table (4) : results of cytological examination related to clinical stage of carcinoma .

Stage	No. of cases	True positive	False negative	Suspicious	Inadequate
Stage I	14	4	3	7	0
Stage II	62	59	1	2	0
Stage III	104	100	1	2	1
Stage IV	52	31	11	6	4
Total	232	194	16	17	5

Table (5) : correlation of cytopathological grading 168 invasive duct cases.

Histological grade	Cytological grade			Agreement %
	I	II	III	
Grade I (1)	0	1	0	0%
Grade II (125)	1	101	23	80%
Grade III (42)	1	15	26	60%

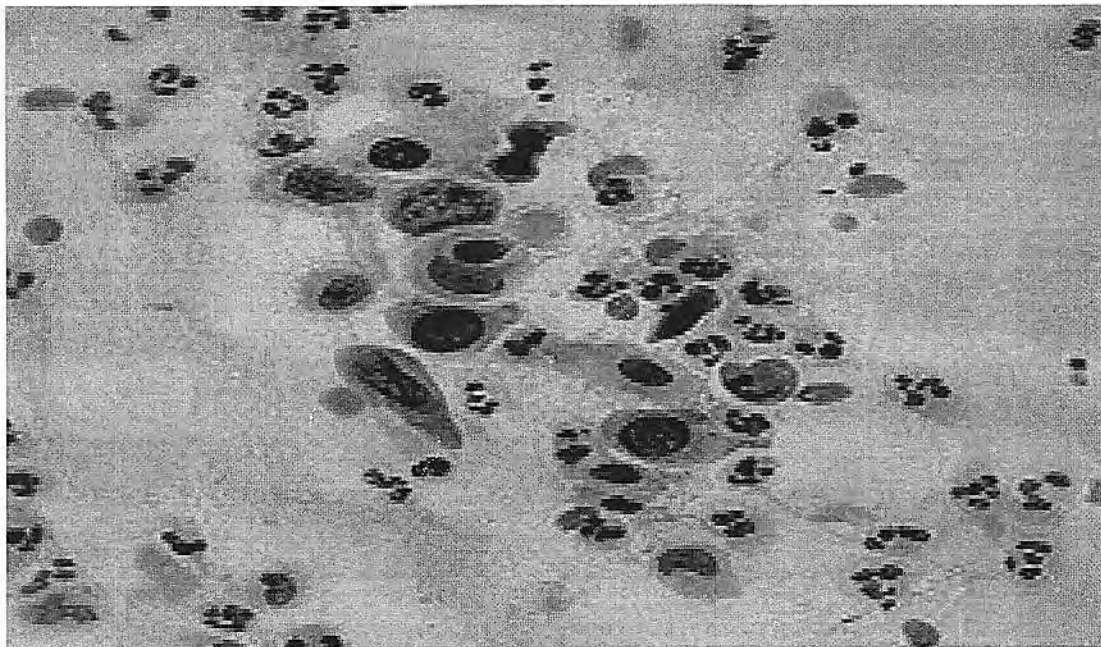


Fig. 1. The cytologic features of Infiltrating ductal carcinoma are demonstrated on FNA smear. The cells show hyperchromatic, pleomorphic nuclei and increased nuclear/cytoplasmic ratio. The background has inflammatory cells(Pap×40).

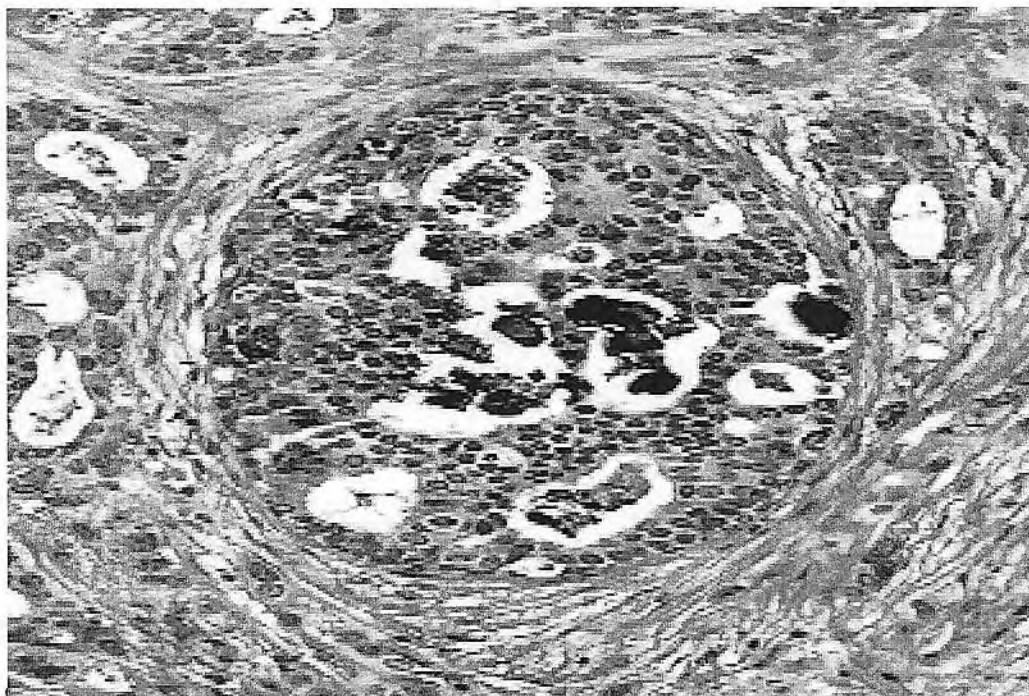


Fig2.Infiltrating ductal carcinoma are seen here. The intraductal component in the center with cribriform pattern and prominent microcalcifications. Surrounding this are infiltrating carcinoma cells(H&E×40)