

—Experimental and Laboratory Notes—

Rapid diagnosis at the outpatient clinic for breast tumors by fine needle aspiration cytology

The utility

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Abstract

The aim of this study was to emphasize the utility and prove the accuracy of rapid diagnosis at the outpatient clinic for breast tumors by fine needle aspiration cytology [FNAC]. Rapid diagnosis for breast tumors by FNAC is performed on the same day just after mammography and echonography are carried out at our hospital and the result reported to the patients while they are waiting at the outpatient clinic. We evaluated FNAC by rapid diagnosis at the outpatient clinic for 1,786 breast tumors during the last ten years.

The cases of no judgement (Class 0) were 11%, negative cases (Class I & II) 72%, suspicious cases (Class III) 7%, and positive cases (Class IV & V) 10%. We experienced only 4 false negative cases and 0 false positive cases among 1,198 cases during the last 5 years, whereas there were 8 false negative cases and 2 false positive cases among 588 cases during the first 5 years. Two false positive cases in the first 5 years were judged as Class IV, but definitive surgery [mastectomy] was not performed because rapid diagnosis during the operation by frozen section confirmed no malignancy. As a result, all the cases in which mastectomies were performed up to now were confirmed malignant.

We emphasize that rapid diagnosis at the outpatient clinic for breast tumors by FNAC is very useful for early detection and treatment and it is very important to consider the histological type of breast tumors by FNAC to prevent misjudgement. (J Nippon Med Sch 1998 ; 65 : 416—420)

Key words: breast tumors, fine needle aspiration cytology (FNAC), rapid diagnosis at the outpatient clinic

Introduction

The occurrence of breast cancer recently has been increasing in Japan¹, so the early detection and treatment of breast cancer is very important. Therefore, rapid diagnosis at the outpatient clinic of breast tumors by fine needle aspiration cytology (FNAC) has been performed at Tama-Nagayama

Hospital, Nippon Medical School for the past ten years and good results have been demonstrated.

Rapid diagnosis of breast tumors by FNAC is performed on the same day just after mammography and echonography are carried out at our hospital and the result reported to the patients while they are waiting at the outpatient clinic. So, firstly we emphasize that rapid diagnosis at the outpatient clinic by FNAC of breast tumors is very useful and

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secondly we discuss how to make a correct judgement for breast tumors by FNAC.

Materials and Methods

Examination using FNAC for breast tumors on 1786 patients in Tama-Nagayama Hospital was carried out over the last ten years from April 1986 to March 1996.

When telephone calls are made by clinicians requesting FNAC, cytotechnologists are sent immediately to the outpatient clinic where they fix slides of FNAC. After 30 minutes' fixation of the slides, Papanicolaou's staining is performed by cytotechnologists. The specimen consists of direct smear and cytocentrifuge preparation. Judgement is immediately made just after considering clinical information on mammography and ultrasonography on the same day and reported to the clinician within one hour while the patient is waiting at the outpatient clinic.

The cytological gradings and the rules concerning the treatment after FNAC in our hospital are as follows:

1) For the cases of no judgement (Class 0) due to insufficient materials, reexamination is performed within 1 hour of performing FNAC.

2) For the negative cases (Class I & II), follow up is carried out.

i) For Class I cases, follow up is carried out every 6 months. ii) For Class II cases, follow up is carried

out every 3 months.

3) For the suspicious cases (Class III), as a general rule, biopsy is performed.

4) For the positive cases (Class IV & V), mastectomy is immediately scheduled.

i) For Class IV cases, mastectomy is performed after rapid diagnosis during the operation by frozen section, which confirmed malignancy. ii) For Class V cases, mastectomy is performed without rapid diagnosis during the operation by frozen section.

Results

The results of FNAC are summarized in **Table 1**. Every year, the number of new patients with breast tumors who come to Tama-Nagayama Hospital has been increasing. A total of 1,786 new patients have undergone FNAC in our hospital during the last 10 years. The number of new patients has doubled in the last 5 years, compared to the first 5 years.

During the last 10 years, the cases of no judgement (Class 0) were 11%, the negative cases (Class I & II) 72%, suspicious cases (Class III) 7%, positive cases (Class IV & V) 10%. Class I cases were only 5% among the negative cases.

Seven cases (5%) among the 131 cases judged as no judgement (Class 0) were also confirmed as malignant by FNAC and/or biopsy. Thirty cases (40%) among the 75 cases judged as suspicious for malignancy (Class III) were confirmed as malignant by biopsy.

Table 1 The result of FNAC of breast tumors

Chronology	Cases	No Judgement (Class 0)	negative (Class I-II)	suspicious (Class III)	positive (Class IV) (Class V)	False negative cases	False positive cases
1986	84	12(14%)	56(66%)	5(6%)	3(4%) 8(10%)	1	0
1987	109	11(10%)	65(59%)	13(12%)	3(3%) 17(16%)	0	0
1988	136	15(11%)	103(75%)	7(5%)	2(2%) 9(7%)	2	0
1989	127	11(9%)	92(72%)	15(12%)	5(4%) 4(3%)	2	1
1990	132	10(7%)	86(69%)	11(7%)	9(6%) 16(11%)	3	1
Subtotal	588	59(10%)	402(68%)	51(9%)	22(4%) 54(9%)	8	2
1991	185	17(9%)	145(78%)	10(6%)	2(1%) 11(6%)	0	0
1992	261	19(7%)	204(77%)	11(5%)	6(2%) 21(9%)	1	0
1993	258	25(10%)	195(75%)	17(7%)	7(3%) 14(5%)	2	0
1994	280	27(10%)	217(77%)	20(7%)	1(1%) 15(5%)	1	0
1995	214	43(20%)	122(57%)	17(8%)	5(2%) 27(12%)	0	0
Subtotal	1,198	131(11%)	883(74%)	75(6%)	21(2%) 88(7%)	4	0
Total	1,786	190(11%)	1,285(72%)	126(7%)	43(2%) 142(8%)	12	2

As far as we have confirmed the histology up to now, twelve false negative cases (1%) among the 1,285 negative cases and 2 false positive cases (1%) among the 185 positive cases have been detected during the last ten years. However, we experienced only 4 false negative cases (0.5%) among the 883 negative cases and 0 false positive cases (0%) among the 109 positive cases during the last 5 years, whereas there were 8 false negative cases (2%) among the 402 negative cases and 2 false positive cases (3%) among the 76 positive cases during the first 5 years.

For these cases of misjudgement, biopsies were performed to confirm the histological type (**Table 2**).

Seven cases (58%) among the 12 false negative cases were invasive lobular carcinoma and invasive ductal carcinoma, scirrhous type.

Both false positive cases were fibroadenomas, and mastectomy was not performed because they were judged as Class IV, and rapid diagnosis during the operation by frozen section confirmed no malignancy just before the scheduled operation. As a result, all the cases in which mastectomies were performed in Tama-Nagayama Hospital up to now were confirmed malignant.

Discussion

The results of this study demonstrate the utility and prove the accuracy of rapid diagnosis at the

outpatient clinic by FNAC of breast tumors as described heretofore²⁻⁴.

The incidence of breast cancer recently has been increasing in Japan. Therefore, the early detection and treatment of breast cancers is extremely important for the following reasons:

i) The result of FNAC can be given to the patients quickly and they can find relief from anxiety more quickly. Consequently, the number of new patients with breast tumors who visit Tama-Nagayama Hospital has been increasing and has doubled in the last 5 years, compared to the first 5 years.

ii) Reexamination of FNAC can be performed immediately in the cases of no judgement (Class 0) due to insufficient materials, for example acellular or extremely scanty aspirates.

iii) Mastectomy for the cases of breast cancer can be performed as soon as possible.

However, it should be noted that it's not so easy to carry out the rapid diagnosis of FNAC because it interferes with the usual activities in the department of pathology if the staff is limited. Therefore, as a condition it is necessary to have adequate staff to perform the rapid diagnosis at short notice because of the extra work involved.

As compared to the results of FNAC during the first 5 years, the results of FNAC during the last 5 years has improved. We experienced only 4 false negative cases and 0 false positive cases among 1,198 cases during the last 5 years, whereas there

Table 2 The cases of misjudgement

Case	Age	Judgement		Histological type
		The first time	Reexamination	
1	43	II	III	Noninvasive lobular carcinoma
2	30	II	II	Invasive ductal carcinoma, scirrhous type
3	42	II	V	Invasive ductal carcinoma, scirrhous type
4	42	II	II	Invasive ductal carcinoma, scirrhous type
5	52	II	N.P.	Invasive ductal carcinoma, scirrhous type
6	40	II	N.P.	Invasive ductal carcinoma, scirrhous type
7	40	II	IV	Invasive ductal carcinoma, papillotubular type
8	44	II	N.P.	Invasive ductal carcinoma, papillotubular type
9	44	II	III	Invasive ductal carcinoma, papillotubular type
10	41	II	III	Invasive lobular carcinoma
11	40	II	IV	Invasive lobular carcinoma
12	62	II	III	Apocrine carcinoma
13	31	IV	III	Fibroadenoma with apocrine metaplasia
14	34	IV	N.P.	Fibroadenoma

N.P. : Reexamination was not performed.

Case 1—case 12 : false negative cases, Case 13—case 14 : false positive cases.

were 8 false negative cases and 2 false positive cases among 588 cases during the first 5 years. The important reason why the results during the last 5 years were good is considered to be as follows:

i) The techniques of FNAC for breast tumors by clinicians have been refined and ii) cytotechnologists and cytopathologists have progressed in judging the FNAC of breast tumors during the last 5 years.

Generally, the most important findings to judge as breast cancer using only FNAC are the following three findings; and any cases which possess these three findings can be judged as malignant with confidence.

i) A large number of tumor cells, ii) loosely cohesive tumor cells, iii) atypical tumor cells with hyperchromasia.

However, when these three findings cannot be seen at the same time, it is sometimes difficult to judge these cases as malignant with confidence. Furthermore, we have to emphasize that the findings of cytology and histology correspond to each other. Therefore, it is important for FNAC to consider the histological type to prevent misjudgement.

Regarding the 12 false negative cases, it would have been possible to prevent misjudgement if the histological type had been considered more carefully. In this study, invasive lobular carcinoma and invasive ductal carcinoma, scirrhus type, occupied 7 cases (58%) among 12 false negative cases. It is well known that the frequency of false negative cases in the FNAC for breast tumors is high in the invasive lobular carcinoma^{5,6} and invasive ductal carcinoma, scirrhus type⁷⁻⁹. So, we should particularly keep in mind the small naked nuclei with "Indian file arrangement" in the invasive lobular carcinoma¹⁰ and a small number of tumor cells with "intracytoplasmic lumina [ICL]"¹¹⁻¹³ in the invasive ductal carcinoma, scirrhus type.

With reference to the 2 false positive cases, which are fibroadenomas, if we had considered the histological type more carefully, it would also have been possible to prevent misjudgement. Fibroadenoma has been considered as the largest cause of equivocal diagnosis¹⁴ and false positive judgement¹⁵, so we should be careful not to overlook myoepithelial cells in the epithelial cluster and stromal cells in the background of the cluster, so

called "dimorphic cellular pattern"¹⁶.

Papanicolaou's classification has not been internationally accepted since it was discarded in the 1988 Bethesda system for reporting cervical/vaginal cytological diagnosis¹⁷. And the Papanicolaou's classification has not been recognized in *Acta Cytologica*, which is the *Journal of the International Academy of Cytology*. As a result, even in Japan, a new cytological grading is under consideration for breast tumors. However, considering the results of this study, we do emphasize that the following three points are very important for FNAC of breast tumors even if the Papanicolaou's classification is not used in Japan.

1) Reexamination should be performed immediately in the cases of no judgement (Class 0) due to insufficient materials because 5% cases among those of no judgement were revealed malignant by reexamination of FNAC.

2) As a general rule, biopsy should be performed for the suspicious cases of malignancy (Class III), because 30 cases (40%) among the 75 cases judged as suspicious cases were confirmed malignant by biopsy.

3) Rapid diagnosis during the operation by frozen section should be performed for the cases of Class IV just before the scheduled operation because of the following reason. Judgement of class IV in our hospital is only given to those cases in which we had any hesitation to perform mastectomy only on the result of FNAC. In fact, mastectomy was not performed for the 2 false positive cases judged as Class IV because rapid diagnosis by frozen section demonstrated no malignancy just before the scheduled operation. As a result, all the cases in which mastectomies were performed up to now were confirmed malignant.

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