COMPARISION OF THE CYTOLOGY TECHNIQUE AND THE FROZEN SECTION RESULTS IN INTRAOPERATIVE CONSULTATION OF THE BREAST LESIONS

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Abstract- ***The cytology study is effective and reliable technique in intraoperative consultation. This study was performed to evaluate the accuracy of the cytology study in intraoperative consultation of the breast lesions. 125 specimens of the breast lesions were examined and studied in Imam Khomeini Hospital during the years 1998-99.***

The sensitivity, specificity and accuracy for cytological method were 87.5%, 95%, 90.5% and for the frozen section 92.4%, 100% and 95.4% respectively.

The false positive reports were 2% in the cytology technique and the most important source of error and false positive reports was fibroadenoma in this method. By reviewing the results. It could be concluded that combination of these two techniques is beneficial and more reliable in intraoperative consultation reports of the breast lesions.

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Key Words: ***Intraoperative consultation, cytology, breast***

INTRODUCTION

Intraoperative consultation is one of the most important tests of every pathology laboratory (1,2). It carries a considerable weight in surgeon's decision for selecting the type of treatment. The frozen section is accepted as a reliable method in intraoperative consultation for many years (3). The cytology is another method used, and because of its advantages such as simplicity, low cost, rapidity, preventing frozen artifacts in tissue and also because it doesn't need Cryostat, is considered as initial steps in intraoperative consultation in some centers (4,5). But, some centers have ignored the importace of this method. According to the material covered earlier and the fact that the breast tissue is one of the most common tissues being sent for intraoperativc consultation, in this research its accuracy, sensitivity and specificity are evaluated.

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MATERIALS AND METHODS

125 specimens of breast lesions in Imam Khomeini pathology center (1998-1999) were included in this prospective cohort study. After receiving fresh breast tissues in pathology department they were sliced by scalpel then blood and the liquid on the surface were cleaned by gas after wards. We provided cytology slides by Imprint method and in some cases by scraping method. Two to three slides were taken from each sample in which one was fixed in alcohol immediately and the other was fixed in alcohol after being air-dried. The slides, which were fixed in alcohol, were stained by rapid H & E method and the slides which were air-dried, stained using Romanovsky method (6). Romanovsky method used in this research was wright-Giemsa as the first method, in which, slides are kept in Wright for 30 second and in Gimsa for 7 min and then washed with water (6). Second method was rapid MGG in which the staining time of MGG was shortened max of 3 min. In two years intervals, beginning the year 1998 till 1999, we took 125 cytology slides of breast samples in which 15 of the slides due to wrong labeling or scant cellularity of them were cancelled out of research. Finally two pathologists without any knowledge of final histologic results, macroscopic, clinical and mammography data examined 110 breast tissues for cytology evaluation. Results were reported as malignant, benign or defer without any initial statically study of diagnosis as true false or defer. After 9 months the same pathologists reviewed the slides. We assumed that 9 months period was enough for forgetting any cytologic details of slides in their memory. The purpose of slides reevaluating was testing the role of pathologists' experience in cytology results. The results gained through 4 times reports by pathologists were compared with final histology results referred as golden standard. Data analysis was performed with the software Epi-info and SPSS and making statistically tests of chi-square and T-test.

RESULTS

From 110 collected samples, 44 cases were malignant and 46 cases benign. The cytology results of each pathologist in either series of slides reading and results from frozen sections are shown in the table 1. It would be much easier to analyze them if we sort them as malignant, benign and defer cases respectively. Per our observation in all of 440 cytology reports 88.7% correct diagnosis, 2% false positive, 5.2% false negative and 4.1% defer existed, whereas the results for frozen sections were 94.6% correct diagnosis, 1.8% false negative and 3.6% defer and false positive results did not exist in this method (Table 1). It must be mentioned that the frozen section reports were in correlation to clinical and macroscopic data therefore the frozen section results are expected to be better than cytology results in this study. But it would be interesting referring to some points and diagnosis of results for errors and defers in this research. In total of 440 cytology reports, 9 false positive have been reported in which, 7 of them were related to fibroadenoma which is known as a pitfall source in cytology and in case of accessibility to macroscopic and clinical data of the patient it would be much easier to diagnosis it as benign lesions and the level of false positive reports was decreased to 4% when deleting these 7 cases. In comparison to the first series of research (all the reports of first and second pathologists in the initial study), an improvement in the reports of the results from the 2nd series of the study was noticed, respecting elimination of all the possible interfering elements. It appears that the experience gained in the initial study has improved the results of the second series. In the 2nd series of study (after 9 months) the level of correct diagnosis was 91.9%, incorrect diagnosis 5.4% (false positive 2.2%, false negative 3.2%) and level of defer were 2.7% respectively in which they were more correlated with results of frozen sections. Sensitivity of first series of cytology study and second series of cytology study were 83.3%, 91.6% respectively (P value= 0.008) and comparison of the sensitivity of the two series of cytology study with frozen sections has not marked differences (P= 0.7) (Table 2). In initial series of study (220 cytology diagnosis) 6 false positive reports existed in which 5 of them were fibroadenoma, they all had cellular smear with mild atypism. These factors and lack of high degree of attention to bipolar naked nucleus of myoepithelial cell had led to misdiagnosis. The other false positive report was related to the proliferative fibrocyctic disease . From 14 false negative reports, some were related to sampling errors, invasive lobular carcinoma and invasive ductal carcinoma with low cellularity. From 12 defer reports, 4 were finally diagnosed as benign lesions such as fibroadenoma or severe ductal hyperplasia and 8 cases were. finally diagnosed as malignant in the form of carcinoma of lobular, tubular, mucinous types, lymphoma and low-grade invasive ductal carcinoma. In second series of study (220 cytology reports) only 3 reports were false positive, of which two were related to fibroadenoma with cellular smear and atypism. The considerable reduction in false positive reports was due to attention of the pathologists to bipolar naked nuclei of myoepithelial cell in the backgrounds of the smears. Nine false negative diagnosis were mostly due to sampling errors. Another interesting point which was noticed after analyzing the frozen sections and cytology results, was the deliberation of false negative and defer causes in the frozen sections and evaluating the cytology results in the samples. Out of 4 defer reports in the frozen sections, 3 cases were finally diagnosed as malignancy as follows. One case had ductal carcinoma insitu (DCIS) and two others had invasive ductal carcinoma (IDS). One of defer reports was due to fatty tissue which could not be sectioned by Cryostat. All the defer causes in the frozen sections were diagnosed correctly by cytology method. Out of two false negative in the frozen sections, one had final diagnosis of DCIS which was diagnosed as malignant lesion in cytology and the other had a small foci of invasive ductal carcinoma in background of granulomatous mastitis which had also false negative by cytology method. It was concluded that a correlation of the two methods and frozen sections will increase the sensivity and specifety of frozen section method tremendously. In this study five cytological criteria:

Cellularity of smear 2- Loss of cohesion 3- cellular atypism 4- Presence of bipolar cells in background 5- intranuclear vacuoles or hole was evaluated in light of malignancy in, cytology samples. In fact these criteria were valued in differentiation of malignant from benign lesions (P< 0.05). In malignant lesions there was more cellularity, loss of cohesion, atypism and nuclear hole and low bipolar naked nuclei in background of smear in comparison to benign lesions.

Table 1. A comparison of cytology, frozen section and histopathology results

Results	Cytology (%)	Frozen section (%)	Histopathology (%)
correct	88.7	94.6	100
False positive	4.2	0	0
False negative	5.2	1.8	0
Defer	4.1	3.6	0
Total	100	too	100

Table 2. A comparison of cytology results of first and second series studies and frozen sections

Type of study	**Number of specimen**	**Sensitivity (%)**
1st series of cytology study	**220**	83.3
2 nd series of cytology study	**220**	91.6
Frozen section study	110	92.4

In base of Yates correct X^2 test
Comparison of cytology sensitivity in first and second series of study
X= 6.84 P value= 0.008
Comparision of cytology sensitivity in first series study and frozen sections
X= 5.67 P value= 0.017
Comparision of cytology sensitivity in second series study and frozen sections
X= 0.08 P value= 0.722

Table 3. A comparison of cytology results of our and Silverberg et al studies

Cytology result	**Our study (%)**	**Silverberg et al study (%)**
Correct	**88.7**	87.5
Incorrect	**7.2**	3.2
Defer	**4.1**	9.3
Total	100	100

DISCUSSION

Breast tissue is one of the most widespread organ that is sent for intraoperative consultation. Also, cytology method is not a common practice for consultation purposes during surgery yet considering the simplicity, fast rate and the low cost of this method, we studied the provided slides of 110 breast lesions and compared the result, with a similar article which was published in 1987 by Esteban and Silverberg (7) since in this article, the clinical and macroscopic data in the cytology results were also ignored. Whereas, in the other published articles, the cytology results were defined using all the available data (macroscopic, clinical & microscopic) (4,7,8). In our research, out of 440 reports accomplished by 2 pathologists reading the slides 4 times, there were 88.7% correct diagnosis, 7.2% incorrect diagnosis (2% false positive, 5.2% false negative) and 4.1% defer (Table 3). These findings in Silverberg and his colleagues' report were as follows:
87.5% correct diagnosis, 3.2% incorrect diagnosis (1.1% false positive,, 2.1% false negative) and 9.3% defer reports. Taking these figures under consideration, we notice that the level of correct diagnosis is better than that of Silverberg and his colleagues' article (7). But wrong results were twice as much and the level of defer reported half of them. With a slight close attention, we could assume that our pathologists, persistence for a definite diagnosis rather than defer reports could be the cause of it. Another point to make is that the attention being paid to the reasoning behind false positive in our research which was mostly related to fibroadenoma in which case they would be correctly diagnosed mostly if the macroscopic and clinical data of the patient were accessible. Although in this research the results of frozen section were better relative to cytology reports but it should be mentioned that the cytology reports, despite frozen section, were done without any knowledge of clinical and macroscopic data. The comparison of the first series of the research results with that of the second series of the slides reviewing, demonstrates noticeable improvement in which pathologists expertise plays a major role in this improvement. Also the results from second series of the study were extremely similar to the frozen section results and they were better than that of Silverberg anal Co-workers. The sensitivity, specificity and accuracy in our research for cytology reports in all were 90.5%, 87.5%, and 95% accordingly and for frozen section they were. 95.4%, 92.4% and 100%, where as these findings in Silverberg and co-workers were 90%, 83.7%, and 97% respectively. In conclusion according to the results achieved, we noticed that the statistical data of our research were an acceptable data and could be considered a reliable procedure if and when correlated with macroscopic and the clinical data of the patient were accessible. We concluded in this research that in order to eliminate any error in sampling or Air-dry artifact (two main sources of errors) as much as possible when preparing the cytology slides, pathologists must have a direct look over it or at least manage to make them on their own. With precise preparation of the slides, and in case of gaining enough experience by pathologist in this field which could be an important factor in confirming cytology result, the need to perform frozen section could be eliminated tremendously (at least in breast lesions), and it could be replaced as a reliable method for frozen section.

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