



ASSESSMENT OF THE POTENTIAL OF FINE NEEDLE ASPIRATION CYTOLOGY (FNAC) IN THE DIAGNOSIS OF TUMOR AT A PUBLIC MEDICAL COLLEGE HOSPITAL IN BANGLADESH

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Abstract: We determined the sensitivity, specificity, positive and negative predictive values of physical examination and fine needle aspiration cytology (FNAC) for diagnosis of tumor's, considering histopathology as standard that included fifty suspected tumor patients. Following the completion of interview for clinical history and physical examination, FNAC and histopathology were performed. Lump was present in 44% cases, weight loss was observed in 42% cases as complaint signs and pain occurred at the site of tumor in 44% cases. Physical examination indicated that 36% cases were malignant and 64% were benign tumors. Histopathological diagnosis of the tumor confirmed that 46% cases were malignant and 54% were benign. Thus, physical examination was sensitive in 52.11%, specific in 77.78%, accurate in 76% and the negative and positive predictive values were 34.37% and 66.57%, respectively. However, FNAC showed 72% neoplasm and 28% non-neoplasm, while histopathology revealed 86% neoplasm and 14% non-neoplasm among the patients. So, the sensitivity, specificity, accuracy, false positive and false negative results, positive and negative predictive values of FNAC were 62.50%, 88.46%, 76%, 16.67%, 28.12%, 83.33% and 71.88%, respectively. Particularly in 28% non-neoplasm's, FNAC showed equal accuracy and sensitivity and that was 50%. In correlation with 27 benign cases and 23 malignant tumors from histopathology, FNAC showed accuracy of 92.60% and 43.48%, respectively. Though FNAC is less sensitive than histopathology in making unequivocal diagnosis of cancer but insignificantly different from histopathology in interpreting atypical or malignant cases of tumors.

Keywords: Tumor, laboratory diagnosis, FNAC, histopathology

Introduction

The character of the complaints, specific symptoms and history of the patients, that's the physical examination has remained as one of the most important diagnostic tool in the medical history, particularly, in the practice of diagnostic pathology devoted in identifying the nature and progression of tumor by studying morphologic changes in tissues and chemical alteration in patients metabolism (Carter *et al.*, 1998). However, Orell *et al.*, reported in 1992 that fine needle aspiration cytology (FNAC) method can be used for most of the assessment of readily palpable lesions in sites such as the breast, thyroid, and lymph nodes. With the time, FNAC has gained popularity as a rapid cost-effective, relatively painless, precise and effective means to diagnose tumor. As of now, Abbas *et al.*, 2004 state that FNAC has yet to be established itself in the routine follow-up of patients. Schwartz, 1995 ascertain that FNAC permits differentiation among

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normal, dysplastic, and cancerous cells and in addition permits the recognition of cellular changes characteristic of carcinoma *in situ*. Again, core biopsy that means histopathology is one of the most sensitive procedures for the detection of cancer. Mordenti *et al.*, 1998 found that histopathological feature of carcinoma varies with a wide degrees of cell differentiation, although distinctive findings associated with each clinical pattern. They also found there was no significant difference between sensitivity of FNAC and histopathology interpreted as either atypia or malignancy, although the sensitivity of histopathological diagnosis interpreted as unequivocal malignancy was greater than that of FNAC.

Carter *et al.*, 1988 ascertained that FNAC and histopathological diagnosis should only be attempted when the pathologists will sure about the details of clinical history, physical examination which might be served as a safeguard in the interpretation of the aspirate/excised material. Hence, the steady drop in cancer mortality rates since the early 1990s has, to a great extent, been due to improvements in early diagnosis (Wilkinson *et al.*, 1993). Martin and Ellis, 1994 reported that a definite diagnosis of benign lesion not only saves the patient from unnecessary physical, emotional and psychological trauma but also relieves the health services from undue burden and pre-operative diagnosis of malignant lesion providing ample opportunity for patient's counseling and planning of possible single-stage surgical treatment. Physicians in developing countries have been found to be dependent upon histopathology reports of the neoplasms even though FNAC is comparatively very much cost effective. Whereas, biopsy is time taking, expensive, more painful, producing unwanted bleeding at times and needs more time for its processing and reporting leading to delay in the planning of definitive treatment. More over many a time a surgeon does not like an encapsulated tumor to be breached. Very few studies found to explore the potential of FNAC for the diagnoses of tumor lesions. In Bangladesh, FNAC and histopathology both are in young stage but practiced rapidly in most of the public and private hospitals. But pathologist has still not assessed the suitability and perfection rate of those diagnosis methods. Considering above mentioned facts, it is imperative to evaluate and compare among the present art of investigative procedures used in cancer diagnosis at a public medical college hospital laboratory in the southern region of Bangladesh.

Materials and Methods

Physical and Cytopathological Examination: Fifty clinically suspected tumor patients were picked up randomly from different wards of Khulna Medical College Hospital and subjected for FNAC and open biopsy during a period of January 2007 to August 2008. Finally, the diagnosis results and correlation was evaluated in terms of medical statistics. The patients were selected randomly on the basis of general physical examination, those who showed the symptoms like swelling, enlargements of lymph node and lump present at any part of body or clinically suspected as tumor patients. Then the history of patients were collected using as per required medical proforma which includes history of present and past illness, general examination, routine examination and afterwards sent for FNAC and histopathological diagnosis. FNAC were performed according to the procedures described by Zajicek (1974) in which we inserted the small bore needle into the lump or site of swelling of the clinically suspected patients and collected cells and fluids from the lump or swelling site subsequently aspirated on the slide and stored in the jar contains alcohol. Then stained according to Papanicolau and observed under microscope after dried.

Histopathological Examination: The excised specimens collected by surgery department and sent to the department of pathology for histopathological examinations. Naked eye examination is very much important as because, it may suggest some provisional diagnosis. Therefore, all biopsy specimens were examined grossly and any gross pathological changes were noted. The excision and incision specimens kept overnight in 10% formal saline for fixation. Fifty specimens were

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processed in the laboratory of Pathology. All blocks were then cut and stained with routine haematoxylin and eosin method. Stained slides were mounted with DPX using no.2 cover slip and observed through microscope.

Statistical Analysis: The data were analyzed in terms of conventional descriptive medical statistics. The sensitivities were compared utilizing chi-square test and the positive predictive value was calculated by means of Fishers exact test and the method of Galen and Gambino. Where, Accuracy = Ratio of true positive and true negative results to the total numbers of the patients; fraction of test results that are correct, Negative predictive value = Ratio of true negative results to predicted negative results, Positive predictive value = Ratio of true positive results to predicted positive results, True Positive = FNAC correctly diagnoses the case as malignant (A), False Positive = FNAC diagnoses falsely as malignant (B), False Negative = FNAC diagnoses falsely as not having malignant (C), True Negative = FNAC correctly diagnoses the case as benign (D), Sensitivity = Ratio of true positive results to all patients with disease: if there is a cancer (or neoplasm) what is the probability that the test will detect? And Specificity = Ratio of true negative results to all patients without disease: if there is no cancer (or neoplasm) what is the probability that the test will confirm it?

Results

Presenting complaints: The commonest mode of presentation of complains was lump in the site of the tumor and weight loss. Twenty-two patients (44%) presented with lump, 34% patients suffered in weight loss as a sign of tumor and seventeen patients had pain in lump (Table 1).

Table 1. Presenting complaints of the patients

Presenting complaints	Numbers of patients
Swelling	11 (22%)
Pain in the swelling	7 (14%)
Weight loss	21 (42%)
Lump	22 (44%)
Pain in lump	17 (34%)
Poor appetite	12 (24%)
Ulcerative growth	4 (8%)
Dehydration	3 (6%)
Enlargement of Lymph node	11 (22%)
Fever	15 (30%)

Correlation between the findings of physical and histopathological diagnosis: In eighteen patients the tumor were diagnosed clinically as malignant and thirty-two as benign. On the other hand, histopathological findings revealed 46% malignant and 54% benign cases (Table 2).

Table 2. Results of physical and histopathological diagnosis

Physical examination	Histopathological diagnosis	Remarks
Types of lesions and their number	Types of lesions and their number	
Malignant-18 (36%)	Malignant-12 (24%)	True positive
	Benign-6 (12%)	False positive
Benign-32 (64%)	Malignant-11 (22%)	False negative
	Benign-21 (42%)	True negative

From the correlation between physical examination and histopathological diagnosis results, it was found that physical examination was sensitive in 52.11 %, specific in 77.78 %, accurate in 76% and negative predictive value was 34.37 %. The positive predictive value was high, that was 66.57% (Table 3).

Table 3. Statistical analysis for physical/clinical examination of patients

Test being evaluated (PE)	Reference standard test (Histopathology)			
	Positive	Positive		Negative
Negative	A = 12	B = 6	C=11	D=21
Sensitivity				52.11%
Specificity				77.78 %
Accuracy				76%
PPV				66.57%
NPV				34.37%

Correlation between the findings of FNAC and histopathological diagnosis: FNAC revealed seven (14%) as lymphoma, six (12%) as breast tumor, six (12%) as ovarian tumor, five (10%) as stomach lesion, five (10%) as leiomyoma. Cervix tumor, lipoma and osteoclastoma each were two (4%), one case was haemangioma and other 28% was non-neoplastic (Table 4).

Table 4. Results of FNAC diagnosis

Type of tumor	Number patients
Lymphoma	7 (14%)
Breast tumor	6 (12%)
Ovarian cancer	6 (12%)
Stomach tumor	5 (10%)
Leiomyoma	5 (10%)
Cervix cancer	2 (4%)
Lipoma	2 (4%)
Osteoclastoma	2 (4%)
Haemangioma	1(2%)
Non-neoplastic	14 (28 %)
Total	50

Where as the histopathology (excised specimens) revealed ten (20%) cases as lymphoma, seven (14%) as breast carcinoma, six (12%) as ovarian cancer, six (12%) as leiomyoma, five (10%) as stomach cancer, lipoma and osteoclastoma each were two (4%) as well as 7% cases diagnoses as non-neoplastic (Table 5).

Table 5. Histopathology examination result of tumor patients

Type of tumor	Number patients
Lymphoma	10 (20%)
Breast carcinoma	7 (14%)
Ovarian cancer	6 (12%)
Leiomyoma	6 (12%)
Stomach tumor	5 (10%)
Lipoma	2 (4%)
Osteoclastoma	2 (4%)
Cervix cancer	1 (2%)
Haemangioma	1 (2%)
Pleomorphic adenoma	1(2%)
Follicular neoplasm	1(2%)
Squamous cell carcinoma	1(2%)
Non-neoplastic	7 (14%)
Total	50

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The analysis of the non-neoplastic cases from FNAC reported that patients affected by TB, fungal infection, colloid goiter, thyroid problem etc. which was not concordance with histopathology and On the other hand histopathology revealed seven (50%) non- neoplastic of fourteen cases that was concordance with FNAC and other seven (50%) were tumor (Table 6).

Table 6. Non –neoplastic cases from FNAC and histopathology with correlation

FNAC report	Number	Histopathology report	Number	Remarks
TB	1	Pleomorphic adenoma	1	False negative
TB	1	Lymphoma	1	False negative
Reactive-lymphadeuieis cell	1	Lymphoma	1	False negative
Fibro- adenosis	1	Ductal carcinoma	1	False negative
Fungal cystic growth	1	Ductal carcinoma	1	False negative
Ectopic thyroid	1	Follicular neoplasm	1	False negative
Nodular colloid goiter	1	Squamous cell carcinoma	1	False negative
Non-neoplastic	7	Non-neoplastic	7	True positive
Total	14	Total	14	

When we analysis only the benign cases found that eighteen cases were diagnosed as benign tumor by FNAC. Seven of these cases were non- neoplastic, two were benign neoplasm and other eighteen were carcinoma on basis of core biopsy (Table 7).

Table 7. Benign tumors from FNAC and histopathology and their correlation

FNAC report	Number	Histopathology report	Number	Remarks
Non-neoplastic	7	Non neoplastic	7	True positive
Adenoma of stomach	5	Adenoma	5	True positive
Lymphoma	3	Lymphoma	3	True positive
Ductal carcinoma	3	Ductal carcinoma	3	True positive
WD-adenocarcinoma	3	WD-Adenocarcinoma	3	True positive
Fibroadenoma	2	Fibroadenoma	2	True positive
Non-neoplastic	2	Benign tumor	2	False positive
Lipoma	1	Lipoma	1	True positive
Cervix cancer	1	Cervix cancer	1	True positive

Among the malignant carcinomas, three cases were diagnosed as Non-Hodgkin lymphoma, five cases were suspected as leiomyoma; one case was haemangioma and another one as neurilemmoma by FNAC. Five cases from non-neoplastic were diagnosed as malignant, such, one was diagnosed as lymphoblastic lymphoma, one melano-carcinoma, one epithelial carcinoma and three adenocarcinomas, one squamous cell carcinoma, and one UD-osteoclastoma were diagnosed on histopathological examination (Table 8).

Table 8. Malignant carcinoma diagnosed from FNAC and their correlation with histopathology findings

FNAC report	Number	Histopathology report	Number	Remarks
Lymphoma	4	non-Hodgkin lymphoma	3	True positive
		Lymphoblastic lymphoma	1	False negative
Breast tumor	2	Melano carcinoma	1	False negative
		Epithelial carcinoma	1	False negative
Ovarian tumor	3	Adeno-carcinoma	3	False negative
Leiomyoma	5	Leiomyoma	5	True positive
Cervix tumor	1	Squamous cell carcinoma	1	False negative
Haemangioma	1	Haemangioma	1	True positive
Non-neoplastic	5	Malignant	5	False negative
Lipoma	1	Neurilemmoma	1	True positive
Osteoclastoma	1	UD-Osteoclastoma	1	False negative

Regarding total patients, the accuracy of FNAC was analyzed for the detection of neoplasm by contrasting, FNAC and Histopathology, FNAC showed sensitivity 62.50%, specificity 88.46%, accuracy 76%, FPR 16.67%, FNR 28.12%, PPV 83.33%, and NPV 71.88% (that is, malignant together with benign neoplasm) (Table 9 and 10).

Table 9. Comparison of FNAC and histopathological examinations tumor patients

FNAC report	Number	Histopathology report	Number	Remarks
Lymphoma	7	Lymphoma	3	True negative
		non-Hodgkin lymphoma	3	True positive
		Lymphoblastic lymphoma	1	False negative
Breast tumor	6	Ductul carcinoma	2	True negative
		Fibroadoma	2	True negative
		Melano-carcinoma	1	True positive
		Epithelial carcinoma	1	True positive
Ovarian tumor	6	WD-Adenoma	3	False positive
		Adeno-carcinoma	3	True positive
Stomach tumor	5	Adenoma	5	True negative
Leiomyoma	5	Leiomyoma	5	True positive
Cervix cancer	2	Cervix cancer	1	True negative
		Squamous cell carcinoma	1	False negative
		Lipoma	1	True negative
Osteoclastoma	2	Neurilemmoma	1	False negative
		Osteoclastoma	1	True positive
		UD-Osteoclastoma	1	False negative
Haemangioma	1	Haemangioma	1	True positive
Non-neoplastic	14	Non-neoplastic	7	True negative
		Malignant	5	False negative
		Benign	2	True negative

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Table 10. Statistical analysis for FNAC tumor detection

Test being evaluated (FNAC)	Reference standard test (Histopathology)	
	Positive	Negative
Positive	A = 15	B = 3
Negative	C = 9	D = 23
Sensitivity	A / (A+C) = 62.5%	
Specificity	D / (B+D) = 88.46%	
Accuracy	(A+D) / (A+B+C+D) = 76%	
False positive result	B / (A+B) = 16.67%	
False negative result	C / (C+D) = 28.12%	
Positive predictive value	A / (A+B) = 83.33%	
Negative predicted value	D / (C+D) = 71.88%	

When only non-neoplastic were taken sensitivity, accuracy and specificity all were 50% (Table 11).

Table 11. Analysis for non-neoplastic diagnosis of patients

Test being evaluated (FNAC)	Reference standard test (Histopathology)	
	Positive	Negative
Positive	A = 7	B = 7
Negative		
Sensitivity	50 %	
Specificity	50 %	
Accuracy	50 %	

The Benign case from FNAC and their relation with histopathological findings showed sensitivity, accuracy and specificity all were 92.60% and NPV 7.40% (Table 12).

Table 12. Analysis for benign tumor of patients

Test being evaluated (FNAC)	Reference standard test (Histopathology)	
	Positive	Negative
Positive	A = 25	B = 2
Negative		
Sensitivity	92.60%	
Specificity	92.60 %	
Accuracy	92.60 %	
Negative predictive value	7.4 %	

When only malignant tumor were taken as numerator keeping in view that malignant and benign nature of the neoplasm be differentiated by the FNAC and histopathological detection, the comparative results were as sensitivity , specificity and accuracy of FNAC were all 43.48% (Table 13).

Table 13. Statistical analysis for malignant tumor

Test being evaluated (FNAC)	Reference standard test (Histopathology)	
	Positive	Negative
Positive	A = 10	C = 13
Negative		
Sensitivity	A / (A+C) = 43.48%	
Specificity	43.48%	
Accuracy	43.48 %	

Discussion

As we studied among different symptoms within the patients, formation of lump and weight loss was the highest record that's were similar to American Cancer Societies listed symptoms of tumor. Schwartz (2003) studied three hundred and forty one cases and showed 88 benign and 27 malignant tumors by physical examination where as histopathology detected 91 benign and 31 malignant tumor. Physical examination by Stewart *et al.*, 1997 showed sensitivity, specificity, and accuracy was 92 %, 100 %, and 98 % respectively in correlation with core biopsy. Our data revealed that the efficacy of clinical and physical examination was low in compared to other researcher findings. This was because of lack of expert, skill and specialists as well as we are in tender age in the field of oncology. Again, Ahmed, *et al.*, 1997 studied 35 benign breast tumor that was diagnosed from FNAC but finally they found 19 cases were benign (54.28%) and 16 cases (45.71%) were malignant by histopathology. However, False-negative results were caused by sampling error, most notably in cystic tumors, or were due to misinterpretation of uncommon neoplasm.

According to Ashcroft and Vanherle (1981) FNAC was shown to achieve a diagnostic accuracy of over 90% in terms of predictive value, sensitivity, specificity and efficiency in the diagnosis of neoplasm. False negative rates of less than 1-2% were reported. In addition, diagnosis of metastatic melanoma performed by Rodrigues and Thomson (1992) showed out of 99 cases where the positive predictive value of fine needle aspiration was 99%. Ahmed, *et al.*, 1997 reported that FNAC showed sensitivity, specificity and accuracy 54.28% and all the malignant lesions turned out to be malignant on final biopsy/ core biopsy (100% sensitivity and PPV). Our result is almost similar to as other reporter. The accuracy of FNAC varies widely both in published literature as well as in the community (Giard and Hermans, 1992). Training and ability in specimen interpretation is important (Zarbo *et al.*, 1991). Studies have shown that the majority of missed diagnoses are due to problems in sampling and specimen preparation (Cohen *et al.*, 1987). In this study the sampling has been adequate in all cases except in three. Of course repeat aspiration had to be performed in five cases for adequacy. The use of FNAC as a diagnostic tool in lymph node based disease has historically been controversial (Katz, 1997). Part of the reluctance in accepting FNAC for the primary diagnosis of lymphoma originates from a time when recognition and classification of malignant lymphomas was difficult even in histological material (Young *et al.*, 1998). Recently, FNAC has become a more common practice in the primary diagnosis, sub-classification, and management of patients with lymphoma. However, the use of FNAC in various centers depends to a large extent on local traditions. The successful application of immunologic markers on material obtained by FNAC has significantly promoted a wider acceptance of the use of FNAC in the final diagnosis of most non-Hodgkin lymphomas (Young and Al-Saleem., 1999). Based on a review of the literature of Das, 1999 and Bizjak-Schwarzbartl, 1997 the value and limitations of FNAC in the diagnosis of lymphomas should not be assessed in terms of cytohistological correlation alone with histology taken as the gold standard.

FNAC is often used as a first line of investigation for screening cases with lymphadenopathy since this method is easy to perform as well as being rapid, and inexpensive. FNAC can help to differentiate between lymphoma, metastasis, nonhemopoietic neoplasms, specific infections such as tuberculosis lymphadenitis, and nonspecific reactive lymphadenitis. In lymphoma patients, FNAC has a role in staging and in the assessment of residual and/ or recurrent disease and may obviate the need for surgical biopsy in cases of lymphoma located in non-accessible areas (Moriarty *et al.*, 1989). An issue recently addressed by Dong *et al.*, 2001 is the availability of material for cytogenetic or molecular genetic analysis for diagnosis and of archival material for correlative scientific studies. When open biopsies are performed for diagnosis, there is always an archive of paraffin-embedded (and often frozen tissue) material that can be used for diagnostic and research purposes, molecular and genetic analyses, and additional immunophenotyping. In the

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present era of emerging technologies of genomics and proteomics, it is important to consider this limitation of FNAC.

Conclusion

We found that accuracy of physical examination is not significant due to low rate of concordance and revealed no significant difference in sensitivity between FNAC and histopathology interpreted as either atypical or malignant where both are sensitive and effective methods of diagnosis of cancer, but histopathology is more sensitive than FNAC in making an unequivocal diagnosis of cancer. Again, Biopsy has been the established diagnostic procedure to confirm the diagnosis of cancerous lesions. But sometimes surgeons do not like to breach the overlying epithelium of the lesions before coming to a probable diagnosis. Moreover, in developing countries, it takes nearly two weeks to get the histopathology report whereas FNAC report can be obtained within a couple of days. Hence keeping these points in mind, this study was carried out to explore the potential of FNAC as an alternative diagnostic procedure. Thus, we suggest for FNAC over the histopathology because FNAC includes the rapidity of procedures, performance in outpatients settings, relative painless, low cost and easy clinico-pathological correlation. FNAC has been highly accurate for the diagnosis of lesions of the tonsils, hard palate and floor of mouth. It was also seen that the study proved to be highly accurate for the malignant lesions which can be of great help in early planning of the definitive course of management. However, FNAC and histopathology can be applied in those institutions where excellent diagnosis services and well skilled pathologist are available. Due to small sample size, the result of this study needs further verification by relatively larger scale studies.

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