The accuracy of fine needle aspiration cytology for the diagnosis of non-thyroid neck masses

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ABSTRACT

Objectives: The aim of the study was to evaluate the accuracy of fine needle aspiration cytology (FNAC) in the diagnosis of neck masses.

Materials and methods: A retrospective study was undertaken of 188 neck masses that had undergone FNAC, over a five-year period from 2010-2015, at Prince Rashid Bin Al-Hasan Hospital. The FNAC reports were reviewed and compared to the final diagnosis. The final diagnosis was determined either by the final histopathological diagnosis or the clinical outcome.

Results: 110 FNACs were included in the study. The sensitivity, specificity and accuracy of FNAC in distinguishing neoplastic from non-neoplastic cervical masses (including salivary gland masses) were 90%, 86% and 94%, respectively. The sensitivity of FNAC in distinguishing malignant from benign neck masses (including salivary gland masses) was 46% with a specificity of 98% and an overall accuracy of 85%. In distinguishing malignant from benign salivary gland masses, the sensitivity of FNAC was 8% with a specificity of 98% and accuracy of 78%. Regarding lymphoma, FNAC had sensitivity of 71% and specificity of 98% with a diagnostic accuracy of 96%. The sensitivity of FNAC in detecting metastatic carcinoma to the neck was 83%, with a specificity of 100%

Conclusion: Although FNAC seems to be an attractive investigation, it should be used cautiously in assessing salivary gland diseases, cystic lumps of the neck and lymphomas.

Keywords: Fine needle aspiration cytology, neck masses, accuracy

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Introduction

Neck masses comprise a wide spectrum of diseases owing to the complex anatomy of the region. The main concern to the clinician is to differentiate between neoplastic and non-neoplastic mass, and whether the mass is benign or malignant.

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Fine needle aspiration cytology (FNAC) is routinely used in the diagnostic work-up of head and neck masses in conjunction with clinical examination and computed tomography.[1] Furthermore, FNAC has been established, or accepted, as pre-requisite investigation in the assessment of a patient presenting with a neck lump.[2-6] The goal of FNAC in the head and neck, as in other anatomic sites, is to provide clinically useful information that exceeds that obtained by palpation or imaging alone.[7] The most attractive feature of FNAC is its minimally-invasive nature,[1,4] and the main advantage is the avoidance of surgical biopsy and its attendant risks.[4,6,7] The fundamental indication for using FNAC is a mass lesion, which is serious enough to warrant consideration of using surgical biopsy as a means of taking a sample.[5] Some proponent of FNAC would consider the presence of any mass lesion in the head and neck to be an indication for the procedure. Others would consider the procedure useful only in answering a specific clinical question.[16] there are relatively few contraindications to FNA in the head and neck. This derives largely from the relatively a traumatic nature of the procedure. Obviously, lesions adjacent to large arteries should be approached with caution. Some authors advise against aspirating carotid body tumors.[16] FNAC has well-documented limitations[10]. Limitations include the potential for false positives and false negatives.[5] Its usefulness has been debated in lymphoma diagnosis,[2,3,8,9,10] and in the investigation of salivary gland diseases.[3,6,11,12,13] In addition, cystic neck lumps pose further challenge to its diagnostic accuracy.[9,15]

As FNAC is considered a primary diagnostic work-up in the management of neck masses, its accuracy needs to be constantly re-evaluated, and an on-going audit of its performance within each institution is required.[11] the aim of the current study was to evaluate the accuracy of FNAC in the diagnosis of neck masses. The study has been approved by the Institutional Review Board of the Jordan Royal Medical Services.

MATERIAL AND METHODS

A retrospective study was undertaken of 188 neck masses that had undergone FNAC, over a five-year period from 2010-2015, at Prince Rashid Bin Al-Hasan Hospital. Inclusion of patients was made irrespective of age or sex. And all aspirates were taken from deep neck masses. The neck masses were evaluated at the department of oral and maxillofacial surgery. Thyroid masses were excluded as they were not managed by an oral and maxillofacial surgeon. The FNAC reports were reviewed and compared to the final diagnosis. The final diagnosis was determined either by the final histopathological diagnosis or the clinical outcome. All FNACs were requested by an oral and maxillofacial surgeon, and were taken by a cytopathologist at the department of pathology. No on-site aspirates were undertaken.

Lesions were assigned to a benign or a malignant category. Masses diagnosed or suggested by FNAC as malignant were considered malignant. All other masses were assigned to the benign category. Masses that had resolved without surgical excision were considered inflammatory or reactive, and so, categorized as benign. Those cases, at the time of presentation, were not considered suspicious and FNACs showed to be reactive or inflammatory and so were kept under clinical follow-up. Masses that were not followed-up surgically or clinically, and FNACs that failed to yield a diagnosis, were excluded. Salivary gland masses were dually evaluated; once as part of the whole neck, and, in another, as a separate entity. The true negative (TN), true positive (TP), false negative (FN), and false positive (FP) rates were calculated. True positives were defined as cases in which FNAC reported malignancy as the diagnosis or in the differential, and a malignant lesion was confirmed on final surgical pathology. True

negatives were defined as cases with benign FNAC and benign surgical pathology, including benign neoplasms, or cases with benign FNAC in which the masses resolved with clinical follow-up. False negatives were defined as cases with benign FNAC and malignant surgical pathology. False positives were defined as cases with malignant FNAC and benign surgical pathology. The sensitivity (TP/TP+FN)x100%, specificity (TN/FP+TN)x100%, and accuracy ([TP+TN]/[TP+TN+FP+FN])x100% of FNAC for determining the various pathological neck masses were calculated.

RESULTS

A total of 188 FNACs of neck masses was performed during the study period. Final diagnosis was reached in 110 FNACs, and 78 aspirates were excluded because they either were non-diagnostic or were not followed surgically or clinically. The study comprised 109 patients of which 49 were females and 60 were males. One male patient had FNACs of two different masses. The age of the studied population ranged from 1 year to 80 years with a mean of 36 years.

The final diagnosis of the biopsied neck masses are shown in ***(Table I).*** Masses of inflammatory or reactive etiology comprised the highest percentage of the diagnosed neck masses (40%). Three masses which were diagnosed by FNAC as inflammatory turned out to be malignant. One of these was taken from the parotid gland, and the others from submandibular and deep cervical lymph nodes. The final diagnoses were carcinoma ex pleomorphic adenoma and Hodgkin's lymphomas, respectively. On the other hand, one mass that was suspicious for non-Hodgkin's lymphoma by FNAC turned out to be a follicular reactive hyperplasia on final diagnosis. In this subgroup, the sensitivity, specificity and accuracy of FNAC in distinguishing malignant from inflammatory masses were 81%, 98% and 93%, respectively ***(Table II).***

In distinguishing neoplastic from non-neoplastic cervical masses, including salivary gland masses, the sensitivity, specificity and accuracy were 90%, 86% and 94%, respectively ***(Table II).***In this group (neck masses including salivary gland masses), the sensitivity of FNAC in detecting malignancy was 46% with a specificity of 98% and an overall accuracy of 85% ***(Table II).***When salivary gland masses were excluded, the sensitivity of FNAC in detecting malignancy was 73% with a specificity of 98% and accuracy of 93% ***(Table II).*** However, in distinguishing malignant from benign salivary gland masses alone, the sensitivity of FNAC was 8% with a specificity of 98% and accuracy of 78% ***(Table II).***FNAC missed the diagnosis of malignant salivary gland tumors in 11 out of 12 cases, most of them were low to intermediate grade mucoepidermoid carcinomas. On the other hand, the positive predictive value of FNAC for detecting benign salivary gland tumors was 98% ***(Table II).***

Regarding lymphoma, FNAC had sensitivity of 71% and specificity of 98%, with a diagnostic accuracy of 96% ***(Table II).***Two neck masses that were diagnosed by FNAC as reactive turned out to be lymphomas. On the other hand, two masses diagnosed by FNAC as lymphomas revealed to be embryonal rhabdomysarcoma and follicular reactive hyperplasia. FNAC correctly diagnosed lymphoma in 5 of 7 patients, with a positive predictive value of 71% ***(Table II).***

Metastatic carcinomas to the neck were diagnosed by FNAC in 5 cases, and all of them were positively correlated with the final diagnosis. However, one mass that was diagnosed by FNAC as infected cyst turned to be a metastatic squamous cell carcinoma (SCC), giving a sensitivity of 83% and specificity of 100%. ***(Table II).***

Table I: Correlation between FNAC diagnosis and definitive diagnosis

FNAC Diagnosis	No.	Definitive diagnosis	No.
• Inflammatory	46	• Inflammatory	43
		• Malignant SG tumors	1
		• Lymphoma	2
• Benign SG tumors	36	• Benign SG tumors	26
		• Malignant SG	10
• Malignant SG tumors	2	• Benign non-SG Tumor	1
		• Malignant	1
• Benign non-SG tumors	5	• Benign non-SG tumors	5
• Metastatic carcinoma	5	• Metastatic carcinoma	5
• Lymphomas	7	• Lymphomas	5
		• Inflammatory	1
		• Rhabdomysarcoma	1
• Non-inflammatory/ Nonneoplastic masses	9	• Branchial cyst	6
		• Epidermoid cyst	1
		• Malignant SG tumor	1
		• Metastatic SCC	1
total	110		110

FNAC, Fine Needle Aspiration Cytology. SG, Salivary Gland. SCC, aquamous Cell Carcinoma

Table II: Performance Characteristics of Fine-Needle Aspiration Procedure in the differentiation between benign and malignant masses

Groups	N	TP	TN	FP	FN	Sensitivity	Specificity	Accuracy
Distinguishing malignant from inflammatory neck masses	60	13	43	1	3	81%	98%	93% (CI 87-99%)
Distinguishing neoplastic from non-neoplastic cervical masses (including salivary gland masses)	110	53	50	1	6	90%	86%	84% (CI 90-98%)
Distinguishing malignant from benign neck masses (including salivary gland masses)	110	12	82	2	14	46%	98%	85% (CI 78-92%)
Distinguishing malignant from benign neck masses (excluding salivary gland masses)	58	11	43	1	4	73%	98%	93% (CI 86-100%)
Distinguishing malignant from benign salivary gland masses	52	1	39	1	11	8%	98%	78% (CI 67-89%)
Diagnostic accuracy of FNAC for lymphoma	110	5	101	2	2	71%	98%	96% (CI 92-100%)
Diagnostic accuracy of FNAC in detecting metastasis to cervical lymph nodes	110	5	104	0	1	83%	100%	99% (CI 97-100%0

CI, Confidence Interval

DISCUSSION

FNAC is being considered an essential tool in the pre-operative work-up of neck masses. In this study, diagnosis of neck masses has been reached through physical examination, computed tomography and FNAC. The main concern was to distinguish between benign and malignant masses, as that will help how to manage the case.

In the current study, neck masses of inflammatory or reactive etiology comprised the highest percentage. The accuracy of FNAC in distinguishing inflammatory from malignant masses was 93%. In two cases, FNAC was falsely negative for lymphoma, and in a third case, was falsely positive for lymphoma. In this context, FNAC had a limitation in differentiation between reactive hyperplasia and low grade lymphoma.[2,10] Nodular sclerosis classic Hodgkin lymphoma (HL) poses a potential pitfall on FNAC as the fibrosis associated with this entity can lead to lower cellularity and lack of Hodgkin and Reed-Sternberg (HRS) cells.[17] In fact, HL accounts for the majority of false negatives in FNAC of

malignant lymphoma.[18] In their study, J.-L Roh et al. (2008) found that FNA prior to tissue biopsy correctly diagnosed lymphoma in only 41 of 109 patients presenting with lymphoma of the head and neck. Y. Houcine et al. (2018), in their series, reported that FNAC of cervical lymph nodes had a sensitivity of 95.5%, specificity of 98.7%, positive predictive value of 97.7%, and negative predictive value of 97.5% in lymphoma diagnosis.

In our study, FNAC correctly diagnosed lymphoma in 5 out of 7 patients presenting with lymphoma. Aspirates from lymphoma may closely resemble that from a reactive lymph node. Conversely aspirates from reactive lymph node may closely resemble lymphoma.[9] varying amounts of neutrophils, lymphocytes, plasma cells, eosinophil's and histiocytes make up the background population of HL. When the proportion is skewed, HL has been reported to mimic suppurative lymphadenitis. By contrast, reactive lymphoid hyperplasia may demonstrate HRS-like cells that can be misinterpreted as true HRS cells.[17] the cytological diagnosis of reactive hyperplasia versus lymphoma can be improved using additional cytological techniques such as flow cytometry. However, these techniques are expensive, and are not widely available outside specialist centers. Furthermore, even when flow cytometry is used there will still be false negative results, and a diagnosis of low grade non Hodgkin lymphoma might be missed unless a tissue biopsy specimen is obtained.[2] Due to the aforementioned mimics and pitfalls, the National Comprehensive Cancer Network (NCCN) guidelines strongly recommend an excisional biopsy for the diagnosis of lymphoma in accessible lymph nodes.[17] And, although the value of FNAC of confirming recurrent or residual lymphoma is well established, its value in the primary diagnosis of lymph node lymphomas remains controversial.[19,20]

FNAC has a high sensitivity in the diagnosis of most neoplasms[9]. In the present study, the sensitivity of FNAC in distinguishing neoplastic from non-neoplastic cervical masses, including salivary gland masses, was 90%. However, the sensitivity of FNAC in distinguishing benign from malignant neck masses, including salivary gland masses, was 46%. And this had risen to 73% when salivary gland masses were excluded. The low sensitivity of FNAC, in the present study, in detecting salivary gland malignancy (8%) attributed to the low overall sensitivity of FNAC in detecting malignant neck masses. Low to intermediate grade mucoepidermoid carcinomas of the parotid gland were the most commonly missed diagnosis and were falsely diagnosed as benign tumors by FNAC. The value of FNAC in the diagnosis of salivary gland neoplasms is debated.[11-14]

FNAC of salivary gland tumors that show uniform histology throughout the lesion has proven to be a reliable and valuable technique for evaluation. On the other hand, neoplasms with a variety of histologic pattern and cell types provide a source of misdiagnosis related to sampling in FNAC.[18] Salivary gland tumors form a heterogeneous group with many different subtypes,[6,12] and a wide variety of morphological features of each type, as a result, they can be difficult to interpret even after excision.[13] K. Balakrishnan et al. (2005) found that FNA biopsy is not sufficiently accurate in distinguishing benign from malignant primary parotid neoplasms to be useful in clinical decision making. In the international literature, several studies analyzing the diagnostic accuracy of FNAC in the diagnosis of salivary gland lesions, reported high sensitivity and specificity for benign lesions, whereas they decrease in cases of malignant tumors.[12] Errors may occur in sampling some tumors such as carcinoma that arise in a pleomorphic adenoma, and FNAC can miss the malignant component , and there are also several benign–malignant "look-alike" tumors such as basal cell adenoma and adenoid cystic carcinoma that can be confused on FNAC.[13] It is also possible to confuse malignant tumors such as mucoepidermoid and

adenoid cystic carcinoma with benign tumors such as pleomorphic adenoma.[13] On the other hand, Jayaram et al. (1994) reported sensitivity and specificity rates of 87.8% and 98%, respectively, for the detection of primary parotid malignant tumors. And S. Aversa et al. (2005) reported specificity, sensitivity and diagnostic accuracy of 100%, 83% and 97%, respectively.. In consistent with other reports, [11, 12] the sensitivity and specificity of FNAC in the diagnosis of salivary gland benign tumors were high in the present study. FNAC appears better at predicting benign than malignant salivary gland diseases, because benign disease is more prevalent, the performance of this diagnostic test appears better than it actually is.[11]

In the context of cervical lymph node metastasis, the present study showed a high correspondence between cytological and histological diagnosis. FNAC correctly diagnosed 5 of 6 lymph node metastasis, and missed the diagnosis of a cystic lymph node metastasis, that was falsely diagnosed as an infected cyst by FNAC. FNAC has high levels of diagnostic accuracy, sensitivity and specificity in diagnosing malignant nodes including metastatic squamous cell carcinoma (SCC) in the head and neck;[2] In the literature, FNAC sensitivity for detecting malignancy in solid masses ranges from 87% to 95%,[21] and diagnostic specificities range from 91% to 100%,[22] therefore, it has clinical utility in the diagnosis of metastatic lymphadenopathy.[8] However, particular caution should be exercised in the case of cystic neck lumps.[9] The rate of accuracy is observed to be lower in cystic lesions than that of the solid forms.[23] FNA sensitivity in detecting malignancy in cystic masses of the lateral neck varies widely in the literature (33%-75%)[21]. In their study, Sheahan et al (2004) found that most malignant lumps which were incorrectly diagnosed by FNAC were cystic, and 25% of cystic lateral neck lumps not considered to be suspicious for malignancy turned to be malignant. Diagnosis of aspirates from cystic lesions may be less specific than the FNAC diagnosis of solid lesions because of the paucity of specific lesional cells in the former, [15] but in a study published by Baykul et al (2010) the value of FNAC in cystic lesions of the maxillofacial region was found as successful as in the solid lesions. The difficulty in distinguishing between benign cysts and cystic carcinomas on the basis of FNAB has been documented by many authors.[9] so, patients who may be at increased risk of SCC and where initial FNAC of neck lumps is negative for malignancy, should be FNAC repeated, [9] and cytodiagnosis should always be considered in the context of clinical findings.[6]

Complications from FNA are infrequent, and reports in the literature are scanty. In one large study of 3267 FNA biopsies from the breast, subcutaneous nodules and lymph nodes, prostate, deep masses, lung, and pancreas, the method was essentially complication-free Needle tract seeding by malignant tumor cells is an exceedingly rare event when needles smaller than 22 gauge are used. And given the large number of head and neck FNACs that are performed relative to the number of reported cases of needle tract seeding, this cannot be considered a significant complication of the procedure.[16] Further, animal studies have shown insignificant tumor cell spillage by this method.[24] In the head and neck the procedure of FNAC may be complicated by ecchymosis and hematoma, tracheal puncture, and vasovagal reactions.[16] Negative pressure during the FNAC may not be necessary to procure a good sample and, occasionally, it may be detrimental. This is especially true in richly vascular anatomic sites, such as the thyroid gland. In such instances, cells can retrieved for cytology by the non-aspiration fine needle cytology technique, which is similar to the conventional FNAC except that the biopsy is performed with the needle alone without the syringe. This method relies on the capillary action to obtain cells within the bore of the needle. The non-aspiration technique is also useful in situations requiring

precise needle placement such as the aspiration of very small skin nodules. However, this technique is less efficient than the traditional method when aspirating hypocellular, fibrous lesions.[16]

CONCLUSION

FNAC is an essential tool in the work-up of neck lumps. Their results may affect clinical judgment and subsequent management, therefore, an on-going audit of the performance of FNAC is required within each institution.[11] Although FNAC has a high diagnostic accuracy, several problems may arise.[23] In the present study FNAC performed well in detecting metastatic carcinoma in solid neck masses, the only missed metastasis was in a cystic cervical mass. False negative rates for cystic masses are as high as 38-63%.[25] so it is wise to consider a cystic neck mass malignant until proven otherwise, especially in old patients. Aspirates from lymphoma may closely resemble that from a reactive lymph node. Conversely aspirates from reactive lymph node may closely resemble lymphoma. The value of FNAC is well established in confirming recurrent or residual lymphoma. However its value in the primary diagnosis of lymph node lymphoma remains controversial.[20] Results of the study showed a very low sensitivity of FNAC in distinguishing malignant from benign salivary gland tumors. Where FNAC missed the diagnosis of malignant salivary gland tumors in 11 out of 12 cases, most of them were low to intermediate grade mucoepidermoid carcinomas.

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