DIAGNOSTIC ACCURACY OF FINE NEEDLE ASPIRATION AND IMPRINT CYTOLOGY OF HEAD AND NECK LESIONS (COMPARATIVE STUDY)

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ABSTRACT

Background

Fine needle aspiration cytology has been considered as the first-step procedure for microscopic evaluation of any mass or swelling in the head and neck area and the entire body following taking a full history and physical examination. It is considered as an alternative procedure to open surgical biopsy. On the other hand, imprint cytology is a well-recognized simple technique. Imprint cytology can be used as an adjunct to or as a substitute for frozen section method; since it has been proven to be more efficient than frozen section, and has higher concordance with histological results

Objectives

To improve clinical and diagnostic cytological experiences among oral pathologists, compare the results of cytological techniques with that of routine histopathological findings, and specify the merits and pitfalls of the above techniques.

Materials and Methods

A prospective study is conducted on 66 patients indicated for FNA. In 27 cases, histological examinations were available for comparison with cytological diagnosis, among which 20 cases had imprint cytology. All samples were stained with H&E and Pap stain, while salivary gland lesions were additionally stained with Diff-quick. Cytological specimens were compared with the histopathological examination to find diagnostic accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV).

Results

Fine needle aspiration cytology was performed on 62 patients, 25 males, and 37 females. The total benign lesions were the commonest (46.7%), followed by inflammatory lesions (38.7%), then malignant lesions (14.5%). The overall diagnostic accuracy of FNAC was 88.8%. The sensitivity, specificity, PPV, and NPV were 75%, 94.7%, 85.7%, and 90% respectively. Whereas in imprint cytology 4 cases were diagnosed as malignant, 11 cases as benign and 5 cases as inflammatory. The diagnostic accuracy of imprint cytology was 90%. The sensitivity, specificity, PPV and NPV were 66.6%, 100%, 100%, 87.5%, and 90% respectively.

Conclusion

Fine needle aspiration cytology FNAC showed 88.8% diagnostic accuracy, while imprint cytology has a slightly higher diagnostic accuracy of 90% for head and neck lesion.

Keywords: *Fine needle aspiration cytology FNA, Imprint cytology, Diagnostic accuracy, Sensitivity, Specificity.*

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INTRODUCTION

Fine needle aspiration cytology (FNAC) has been considered as a first-step procedure next to a full history and physical examination. It is used to evaluate any mass or swelling in the head and neck area and the entire body, and considered as an alternative procedure to open surgical biopsy [1]. It has the advantages of being a safe, cost-effective, requires very few equipment, less traumatic than biopsy, leaves no scar and allows immediate pre-operative diagnosis, thereby avoiding unnecessary harm to vital structures of the oral cavity [2, 3]. The fundamental indication of this technique is any lesional mass that is palpable or visible by radiological imaging (intraosseous lesions with thinned cortical bone) [4]. There are no absolute contraindications for FNAC, but in case of uncooperative patients, it may not be suitable. However, patients with bleeding disorders or on anticoagulant medications require consultation, while those with prosthetic heart valve require prophylactic antibiotics before the procedure. Although it may be associated with certain complications such as bruising, soreness, the risk of false negative/positive results and the controversy of spreading of tumor cells (which is considered quite rare), it is all considered minor to the benefits obtained [5].

Imprint cytology (IC) is a well-recognized simple intra-operative method, used to provide valuable, accurate diagnostic information in the theater and can be used as an adjunct to or as a substitute for frozen section method. [6, 7]. The technique is quite straightforward, accurate, rapid, cost-effective, and does not require special equipment [8]. Although it has some drawback and limitation since it does not provide reliable information regarding the depth of infiltration of the tumor and cannot diagnose well-differentiated tumors and tumors with a dense fibrous stroma, it is still considered a valuable diagnostic tool for tumors in various body sites [9,10].

By cytology, lesions can be categorized as inflammatory (septic or non-septic) or non-inflammatory (hyperplastic, dysplastic or neoplastic). If neoplastic, it is essential to find the origin of the cells and determine whether it is benign or malignant. However, others have classified the lesions into five categories; inflammatory, cystic, hemorrhagic, neoplastic and mixed cell population (epithelial or mesenchymal) [11].

Smear background, cell arrangement, density, and cellular features (nucleus and cytoplasm) should all be considered during interpretation of a cytological smear as they point to the diagnosis [12]. The diagnostic accuracy of FNAC method varies from 90-to-97% depending on the clinical data, anatomical site, adequate material obtained, proper sampling, smearing, fixing and staining techniques as well as the expert interpretations [13]. It is highly suggested that the best results can be achieved by using imaging guidance to improve sampling accuracy [14]. Despite the easy accessibility of neck lesions, FNAC of these lesions can pose a challenging diagnostic problem. The variety of inflammatory and neoplastic lesions in this area, along with the anatomical overlap of the structures makes the diagnostic accuracy of the area approaches 50% [15]. However; FNA cytology of lymph node almost offers a near accurate diagnosis for reactive lymphoid hyperplasia, infectious diseases, granulomatous lymphadenitis, and metastatic malignancy [16, 17]. The diagnostic accuracy of FNAC in salivary gland can be quite problematic. Masses that appear in the area of salivary glands can represent the gland itself, intra-parotid lymph nodes or high cervical lymph nodes, cysts of the neck or a soft tissue mass, resulting in a broad differential diagnosis. Many salivary gland lesions sometimes presented with secondary alterations like cystic changes, prominent lymphoid stroma, clear cell changes, sebaceous differentiation and mucin production resulting in difficulty in the interpretation [18]. Some salivary gland lesions may be confused with others, like in case of acinic cell carcinoma with basal cell carcinoma or oncocytoma, and in the case of pleomorphic adenoma and adenoid cystic carcinoma. The presence of both stromal and epithelial component is required for accurate diagnosis [14]. Imprints prepared from fresh surgical specimens give excellent cytological clarity and few artifacts. This technique is considered reliable in the diagnosis of a surgical specimen of salivary glands, lymph nodes, and other lesions, but its role in the evaluation of margins of squamous cell carcinoma is unclear [19]. Even though efforts to be as accurate as possible, both false negative and positive diagnosis can still occur [20]. False negative diagnoses are most commonly related to desmoplasia, well-differentiated tumor cells, and sampling problems [21]. On the other hand, a false-positive diagnosis is usually caused by contamination, changes due to radiation and chemotherapy effects, the presence of necrotic material and blood elements, and inexperience by the cytopathologist [22].

The aim of this study is to find the accuracy of FNA cytology and imprint cytology in the diagnosis of head and neck lesions.

PATIENTS AND METHODS

This prospective study was conducted during the period from 1st April to 30th November 2015. It included patients having either salivary gland lesions or palpable soft tissue lump in the head and neck area (excluding thyroid lesions) or radiolucent intra-osseous lesions indicated for FNAC. The patients were collected from Sulaimani Teaching Hospital/ Oral and

Maxillofacial Department and Shaheed Saif Al-Din Dispensary Clinic. The demographic and clinical data and investigations for every patient were registered in a case sheet.

The study was approved by the Ethical and Scientific Committee in the Faculty of Medical Sciences/ University of Sulaimani. Although all cases were indicated for cytology and referred by a surgeon, the researcher explained for each participant the purpose of the study and was assured confidentiality of information and a verbal consent was obtained.

After establishing a comfortable position for the patient, the skin over extra-oral mass was disinfected by antiseptic solution, while for the intra-oral lesion, the mucosa was washed thoroughly with water and wiped with gauze. A local anesthetic was given when needed. The operator properly fixed the mass by two fingers and inserted a needle (22-23) gauge with a length of 1.5 inches (3-8 cm) attached to disposable plastic syringe that have been previously aspirated to the mark of 2 ml. The operator aspirated in different directions, with or without the ultrasound image guiding (according to the case). After many passes, the operators released the pressure and withdrew the needle and cover the site of needle insertion by a cotton pack with or without an ice pack. The material then was spread on a glass slide (conventional preparation) [23]. Any specimen contained blood or fluid was centrifuged (6-8min, 600-1000 rpm), then the obtained cells were spread on a slide by pouring and then slides were pulled apart against each other to help to get a single layer smear. Immediate fixation was carried by either using 95% ethanol for 30 min (wet smear) or leaving it to dry (dry smear) depending on the staining method.

For imprint smear, the surgical specimen was sectioned, and the blood on the surface of the suggestive diseased area was removed by gently pressing with dry gauze. Then slide gently touched on to the freshly cut surface of the specimen, avoiding a gliding movement. Pressure applied according to the consistency of the tissue [24, 25]. Then some slides were fixed in 95% alcohol, others were air dried. The surgical samples were sent for routine histopathological preparation for comparing the results.

Two different sets of wet-fixed smears were prepared from each lesion; one stained with Hematoxyline and eosin, and the other with Papanicolaou stain. Salivary gland lesions had an additional set of dry-fixed smears stained with Diff-quick. The number of the slides depended on the availability of the obtained material, but generally, there were two slides for each stain. Finally, the slides were cleared, mounted with DPX and covered. The staining procedure was done in the histopathological lab/ College of Dentistry/University of Sulaimani. The stained slides examined under a light microscope by two pathologists.

The cytological and histological analysis was reported regarding frequencies and percentages. Furthermore, the diagnostic accuracy for head and neck lesions was measured using histopathology as the gold standard. Sensitivity, specificity, negative predictive value (NPV) and positive predictive value (PPV) were calculated using certain formula listed below:

A true positive (TP) FNA is defined as a malignant cytological diagnosis from a lesion determined to be malignant on histopathological examination. A false positive (FP) is defined as a malignant cytological diagnosis found to be benign on histopathological examination. A true negative (TN) is defined as benign cytological results from a lesion proved to be benign on histopathology. A false negative (FN) is defined as benign cytological results that are found malignant on histopathological examination (26).

Sensitivity: It is defined as the proportion of patients having malignant lesions and positive cytological diagnosis, calculated by TP/ (TP+FN) x100%. Specificity: It is defined as the proportion of patients with non-malignant lesions and negative cytological finding, calculated by TN/ (TN+FP) x100% (27). Positive predictive value (PPV): It is the probability of having a malignant lesion with positive cytological finding calculated by TP/ (TP+FP) x100%. Negative predictive value (NPV): It is the probability that the patient did not have a malignant lesion with negative cytological finding, calculated by TN/ (TN+FN) x100%. Accuracy: It is the proportion of correct results (TP and TN) about all cases studies. Calculated by (TP+TN) / (TP+FP+TN+FN) x100% (28).

Descriptive statistics including mean, IQR (Inter-Quartile Range), minimum and maximum values, frequency, percentage, and ratio were analyzed by using Microsoft Excel 2010. Furthermore, Inferential statistics were calculated to determine sensitivity, specificity, positive and negative predictive values, and diagnostic accuracy.

RESULTS

Fine needle aspiration cytology FNAC was performed on 62 patients (27 males and 39 females) with a 1:1.4 male to female ratio. The age ranged from 3-85 years with a median of 43.5, the IQR was 36, and the maximum number of cases was in the age group of 21-57 years. Among 62 cases, 27 cases were presented with histological diagnosis and considered for comparison with cytological diagnosis, among which 20 cases had imprint cytology. Difficulty in obtaining a surgical biopsy of remaining cases was either due to the patient being reluctant to surgery or had poor socioeconomic status.

Regarding the anatomical site distribution, 17 cases (27.4%) basis of lesions arises in lymph node and another 17 cases in salivary gland (27.4%). They were sub-grouped into three categories: inflammatory, benign, and malignant lesions. The remaining cases (n=28, 45.1%) arose from different sites including; maxillary and pre-maxillary region, forehead, submandibular area, upper lateral cervical neck area, parotid region, nose, and palate. They were subdivided into inflammatory (38.7%), cystic, benign growth (46.7%) (Central giant cell granuloma, lipoma, and hemangioma) and malignant neoplasm (14.5%) (Basal cell carcinoma)(Table 1).

Out of the total 62 examined cases, 9 cases were diagnosed as malignant, 29 cases were diagnosed as benign, and 24 cases were diagnosed as inflammatory (Table 2). The overall diagnostic accuracy of FNAC was 88.8%. While in imprint cytology 4 cases were diagnosed as malignant, 11 cases as benign and 5 cases as inflammatory (Table 2). The diagnostic accuracy of imprint cytology was 90%. The sensitivity, specificity, PPV, and NPV of the two procedures were shown in (Table 3). The statistical analysis of both FNAC and imprint cytology was compared and showed a slight difference between the two methods. Imprint cytology had a minor advancement over FNAC regarding the diagnostic accuracy, along with specificity and PPV.

Table 1. Anatomical site based distribution of cases depending FNA cytological diagnosis.

Site	Inflammatory		Tumors				Total	
			Benign		Malignant			
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Lymph node	10	41.6	0	0	7	77.7	17	27.4
Salivary gland	6	25	10	34.4	1	11.1	17	27.4
Others	8	33.3	19	65.5	1	11.1	28	45.2
Total	24	38.7	29	46.7	9	14.5	62	

Table 2. Diagnostic accuracy of FNAC and imprint cytology in the studied cases.

cytological technique	Diagnosis group	Cases number		Matching diagnosis	False Positive	False negative
		Cytology	Biopsy			
FNAC	**Malignant**	9	7	6 TP	1	0
	Benign	29	15	14 TN	0	1
	Inflammatory	24	5	4 TN	0	1
	Total	62	27	24	1	2
Imprint	**Malignant**	4	4	4 TP	0	0
	Benign	11	11	10 TN	0	1
	Inflammatory	5	5	4 TN	0	1
	Total	20	20	18	0	2

Table 3. Interferential analysis of FNAC and imprint cases.

	Sensitivity	Specificity	PPV	NPV	Accuracy
FNA	75%	94.7%	85.7%	90%	88.8%
Imprint	66.6%	100%	100%	87.5%	90%

DISCUSSION

FNAC is a cytodiagnostic method based on the morphological finding of individual cells, group of cells and micro-particles of tissue acquired by using a needle. It is easy done procedure with minimal incidence of complication and no risk of implantation of tumor cells (less than 1%). It is considered to be superior to physical and radiological evaluation [1]. The accuracy of the procedure depends on the expertise of the cytopathologist, technician, the site of the lesion and the adequacy of the sample and sampling method [29]. FNAC is considered to have high diagnostic accuracy. In this study, the total diagnostic accuracy of different head and neck lesions was 88.8%, which is less than that reported by Tatomirovic et al (91.8%) and higher than the findings of Saleh et al (86.8%) [30, 31] and Rajbhandari et al (83.8%). Furthermore, we reported 75% sensitivity and 94.7% specificity, which were slightly less than those reported by other studies (Rajbhandari et al., Kishor et al.) [32, 33].

On the other hand, imprint cytology is considered simple, rapid and does not require sophisticated instruments. The smear has a good diagnostic accuracy that allows this procedure to be considered as an adjunctive procedure to histopathological examination [34]. Improper dissection of a specimen during operation for the purpose of imprint smearing may result in disruption of surgical margins, and extra care should be exercised to maintain specimen integrity as much as possible. In this study, imprint cytology had an accuracy of 90%, which is in line with that found by Hussein 2005 [35]. However, the sensitivity (66.6%) was less, and the specificity (100%) was higher than their findings since they concerned only the presence or absence of LN metastasis. Herein, this study concerned reaching the diagnosis whether it is benign or malignant. Review of literature concerning imprint cytology of head and neck lesions showed no updated published articles.

The use of FNAC for lymph nodes are widely debated. It has certain advantages of being a simple, convenient procedure for some high-risk surgical candidates or for patients in whom masses are located in relatively inaccessible sites. The usefulness of FNA cytology for establishing a diagnosis of metastatic carcinoma is now commonly accepted practice; however, sub-classification of Hodgkin lymphoma is not possible by using FNAC only. The diagnosis and classification of lymphomas should be based on consideration of the cytomorphologic findings, histologic pattern, and immunophenotype [36]. In our study, the diagnostic accuracy of FNAC of lymph node lesions was found to be 87.5%, which was higher than that reported by Hafez and Tahoun (82.2%) [16]. On the other hand imprint cytology had a less diagnostic accuracy of 83.3% and sensitivity of 66.6%, but a higher specificity of 100% than those found by Arif et al. (97.8%,95%,98.6%) [37].

Moreover, specific interpretation difficulties may arise during the studying FNAC from salivary gland neoplasms as a result of the extraordinary diversity of their morphology [38]. Pre-operative core needle biopsy is hazardous and may damage the facial nerve in case of the parotid gland, lead to fistula formation or associated with tumor seeding. However, FNAC is considered virtually risk-free [39]. It provides two roles, first identifying the origin of the swelling as pre-auricular area and submandibular lymph-node swellings can mimic salivary gland neoplasms clinically and second to get a preliminary diagnosis about the nature of the disease. Therefore, FNAC is considered a reliable procedure to differentiate between inflammatory and neoplastic of salivary gland lesions [40].

Basically, there are three types of aspiration of salivary gland lesions; first is the aspiration of a normal salivary gland tissue that may be due to failure to targeting the lesion accurately or not having enough material or it is a case of sialosis. In sialosis, clinical examination of bilateral involvement along with a history of malnutrition, diabetes mellitus, or alcoholism should be taken into consideration. However, unilateral and

idiopathic cases of sialosis were reported. The second type of aspiration is the one that shows inflammation. Most aspirations yielding purulent material represent a secondary infection superimposed on sialolithiasis. Thirdly is the neoplastic aspiration whether benign or malignant [41].

In this study, the diagnostic accuracy and specificity of FNAC for salivary gland lesions were (77.7%, 100%) which were higher than that reported by Faizal et al. (70.8%, 97.1%) and a sensitivity of 33.3% which was lesser than that reported by Faizal et al (66%) [41]. On the other hand, the diagnostic accuracy of imprint cytology was even higher than that of FNAC (87.5%), but unfortunately, no previous published article concerning the diagnostic accuracy of imprint cytology of salivary gland lesions could be found.

Last but not least, the other diagnosed lesions were heterogeneous and from different anatomical cites what made it quite difficult to be categorized.

The limited number of studied cases was restricted by the difficulty to obtain IC from patients who underwent surgical operation in private hospitals. On the other hand, other patients were uncooperative (uneducated) and refused to do surgery.

Regarding Staining procedures used (H&E and Pap) showed a similar cytological reading. While the reading of Diff-quick salivary gland smear was quite difficult, partly due to lack of experience regarding reading air-dried stains, since it is not used in routine cytological diagnosis in our hospitals as they depend on Pap and H&E staining in their diagnosis. It is highly recommended to be used in salivary gland lesions, aiming to increase the diagnostic accuracy and the experience among cytopathologists regarding salivary gland lesions interpretation.

In conclusion, FNAC can help improve the preoperative diagnosis of head and neck lesions with an accuracy of 88.8%. And, Imprint cytology performed at the time of operation can provide a reasonably accurate intra-operative diagnosis of lesions as non-neoplastic versus neoplastic, and benign versus malignant. This can guide the surgeon in making decisions about the extent of surgical excision. The accuracy of imprint cytology is slightly higher than FNAC at 90%. Imprint cytology for intra-operative diagnosis of salivary gland lesions is higher than that of FNAC at 87.5%.

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