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## Diagnostic Value of Fine Needle Aspiration in Salivary Gland Tumors Compared with the Histopathological Results after Mass Excision

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### ABSTRACT

Fine Needle Aspiration (FNA) is a relatively painless, safe and inexpensive diagnostic method, which is a widely accepted for the diagnosis of salivary glands neoplastic and inflammatory lesions before surgery. The aim of this study was to evaluate the diagnostic value of FNA in the diagnosis of salivary gland tumors nature compared with the histopathological results after mass excision. This is a cross-sectional study, where since April 2009 to March 2012, all patients complaining about salivary gland tumors referred to the ear, nose and throat ward of Ahvaz Imam Khomeini hospital and undergone FNA and biopsy have been studied. Then, the results of FNA were compared with pathology results after mass excision, as well as the diagnostic accuracy of FNA was calculated. In this study, 160 patients were studied including 88 females (55%) and 72 males (45%). Most patients were in the age group of 31-40 years and lowest in patients aged over 80 years. The mean age of patients was  $41.7 \pm 18.9$  with a minimum 3 years and the maximum was 85 years old. The FNA sensitivity in salivary gland tumor to pathological findings after mass excision was calculated 92.3% and its characteristics 99%. The positive predictive value was 96% and negative predicted value 97.9%. As shown in this study, FNA sensitivity has a high specificity and diagnostic value in the detection of the salivary gland lesions. Given that it is an inexpensive, safe and reliable method, it is recommended to be used more widely.

**Key words:** Salivary glands, fine needle aspiration, sensitivity, specificity, diagnostic accuracy

### INTRODUCTION

Salivary gland tumors are relatively rare and unusual neoplasms and account for about 2-10% of head and neck neoplasms. These tumors commonly occur in the parotid gland (Capone *et al.*, 2002). The incidence of salivary gland neoplasms was approximately 1.5 cases per 100,000 in America and about 700 deaths per year (0.4 per 100,000 for men and 0.2 per 100,000 for women). Salivary gland neoplasms are more frequent in the sixth decade of life (Mandel, 2014). Salivary gland tumors are divided into two categories: Benign and malignant. Benign tumors are more common in women but the incidence of malignant tumors is the same in both sexes. Salivary malignant lesions appear after 60 years old, while, benign lesions are appearing over 40 years of age. Treatment of salivary gland tumors is determined based on clinical evidence, radiological and histopathological examinations (Capone *et al.*, 2002; Mandel, 2014).

For histopathological diagnosis, biopsy lesion is necessary. A biopsy can be done in different ways, of which one of its fast and easy ways is Fine Needle Aspiration (FNA). In FNA, part of the lesion is removed by a fine needle from other parts. Then, the contents of the needle are put on a slide and examined under a microscope (Capone *et al.*, 2002; Maiorano *et al.*, 1997; Mandel, 2014). Using FNA for the diagnosis of salivary glands neoplastic and inflammatory lesions is a widely accepted method before surgery. This aspiration method is relatively painless and safe method for early detection of lesions available (Maiorano *et al.*, 1997). The sensitivity of this method in the study of salivary gland tumors is reported to be 85.5-90% and its specificity 96.3-100% (Capone *et al.*, 2002; Guzzo *et al.*, 2010; Maiorano *et al.*, 1997; Bozinovic *et al.*, 2015). This aspiration method allows counseling before surgery for patients based on the tumor nature and possible spread of resection, preservation of the facial nerve during surgery and probability of cervical dissection. Such information is important not only in the treatment plan but also is effective in reducing and relieving anxiety in patients (Guzzo *et al.*, 2010; Bozinovic *et al.*, 2015). The aim of the present study was to evaluate the diagnostic value of FNA in the diagnosis the nature of the salivary gland tumors compared to the histopathological results.

## **MATERIALS AND METHODS**

**Study design and population:** This cross-sectional study, was performed on all patients with complaints of salivary gland mass, have undergone FNA and excisions biopsy referring to otolaryngology (ENT) ward of Ahwaz Imam Khomeini Hospital since April 2009 to March 2012. This study was approved by the ethical committee of Ahwaz Jundishapur University of Medical Sciences and all patients have signed the inform consent for participating in this study.

**Methods:** The FNA was performed in such a way that after the preparation of the skin and local anesthesia, we enter the aspirated needle (no. 22-25) that is connected to a 10 cc syringe with an inclined approach to the mass. Then, we enter a negative pressure by hand or needle holder and we pass the mass. After cutting the negative pressure, we bring out the needle. Using a syringe, we send some air into the needle and we unload the needle contents on a prepared slide. Then, we widen the sample using another slide and fix the sample with a fixture which it will be sent to the Department of Pathology for review. Usually, in the Department of Pathology, the slides are studied after staining with papanicolaou stain. For this purpose, we put them in alcohol 96 degrees for at least 30 min to be totally fixed. Next, we enter samples into 80 degrees alcohol for 10 times and in 70 degrees alcohol for 10 times, respectively and then we wash them using water. Then, for core staining, we put samples for 5 min in hematoxylin stain, which is specific to the core. We then wash slides with alkaline or municipal water without chlorine. Then, we enter slides into the acid alcohol solution, until the cytoplasm hematoxylin stain is disappeared and then we wash them again. Next, we enter the slides three times in lithium carbonate solution to fix the core color; we then wash the slides with water. To stain the cytoplasm, we initially enter slides in 96 degrees alcohol for 10 times. Then for 4 min, samples will be put into the Orange (Og6) solution and we enter the samples two times in alcohol 96 degrees and we then enter it in EA50 color for at least 5 min. In the next step, the samples are dehydrated with the help of alcohol, so that we enter the slides into the containers containing low-grade alcohol, high-grade alcohol and xylenol, respectively. Then, some xylenol were taken by the slide and we put the coverslip on it, while putting the coverslip, we should be careful not to create any bubble. After staining slides, we paste a label called canada bond on them. The prepared slides are studied with the microscope (Chung *et al.*, 2007; Escudier and McGurk, 1999; Grases *et al.*, 2003).

Mass excision specimens will be transported to the pathological laboratory after placing in appropriate fixture (usually 10% formalin). There, after passing the sample, they place it in the tissue processor device (Automated Vacuum Tissue Processor ASP6025, Leica Biosystems Nussloch GmbH, Spain) for 12 h. In this device, some changes will be created in the sample during 4 stages: Fixation, dehydrogenation, transparency and contamination. During fixation, samples must pass at least three separate containers containing fixator to be fixed well. In the dehydrogenation step, tissue water is separated by a dehydratase substance such as alcohol. Samples should pass three containers containing alcohol with percentages, 80, 96, 99 and 100%, respectively to let dehydrogenation is well done. In transparent step, some gaps are created in tissue by xylol. In the contamination step, gaps created in transparency are filled with fully melted paraffin containing citrate and the samples have lost their fragility state and will be, relatively robust and firm. Then in molding stage, we prepare molds such as blocks using paraffin. After the samples were completely tightened, we cut them by a machine called microtome (Leica Biosystems Nussloch GmbH, Spain), with a thickness of 5-10  $\mu\text{m}$ . After cutting, we put slides for at least 1 h in the oven. After which, prepared cuts were placed on slides containing gelatin to be cohered on the slide. Finally, the prepared sample was stained and studied using a microscope (Motic<sup>®</sup> BA210 Biological Light Microscope, TED Pella, INC., USA).

**Data collection tools:** Data is extracted from the archives of the Department of Pathology of Imam Khomeini hospital in Ahwaz. This information includes age, sex, FNA results and histopathological results after mass excision (tumor type) and tumor site (parotid or etc).

**Statistical analysis:** The report of benign tumors in histopathology as benign tumors in FNA are considered as the true positive result and benign tumors as false positive result and the reports of malignant tumors as a result of FNA histopathology as malignant tumors in true negative and as malignant tumors as a result of false negative. Sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated according to the following formulas (Rahim and Keikhaei, 2009):

$$\text{Sensitivity} = \frac{\text{True positive} + \text{False negative}}{\text{True positive}}$$

$$\text{Specificity} = \frac{\text{True negative} + \text{False positive}}{\text{True negative}}$$

$$\text{Accuracy} = \frac{\text{Total}}{\text{True negative} + \text{True positive}}$$

$$\text{Positive predictive value} = \frac{\text{People with positive test}}{\text{True positive}}$$

$$\text{Negative predictive value} = \frac{\text{People with negative test}}{\text{True negative}}$$

**RESULTS**

In this study, 160 patients with complaints of salivary gland mass were enrolled. The FNA and pathological results were extracted after mass excision, age, sex and the tumor site from the archives of the Department of Pathology and the results of which was compared to pathological results after mass excision to evaluate the diagnostic value of FNA. Obviously, FNA results of patients who had no pathologic results after mass excision were excluded. Also, the FNA results that were "inadequately" reported were invalid in evaluating the diagnostic value and only the pathologic findings after mass excision of these patients were used for other research purposes (review of prevalence of salivary gland tumors by age, sex and pathology type). In addition, 19 patients (11.9%) of the subjects with probable diagnosis of tumor in the tail of parotid gland had undergone FNA and therefore were included in the study but they were excluded after determining the definitive diagnosis (with pathology results after mass excision). From 160 patients, 88 (55%) were female and 72 (45%) were males. Age distribution in patients is presented in Table 1, that showed most patients were in the age group of 31-40 years and the least in the age group over 80 years (Fig. 1). Mean age of patients was 18.9±41.7 years old, with a minimum age of 3 years and maximum 85 years.

The most common site of involvement was in the parotid gland (56.3%) and lowest in the sublingual gland (3.8%). Nineteen cases with a presumptive diagnosis of parotid gland mass had undergone aspiration. After excision and determining the results of pathology, the mass origin was the cervical tissue (Table 1).

Most frequency was related to the pleomorphic adenoma (25%) and the lowest frequency to undifferentiated carcinoma and parotid large cell lymphoma arising from pleomorphic adenoma (Table 2). Four (2.5%) adenoid cystic carcinoma and 6 (3.8%) mucoepidermoid carcinoma have been reported. The frequency of acinic cell carcinoma was 2 (1.3%) and monomorphic adenoma 3 (1.9%).

Table 1: Frequency of sites studied in patients under study

Sites	Frequency	Percentage
Parotid	90	56.3
Submandibular	45	28.1
Sublingual	6	3.8
Cervical	19	11.9
Total	160	100.0

Table 2: Frequency of salivary gland tumor by pathology type

Pathology results	Frequency	Percentage
Inflammation	30	18.8
Pleomorphic adenoma	40	25.0
Paroditis+stone	11	6.9
Mucocele	6	3.8
Lipoma	5	3.1
Warthin tumor	6	3.8
Mucoepidermoid carcinoma	6	3.8
Non-hodgkin lymphoma	7	4.4
Hodgkin lymphoma	2	1.3
Sialadenitis	8	5.0
Squamous cell carcinoma	6	3.8
Myoepithelioma	3	1.9
Adenoid cystic carcinoma	4	2.5
Monomorphic adenoma	3	1.9
Reactive lymphnode	19	11.9
Acinic cell carcinoma	2	1.3
Poorly differentiated carcinoma arising within pleomorphic adenoma	1	0.6
Lymphoma of large cell of parotid	1	0.6
Total	160	100.0

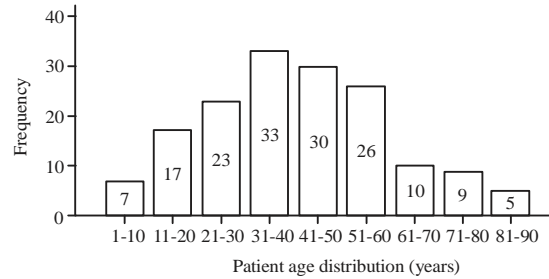


Fig. 1: Frequency distribution of different age groups

Pleomorphic adenomas were 80% in the parotid gland and the rest 20% was in submandibular gland. All reported cases of Warthin's tumor were related to the parotid gland. Sixty six percent of the mucoepidermoid carcinoma was in the parotid gland and other cases in submandibular glands. Out of four cases of adenoid cystic carcinoma, 3 cases (75%) were in the submandibular gland and one (25%) in the parotid gland. 66.6% of myoepithelioma was in parotid and the rest in the submandibular glands. The highest rate of mucocele was in submandibular gland with 66.6% and the highest rate of inflammation followed by the salivary gland stones in the parotid glands (81.8%). One case of large cell lymphoma was in parotid and one "undifferentiated carcinoma from the Pleomorphic Adenoma" in the parotid.

As already explained in the previous sections, cervical samples were in fact cases that have undergone FNA with early diagnosis of a mass in the tail of the parotid gland. After pathological results (after mass excision) were determined, they were excluded from the study, meaning that, the results were not included in the calculation of sensitivity and specificity. Although the sensitivity and specificity were 100% for this category, the sensitivity of FNA in masses of salivary gland compared to the pathological findings after mass excision was obtained as 92.3% and its specificity as 99%. Positive predictive value was calculated as 96% and negative predictive value as 97.9%.

## DISCUSSION

In this study, which aims to examine the diagnostic value of FNA in the diagnosis of the nature of salivary gland tumors compared with histopathological results on 160 patients, found that a significant compliance exists between FNA and histopathological findings (92.3%). The most common site of involvement was located in the parotid gland (56.3%) and lowest in the sublingual gland (3.8%). Nineteen cases with a presumptive diagnosis of a mass in the tail of the parotid gland had undergone aspiration. After excision and determining the pathological results, mass origin was the cervical tissue. These are not included in the calculation of sensitivity and specificity.

The 66 cases of neoplasm were reported in pathologic consequences, of which 52 (78%) were benign and 14 (22%) were malignant. Most of the involvement was in the parotid gland (74%). The present results are consistent with the results of Gonzalez *et al.* (1999), who have reported the possibility of benign tumors as 80% and the probability of malignancy 20% and parotid involvement up to 83%. Ma'aita *et al.* (1999) have reported similar results in Jordan. In a study Halimi *et al.* (2009) reported histopathological results of the samples of tumor excision as 80.4% benign and 19.6% malignant.

All the 66 cases of neoplasm in this study were in the parotid and submandibular glands and no neoplasm in sublingual glands have been reported. This shows the low risk of the gland tumors that were consistent with previous studies. In this regard, Ma'aita *et al.* (1999) also showed that the incidence of tumors of the sublingual gland is only 0.04%. In contrast, in a survey conducted

among 1, 021 patients, 33 sublingual gland involvements was observed that has occurred with a ratio of 3.2% even more than minor gland tumor involvement (3%) (Califano and Eisele, 1999).

In this study, the most common neoplasm reported was pleomorphic adenoma (60%) that has constituted 65% of parotid gland tumors. All studies on salivary gland tumors have declared the incidence of the tumor between 50 and 80%. On the other hand, 80% of pleomorphic adenoma was in the parotid gland and the rest 20% in submandibular gland. All 6 cases reported of Warthin's tumor (9% of all neoplasms) were related to parotid gland. In other studies, the prevalence of this tumor has ranged between 9 and 28% (Chulam *et al.*, 2013; De Oliveira *et al.*, 2009; Luksic *et al.*, 2012). In our study, the share of mucoepidermoid carcinoma was 9% of neoplasms, with more incidences in men and at ages over 50 years, 66% were in the parotid gland and the rest in submandibular glands. The results of this study were consistent with the study by Rice (1999) in Brazil, who have reported its prevalence between 7-10% and involvement of the parotid as 55-70%. Consistent with previous studies, 3 (75%) out of 4 adenoid cystic carcinoma cases were in the submandibular gland and one (25%) in the parotid gland.

In our study, a high diagnostic value for fine needle aspiration was obtained in malignant lesions. Generally, fine needle aspiration sensitivity in salivary gland tumors was obtained 92.3% and its specificity 99%. The positive predictive value was calculated 96% and negative predictive value 97.9%. These results are in line with results of Behzatoglu *et al.* (2004), who have reported the sensitivity and specificity of FNA in the diagnosis of parotid gland tumors as 91 and 98%, respectively. Positive predictive value was reported 100% and negative predictive value 95.9%. In another study, Madani *et al.* (2011) reported the sensitivity as 67, specificity 91 and diagnostic accuracy to be 83%. In his study, the positive and negative predictive values were 78 and 85%, respectively. In the study by Al-Khafaji *et al.* (1998), reported the sensitivity of 82%, a specificity of 86% and an overall diagnostic accuracy of 84%. In the study by Stramandinoli *et al.* (2010) after comparing 79 cases of result of aspiration and pathological results, the sensitivity was reported 86.2%, specificity 87.7% and the diagnostic value 82.3%, positive predictive value 86.2% and negative predictive value 87.7%.

But in the study, by Halimi *et al.* (2009) on 51 patients, the sensitivity was 85.4%, both specificity and positive predictive values were 83.3% and negative predictive value was 43.3%, as well as diagnostic accuracy was 74.5%. Likewise, in the study by Madani *et al.* (2011), after comparing cytology and pathology results in 169 patients, sensitivity was obtained 67%, specificity 91% and diagnostic accuracy 83%. Various reasons are raised to explain different results in this area. Some of which are difference in the study sample size, frequency of types of salivary gland tumors, especially in malignant ones, how to obtain and examine samples and the expertise of the tested person and pathologist precision and experience. As shown, a high concordance exists between the results of FNA and final histopathological findings in salivary gland tumors. These results may be due to the good sampling technique, proper preparation of samples for study, enough precision and experience in studying samples.

## **CONCLUSION**

Fine needle aspiration is an inexpensive, fast, effective and economical method and according to the results of this study, it is reliable in salivary gland lesions diagnosis. In case the association with clinical judgment, can make a substantial contribution to evaluate the patient before surgery. According to the results, it is recommended to use this method more in the diagnostic procedures of salivary gland tumors.

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