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Role of Fine-Needle Aspiration Biopsy in the Management of Salivary Gland Masses

Tükrük Bezi Kitlelerininin Tedavisinde İnce İğne Aspirasyon Biyopsisinin Rolü

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Abstract

Objective: Fine-needle aspiration biopsy (FNAB) is widely used in the management of salivary gland masses. Its main advantage is its ability to differentiate benign from malignant disease. In this study, we aimed to evaluate the diagnostic ability of FNAB in salivary gland masses.

Methods: The records of patients who had undergone FNAB before parotidectomy or submandibular gland excision between 2005 and 2013 were retrospectively analyzed. FNAB results were classified as negative, positive, suspicious for malignancy, and non-diagnostic. Preoperative FNAB results were compared with definitive histopathological results. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of FNAB results were calculated.

Results: A total of 285 patients were enrolled. Among them, 230 (80.7%) had parotid gland and 55 (19.3%) had submandibular gland masses. Following a definitive histopathological examination, the most common benign tumor was pleomorphic adenoma (52.6%), whereas malignant tumors were mucoepidermoid carcinoma (2%) and squamous cell carcinoma (2%). The sensitivity, specificity, PPV, NPV and accuracy of FNAB results were 76.9%, 95.4%, 75%, 95.9%, and 92.6%, respectively. The rate of a suspicious cytology was 5.2% (15 patients) and that of a non-diagnostic cytology was 8.8% (25 patients).

Conclusion: FNAB is a safe and simple diagnostic tool for the diagnosis of salivary gland masses and has a relatively high sensitivity and specificity. It may provide valuable information for patient counselling and surgical planning. The major drawbacks include a lower sensitivity than specificity and a relatively high rate of non-diagnostic results.

Keywords: Salivary gland, fine-needle aspiration biopsy, neoplasia, management

Öz

Amaç: İnce iğne aspirasyon biyopsisi (İİAB), tükrük bezi kitlelerinin yönetiminde yaygın olarak kullanılmaktadır. Benign hastalığı, malign hastalıktan ayırabilme özelliği, bu tekniğin en önemli avantajı olarak bilinmektedir. Bu çalışmada, tükrük bezi kitlelerinde İİAB'nin tanısal değerlendirmedeki rolü incelenmeye çalışılmıştır.

Yöntemler: 2005-2013 yılları arasında, parotidektomi ve submandibüler bez eksizyonu öncesinde İİAB yapılmış hastaların kayıtları geriye dönük olarak incelendi. İİAB sonuçları malignite açısından negatif, pozitif, şüpheli ve tanısal olmayan olarak sınıflandırıldı. Preoperatif İİAB sonuçları, postoperatif histopatoloji sonuçları ile karşılaştırıldı. İİAB'nin duyarlılık, özgüllük, pozitif öngörü değeri (PÖD), negatif öngörü değeri (NÖD) ve doğruluk değerleri hesaplandı.

Bulgular: Toplamda 285 hasta çalışmaya dahil edildi. 230 (%80.7) hastada parotis bezi, 55 (%19.3) hastada ise submandibüler bez kitlesi mevcuttu. Kesin histopatolojik inceleme sonrasında en sık tespit edilen benign tümör pleomorfik adenom (%52.6) iken, en sık tanı koyulan malign tümörler mukoepidermoid karsinom (%2) ve yassı hücreli karsinom (%2) idi. İİAB'nin duyarlılık, özgüllük, PÖD, NÖD ve doğruluk oranları, sırasıyla %76.9, %95.4, %75, %95.9 ve %92.6 olarak belirlendi. Şüpheli sitoloji oranı %5.2 (15 hasta) ve tanısal olmayan sitoloji oranı %8.8 (25 hasta) idi.

Sonuç: Tükrük bezi kitlelerinin tanısında kullanılan İİAB, göreceli olarak yüksek duyarlılık ve özgüllüğe sahip olan güvenli ve basit bir testtir. Hasta bilgilendirme ve cerrahi planlama açısından değerli bilgiler sağlamaktadır. En önemli dezavantajları arasında duyarlılık değerinin özgüllük değerinden düşük olması ve göreceli olarak tanısal olmayan sonuçların yüksek olması yer alır.

Anahtar Kelimeler: Tükrük bezi, ince iğne aspirasyon biyopsisi, neoplazi, tedavi

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Introduction

Salivary gland tumors account for 3–10% of head and neck tumors (1-3). Fine-needle aspiration biopsy (FNAB) of the salivary gland mass is considered as an important diagnostic tool, although some controversy exists (4, 5). FNAB is a reliable and minimally invasive method and carries a minimum risk of complications (3, 6). Differentiation between benign and malignant lesions may be possible with FNAB; this is one of the most important advantages of FNAB (7). Additionally, the degree of differentiation of neoplastic cells can be determined, which may aid in the selection of the type of surgical intervention. However, in the management of salivary gland masses, the cytology results of FNAB should be interpreted along with the clinical findings and radiological investigations (2). When performed and analyzed by experienced hands, FNAB has the advantage of providing valuable diagnostic data in a relatively short period of time (6).

This article aimed to present the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy of FNAB results for salivary gland masses in a tertiary referral center through a review of the literature.

Methods

The medical records of 423 patients who had undergone parotid or submandibular gland excision (between 2005 and 2013) with or without neck dissection were retrospectively analyzed in the Otorhinolaryngology Department of the İstanbul Training and Research Hospital. Only patients with both a preoperative FNAB and postoperative definitive histopathologic examination were included. This study was approved by the Local Ethics Committee of the İstanbul Training and Research Hospital (531, 5th September 2014).

The age, sex, complaints, and FNAB and definitive histopathological results of the patients were recorded. We included only patients who underwent FNAB in our hospital. All FNAB procedures were performed with a 23 G or 25 G needle under ultrasound guidance, and the materials were stained with Papanicolaou stain following alcohol fixation and drying. The results were interpreted by three experienced cytopathologists due to the relatively longer study duration.

The FNAB results were classified into four categories:

i. Negative for malignancy: No evidence of malignancy (including both benign neoplasia and non-neoplastic diseases).
ii. Positive for malignancy: Presence of clear malignancy findings.
iii. Suspicious for malignancy: Differentiation between benign and malignant disease was not possible, although the result was suggestive of a neoplasm.
iv. Non-diagnostic: Insufficient acellular or hypocellular material or elements of peripheral blood. The cytology report was accepted as non-diagnostic following at least two FNABs.

The preoperative FNAB results were postoperatively compared with the definitive histopathological results. Sensitivity, specificity, PPV, NPV, and accuracy were analyzed not only totally but also unique to the parotid and submandibular glands individually. Two different methods were utilized for calculating these variables. In the first evaluation method, suspicious and non-diagnostic FNAB results were omitted, and in the second, suspicious results were included in the malignant group and non-diagnostic results were omitted.

Statistical Package for the Social Sciences (SPSS Inc.; Windows version 15.0, IBM Corporation; USA) was used for statistical analysis. Descriptive values were given as numbers and percentages for categorical variables, and numerical variables were given as mean±standard deviation. The Student's t test was used for intergroup comparisons and the chi-square test for intergroup comparisons of categorical variables. A p-value less than 0.05 was considered statistically significant. We compared the FNAB results with definitive histological results from the perspective of malignancy and categorized the results as true negative when the malignancy was not cytologically and histologically present, true positive when the malignancy was present both cytologically and histologically, false negative when the FNAB result was negative for malignancy but the definitive histological examination showed malignancy, and false positive when the FNAB result was positive for malignancy but the definitive histological examination showed a benign result. A positive predictive result is defined as the probability that a positive FNAB result indicates malignancy following the histological examination. A negative predictive result is defined as the probability that a negative FNAB result indicates the absence of malignancy following the histological examination. Accuracy refers to how close a FNAB result is to the histological examination result and is calculated as the ratio of the sum of both true-positive and true-negative results to the total population number. Sensitivity measures the ratio of actual positives that were correctly identified as malignant on the histological examination, and specificity measures the ratio of actual negatives that were correctly identified as benign on the histological examination.

Results

Two hundred eighty-five patients were included. Among them, 166 (58.2%) were males and 119 (41.8%) were females. Parotid gland excision (PG group) was performed for 230 (80.7%) patients and submandibular gland intervention (SG group) for 55 (19.3%) patients. In the PG group, 135 (58.7%) were males and 95 (41.3%) were females, whereas in the SG group, 31 (56.4%) were males and 24 (43.6%) were females. The mean age of the patients was 53.9±16.7 (9–90) years; the mean ages of the patients in the PG and SG groups were 54.1±16.2 (11–90) years and 52.8±18.06 (9–86) years, respectively. Three patients (1%) developed hematoma following needle aspiration of the parotid mass, and these hematomas completely regressed following a pressure dressing. No other complications were encountered.

The FNAB results were as follows: 220 (77.2%) benign, 25 (8.8%) malignant, 15 (5.2%) suspicious, and 25 (8.8%) non-di-

Table 1. Fine-needle aspiration biopsy results

FNAB result*	Benign (n, %)	Malignant (n, %)
PG	Pleomorphic adenoma (109, 38.2%)	Malignant cytology[2] (12, 4.2%)
	Warthin's tumor (42, 14.7%)	Mucoepidermoid carcinoma (2, 0.7%)
	Benign cytology[1] (27, 9.4%)	Acinic cell carcinoma (1, 0.3%)
	Acute inflammatory cells (4, 1.4%)	
	Chronic inflammatory cells (3, 1%)	
	Oncocytic cell neoplasia (1, 0.3%)	
SG	Pleomorphic adenoma (26, 9.1%)	Malignant cytology[2] (5, 1.7%)
	Benign cytology[1] (5, 1.7%)	Adenoid cystic carcinoma (4, 1.4%)
	Chronic inflammatory cells (3, 1%)	Lymphoma (1, 0.3%)

*excluding suspicious and non-diagnostic cytologies; FNAB: fine-needle aspiration biopsy; PG: parotid gland; SG: submandibular gland
[1]not giving any specific result
[2]not giving any specific result; consisting of only malignant cells

Table 2. Definitive histopathological results

Parotid gland (230)	Submandibular gland (55)
Benign (199, 86.5%)	**Benign (45, 81.8%)**
Pleomorphic adenoma (121)	Pleomorphic adenoma (29)
Warthin's tumor (58)	Plexiform neurofibroma (1)
Monomorphic adenoma (4)	Sialadenitis (15)
Myoepithelioma (3)	
Oncocytoma (2)	
Benign PNST[1] (1)	
Other[2] (10)	
Malignant (31, 13.5%)	**Malignant (10, 18.2%)**
Mucoepidermoid carcinoma (6)	Adenoid cystic carcinoma (5)
Squamous cell carcinoma (6)	Lymphoma (2)
Acinic cell carcinoma (4)	Mucoepidermoid carcinoma (1)
Lymphoma (3)	Ductal carcinoma (1)
Myoepithelial carcinoma (2)	Papillary carcinoma metastasis (1)
Other[3] (10)	

[1]peripheral nerve sheath tumor
[2]includes sialadenitis (two cases), tuberculosis (three cases), cysts (two cases), and reactive lymphadenitis (three cases)
[3]includes a high-grade pleomorphic undifferentiated sarcoma, a pleomorphic malignant fibrous histiocytoma, a carcinosarcoma, an adenoid cystic carcinoma, an oncocytic carcinoma, a ductal carcinoma, a papillary cystadenocarcinoma, a spindle cell carcinoma, a round cell tumor, and a renal cell carcinoma metastasis

agnostic. The corresponding FNAB results specific to the PG group were 186 (80.8%), 15 (6.5%), 13 (5.7%), and 16 (7%) and those specific to the SG group were 34 (61.8%), 10 (18.2%), 2 (3.6%), and 9 (16.4%). The most common FNAB result was pleomorphic adenoma (135 patients, 47.3%), followed by Warthin's tumor (42 patients, 14.7%). FNAB results (excluding suspicious and non-diagnostic cytologies) are given in Table 1.

Regarding definitive histopathological results, 244 (85.6%) were benign, whereas 41 (14.4%) were malignant. The distribution of definitive results for the PG and SG groups is given in Table 2. The most common benign result in the PG and SG groups was pleomorphic adenoma, whereas the most common malignant results were mucoepidermoid carcinoma (six patients) and squamous cell carcinoma (six patients) in the PG group and adenoid cystic carcinoma in the SG group.

The definitive histopathologic examination of 15 suspicious FNAB results consisted of six benign (40%) and nine malignant (60%) results, whereas that of 25 non-diagnostic FNAB results consisted of 23 benign (92%) and two malignant (8%) results. Regarding the 25 non-diagnostic FNAB results, two malignancies (squamous cell and adenoid cystic carcinomas) were diagnosed by definitive histopathological results, whereas 23 (92%) of these non-diagnostic results were proved to be benign. The definitive results of suspicious and non-diagnostic FNAB results in the PG and SG groups are given in Table 3.

For analyzing sensitivity, specificity, PPV, NPV, and accuracy, we excluded 40 results with suspicious (n: 15) and non-diagnostic (n: 25) cytology. For the remaining 245 results, sensitivity, specificity, PPV, NPV, and accuracy were 70%, 98.1%, 84%, 95.9%, and 94.6%, respectively. Considering the 15 suspicious FNAB results to be malignant and excluding only the non-diagnostic cytology, sensitivity, specificity, PPV, NPV, and accuracy were 76.9%, 95.4%, 75%, 95.9%, and 92.6%, respectively. Sensitivity, specificity, PPV, NPV, and accuracy of the results for each salivary gland are given in Table 4.

The false-negative rate in terms of diagnosing malignancy was 23.1% (nine patients) and the false-positive rate was 4.6% (10 patients). The FNAB and definite histopathological results of both false-positive and false-negative results are given in Table 5. None of the false-negative and three of the false-positive results were detected in the SG group.

Among 135 cases where the FNAB result was indicative of a diagnosis of pleomorphic adenoma, three were erroneous: Warthin's tumor, mucoepidermoid carcinoma, and myoepithelial carcinoma. On the other hand, FNAB results were non-diagnostic in five pa-

Table 3. Definitive suspicious and non-diagnostic FNAB results

	Definitive results of suspicious FNAB (n: 15)	Definitive results of non-diagnostic FNAB (n: 25)
Benign	6 (40%)	23 (92%)
PG	5 (33.3%)	15 (60%)
	Warthin's tumor, 3 (20%)	Warthin's tumor, 6 (24%)
	Pleomorphic adenoma, 1 (6.6%)	Pleomorphic adenoma, 3 (12%)
	Myoepithelioma, 1 (6.6%)	Monomorphic adenoma, 2 (8%)
		Cyst, 2 (8%)
		Sialadenitis, 1 (4%)
		Myoepithelioma, 1 (4%)
SG	1 (6.6%)	(32%)
	Sialadenitis, 1 (6.6%)	Sialadenitis, 6 (24%)
		Pleomorphic adenoma, 2 (8%)
Malignant	9 (60%)	2 (8%)
PG	8 (53.3%)	1 (4%)
	Oncocytic carcinoma, 1 (6.6%)	Squamous cell carcinoma, 1 (4%)
	Acinic cell carcinoma, 1 (6.6%)	
	Adenoid cystic carcinoma, 1 (6.6%)	
	Myoepithelial carcinoma, 1 (6.6%)	
	Squamous cell carcinoma, 1 (6.6%)	
	Lymphoma, 3 (20%)	
SG	1 (6.6%)	1 (4%)
	Lymphoma, 1 (6.6%)	Adenoid cystic carcinoma, 1 (4%)

FNAB: fine-needle aspiration biopsy; PG: parotid gland; SG: submandibular gland

Table 4. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of FNAB

	Sensitivity	Specificity	PPV	NPV	Accuracy
Total[1]	70%	98.1%	84%	95.9%	94.6%
Parotid gland	59%	98.8%	86.6%	95.1%	94.5%
Submandibular gland	100%	94.4%	80%	100%	95.4%
Total[2]	76.9%	95.4%	75%	95.9%	92.6%
Parotid gland	70%	93.6%	75%	95.1%	92.5%
Submandibular gland	100%	91.8%	75%	100%	93.4%

[1]excluding suspicious and non-diagnostic FNAB results

[2]considering suspicious FNAB results as malignant and excluding non-diagnostic results

FNAB: fine-needle aspiration biopsy; PPV: positive predictive value; NPV: negative predictive value

tients, suspicious in one patient, and a benign cytology without any specific result in 12 patients who had been diagnosed to have pleomorphic adenomas following the definitive examination.

Among 42 cases where the FNAB result was indicative of a diagnosis of Warthin's tumor, two were inaccurate: mucoepidermoid carcinoma and acinic cell carcinoma. The FNAB result was non-diagnostic in six patients and suspicious in three patients who had a definitive diagnosis of Warthin's tumor.

In cases where the FNAB result was indicative of malignancy (25), four definitive results were benign: two sialadenitis and two reactive lymphadenopathies. In 41 cases where the definitive diagnosis was a malignant tumor, the FNAB result was benign in nine, suspicious in nine, and non-diagnostic in two.

Discussion

Fine-needle aspiration biopsy of salivary gland masses is widely performed due to its safety, technical ease, low cost, and relatively high accuracy (5). The cytological result is useful in terms of both surgical planning and patient counselling (8). The cytological diagnosis mainly aims to differentiate malignant from benign lesions (2). Preoperative knowledge of the malignant nature of the tumor may modify the postoperative course, and the

Table 5. Definitive histopathological results of false-negative and false-positive FNAB results

False-negative FNAB (9)	**Definitive histopathology**
Benign cytology (3)	Mucoepidermoid carcinoma (3)
Pleomorphic adenoma (2)	Mucoepidermoid carcinoma
	Myoepithelial carcinoma
Warthin's tumor (2)	Acinic cell carcinoma
	Mucoepidermoid carcinoma
Acute inflammatory cells (2)	Acinic cell carcinoma
	Squamous cell carcinoma
False-positive FNAB (10)	**Definitive histopathology**
Suspicious cytology (6)	Warthin's tumor (3)
	Pleomorphic adenoma (1)
	Myoepithelioma (1)
	Sialadenitis (1)
Malignant cytology (4)	Sialadenitis (2)
	Reactive lymphadenopathy (2)

FNAB: fine-needle aspiration biopsy

surgeon may consider a more extensive surgery with concurrent neck dissection (7, 9). On the other hand, some authors claim that FNAB is not a systematic procedure for the management of the salivary gland masses, whereas others suggest that FNAB does not affect the treatment algorithm of benign lesions in particular (10, 11). Nevertheless, FNAB should not be considered more important than the clinical impression and should be interpreted along with the physical examination findings (6). It is of paramount importance to work with an experienced cytopathologist when evaluating FNAB material (12). Accurate interpretation of the cytopathology and straightforward preparation of the aspirated material are cornerstones for making a correct diagnosis. Cytopathologists must have enough and necessary information on the clinical features of the mass, including the duration of the mass, associated pain and/or facial paralysis, and cervical lymphadenopathy, to make a more accurate interpretation (12). Ultrasound guidance along with immediate assessment of the material by a cytopathologist has been reported to increase the accuracy of FNAB (13).

The accuracy of 94.6% obtained in this study is in accordance with that found in the literature (4, 14). The sensitivity of FNAB clearly seems to be lower than its specificity, which means that the false-negative rate is higher than the false-positive rate (15, 16). The relatively high rate of false negatives may limit the usefulness of FNAB. In a review of the literature of the last decade, the sensitivity was reported to range between 60% and 92% and the specificity was reported to range between 87.7 and 100% (14-21). In our study, the sensitivity and specificity were 76.9% and 95.4%, respectively.

If we examine the sensitivity and specificity of FNAB for the PG and SG groups individually, the sensitivity for the SG group seems significantly higher than that for the PG group (100% vs 70%, respectively), whereas the specificity was similar (93.6% vs 91.8%, respectively). In other words, the false-negative rate for the SG group is much lesser than that for the PG group.

A non-diagnostic cytology is one of the major drawbacks of FNAB, and it ranges between 3% and 34% (8, 16). This may be due to low cellularity, necrosis, bleeding, or improper technique (3, 8). Atypical cellular findings and architectural changes are similar in many malignant tumors, and some of these are diagnosed only if capsular or perineural invasion is demonstrated (3). These findings are almost impossible to identify with FNAB (22). To decrease the rate of non-diagnostic cytology, evaluation of the adequacy of the specimen by an experienced cytopathologist is advised and re-aspiration, if necessary, should be considered (3). In our series, FNAB was performed two times in all non-diagnostic cytology cases (25 patients, 8.8%). In these non-diagnostic FNAB results, two malignancies (squamous cell and adenoid cystic carcinomas) were identified by the definitive histopathological results.

A suspicious cytology, due to its relatively high rate of malignant disease, may be managed similar to a malignant cytology (18). In our series, the rate of a suspicious cytology was 5.2%, and a majority (86.6%) were obtained from the PG group. More importantly, 60% of these cases proved to be malignant following the definitive histopathological examination. Fundakowski et al. (23) reported a malignancy rate of 31.3% in a series of 115 suspicious FNABs of the parotid gland, and a suspicious cytology was accepted as a significant risk factor for malignancy.

A pleomorphic adenoma, due to its unique characteristics, can be easily identified by FNAB (24, 25). However, the presence of atypical cytological findings may be indicative of malignancy (26). Differentiation from carcinoma ex pleomorphic adenoma or adenoid cystic carcinoma may be difficult (25). In our series, the FNAB result was consistent with pleomorphic adenoma in 135 patients. Three of these results were false positives for pleomorphic adenoma (two were proved to be malignancies).

In this study, pleomorphic adenoma was the most common salivary gland mass (52.6%), followed by Warthin's tumor (20.3%). The most common malignant disease was mucoepidermoid carcinoma (seven cases, 2.4%), six of which were located in the parotid gland. In the submandibular gland, an adenoid cystic carcinoma was the most common malignancy. All cases of squamous cell carcinoma were located in the parotid gland, whereas five of the six adenoid cystic carcinoma cases were located in the submandibular gland. Five cases of lymphoma were diagnosed following the definitive histopathological examination. All were non-Hodgkin lymphomas. FNAB results of these cases were benign (two patients), suspicious (two patients), and malignant (one patient). Making a diagnosis of a lymphoma with the help of FNAB has some difficulties, including a relatively high rate of false negativity. Immunophenotyping studies have been reported to help in the interpretation of the lymphoproliferative processes (27).

Fine-needle aspiration biopsy may have some disadvantages including bleeding, squamous metaplasia, fibrosis, and necrosis in the final histopathological examination. Nevertheless, it is generally accepted that these complications, if they do exist, do not interfere with the definitive diagnosis (14, 21).

Recently, a new technique, core needle biopsy (CNB), has emerged in diagnosing salivary gland masses. Intact tissue cores can be obtained with CNB, which in turn results in improved specimen adequacy (28). CNB can overcome the disadvantage of the low sensitivity of FNAB. Increased risks related to bleeding, facial nerve injury, and tumor seeding are the main concerns of CNB (29). However, the safety of CNB has been widely accepted (30). Although long-term follow-up results have not yet been published, the effect of CNB in the preoperative diagnosis of salivary gland masses seems promising.

Conclusion

To differentiate between benign and malignant diseases is an important feature of FNAB of salivary gland masses in terms of patient counselling and proper surgical planning. This retrospective study demonstrated that FNAB is a useful technique for the diagnosis of salivary gland masses and should continue to be used in the management of salivary gland masses. The technique is simple and safe and has a minimal complication rate. The ratio of non-diagnostic results may be improved using proper techniques in with the cooperation of the cytopathologist.

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