Original Article

Reliability of Fine Needle Aspiration Cytology for Salivary Gland Lesions

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Abstract

Background and Aim: Fine needle aspiration (FNA) cytology is a safe, reliable, minimally invasive and cost-effective technique for the diagnosis of salivary gland lesions. This study aimed to assess the accuracy, reliability and diagnostic value of FNA cytology in Iran.

Materials and Methods: A total of 200 records of patients with a history of biopsy or surgical excision of salivary gland lesions along with their histological and cytological examination results were retrieved and evaluated in the Pathology Department of Amir Alam Hospital during 2007-2013. The results of cytological diagnosis were divided into 4 groups of unfavorable, benign, suspicious and malignant. The cytological results were compared with the histological data. The accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of FNA cytology were calculated using SPSS version 16.00.

Results: Of the specimens chosen for the study, 173 were from the parotid, 22 from the submandibular and 5 from the minor salivary glands. FNA cytological diagnosis was benign in 161 cases, suspicious for malignancy in 4 cases, and malignancy in 35 cases. Of 161 cases diagnosed as benign by FNA cytology, 25 were malignant and the frequency of false positive results was 15.5%. The accuracy, sensitivity, specificity, PPV and NPV of the FNA test were 82, 53, 93, 72 and 84%, respectively.

Conclusion: A good agreement exists between the FNA results and final histopathological diagnosis of salivary gland tumors. Also, this study showed that FNA cytology has moderate accuracy and relative diagnostic value for diagnosis of salivary gland lesions.

Key Words: Salivary gland, Fine needle aspiration biopsy, Sensitivity, Specificity, Diagnostic accuracy

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Introduction

Salivary gland tumors are among the less common cancers with an incidence rate of 0.4-13.5 cases/100,000 population worldwide [1]. Salivary gland tumors comprise 2-6.5% of the head and neck cancers and 21-46% of them are malignant [1]. The prevalence of these tumors is variable among different ethnicities and populations in different geographical locations. The parotid gland is the most commonly involved salivary gland and 34-86% of salivary tumors occur in this gland. However, other major and minor glands may be involved as well [2]. The frequency of benign salivary gland tumors is higher than that of malignant salivary gland tumors and the prevalence of these tumors is generally higher in women [3]. Thus, prompt diagnosis with a simple and highly accurate technique is necessary.

FNA cytology plays an important role in diagnosis of salivary gland lesions. FNA was first introduced

in 1920 for assessment of parotid lesions and gained popularity 50 years later. This method is commonly used to differentiate neoplastic and non-neoplastic lesions and discriminate malignant from benign cases. On the other hand, this method can be used for lesions such as cysts, masses and large lymph nodes visible with naked eye or those diagnosed with advanced techniques such as ultrasound and CT scan. The most common application of this test is for breast and thyroid masses and the head and neck glands. This method has fewer complications than biopsy and local tumor spread less commonly occurs in this technique. It is also well accepted by patients [4, 5]. This method is safe, simple and cost effective. Buley et al. reported its sensitivity to be 60-73% for salivary gland malignancies [6].

Although this test cannot serve as a definite diagnostic tool, it can prevent unnecessary surgical procedures [7, 8]. However, for management of patients suffering from salivary gland conditions, cytology alone is not enough and it must be used in conjunction with physical and radiographic examinations such as CT scan and MRI to achieve higher diagnostic value [9, 10].

A general concern regarding FNA is dissemination or seeding of tumor along the path of needle.

However, a 15-year retrospective study refuted this theory. FNA is performed in many clinics for detection of salivary gland lesions. Based on previous studies, FNA has 10-62% sensitivity, 86-100% specificity and 77-98.2% accuracy for diagnosis of salivary gland lesions [4, 5, 11-14]. This diagnostic test is widely used in the United States, Europe and Asia. However, the diagnostic value of this test for management of salivary gland tumors remains questionable [14, 15].

This study aimed to assess the accuracy, sensitivity and specificity of FNA for diagnosis of salivary gland tumors in comparison with biopsy as the definite, gold standard diagnostic method for these tumors.

Materials and Methods

This analytical cross sectional study was performed on patient records in the archives of the Pathology Department of Amir Alam Hospital in Tehran regarding FNA and histopathological reports of salivary gland lesions from 2007 to 2013. First, medical records of patients with salivary gland tumors were found and the clinical reports of these patients (filled out in the pathology department) were also retrieved to complete data and make a comparison between the efficacy of FNA and histopathological analysis. The accuracy of FNA test was compared with that of pathology report, which is the gold standard for diagnosis of salivary gland tumors.

In Amir Alam Hospital, FNA test is often performed by expert technicians using a 22-23 gage needle and a 10cc syringe.

Tissue specimens were fixed in 95% alcohol and stained with Papanicolaou stain, which is commonly used for detection of cell components to assess cell structure and benign or malignant nature of the tumor [14]. Next, the specimens were evaluated under a light microscope. Biopsy specimens were conventionally sectioned and stained with hematoxylin and eosin. Specimens were then evaluated under a light microscope.

Histopathological type of salivary gland tumors was determined using the classification by World Health Organization (WHO) [16]. One pathologist assessed and reported both FNA and histopathological results, who was expert enough for reading cytology specimens. Considering the high volume of salivary gland specimens evaluated in the Pathology Department of Amir Alam Hospital and also high volume of referral cases to this department, the accuracy of diagnoses can be assumed to be high.

Based on the opinions of two pathologists and the clinical and radiographic information present on patient files, the results of FNA diagnosis were classified into 4 groups of unfavorable, benign, suspicious for malignancy and malignant.

Unfavorable specimens were excluded and were not analyzed statistically. Cases suspected for malignancy were combined with malignant cases in one group. Data were analyzed using SPSS version 16 with 95% confidence interval to assess the accuracy, sensitivity, specificity, PPV and NPV.

Accuracy=True positive + true negative/ true positive and false positive + true negative and false negative

Sensitivity=True positive/True positive + false negative

Specificity= True negative/True negative + false positive
Positive predictive value=True positive/cases with a positive test
Negative predictive value=True negative/cases with a negative test

Results

In total, FNA and histopathological results of 200 patients were compared; out of which, 119 were males and 81 were females. Lesions in major salivary glands were all aspirated using a fine needle. There were 22 cases of submandibular gland involvement, 173 cases of parotid gland involvement and 5 cases of minor salivary gland involvement. Involvement of salivary glands in different anatomical locations along with FNA and histopathological results are shown in Table 1. Based on the results of FNA, 147 cases were benign and 53 were malignant.

Based on histopathological data, there were 100 benign and 60 malignant cases. In 165 cases, the diagnoses of FNA and histopathology were the same. In 35 cases, the diagnoses were different. Table 2 shows the diagnoses of benign and malignant tumors by FNA and histopathological analysis. The agreement between FNA and histopatho-logical analysis was relatively excellent (94%) for neoplastic benign tumors. This rate was 92.5% for non-neoplastic benign tumors.

The diagnostic agreement of FNA and histopathological analysis for malignant tumors is shown in Table 3. In general, the two methods showed agreement in approximately 57% of cases. In 43%, the malignant cases were shown as benign by FNA.

Table 4 shows the accuracy, sensitivity, specificity, PPV and NPV of FNA. Based on the results, the sensitivity of FNA in the understudy population was moderate (53%); whereas, its specificity was excellent (97%).

Discussion

Salivary glands have complex structures, making the detection of neoplasms in them very difficult. Clinically, many of the malignant salivary gland tumors behave like the benign types. Thus, the priority for use of FNA is to differentiate benign from malignant tumors and this issue is superior to detection of the type of tumor. Thus, this study sought to assess the accuracy, reliability and diagnostic value of FNA cytology for accurate diagnosis of malignant and benign salivary gland tumors and to make a comparison with histopathological analysis.

The results of this study showed that the agreement between FNA and histopathological analysis was 57% for malignant and 93.5% for benign salivary gland tumors. In most parts of the world, FNA is routinely used for preoperative diagnosis of salivary gland lesions. This is usually done in the first clinical examination of patients. During the 6-year period of this study, 200 cases of FNA cytology for salivary glands were re-evaluated. Some cases did not have a histopathology report; which may be attributed to the fact that they were confirmed to be benign and FNA cytology had yielded no sign of tumoral cells. Preoperative FNA provides the clinicians with valuable information and helps making a decision whether a specific patient should be operated on or not [17, 18].

A previous study reported that use of FNA as a primary diagnostic tool caused 30% reduction in salivary gland surgeries and saved some patients from unnecessary invasive procedures [19]. FNA test is especially important for clinical management of patients with head and neck tumors particularly for diagnosis of malignant cases.

In our study, the diagnostic accuracy, sensitivity, specificity, PPV and NPV of preoperative FNA specimens of salivary glands were found to be 82%, 53%, 97%, 72% and 84%, respectively. These results are in accord with the findings of previous studies [4, 5, 12, 13, 20, 22]. However, other studies have reported a wide spectrum of sensitivity and specificity for FNA cytology of salivary glands in diagnosis of malignant tumors ranging from 29-97% and 84-100% [23]. The reason for this wide variability may be technical factors, medical experience with FNA and experience and expertise of the cytopathologist [23].

Rate of non-neoplastic benign lesions in this study was 50%. This is in accord with the rates reported in other studies ranging from 20-72.9% [20, 24, 25]. Inflammatory and lymphatic hyperplasia comprise a high percentage of non-neoplastic benign lesions. Some authors have stated that high

Table 1. Comparison of results of FNA and histopathological analysis

FNA	Histopathology		
	Benign	**Malignant**	**Total**
Benign	(True negative) 136	(False negative) 25	161
Suspicious	(False positive) 2	(True positive) 2	4
Malignant	(False positive) 9	(True positive) 26	35
Total	147	53	200

Table 2. Results of FNA for histopathologically benign tumors based on the type of tumor

Histopathological diagnosis	Number of specimens	FNA	
Neoplastic benign tumor	100	Benign	Malignant
Pleomorphic adenoma	95	89	6
Warthin's tumor	3	3	0
Basal cell adenoma	1	1	0
Myoepithelioma	1	1	0
Non-neoplastic benign tumor	40		
Sialadenitis, lymphoid hyperplasia, etc	33	30	3
Oncocytoma	7	7	0

percentage of inflammatory lesions may be due to geographical differences [25, 26]. The rate of agreement between FNA and histopathological diagnosis in benign neoplasms was relatively excellent (94%) in our study. In the current study, pleomorphic adenoma was the most common benign tumor accounting for 47.5% of all benign cases. In terms of prevalence, Warthin's tumor ranked second among benign neoplastic tumors accounting for 1.5% of all tumors. The prevalence rate of these two benign neoplasms is in accord with the results of previous studies [4, 11, 20, 26]. In our study, there were 60 cases (30%) of malignant neoplasms. In other studies, the reported rates varied from 15 to 30% among different populations [13, 20, 24, 27]. The most common malignant salivary gland tumors were mucoepidermoid carcinoma and squamous cell carcinoma with 5 and 8% prevalence, respectively; these rates were also in accord with previous reports [5, 20, 23].

In the current study, 4 cases were suspicious for malignancy, which were included in the malignant category. Re-aspiration is highly recommended for suspicious cases. Although FNA enables possible diagnosis of lymphoma, there is a general consensus that this diagnosis must be confirmed with surgical biopsy and immunohistochemical analysis.

Moreover, diagnosis of mucoepidermoid carcinoma must also be confirmed since it may occur in high-grade or low-grade forms.

Low-grade mucoepidermoid carcinoma may be mistaken for chronic sialadenitis, mucosal retention cyst, Warthin's tumor or adenomatoid hyperplasia of the mucosal salivary glands. Cells may not show significant pleomorphism for diagnosis of malignancy. Thus, to prevent false negative results, these specimens must be evaluated with utmost precision [7]. Pleomorphic adenoma is comprised of glandular epithelium and mesenchymal stroma and the results of FNA test for this tumor are often correct. However, in some cases, it may be mistaken for adenoid cystic carcinoma, monomorphic adenoma, or mucoepidermoid carcinoma; this results in increased frequency of false positive and false negative results.

Pleomorphic adenocarcinoma is hardly diagnosed with FNA. Adenoid cystic carcinoma can be diagnosed by FNA test.

However, it is difficult to diagnose its benign or malignant nature with FNA and biopsy needs to be performed for this purpose. Squamous cell carcinoma can be easily mistaken for mucoepidermoid carcinoma and sialadenitis. To differentiate squamous cell carcinoma and mucoepidermoid carcinoma, immunohistochemical

Table 3. Diagnostic results of FNA for histopathologically malignant tumors based on the type of tumor

Histopathological diagnosis	Number of specimens	FNA	
Malignant tumor	60	Benign	Malignant
Mucoepidermoid carcinoma	16	6	10
Squamous cell carcinoma	10	4	6
Clear cell tumor	2	1	1
Metastatic tumor	3	0	3
Salivary duct carcinoma	1	0	1
Melanoma	1	0	1
Adenoid cystic carcinoma	9	5	4
Acinic cell carcinoma	8	6	2
Basal cell carcinoma	5	2	3
Lymphoma	5	2	3

Table 4. Diagnostic accuracy of FNA for salivary gland tumors

Parameter	Value	95% confidence interval
Accuracy	82%	87%-76%
Sensitivity		
Specificity	93%	96%-87%
Positive predictive value	72%	83%-56%
Negative predictive value	84%	89%-78%

analysis and detection of high rate of mucin indicative of mucoepidermoid carcinoma can greatly help [27].

After combining the suspicious and malignant cases in one group, the frequency of false positive results was found to be 5.5% (11 cases) in our study, which is close to the range of 0.0-4.7% reported by other studies [12, 18].

Some cases of NPV may be due to errors in interpretation of lesions and it should be noted that both neoplastic and non-neoplastic lesions of salivary glands may show involvement of squamous cells, which is an unexpected finding and may lead to misdiagnosis [29]. Rate of false negative results in this study was 12.5%, which is in line with the range of 4.7-24.5% reported in previous studies [7, 9, 12]. But, this rate has reported to be 2.2% in another study [17]. According to the reports by the American Association of Pathologists, many of the cases of false negative reports and disagreements are related to malignant tumors i.e. lymphoma, acinic cell carcinoma, mucoepidermoid carcinoma and adenoid cystic carcinoma, which is in accord with the current study results (Table 3) [30].

Differential diagnoses of lymphoma include lymphoid hyperplasia, benign lymphoreticular lesions, chronic sialadenitis and adenolymphoma and their differentiation with the use of FNA alone is very difficult [17]. On the other hand, in some cases, lymphoma manifests as accumulation of populations of lymphoid cells along with primary, immature inflammatory cells, making the diagnosis more difficult by cytology alone. In such cases, FNA cytology along with other methods such as immunohistochemistry and flow cytometry may be helpful for diagnosis and classification of lymphoma and other tumors with high rate of false negative results [23].

Some other reasons for the disagreement between FNA and histopathology results may be the experience and expertise of the person reading the FNA slide. Some individual errors may lead to misinterpretation. Inappropriate sampling may also

lead to misdiagnosis. Thus, assessment of higher number of specimens may play a role in correction of human errors. Four main reasons have been described for errors in diagnoses based on cytology results including inadequate number of specimens, selection of degenerated cells, errors in marking of specimens and the cytologist being unfamiliar with the morphology of rare salivary gland tumors [31]. Another method used for assessment of salivary gland lesions is incisional biopsy and frozen section (FS) for management of salivary gland lesions.

Some researchers prefer this method to FNA and believe that aspiration with a fine needle alone is not reliable for surgical management of cases of primary parotid carcinoma. However, some other studies have shown that FNA is much more sensitive than FS; while FS has higher specificity. The accuracy of both methods is the same and some researchers have concluded that these methods in conjunction with one another are helpful for management of malignant salivary gland tumors [14, 17, 32].

Conclusion

A suitable agreement exists between the results of FNA and final histopathological diagnoses for salivary gland tumors. Also, this study showed that FNA cytology has moderate accuracy and relative diagnostic value for diagnosis of salivary gland lesions.

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