Role of Fine Needle Aspiration Cytology in the Diagnosis of Swellings in the Salivary Gland Regions: A Study of 712 Cases

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Key Words

Salivary gland · Parotid · Submandibular gland · Fine needle aspiration cytology · Sialadenitis · Pleomorphic adenoma · Warthin's tumor · Adenocarcinoma

Abstract

Introduction: A mass in the salivary gland region often presents a diagnostic challenge with regard to its site of origin (salivary versus nonsalivary), benign or malignant nature, and tissue-specific diagnosis. The present study describes the utility of fine-needle aspiration (FNA) cytology in the diagnosis of these lesions. **Subjects and Methods:** Over a 6-year period (January 1994 to December 1999), 712 patients aged between 6 months and 91 years (median, 37 years) were subjected to FNA of swellings in their salivary gland regions. Male:female ratio was 1.28:1. The swellings were mostly located in the parotid (323 cases), submandibular (343 cases), and upper cervical region (27 cases). Swellings of oral (5 cases) and sublingual (2 cases) sites were rare. The lesions diagnosed by FNA cytology were compared among the major salivary glands. Cytologic diagnoses were correlated with histology in 45 cases. **Results:** Benign nonneoplastic lesions were the most common (73%), followed by neoplasms (20%), and those with atypical cytology (1%).

Cytologic material was inadequate in 6% cases. Parotid gland region was involved more frequently by neoplasms (27.1%) than the submandibular gland region (13.7%, $p < 0.0001$). Inflammatory processes affected the submandibular gland region more commonly (42.0%) than the parotid (32.6%, $p = 0.0164$). Pleomorphic adenoma was the most common neoplasm (61.5%), followed by Warthin's tumor (12.6%). Malignancies accounted for 10.5% of neoplasms. Frequency of involvement of parotid by Warthin's tumor (16.7%) was significantly higher than that of submandibular gland (2.3%, $p = 0.0191$). However, the submandibular gland was more commonly affected by malignancy than the parotid gland ($p = 0.0003$). Sensitivity, specificity, and diagnostic accuracy of FNA cytology for all neoplastic lesions of the salivary gland were 94.6, 75.0, and 91.1%, respectively. The corresponding figures for malignancies were 60.0, 95.0, and 91.1%, respectively. **Conclusion:** FNA cytology is very useful for the diagnosis of salivary gland lesions. However, sampling and interpretation errors may occur. The low specificity for the diagnosis of neoplasms as a whole and the poor sensitivity for malignancies found in our study can be attributed to the relatively small number of benign nonneoplastic and malignancy cases with available histopathologic diagnoses.

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Introduction

A mass in the salivary gland region is often a diagnostic and therapeutic challenge. Important questions include whether it is inflammatory, a benign or malignant neoplasm, whether surgery is indicated and, if so, how radical it should be [1]. Since not all lesions of the salivary glands are subjected to surgical procedures, information on the distribution of these lesions between the major salivary glands, based on histopathological diagnoses, may not be complete. Fine needle aspiration (FNA) cytology has a recognized role in the evaluation of all swellings in the salivary gland region. It may be used to differentiate non-neoplastic lesions from neoplasms, and benign from malignant neoplasms [2]. FNA diagnosis is also useful in planning definitive treatment, including the avoidance of unnecessary surgery, and ultimately in reduction in hospital cost [1, 2].

The present study describes the cytologic features of masses in the salivary gland regions and the relative distribution of these lesions between the major salivary glands. The efficacy of FNA cytology was determined by comparing cytodiagnoses with histopathology results in 45 cases, including 38 neoplastic lesions.

Subjects and Methods

During a 6-year period (January 1994 to December 1999), masses in the salivary gland region of 712 patients were investigated by FNA in the Department of Cytology, Mubarak Al-Kabeer Hospital, Kuwait. Patients with localized or diffuse swellings in the salivary gland

region were sent for FNA from the medical, surgical, and ENT outpatient departments of six major hospitals as well as from some polyclinics. The ages of these patients ranged from 6 months to 91 years with a median of 37 years. Male:female ratio was 1.28:1. The swellings were mostly located in the parotid (323 cases), submandibular (343 cases), and upper cervical region (27 cases). Involvement of oral (5 cases) and sublingual salivary glands (2 cases) was less frequent.

Pathologists with experience in FNA cytology ranging from 5 to 18 years performed the FNA. Aspiration was accomplished using 10-ml disposable plastic syringes and 22- to 23-gauge disposable needles fitted to a Franzen handle (Cameco syringe pistol). The air-dried smears were stained using the May-Grünwald-Giemsa (MGG) method and wet-fixed smears by Papanicolaou stain. Histopathology slides and reports of surgically resected specimens were available from two of the six major hospitals for 45 cases only. The FNA smears and hematoxylin and eosin-stained paraffin sections of these cases were blindly reviewed by 2 pathologists (D.K.D. and J.T.A., respectively) and subsequently examined together without further alterations of the reviewed diagnoses to determine sampling and interpretation errors. Special stains (PAS-Alcian blue and mucicarmine) and immunohistochemistry (cytokeratin, epithelial membrane antigen, carcinoembryonic antigen, leukocyte common antigen, S-100 protein, CD-3, CD-20, CD-68, and CD-79α) were also employed in selected cases.

Fisher's Exact Test was used to determine the significance of differences between two sets of values. A p value of less than 0.05 was considered significant. The sensitivity, specificity and diagnostic accuracy of FNA cytology in comparison to histopathology was also calculated.

Results

Lesions were categorized on the basis of their anatomical location and cytological characteristics. Lesions were categorized on the basis of cytology into 519 (73%) benign

Table 1. FNA cytodiagnosis of salivary gland lesions

FNA cytodiagnosis	Cases		Sites of FNA					
	n	%	parotid	sub-mandibular	sub-lingual	upper cervical	oral	NOS
Benign salivary aspirate	122	17.1	72	36	—	12	1	1
Inflammatory lesions	245	34.4	101	132	1	5	1	5
Reactive lymphoid hyperplasia	93	13.1	22	71	—	—	—	—
Benign cystic lesions	41	5.8	23	16	—	—	2	—
Lipomatous lesions	18	2.5	6	12	—	—	—	—
Atypical cytology	6	0.8	2	4	—	—	—	—
Neoplasm	143	20.1	84	43	1	10	1	4
Inadequate	44	6.2	13	29	—	—	—	2
Total	712		323	343	2	27	5	12

NOS = Not otherwise specified.

nonneoplastic lesions consisting of benign salivary gland aspirates, inflammatory lesions, reactive lymphoid hyperplasia, benign cystic and lipomatous lesions, 6 (1%) atypical cytology, 143 (20%) neoplasms, and 44 (6%) inadequate aspirates (table 1). Thirteen (4.0%) aspirates from the parotid and 29 (8.5%) from the submandibular region were inadequate ($p = 0.0241$). Of the 668 cases with adequate material, 310 were from the parotid and 314 from the submandibular region. A significantly higher proportion of cases (42.0%) from the submandibular gland region were inflammatory in nature compared to the parotid (32.6%, $p = 0.0164$). A significantly higher proportion of samples from the submandibular region (22.6%) also showed reactive lymphoid tissue compared to the parotid (7.1%, $p < 0.0001$). On the other hand, 27.1% of parotid and 13.7% of submandibular lesions were neoplastic ($p < 0.0001$). The difference between these two sites with respect to benign cystic lesions was not significant ($p = 0.2503$).

Neoplastic Lesions

The types and distribution of the neoplastic lesions are summarized in table 2. Of these, 126 (88.1%) were benign; 15 (10.5%) were malignant, and in 2 (1.4%) the decision between benign and malignant lesions was difficult. The correlation between initial FNA cytodiagnosis and

histopathological diagnosis is shown in table 3 and alterations in diagnoses following review in table 4.

Pleomorphic adenoma was the most common salivary gland tumor, constituting 88 (61.5%) of all neoplasms and 69.8% of the benign tumors. Cytologically, it showed a variable mixture of poorly cohesive sheets and single epithelial cells as well as fibrillar myxoid or chondromyxoid ground substance (fig. 1A) entrapping spindle-shaped mesenchymal cells (fig. 1B). Histopathology of these tumors also revealed sheets and strands of epithelial/myoepithelial cells with evidence of acini or duct formation. The epithelial/myoepithelial element was dispersed within a myxoid matrix (fig. 1C). Squamous metaplasia of the epithelial component was present in 24% of cases and chondroid differentiation of the mesenchyme-like matrix was observed in 44% of cases. Warthin's tumor was the second most common salivary gland tumor accounting for 18 (12.6%) of all tumors and 14.3% of the benign neoplasms. The aspirates revealed cohesive sheets of bland oncocytic cells against a background material of lymphoid cells and cell debris (fig. 1D). The histology of these tumors showed spaces lined by a double layer of oncocytic epithelial cells resting on a dense lymphoid stroma (fig. 1E), which had dispersed germinal centers. The four monomorphic adenomas constituted 2.8% of all salivary gland tumors and 3.2% of the benign tumors. FNA smears

Table 2. FNA cytodiagnosis of neoplasms in salivary gland region

FNA cytodiagnosis	Cases		Sites of FNA					
	n	%	parotid	sub-mandibular	sub-lingual	upper cervical	oral	NOS
Monomorphic adenoma	4	2.8	2	–	1	1	–	–
Pleomorphic adenoma	88	61.5	58	25	–	3	1	1
Warthin's tumor	18	12.6	14	1	–	3	–	–
Vasoformative tumor	3	2.1	1	2	–	–	–	–
Lipoma	8	5.6	2	5	–	–	–	1
Benign neoplasm (NOS)	5	3.5	4	–	–	1	–	–
Acinic cell tumor	1	0.7	–	1	–	–	–	–
Pleomorphic adenoma with atypia/mucoepidermoid ca.	1	0.7	1	–	–	–	–	–
Mucoepidermoid ca./Warthin's tumor	1	0.7	–	–	–	–	–	1
Carcinoma	7	4.9	–	5	–	2	–	–
Lymphoma	5	3.5	1	4	–	–	–	–
Malignancy (NOS)	2	1.4	1	–	–	–	–	1
Total	143		84	43	1	10	1	4

NOS = Not otherwise specified; ca. = carcinoma.

Table 3. Correlation of initial FNA cytologic and histopathologic diagnosis in salivary gland lesions

Initial FNA cytodiagnosis	Cases	Initial histopathological diagnosis	
		consistent	inconsistent
Benign salivary gland aspirate	3	3	–
Sialadenitis	3	2	1 (carcinoma ^c)
Pleomorphic adenoma	28	25	3 (2 monomorphic adenoma ^a , 1 acute lymphadenitis ^b)
Pleomorphic adenoma with atypia	1	–	1 (pleomorphic adenoma ^a)
Warthin's tumor	3	3	–
Warthin's tumor/mucoepidermoid carcinoma	1	–	1 (Warthin's tumor ^a)
Pleomorphic adenoma with atypia/mucoepidermoid carcinoma	1	–	1 (carcinoma ^a)
Carcinoma	2	2	–
Reactive lymph node	2	–	2 (1 atypical lymphoid proliferation ^b , 1 mucolith ^a)
Atypical lymphoid proliferation	1	–	1 (actinomycosis ^b)
Total	45	35	10

^a Minor discrepancy (n = 6).

^b Moderate discrepancy (n = 3).

^c Major discrepancy (n = 1).

Table 4. Alterations in FNA cytodiagnosis and histopathological diagnosis in salivary gland lesions following review

Sr. No.	Initial FNA cytodiagnosis	Initial histopathologic diagnosis	Reviewed FNA cytodignosis	Reviewed histopathologic diagnosis
1	Pleomorphic adenoma	monomorphic adenoma	monomorphic adenoma	monomorphic adenoma
2	Pleomorphic adenoma	suppurative lymphadenitis, <i>normal salivary gland</i>	organizing inflammation	actinomycosis in lymph node, normal salivary gland
3	Atypical lymphoid proliferation	actinomycosis	reactive lymph node	reactive lymph node
4	Chronic sialadenitis	carcinoma ex pleomorphic adenoma	chronic sialadenitis	carcinoma ex pleomorphic adenoma
5	Pleomorphic adenoma	pleomorphic adenoma	pleomorphic adenoma with atypia	pleomorphic adenoma
6	Pleomorphic adenoma with atypia/ mucoepidermoid carcinoma	low-grade adeno-carcinoma	suspicious of malignancy	low-grade adenocarcinoma
7	Reactive lymph node	mucolith	reactive lymph node	chronic sialadenitis
8	Pleomorphic adenoma	pleomorphic adenoma	suspicious of malignancy	terminal duct carcinoma
9	Pleomorphic adenoma	monomorphic adenoma	monomorphic adenoma	monomorphic adenoma
10	Reactive lymph node	atypical lymphoid proliferation	reactive lymph node	non-Hodgkin's lymphoma
11	Warthin's tumor/ mucoepidermoid carcinoma	Warthin's tumor	Warthin's tumor	Warthin's tumor
12	Pleomorphic adenoma with atypia	pleomorphic adenoma	pleomorphic adenoma	pleomorphic adenoma

of monomorphic adenomas showed cohesive masses or strands of monomorphic basaloid cells along with scanty stromal material. The fibrillar mesenchymal matrix of pleomorphic adenoma was conspicuously absent. Of the 28 pleomorphic adenomas with subsequent histology, there was agreement with FNA cytology in 25 (89.3%) cases. The 3 discrepant cases included 2 histologically

diagnosed monomorphic adenomas (fig. 2A). Review of FNA cytology also proved them to be monomorphic adenomas (fig. 2B). The remaining case was acute lymphadenitis in histology, which showed actinomycosis during review, but the FNA smear showed only organizing inflammation. Even the review of 25 concordant cases of pleomorphic adenoma revealed discrepancy between cy-

Fig. 1. A Pleomorphic adenoma. FNA from a 2.5-cm-diameter right parotid swelling from a 36-year-old man. Smear shows sheets of epithelial cells and fibrillar myxoid matrix. May-Grünwald-Giemsa. $\times 200$. **B** Oval to spindle-shaped nuclei of stromal cells embedded in mesenchymal matrix. Same case as shown in **A**. Papanicolaou. $\times 100$. **C** Pleomorphic adenoma. Histopathology of the case shown in **A** and **B**. Sheets of epithelial cells forming occasional acini and surrounded by mesenchymal matrix. Hematoxylin and eosin. $\times 200$. **D** Warthin's tumor. FNA from a 2.5-cm-diameter swelling in the peripheral part of the right parotid gland from a 61-year-old woman. Smear shows sheets of bland oncocytic cells and lymphocytes. Papanicolaou. $\times 200$. **E** Warthin's tumor. Histopathology of the case shown in **D**. Cystic space lined by a double layer of oncocytic cells, which rests on dense lymphoid stroma. Hematoxylin and eosin. $\times 200$.

tology and histology in 2 cases. FNA smear in 1 of them showed mild cytologic atypia during review and the other case raised suspicions of malignancy (fig. 2C). Histopathology of the latter case proved to be a terminal duct carcinoma (fig. 2D), indicating interpretation error at initial diagnosis. All the 3 cases of Warthin's tumor were confirmed by histology. A cytologically diagnosed pleomorphic adenoma with atypia and a case in which differentiation between Warthin's tumor and mucoepidermoid carcinoma was difficult turned out to be pleomorphic adenoma and Warthin's tumor, respectively, thus correlating with histopathologic diagnosis.

The 7 cases of carcinoma constituted 4.9% of all salivary gland tumors and 46.7% of all malignancies in this

study. These included 3 cases of mucoepidermoid carcinoma, 2 metastatic carcinomas and 1 each of papillary adenocarcinoma and poorly differentiated carcinoma. Two cases of carcinoma (mucoepidermoid and poorly differentiated) had subsequent histology, confirming the cytodiagnosis. The smears in the mucoepidermoid carcinoma contained cohesive sheets of tumor cells with abundant cytoplasm showing squamous differentiation as well as cells containing intracytoplasmic mucin vacuoles (fig. 3A). Histologically the tumor showed cysts filled with mucin and lined by sheets of intermediate cells, squamous cells, and cells containing variable amounts of mucin (fig. 3B), which yielded positive staining for PAS-Alcian blue and mucicarmine stain. The poorly differentiated

Fig. 2. **A** Monomorphic adenoma. Section from a right upper cervical swelling from a 27-year-old woman showing strands of basaloid cells and scanty matrix. Hematoxylin and eosin. $\times 200$. **B** FNA smear from the swelling described in **A** shows masses or strands of basaloid tumor cells, and scanty stromal material. Initial cytodiagnosis was pleomorphic adenoma. May-Grünwald-Giemsa. $\times 100$. **C** FNA from a submandibular swelling in a 36-year-old woman. Smear shows groups of tumor cells with mild to moderate pleomorphism, raising suspicions of malignancy. Hematoxylin and eosin. $\times 200$. **D** Terminal duct carcinoma. Histopathology of the case shown in **C**. Section shows strands of malignant cells with scanty cytoplasm, surrounded by a stroma rich in lymphocytes and eosinophils. Mucin-like secretion is seen in occasional areas. Hematoxylin and eosin. $\times 400$.

carcinoma showed pleomorphic and discohesive tumor cells in the smears and invasive clusters of malignant cells with numerous mitotic figures in the paraffin sections. There were features of a preexisting pleomorphic adenoma in the latter case. There was only 1 acinic cell tumor but no adenoid cystic carcinoma in this series. The 5 lymphomas accounted for 3.5% of all salivary gland tumors and 33.3% of the malignancies. Cytologically 2 were Hodgkin's disease (lymphocytic predominance and mixed cellularity) and 3 were non-Hodgkin's lymphoma (low-grade small lymphocytic in 1 and intermediate-grade mixed small and large cell type in 2). Amongst the cases where a decision between benign and malignant neoplasm was difficult, there was 1 case in which cyto-

diagnosis was pleomorphic adenoma with atypia or mucoepidermoid carcinoma. During review the cytologic features were indicative of malignancy (fig. 3C). It was determined to be a low-grade adenocarcinoma in histology (fig. 3D).

The distribution of various tumors varied widely between the major salivary glands. Of the 143 cases with neoplastic lesions, 84 were from the parotid and 43 from the submandibular gland. The pleomorphic adenomas constituted 69.0% of parotid tumors and 58.1% of tumors in the submandibular region ($p = 0.2418$). Warthin's tumors occurred more frequently in the parotid gland region (16.7%) compared to the submandibular gland (2.3%, $p = 0.0191$). However, malignant tumors consti-

Fig. 3. A Mucoepidermoid carcinoma. FNA from a left parotid swelling in a 30-year-old man. Smear contains a group of intermediate cells showing squamous differentiation and presence of mucin globules in a few cells (arrows). Papanicolaou. $\times 400$. **B** Mucoepidermoid carcinoma. Histopathology of the case shown in **A**. A sheet of intermediate cells shows evidence of squamous differentiation and mucin secreting cells line the cystic spaces filled with mucin. Hematoxylin and eosin. $\times 200$. **C** FNA from a left parotid swelling of 10 years' duration in a 50-year-old man. Initial FNA cytology diagnosis was pleomorphic adenoma with atypia/mucoepidermoid carcinoma. Smear on review showed sheets of pleomorphic tumor cells, highly suspicious of malignancy. Papanicolaou. $\times 400$. **D** Low-grade adenocarcinoma. A group of pleomorphic and infiltrating tumor cells. Histopathology of the case shown in **C**. Hematoxylin and eosin. $\times 400$.

tuted 23.3% of all submandibular tumors and only 2.4% of parotid tumors, the difference being highly significant ($p = 0.0003$).

Nonneoplastic Lesions

These included 122 benign salivary gland aspirates, 245 inflammatory lesions, 93 reactive lymphoid tissue, 41 benign cysts, and 18 lipomatous lesions. The inflammatory lesions included 59 (24.1%) acute sialadenitis cases with or without evidence of organization, 99 (40.4%) chronic inflammatory lesions including 8 lymphoepithelial lesions, 60 (24.5%) cases of granulomas with or without necrosis, and 6 (2.4%) cases of necrotic material mixed with a variable number of lymphocytes and neutro-

phils. The benign cystic lesions included 20 cases of epidermal inclusion cysts, 7 retention cysts, 2 branchial cysts, and 12 benign cysts not otherwise specified.

Three cases with benign salivary gland aspirates and 2 cases of chronic sialadenitis were confirmed by histology whereas 1 case of cytologically diagnosed chronic sialadenitis (fig. 4A, B) proved to be a carcinoma ex pleomorphic adenoma on histological review (fig. 4C, D). This was a case of sampling error in FNA cytology. Two cases showing reactive hyperplasia in FNA smear had subsequent histopathological analysis. One turned out to be a case of chronic sialadenitis and the other case (fig. 5A, B), originally diagnosed by histology as atypical lymphoid proliferation, proved to be a non-Hodgkin's lymphoma at

Fig. 4. **A** FNA smear from the right parotid swelling of 14 years' duration in a 48-year-old woman. Smear shows benign salivary duct cells and chronic inflammatory cells indicating chronic sialadenitis. Papanicolaou. $\times 200$. **B** FNA smear shows a small group of partially degenerated acinar cells and lymphoid cells including immunoblasts. Same case as shown in **A**. May-Grünwald-Giemsa. $\times 400$. **C** Carcinoma ex pleomorphic adenoma. Groups of infiltrating malignant cells against a background of chondromyxoid matrix. Histopathology of the case shown in **A** and **B**. Hematoxylin and eosin. $\times 100$. **D** Higher magnification of the case shown in **C**. Two groups of tumor cells intervened by chondromyxoid matrix. Hematoxylin and eosin. $\times 200$.

review (fig. 5C, D). It was further characterized as a B-cell neoplasm following a positive reaction for CD-20 (fig. 5E) and CD-79 α . This was considered as a case of interpretation error by FNA cytology.

Diagnostic Accuracy of FNA Cytology

Correlation of initial cyto- and histopathological diagnoses in 45 cases revealed that there was complete tissue-specific agreement between the two morphological methods in 35 cases (77.8%). The sensitivity, specificity, and diagnostic accuracy of initial FNA cytology diagnosis for the neoplasms were 94.6, 75, and 91.1%, respectively. The sensitivity, specificity, and diagnostic accuracy of initial FNA cytodiagnosis for malignancy (frank malignant

and suspicious) versus benign lesions (nonneoplastic and neoplastic) were 60.0, 95.0, and 91.1%, respectively.

Discussion

Head and neck masses presenting clinically as salivary gland lesions are difficult to diagnose since the anatomic site can be misleading [3]. Perisalivary or intrasalivary lymphoid tissue or lymph nodes occur in the parotid region, and the submandibular group of lymph nodes are located lateral to the submandibular salivary gland, as does ectopic salivary gland tissue in unexpected sites including upper cervical and submandibular lymph nodes

Fig. 5. **A** FNA from a left parotid swelling of 10 days' duration in a 40-year-old man. Smear shows a polymorphic population of lymphoid cells indicating reactive hyperplasia of lymphoid tissue. Papanicolaou. $\times 400$. **B** Same case as shown in **A**. Smear contains a nearly polymorphic population of lymphoid cells including a few cleaved cells. May-Grünwald-Giemsa. $\times 400$. **C** Non-Hodgkin's lymphoma of salivary gland. Histopathology of the case shown in **A** and **B**. Lymphoid cells completely replace acini and surround salivary gland ducts. Hematoxylin and eosin. $\times 200$. **D** Higher magnification of the case shown in **C**. Numerous atypical lymphoid cells with nuclear cleaving and irregularity are seen. Hematoxylin and eosin. $\times 400$. **E** Non-Hodgkin's lymphoma of the salivary gland. Same case as shown in **C** and **D**. Lymphoid cells are uniformly positive for B-cell marker. CD 20. $\times 400$.

[4]. Tumors of the skin appendages and soft tissues as well as developmental anomalies such as branchial cleft cyst and thyroglossal duct cyst can also occur at these sites [5]. The sites of FNA included in the earlier salivary gland studies were parotid, submandibular, sublingual, and oral [2, 5, 6]. In the present study, the major sites were also parotid including preauricular swellings, submandibular region, sublingual and oral. In addition, we have taken into consideration swellings in the upper cervical region, which showed definitive features of either benign salivary gland tissue or its pathological lesions. The present study, involving 712 cases, is one of the largest reported in recent years [2, 5, 7–9].

Type-specific FNA cytologic diagnosis for neoplastic and nonneoplastic salivary gland lesions is possible in most cases, as is evident from the literature of the past three and a half decades [2, 6, 10–15]. The lesions of salivary glands have been described for diagnostic purposes under five major headings: benign nonneoplastic lesions (benign aspirate, inflammatory lesions, reactive lymphoid tissue, benign cystic lesions, and lipomatous lesions), benign neoplasms, malignancies, atypical cytology, and inadequate material. The cases of reactive hyperplasia of lymphoid tissue and granulomatous lesions from the parotid and submandibular regions could be either from the salivary gland or intra-/perisalivary lymph nodes. This may be considered a limitation of FNA cytology. Further-

more, although lesions like epidermal inclusion cyst find a place in this study because of their anatomic locations and clinical characteristics, they are not true salivary gland lesions.

The proportion of benign nonneoplastic lesions in the medical literature ranges from 20.0 to 61.6% with an average of 37.0% [5–7, 9, 10, 16–18]. In the present study, 72.9% were benign nonneoplastic lesions. This higher frequency was largely a result of benign salivary gland aspirates from enlarged salivary glands due to lipomatosis or sialadenosis, inflammatory lesions and reactive lymphoid tissue. The proportion of inflammatory lesions in the present study was much higher than in other FNA-based studies and may be due to geographical differences [6, 9]. The frequency of benign neoplasms in the above-cited studies [5–7, 9, 10, 16–18] ranged from 21.2 to 51.4% with an average of 38.4%. In the present study, only 17.8% of the aspirates were benign neoplasms, which largely consisted of pleomorphic adenomas and Warthin's tumor. The predominance of these two tumors in the salivary gland aspirates has been reported in a number of studies [2, 6, 16–18]. The frequency of malignancy in the present study (2.1% of all salivary gland aspirates) is one of the lowest reported in the literature. Mucoepidermoid carcinoma represents the most common malignant tumor of the salivary gland [19]. However, in FNA-based studies its frequency varies from rare [6] to the most common salivary gland malignancy [8, 18]. Although mucoepidermoid carcinoma was the most frequent carcinoma in our study, lymphomas were the most common form of malignancy. Five lymphoma cases in our study constituted 3.5% of all neoplasms and 33.3% of malignancies. Lymphomas are reported to be as low as 5.6% [18] and as high as 40% [6] of all malignancies in FNA-based studies on salivary gland lesions.

The inadequacy rate in our material was close to the average encountered in various studies. A significantly higher number of our aspirates from the submandibular gland (8.5%) were inadequate compared to the parotid (4.0%, $p = 0.0241$). This may be due to relative inaccessibility of the former for FNA. A significantly higher number of the aspirates from the parotid (27.1%) were neoplasms compared to the submandibular gland (13.7%, $p < 0.0001$). However, the frequency of malignant tumors as a whole was significantly higher in the submandibular gland than the parotid ($p = 0.0003$). An overwhelming predominance of neoplastic lesions in the parotid gland had been reported [6, 10]. It is also known that pleomorphic adenomas represent about 60% of tumors in the parotid, are less common in the submandibular gland,

and are relatively rare in the minor salivary glands. Pleomorphic adenomas constituted 69.0% of the parotid tumors in our material. The frequency of this neoplasm was lower in the submandibular gland (58.1%), but the difference was not significant. Further, Warthin's tumor is also known to be virtually restricted to the parotid gland [20, 21], whereas mucoepidermoid carcinomas occur predominantly in the parotid, and adenoid cystic carcinomas are more common in the other salivary glands [20]. Warthin's tumors were significantly more common in the parotid compared to the submandibular ($p = 0.0191$) in our material. Occurrence of a small number of Warthin's tumors in the submandibular gland can be explained by lesions in the tail of the parotid gland that may appear as a submandibular tumor. However, according to the files of the Armed Forces Institute of Pathology, although an overwhelming number of Warthin's tumors (95%) affect the parotid gland, a small number of cases involve other sites such as submandibular, tonsil, lip, palate, buccal mucosa, mandible, oral cavity, and pharynx [22].

The accuracy of FNA cytology for the diagnosis salivary gland tumors has been questioned [7]. In six studies, the sensitivity of FNA cytology for the diagnosis of neoplasms, especially malignancies of the salivary glands, ranged from 55.0 to 98.0% (average 81.9%), the specificity from 92.0 to 99.0% (average 97.1%), and the diagnostic accuracy from 84.0 to 98.0% (average 92.6%) [1, 2, 5–7, 10]. In our material, the specificity was poor (75.0%) for the diagnosis of neoplasms as a whole during the initial diagnosis. The sensitivity was also poor (60.0%) for the diagnosis of malignancy. This was probably due to the small number of nonneoplastic lesions and malignancy cases, for which subsequent histopathology information was available. Many studies in the past reported high (>90.0%) sensitivity [1, 2, 5, 6], but a few showed poor sensitivity (<60.0%) [7, 10]. According to Atula et al. [7], high false negative rates have been reported in a number of studies [10–12, 23, 24].

From the results of this histocytology correlation, the pitfalls of FNA cytology appear to be in the cytodiagnosis of pleomorphic adenoma, carcinoma and lymphoma cases. According to Layfield et al. [23] mucoepidermoid carcinoma, pleomorphic adenoma, chronic sialadenitis and malignant lymphoma were responsible for most of the diagnostic errors. Review of our cases shows that while FNA cytology had sampling and interpretation errors, the histopathology diagnosis was also not free from interpretation errors.

Cellular atypia, cystic transformation, and presence of cylindrical pattern resembling adenoid cystic carcinoma

are the most common cytologic variations in pleomorphic adenoma and are responsible for the majority of errors [8]. The presence of a few atypical cells is compatible with pleomorphic adenoma [25] and as a general rule a few atypical cells in classic pleomorphic adenoma should not be regarded as evidence of malignancy [6]. Terminal duct carcinoma is a polymorphous low-grade adenocarcinoma, which occurs in the fifth through eighth decades of life and affects almost exclusively the minor salivary glands [19]. Histologically, it is characterized by a homogeneous population of cells with bland nuclei and scanty cytoplasm, arranged in lobules, tubules, nests and trabeculae. Our case had all the above clinicopathologic features except the site of origin. It was in the preauricular region rather than the common site, palate. Carcinoma ex pleomorphic adenoma is a rare neoplasm of the salivary gland [26]. In a study of 26 histologically proven cases, 17 were of high grade, and 9 low grade; the FNA cytology diagnosis being malignancy in 13 (50.0%), suspicious in 2 (7.7%), and negative for malignancy in 11 (42.3%) [27]. According to these authors, while accurate diagnosis of malignancy on preoperative fine-needle sampling was achieved in high-grade tumors, most negative results were encountered in low-grade carcinomas as happened in our study. A case of B-cell non-Hodgkin's lymphoma was diagnosed as reactive hyperplasia in FNA smears and this diagnosis did not change after blind review of the cytologic material. When correlation with histopathology diagnosis was undertaken, the interpretation error in FNA cytology was apparent. The value and limitations of FNA cytology in differentiating reactive hyperplasia from lymphoma have been highlighted by Das [28] in a review. FNA cytology along with ancillary studies has been uti-

lized successfully for diagnosis of lymphomas and separation of these cases from reactive hyperplasia [29]. The differential diagnosis of FNA biopsy material from salivary gland lesions with numerous small-to-medium-sized lymphocytes includes myoepithelial sialadenitis, benign lymphoepithelial cyst, chronic sialadenitis, Warthin's tumor, intra- and perisalivary lymph node, follicular center cell lymphoma (grade I), small lymphocytic lymphoma/chronic lymphocytic leukemia, lymphoplasmacytoid lymphoma, and mantle cell lymphoma [30]. According to Chai et al. [31], careful examination of the morphologic features of the lymphoid population may allow separation of lymphomas from reactive or autoimmune proliferations. However, based on the difficulties encountered in the histologic recognition of malignant lymphoma originating in benign lymphoepithelial lesions, it would appear that diagnosis of such a change by FNA alone would be extremely difficult, if not impossible.

Conclusions

The present study highlights the utility and pitfalls of FNA cytology in the diagnosis of salivary gland lesions. It demonstrates significant differences in the distribution of various pathological lesions involving the parotid and submandibular glands in our study group.

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