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Research Article

The Correlation between Fine Needle Aspiration and Histopathological Diagnosis of the Salivary Gland Lesions of 77 Cases

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Abstract: The aim of the study is to determine the diagnostic value and accuracy of fine-needle aspiration (FNA) of salivary gland lesions and to detect the most challenging lesions that cause difficulties cytopathologically. Salivary gland FNAs and postoperative histopathological diagnosis of 77 cases evaluated in the Department of Pathology at Ankara Numune Training and Research Hospital in a seven-year period were reviewed and compared retrospectively. Forty-nine (63.6%) FNAs were diagnosed as benign, 7 (9.1%) were diagnosed as suspicious for malignancy, 2 (2.6%) were diagnosed as malignant, and 19 (24.7%) were reported as inadequate cytology. Sixty-five (85%) cases were benign, and 12 (15%) were malignant histopathologically. Four cases that were reported as inadequate cytology were diagnosed histopathologically as malignant. Forty-six FNAs were true negative(TN), three were false negative(FN), five were true positive(TP), and four were false positive(FP). Specific diagnoses were reported in 39 (67.2%) FNAs. Thirty-two (82%) of them were verified histopathologically, 7 (18%) were incompatible with the histopathological diagnoses. The rate of true positivity of FNA was 8.6%, true negativity was 79.3%, false negativity was 5.2%, false positivity was 6.9%, sensitivity was 62.5%, specificity was 92%, positive predictive value was 55.6%, negative predictive value was 93.9%. The diagnostic accuracy was estimated as 87.9%. It is noteworthy that sufficiency of the cytological material, the experience and knowledge of the pathologist, and a comprehensive clinical and radiological findings are crutial for obtaining a higher rate of diagnostic accuracy in salivary gland FNA.
Keywords: Cytology, Fine needle aspiration, Histopathology, Salivary gland, Correlation.

INTRODUCTION

FNA is a minimally invasive method that was initially used in 1920 in the USA and Europe [1, 2]. It is widely used for the diagnosis of the salivary gland lesions for a fast clarification of the nature of the lesion whether it is benign or malignant. It is useful to avoid unnecessary surgery for nonneoplastic benign lesions such as sialadenitis. Also, it is usually used for staging and determining the surgical modality and the follow-up of the neoplastic salivary gland lesions [3]. Nevertheless, controversial opinions still exist in the literature about its diagnostic value due to the limitations of it and the consideration that it does not generally alter the surgical modality of the salivary gland masses [4, 5].

The diagnostic value of FNA in the salivary gland lesions are mostly reported to be high in the literature, however conflicting results are also available [6].

The aim of the study is to review our experience about the FNA of salivary gland lesions, compare the histopathological and the cytopathological diagnoses in order to evaluate the accuracy and the diagnostic value of FNA, and analyze the possible conditions that may cause diagnostic error.

MATERIALS AND METHODS

Salivary gland FNAs and postoperative histopathological diagnosis of 77 cases evaluated in the Department of Pathology at Ankara Numune Training and Research Hospital in 7 years (between January 2006 and January 2013) were compared retrospectively. Ultrasound-guided FNAs were performed by different radiologists that were moderate or well-experienced about salivary gland FNA. 23-24- gauge needles attached to 10-ml syringes holder were used during performing FNA. The specimens were expelled onto two-six slides, and thin smears were prepared between two slides and immediately fixed. Air-dried slides were stained with May-Grunwald Giemsa and Hematoxylin and eosin (H&E). Ethyl alchohol (95%)-fixed slides

were stained with Papanicolaou (PAP). The slides of FNA and the operation materials from salivary gland lesions were reviewed by a pathologist under light microscope. The paraffin sections obtained from salivary gland operation materials were also examined. The salivary gland FNA results were evaluated according to the categories as following: true-negative (the case diagnosed as "benign" both cytologically and histopathologically); true-positive (histopathologically "malignant" case that was diagnosed as "malignant" or "suspicious for malignancy" with FNA); false-negative (the cytological specimen failed to diagnose a malignancy); and false-positive (the benign cytological specimen that was diagnosed incorrectly as malignancy); inadequate cytology (the specimen that was insufficient for diagnosis due to hypocellularity, fixation artefact, etc.). Study design included a comparison between results of preoperative FNA with postoperative histopathological diagnoses. Data analysis was based on the formulas of Galen and Gambino method described below. Sensitivity for the presence of malignancy (true positive/true positive + false negative), specificity for absence of malignancy (true negative/ true negative + false positive), positive predictive value (PPV) (true positive/true positive + false positive), negative predictive value (NPV) (true negative/true negative + false negative) and accuracy of FNA (true positive + true negative/total diagnostic cases) were calculated. Informations about the patients were obtained from the pathology reports and the automation system of the hospital.

RESULTS

FNA of salivary gland lesions obtained from 77 patients were included in the study. Sixty-nine (89.6%) of them were operated for the parotid gland lesions, and 8 (10.4%) were operated for the submandibular gland lesions. Forty-four (57.1%) of the patients were male, 33 (42.9%) of them were women. The mean age was 48 years (range: 10-83) (Table 1). Cytologically, 49 (63.6%) of the patients were diagnosed as benign, 7 (9.1%) were diagnosed as suspicious for malignancy, 2 (2.6%) were diagnosed as malignant, and 19 (24.7%) were reported as inadequate cytology (Table 1).

Sixty-five (85%) of the cases were benign, and 12 (15%) were malignant histopathologically (Table 2).

Four (21.1%) of the 19 cases that were diagnosed as inadequate cytology with FNA were diagnosed histopathologically as malignant [1 carcinoma ex pleomorphic adenoma (PA), 1 acinic cell carcinoma, 1 adenoid cystic carcinoma, 1 squamous cell carcinoma (SCC)], 15 (78.9%) were diagnosed as benign [4 PAs, 2 basal cell adenomas (BCA), 3 sialadenitis, 2 keratinous cysts, 1 papillary oncocytic cystadenoma, 1 lymphoepithelial cyst, 1 sialolipoma, 1 sebaceous lymphadenoma].

Forty-six (93.9%) of the 49 cases that were diagnosed as benign with FNA were confirmed by histopathological examination (true negative) (Table 3).

Twenty-six (56.5%) of those cases were PA (Fig. 1a, Figure 1b), 9 (19.6%) were Warthin's Tumor (WT), and 2 (4.3%) were sialadenitis, 2 (4.3%) were lymphoepithelial cyst, 2 (4.3%) were necrotizing granulomatous inflammation, and the rest 5 cases were sialolipoma, lymphoepithelial sialadenitis, nodular oncocytosis, salivary duct cyst, and sialadenosis histopathologically. Three (6.1%) of the 49 cases that were diagnosed as benign with FNA were diagnosed as malignant [an epithelial-myoepithelial carcinoma (EMC) (Fig. 1c-1d), a carcinoma ex PA and a Hodgkin's lymphoma] (false negative) histopathologically (Table 4).
The 2 cases that were diagnosed as malignant cytologically were confirmed histopathologically (true positive) (Table 3). One of them was SCC and the other one was small lymphocytic lymphoma.

Three (42.9%) of the 7 cases that were reported cytopathologically as "suspicious for malignancy" were diagnosed as malignant lesions [2 mucoepidermoid carcinomas (MECs) (Fig. 2a-2b) and a carcinoma ex PA] histopathologically (true positive) (Table 3). Four (57.1%) of them were found to be benign [2 PAs, a WT (Fig. 2c-2d), and a BCA] (false positive) (Table 4).

In the present study, the rate of true positivity of FNA was 8,6%, true negativity was 79.3%, false negativity was 5.2%, false positivity was 6.9%, sensitivity was 62.5%, specificity was 92%, PPV was 55.6%, NPV was 93.9%, and diagnostic accuracy was 87.9% (Table 5).

Specific diagnoses were reported in 39 (67.2%) FNAs. Thirty-two (82%) of them were verified histopathologically. The cytopathological diagnosis of 7 (18%) cases were incompatible with the histopathological diagnoses.

The lesions that were confirmed histopathologically were as follows: 23 PAs, 6 WTs, one SCC, one small lymphocytic lymphoma, and one MEC. The three cases reported as compatible with WT cytopathologically were diagnosed histopathologically as sialadenosis, salivary duct cyst, and lymphoepithelial cyst. A case that was considered to be acinic cell carcinoma with FNA was diagnosed as PA histopathologically. The histopathological diagnosis of a case that was reported as chronic sialadenitis with FNA was found to be necrotizing granulomatous inflammation. One of the 2 cases compatible with PA cytologically was carcinoma ex PA, and the other one was lymphoepithelial cyst histopathologically.

Table 1: The clinicopathological features of the patients (n: 77)

Clinicopathological features	
Age	
Mean	48
Range	10-83
Gender	
Female	44 (57.1%)
Male	33 (42.9%)
Localisation	
Parotid gland	69 (89.6%)
Submandibular gland	8 (10.4%)
Cytological diagnosis	
Benign	49 (63.6%)
Suspicious for malignancy	7 (9.1%)
Malignant	2 (2.6%)
Inadequate cytology	19 (24.7%)
Histopathological diagnosis	
Benign	65 (85%)
Malignant	12 (15%)

Table 2: The histopathological diagnosis of the lesions (n:77)

Benign lesions	n: 65 (85%)
Neoplastic	
Pleomorphic adenoma	32 (41.6%)
Warthin's tumor	10 (13%)
Basal cell adenoma	3 (3.9%)
Sialolipoma	2 (2.6%)
Sebaceous lymphadenoma	1 (1.3%)
Oncocytic papillary cystadenoma	1 (1.3%)
Nonneoplastic	
Sialadenitis	
Chronic sialadenitis	5 (6.5%)
Granulomatous sialadenitis	2 (2.6%)
Lymphoepithelial sialadenitis	1 (1.3%)
Cystic lesions	
Lymphoepithelial cyst	3 (3.9%)
Keratinous cysts	2 (2.6%)
Salivary duct cyst	1 (1.3%)
Other	
Nodular oncocytosis	1 (1.3%)
Sialadenosis	1 (1.3%)
Malignant lesions	**n:12 (15%)**
Carcinoma ex pleomorphic adenoma	3 (3.9%)
Squamous cell carcinoma	2 (2.6%)
Mucoepidermoid carcinoma	2 (2.6%)
Adenoid cystic carcinoma	1 (1.3%)
Acinic cell carcinoma	1 (1.3%)
Epithelial myoepithelial carcinoma	1 (1.3%)
Small lymphocytic lymphoma	1 (1.3%)
Hodgkin lymphoma	1 (1.3%)

Table 3: The cases with accurate diagnosis (n: 51).

The rate of true negativity = 79.3% (n: 46)	**Number of cases (n) and percentage(%)**
Pleomorphic adenoma	26 (56.5%)
Warthin's tumor	9 (19.6%)
Sialadenitis	2 (4.3%)
Lymphoepithelial cyst	2 (4.3%)
Necrotizing granulomatous inflammation	2 (4.3%)
Sialolipoma	1 (2.2%)
Lymphoepithelial sialoadenitis	1 (2.2%)
Oncocytic nodular hyperplasia	1 (2.2%)
Salivary duct cyst	1 (2.2%)
Sialadenosis	1 (2.2%)
The rate of true positivity = 8.6% (n: 5)	
The cases diagnosed as "**malignant**" with FNA	
• Squamous cell carcinoma	1 (20%)
• Small lymphocytic lymphoma	1 (20%)
The cases diagnosed as **"suspicious for malignacy"** with FNA	
• Mucoepidermoid carcinoma	2 (40%)
• Carcinoma ex pleomorphic adenoma	1 (20%)

Table 4: The cases with cytopathological and histopathological discordance (n: 7).

	Cytopathological diagnosis	**Histopathological diagnosis**	**Number of cases (n)**
False Negative Cases	Benign	Malignant	3
	• Epithelial neoplasia (Distinction can not be made between BCA and PA) • PA • Reactive lymph node	• EMC • Carcinoma ex PA • Hodgkin's lymphoma	1 1 1
False Positive Cases	Suspicious for malignancy	Benign	4
	• Low-grade carcinoma (Suspicious for acinic cell carcinoma) • Unable to distinguish low-grade carcinoma from PA • Carcinoma showing squamous differentiation • Acinic cell carcinoma	• PA • PA • WT • BCA	1 1 1 1
Abbreviations: BCA: Basal cell adenoma, EMC: epithelial myoepithelial carcinoma, PA: pleomorphic adenoma, WT: Warthin's tumor			

Table 5: The correlation between cytopathological and histopathological diagnosis

	FNA diagnosis Malignant (n)	**FNA diagnosis Suspicious for malignancy (n)**	**FNA diagnosis Benign (n)**	
Histopathological diagnosis = Malignant (n)	2	3	3	Sensitivity 62.5% (5/8)
Histopathological diagnosis = Benign (n)	0	4	46	Specificity 92% (46/50)
	Positive predictive value 55.6% (5//9)		Negative predictive value 93.9% (46/49)	Accuracy 87.9% (51/58)

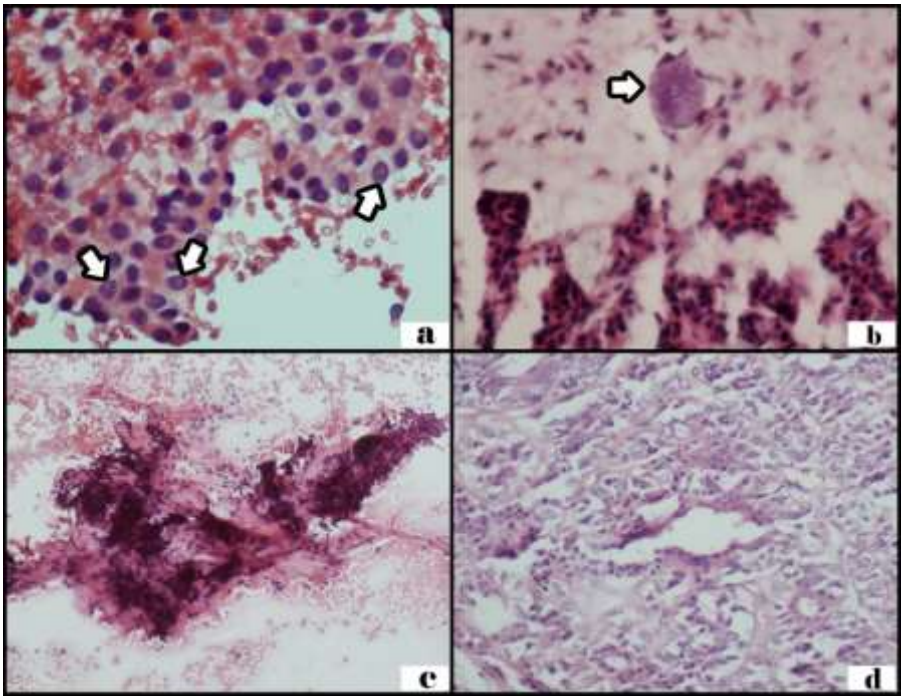

Fig. 1: (a) Intranuclear cytoplasmic inclusions (*arrows*) in a FNA of PA (HE, x400). (b) A flower-shaped tyrosine crystalloid (*arrow*) in a tissue section of PA (HE, x400). (c) The FNA of epithelial-myoepithelial carcinoma considered as PA or BCA (*false negative*) including acellular eosinophilic matrix in the background and many myoepithelial cells (HE, x40). (d) The histopathological photomicrograph of the epithelial-myoepithelial carcinoma (mentioned in Figure 1c) consisting of luminal cuboidal ductal cells and abluminal myoepithelial cells with large polygonal clear cytoplasm (HE, x100).

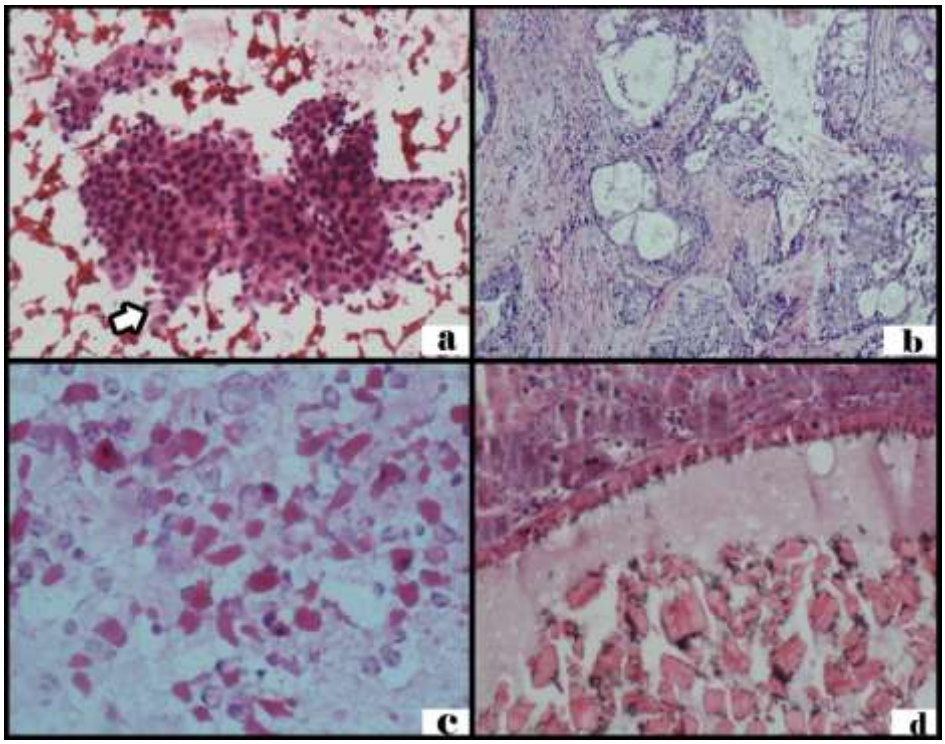

Fig. 2: (a) The FNA of a low grade MEC showing many intermediate cells and a few nonkeratinized squamous cells, and a mucin-containing mucus cell (*arrow*) (HE x100). (b) The tissue section of the low grade MEC mentioned in Figure 2a (HE, x40) (c) The FNA of the WT reported as suspicious for malignancy (*false positive*) due to the atypical squamous cells and the eosinophilic polygonal structures resembling keratin (HE, x100). (d) The tissue section of WT (mentioned in Figure 1c) showing a cystic area containing polygonal materials lined by cells with large eosinophilic cytoplasm and hyperchromatic nuclei similar to the content of FNA (HE, x100).

DISCUSSION

FNA is an easily applicable preoperative method for the diagnosis of salivary gland lesions. If FNA is performed by experienced physicians, it is very effective for the definite diagnosis [6]. In the literature, the rate of diagnostic accuracy of salivary gland FNA is high that ranges from 74% to 100% [3, 6, 7] Sensitivity of FNA has a wide range from 27% to 100%, and specificity of FNA ranges from 84% to 100% in the literature [3, 6]. The rate of diagnostic accuracy, sensitivity and specifity of the present study were consistent with the literature and they were estimated as 87.9%, 62.5%, 92%, respectively. Higher sensitivity indicates a higher accuracy in detecting the malignancy, however higher specificity indicates a higher efficiency in detecting the benign lesions. Similar to the literature, the rate of sensitivity is lower than the specifity in our study. The sensitivity is inversely correlated with false negativity (sensitivity: TP/TP+FN) [8]. Technical factors such as sampling error due to the inefficiency of the physicians performing the FNA, the hypocellular FNA due to the cystic nature of some malignant lesions such as low grade MEC, using inadequate technique in preparation of the slides, the lack of well-experienced pathologists about evaluation of FNA, and underdiagnosing low grade malignant tumors due to their bland cytological findings may be the possible reasons that cause false negativity as well as lower sensitivity [4, 9]. The rate of false negativity of the present study was 5.2% that was a relatively lower rate reported in the literature (0-48%) [1, 10]. MEC, adenoid cystic carcinoma, lymphoma, SCC, carcinoma ex PA, acinic cell carcinoma and myoepithelial carcinoma have been reported as the false negative cases in the literature [4]. Carcinoma ex PA, Hodgkin lymphoma, and EMC were the false negative cases (discussed later) in our study.

The rate of false positivity ranges from 0% to 12% in the literature, and our result was 6,9%, consistent with the literature [1]. One of the main reasons for false positivity is overdiagnosing of reactive changes and metaplasia as malignancy due to the inflammation, etc. The heterogeneity of benign and malignant tumors with similar cytologic findings might be considered as another reason. Two PAs, a WT, and a BCA were the false positive lesions (discussed later) in the present study.

PPV that signifies the probability of malignancy ranges from 70% to 100% in the literature [4]. This rate infers that a case considered as malignant with FNA may be diagnosed as benign histopathologically with a rate of up to 30%. The PPV of the present study was 55.6% that was lower than the rates reported in the literature. PPV is directly correlated with the number of true positive cases, however it is inversely correlated with the number of false positive cases (PPV: TP/TP+FP) [8]. In the present study, the lower rate of PPV was particularly attributed to the presence of relatively higher number of false positive cases (n: 4) that was closer to the number of true positive cases (n: 5) in the study. Therefore, the reasons mentioned previously for false positivity may also be considered to cause low rate of PPV.

The rate of NPV that indicates the probability of benign lesions ranges from 84% to 94% in the literature [4, 8]. This rate demonstrates that a case considered as benign with FNA may be diagnosed as malignant histopathologically with a rate of up to 16%.The rate of NPV of the present study was 93.9% that was compatible with the literature. NPV is directly correlated with the number of true negative cases, however it is inversely correlated with the number of false negative cases (NPV= TN/TN+FN). The NPV of our study that was relatively higher than many studies in the literature was attributable to the presence of smaller number of false negative cases (n: 3) than the number of true negative cases (n: 46) in the study. Similar to our study, the frequency of the benign lesions of the salivary glands are higher than the malignant tumors in the literature. This fact may probably play a role to gain the pathologists more experience about the FNA of benign lesions than the malignant tumors, and obtain a higher rate of NPV indirectly.

The rate of inadequate cytology ranges from 2% to 15% in the literature [1, 6, 11, 12]. In this study, the rate of inadequate cytology was higher (24.7%) than the literature.This was attributable to the varying efficiency of the physicians performing the FNAs and the cystic component of some lesions that caused scant cellularity.

PA also known as “benign mixed tumor” is the most common tumor of the parotid gland [3, 13]. Similar to the literature, PA was the most common tumor of the parotid in this study, and also it was the most accurate and specific diagnosis of FNA. In FNA, PA exhibits various amounts of three basic components as extracellular matrix, ductal cells and myoepithelial cells [9]. Ductal cells are usually small cuboidal-shaped cells that form honeycomb layers. Myoepithelial cells are composed of plasmacytoid, spindle, stellate, polygonal, or epithelioid cells.9 Extracellular matrix has a fibrillary structure frayed with indistint margins and it shows mucoid, myxoid or chondromyxoid features [9, 13]. It should be noted that, some benign (BCA, myoepithelioma, etc.) and malignant lesions (adenoid cystic carcinoma, polymorphous low grade adenocarcinoma, EMC, carcinoma ex PA, etc.) contain various amount of matrix in the background similar to PA cytologically [13]. It should be kept in mind that multinucleated giant cells, focal and mild to moderate cytologic atypia may be detected in some PAs that do not indicate malignancy. Intranuclear cytoplasmic inclusions may be seen rarely in PA. In this study, there were two FNAs that contained intranuclear cytoplasmic inclusions [14].

Metaplastic squamous epithelial cells, mucinous or oncocytic metaplasia, cystic contents, sebaceous cells, inflammatory cells, calcifications resembling psammoma bodies, and non-birefringent flower-shaped tyrosine crystalloids may be detected in PA [13, 14]. In this study, tyrosine crystalloids were observed in a case histopathologically. The diagnosis of PA with FNA is straightforward when 3 major components are present, however matrix-poor or hypercellular cases may be confused with other tumors such as BCA. Myoepithelial cell rich PAs may also be misdiagnosed as myoepithelioma or acinic cell carcinoma. Low grade MEC should be considered particularly in the FNAs with extensive mucinous and squamous metaplasia. Cylindromatous pattern occurs rarely in PA that may cause confusion with adenoid cystic carcinoma. [13, 16] Differential diagnoses of PA should include carcinoma ex PA if cytologic atypia is prominent [16]. The 4 of the 32 PAs could not be diagnosed cytologically due to the inadequate FNAs. Twenty-six of the remaining adequate 28 FNAs were diagnosed as benign, and 2 of them were diagnosed as suspicious for malignancy. Thus, the rate of diagnostic accuracy of PA was 92.9% that was consistent with the literature (80-94%) [6, 15]. In addition, 23 (82.1%) of PAs were found to be considered as PA in FNA reports. One of the false positive 2 cases of FNA was reported to be suspicious for low-grade carcinoma particularly for acinic cell carcinoma. The other case was reported to be suggestive of priorly a benign neoplastic process (especially a PA?) but a note was added that a low-grade carcinoma could not be ruled out.

In the review of those FNAs, hypercellular slides containing papillary and tubular structures and solid layers with myxoid matrix were detected. The suspicion for malignancy was attributed to the hypercellularity, lack of significiant cellular pleomorphism, and the fact that many low-grade malignant salivary gland tumors may produce matrix.

WT was the second most frequent lesion that had accurate diagnosis with FNA following PA in the present study. WT has characteristic appearence composed of oncocytic cells with eosinophilic granular cytoplasm with a background containing mature lymphocytes and foamy histiocytes compatible with cystic contents [9, 14]. Sebaseous metaplasia, mucinous metaplasia and squamous metaplasia may be detected in FNA that may cause difficulty in excluding low grade MEC and branchial cleft cyst [14]. In this study, there were 10 WTs histopathologically. Nine of them were diagnosed as benign with FNA. Six (66.7%) of these FNAs were indicated to be WTs. The remaining one case was diagnosed as suspicious for malignancy with FNA due to the atypical squamous epithelial cells and in the background containing histiocytes. Histopathologically, it was detected that the tumor had dense and fragmented cystic content lined with degenerated epithelial cells showing focal squamous metaplasia.

Suspicion of malignancy was attributed to the history of SCC of the lip of the patient as well as absence of oncocytic cells and lymphocytes in the FNA.

In the present study, a case of EMC was detected to be considered primarily as PA and less likely to be BCA cytopathologically (false negative).

EMC is a low-moderate grade malignancy often develops in parotid gland. In FNA, it represents a biphasic tumor composed of dominantly myoepithelial cells and some ductal cells. Myoepithelial cells have large polygonal glycogen-rich clear cytoplasms, small nucleoli, and oval vesicular nuclei. Ductal cells are cuboidal shaped cells that have small amount of cytoplasms without significant cytological atypia. Acellular hyaline material and fibrous tissue fragments may be detected in the background. In our case, false negativity might be attributed to some of the features of the FNA as follows: consisting of acellular eosinophilic matrix in the background, presence of many myoepithelial cells and showing no cytological atypia.

BCA is a benign tumor that arises most frequently in the parotid gland. It may demonstrate a variety of histologic patterns such as tubular, trabecular, solid, membranous, and mixed patterns. Cytologically, it exhibits small and/or intermediate-sized basaloid cells with peripheral palisading. A dense, nonfibrillary stroma usually accompanies the cell groups peripherally. This stroma usually causes difficulty in differentiating BCA from PA. BCA does not exhibit necrosis, cellular atypia, and high mitotic activity. However, the absence of these malignant features does not rule out some low grade malignancies such as solid type adenoid cystic carcinoma and basal cell adenocarcinoma (the diagnosis relies on infiltrative growth pattern histologically) [16]. In the present study, a BCA was diagnosed as suspicious for acinic cell carcinoma, a low grade malignancy cytologically (false positive).

Acinic cell carcinoma is composed of cells similar to the normal acinar cells of salivary gland that have large granular cytoplasms containing vacuoles, and eccentric nuclei [16]. Cellular pleomorphism is absent or minimal. It shows low mitotic activity. The morphological resemblance of the normal acinar cells to the tumor cells of acinic cell carcinoma may cause misdiagnosing the benign FNA as malignant similar to our case. In contrast, the bland cytological characteristics of the tumor cells may also cause skipping the malignancy.

In this study, two low grade MECs were diagnosed as suspicious for low grade carcinoma with FNA (true positive). Low grade MEC is usually hypocellular in FNA due to its major cystic growth

pattern [9, 16]. It is composed of three main cell components without significant cytologic atypia. These are nonkeratinizated squamous cells, intermediate cells that resemble to the metaplastic cells of the cervix, and mucin-containing mucus cells. In general, a thick blue-violet colored mucoid plaque containing cellular debris, lymphocytes, foamy histiocytes may be seen in the background. In addition, some cells with clear cytoplasm, columnar and oncocytic cells may be detected. It is devoid of myoepithelial cells. The benign lesions showing squamous metaplasia such as mucocele, retention cyst and WT may cause difficulty in the differential diagnosis of low grade MEC. In the literature, low grade MEC has been reported to be the most difficult diagnosis of FNA due to exhibiting a high potential for false negativity [15, 17, 18]. The pitfalls for false negativity may be considered as bland cytological features, and lacking coexistence of three main cell components (mentioned before) in each case due to hypocellular and cystic nature of it. High grade MEC is consisted of mature squamous cells that show significant cytological atypia and form three-dimensional groups cytologically. In contrast to low grade MEC mucoid cells are rarely seen in high grade MEC. Although, high grade MEC is diagnosed more easily than low grade MEC with FNA, metastatic SCC, primary or secondary adenocarcinomas may cause difficulty in the differential diagnosis [9]. In our cases, the presence of a few mucoid cells and the absence of cellular atypia in the FNA slides were the possible causes of failing to make clear distinction between benign or malignant lesions, and achieving an exact diagnosis.

A carcinoma ex PA was considered as PA with an adequate FNA that showed typical cytological features of PA in the present study (false negative). Misdiagnosis was attributed to the failure to sample the cells of the carcinoma component with FNA.

Similarly, an intraparotid lymph node with Hodgkin lymphoma was observed to be diagnosed as reactive lymph node with FNA that was devoid of Reed-Sternberg/Hodgkin's cells (false negative). Also, a case of necrotizing granulomatous inflammation was misdiagnosed as chronic sialadenitis with FNA that lacked epithelioid histiocytes due to sampling error. It is obvious that performing many samples of FNA by the guide of ultrasonography will be of assistance to maintain the correct diagnosis of the lesions demonstrating partial involvement. In addition, it is rational that not only the features of FNA, but also the radiological and clinical findings should be evaluated together in order to make an exact diagnosis.

Intraparotid lymph nodes or lymph nodes around the salivary glands may be sampled with FNA. Particularly, there are some difficulties in the differential diagnosis of low-grade lymphomas such as follicular lymphoma and MALT lymphoma, and the Hodgkin's lymphoma that contains reactive lymphoid cells in the background [9].

These cases may be misinterpreted as sialadenitis, reactive lymph node or WT. Even if lymphoma is diagnosed by FNA, subtyping or the specific diagnosis can not be usually determined [9]. In this study, a Hodgkin's lymphoma-as mentioned previously-was misdiagnosed as a reactive lymph node with FNA.

Another case considered as lymphoma with FNA was diagnosed as small lymphocytic lymphoma histopathologically.

In FNA, the metastatic tumors (particularly SCC and malignant melanoma) in the salivary gland, intraparotid lymph nodes or the lymph nodes around the salivary glands are usually observed [6]. The specifity of FNA for metastatic tumors of parotid are reported to be more than 90% in the literature [6]. In this study, a FNA of a patient with a history of SCC of the larynx was diagnosed as metastatic SCC in the salivary gland.

CONCLUSION

In conclusion, the rate of diagnostic accuracy of FNA that signifies the benign or malignant nature of the salivary gland lesions is generally reported to be high in the literature [3, 6, 7]. However, the rate of identification of exact histopathological diagnoses with FNA seems to be lower because of some limitations originated from the difficulties in evaluation of the FNA due to the morphological variability and rarity of the salivary gland lesions, and the overlapping of the cytologic findings of some benign and malignant tumors. It should be noted that technically adequate cytological material, the experience and knowledge of the pathologist about the FNA, and a comprehensive clinicopathological correlation are necessary for obtaining a higher diagnostic value in salivary gland FNA.

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