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VALUE OF FINE NEEDLE ASPIRATION CYTOLOGY IN DIAGNOSIS FOR SALIVARY GLAND LESIONS: OUR EXPERIENCE

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Summary

The retrospective study was designed to evaluate salivary gland lesions diagnosed in the Department of Clinical Cytology and surgically treated in the Department of Head and Neck Surgery in the University Hospital for Tumors, Zagreb, Croatia between 1990 and 2004. We analyzed localization, histological type and concordance between cytology and final histological diagnosis.

The study includes 286 patients treated for salivary gland lesions. All patients had fine-needle aspiration (FNA) cytology of the lesion before surgery. All the cytological specimens obtained were aspirated from palpable lesion or revealed during sonographic examination.

The majority of lesions was localized in the parotid gland. There were 213 benign tumors, 40 benign lesions and 33 malignant tumors. The most common benign tumors were pleomorphic adenoma and Warthin's tumor, while the most common malignant tumor was adenoid cystic carcinoma.

Our results show overall accuracy of fine-needle aspiration cytology of 91%. The sensitivity in differentiating benign from malignant lesions was 61% and specificity was 95%. The positive predictive value was 61% and negative predictive value 95%.

FNA cytology of salivary gland lesions is safe, easy to perform and valuable noninvasive method of preoperative diagnosis. It is accurate method and differentiates non-tumorous benign lesion, benign and malignant tumor, as well as grade of tumor malignancy.

KEY WORDS: *salivary gland lesions, FNA cytology*

VRIJEDNOST CITOLOGIJE U DIJAGNOSTICI LEZIJA ŽLIJEZDA SLINOVNICA: NAŠE ISKUSTVO

Sažetak

U retrospektivnoj studiji analizirane su lezije žlijezda slinovnica dijagnosticirane u Službi za kliničku citologiju i kirurški liječene u Službi za tumore glave i vrata Klinike za tumore u Zagrebu između 1990. i 2004. Analizirali smo lokalizaciju, histološki tip i podudarnost između citološkog i konačnog patohistološkog nalaza.

Studija je uključila 286 bolesnika liječenih zbog lezija žlijezda slinovnica. Predoperativna obrada uključivala je citološku analizu kod svih bolesnika. Materijal za citološku analizu dobiven je aspiracijom iz palpabilne promjene ili pod kontrolom ultrazvuka.

Većina lezija nalazila se u parotidnoj žlijezdi. Bilo je 213 dobroćudnih tumora, 40 dobroćudnih netumorskih promjena i 33 zloćudna tumora. Najčešći dobroćudni tumori bili su pleomorfni adenom i Warthinov tumor, najčešći maligni tumori bio je adenoid cistični karcinom.

Naši rezultati pokazuju ukupnu točnost citološke analize 91%. Senzitivnost metode u razlikovanju benignih i malignih lezija bila je 61%, a specifičnost 95%. Pozitivna prediktivna vrijednost bila je 61%, a negativna prediktivna vrijednost bila je 95%.

Citološka analiza lezija žlijezda slinovnica je sigurna, jednostavna i vrijedna neinvazivna metoda u preoperativnoj dijagnostici. Metoda je točna i razlikuje netumorske dobroćudne lezije, dobroćudne i zloćudne tumore, kao i stupanj diferenciranosti zloćudnih tumora.

KLJUČNE RIJEČI: *lezije žlijezda slinovnica, aspiracijska citodijagnostika*

INTRODUCTION

FNA cytology of salivary gland lesions is obligatory in the preoperative clinical management of patients. Although diagnosis of some common tumors is not difficult in most cases, sampling error may cause difficulties in interpretation. One of the most important roles of salivary gland FNA cytology is to distinguish between neoplasms and non-tumorous benign lesions and thus avoid surgery in conditions that clinically mimic neoplasm (1).

Primary salivary gland tumors (SGTs) are uncommon, accounting for less than 0.3% of all cancers (2). SGTs account for about 3% of all head and neck tumors (1). The world wide annual incidence of SGT ranges from 0.4 to 13.5 cases per 100,000 (3). Two-thirds of SGTs are benign and one-third is malignant. The age-adjusted incidence is approximately 1.3 for males and 1 for females. There is slight female predominance for benign tumors, but carcinomas are equally represented in both sexes (2). Incidence rates for both benign and malignant tumors increase with age until age 65-74 years and then decline (4). The repertoire according to age groups is identical except for a different frequency of histologic types. SGTs occur primarily in older adults, commonly affecting females, except Warthin's tumor and high-grade malignant SGT. In children under age of 18, SGTs are rare in general with only 1.7-3% of all SGTs. Mesenchymal tumors predominate in infants, while in older children epithelial tumors are the most common, being malignant in 60%. However, tumor mortality and morbidity in children are low thanks to mostly low grade of malignant SGT (3-7). The most frequent sites of occurrence are, in descending order of appearance: parotid gland, submandibular gland, sublingual gland and small salivary glands which include palate, cheek, and tongue. SGTs are emphasized in pathology by the fact: the smaller gland the higher chance of malignancy. Namely, the highest chance of being malignant have the SGT arising from retromolar area (89.7%), floor of mouth (88.2%), tongue (85.7%), and sublingual gland (70.2%). On the contrary, only approximately 20% of all parotid tumors are malignant (8).

The majority of adult SGTs are epithelial in origin (90%) being benign in 75% with pleomorphic adenoma on the head (about 65% of all epithelial tumors) (3). According to their behavior, malignant SGTs can be broadly categorized into low, intermediate and high grade tumors. Low grade malignant SGTs are locally invasive with tendency to recur, but distant metastasis and mortality are rare. The high grade malignant SGTs grow rapidly and are often bulky at presentation with early dissemination to regional lymph nodes and distant sites. The 5-year survival rate for low grade, intermediate grade and high grade SGTs are in the range of 80-95%, 50-75%, and 5-45%, respectively (3).

Non-neoplastic and inflammatory lesions can be mistaken for tumors, because of similar clinical presentation, painless swelling being the leading one.

PATIENTS AND METHODS

This retrospective study was designed to evaluate salivary gland lesions diagnosed in the Department of Clinical Cytology and surgically treated in the Department of Head and Neck Surgery in the University Hospital for Tumors, Zagreb, Croatia between 1990 and 2004. The present study included 286 patients, 129 male and 157 female patients, aged 16 to 79 years.

FNA cytology was performed in all patients. The specimens were either aspirated from palpable nodular lesion or revealed during sonographic examination. The majority was obtained by US-guided fine needle aspiration. The specimens were stained according to May-Grünwald-Giemsa (MGG).

All patients were surgically treated. Surgical material was embedded in paraffin and 5µm sections were hematoxylin-eosin (H&E) stained.

We analyzed accuracy and possibilities of FNA cytology in recognizing salivary gland lesions. Cytological reports and final histological analysis were compared. Cytological findings were classified as correct, concordant or incorrect compared to final histological diagnosis.

Correct cytological report means morphologically the same diagnosis in cytological and histological report. Concordant report means that FNA cytology recognized a benign lesion as benign and a malignant lesion as malignant, but it did not recognize the histological type of the lesion. Incorrect report means unrecognizing a benign or malignant lesion as benign or malignant.

RESULTS

Localization of salivary gland lesions showed a typical distribution. The most common gland involved was the parotid gland (n= 244; 85%), followed by the submandibular gland (n=37; 12%), small salivary glands (n=4; 1.4%) and the sublingual gland (n=1; 0.3%) (Fig. 1).

There were 213 benign tumors (74%), 40 benign non-tumorous lesions (14%) and 33 malignant tumors (12%). Male to female ratio was 1 to 1.3 for benign lesions and 1.5 to 1 for malignant tumors (Fig. 2). Age distribution for benign and malignant tumors was similar, with the peak incidence for the benign between 61 and 70 years, and for the malignant the highest and equal incidence in 61-70 and 71-80 age groups (Fig. 3).

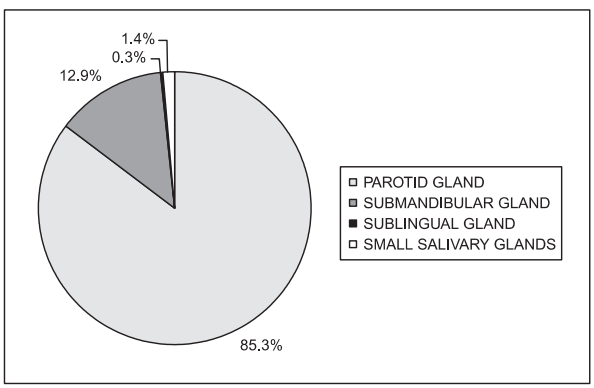


Figure 1. Localization of salivary gland lesions.

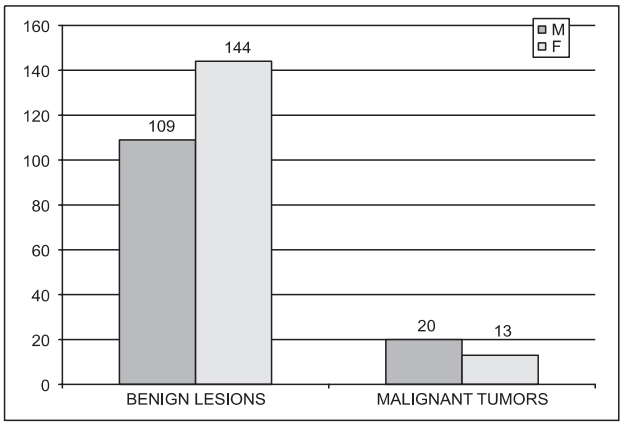


Figure 2. Gender distribution for benign and malignant lesions.

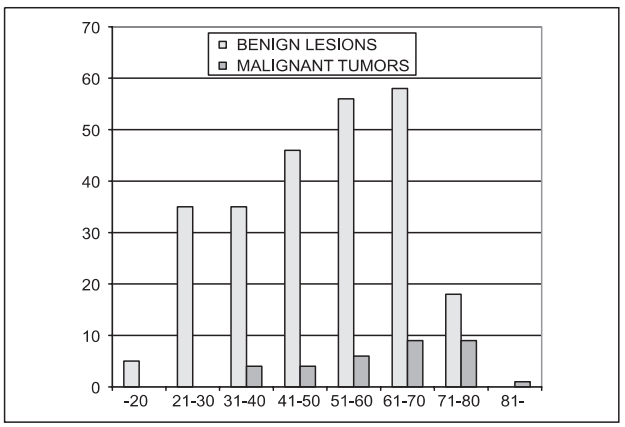


Figure 3. Age distribution for benign and malignant lesions.

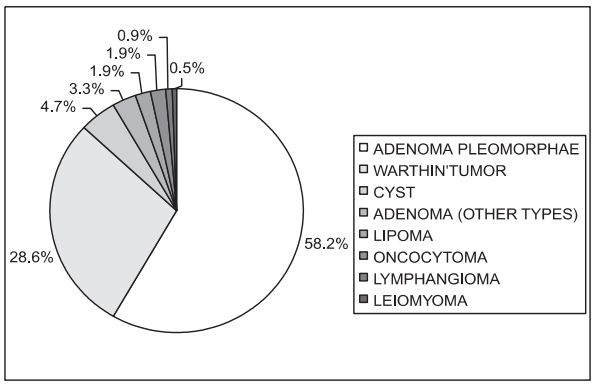


Figure 4. Histology of benign tumors.

The most frequent histological diagnosis were pleomorphic adenoma (n=121; 42%), Warthin's tumor (n=61; 21%), chronic sialoadenitis (n=24; 8%), cyst (n=10; 3.5%) and adenoid cystic carcinoma (n=10; 3.5%)

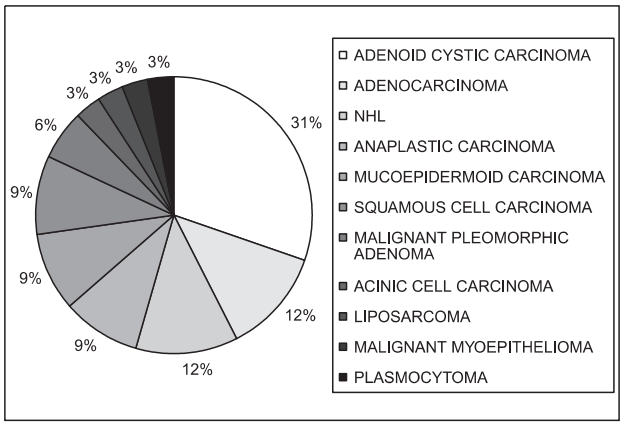


Figure 5. Histology of malignant tumors.

Among benign tumors, the most common was pleomorphic adenoma (57 %), followed by Warthin's tumor (29%) (Fig. 4). The most common benign non-tumorous lesion was sialoadenitis, while the most common malignant tumors were adenoid cystic carcinoma (n=10), followed by adenocarcinoma (n=4) and non Hodgkin lymphoma (n=4) (Fig. 5).

In 214 patients, cytological finding was correct (75%), in 46 concordant (16%) and in 26 patients incorrect (9%). Among benign lesions (benign tumors and non-tumorous benign lesions), the cytological finding was correct in 197 patients (78%), concordant in 43 (17%) and incorrect in 13 (5%). Among malignant lesions it was correct in 17, concordant in 3 and incorrect in 13 patients (Fig. 6).

Further analysis of incorrect cytological reports was done. For benign lesions, the highest false positive rates were for pleomorphic adenoma, Warthin's tumor and chronic sialoadenitis, and most of them were cytologically misdiagnosed as carcinoma (Table 1). Among malignant tumors, the highest false negative rates were for adenoid cystic carcinoma, malignant pleomorphic adenoma and mucoepidermoid carcinoma, and most of them were misdiagnosed as pleomorphic adenoma (Table 2).

Our results show overall accuracy of FNA cytology of 91%. The sensitivity in differentiating benign from malignant lesions was 61% and specificity was 95%. The positive predictive value was 61% and the negative predictive value was 95%.

Table 1.

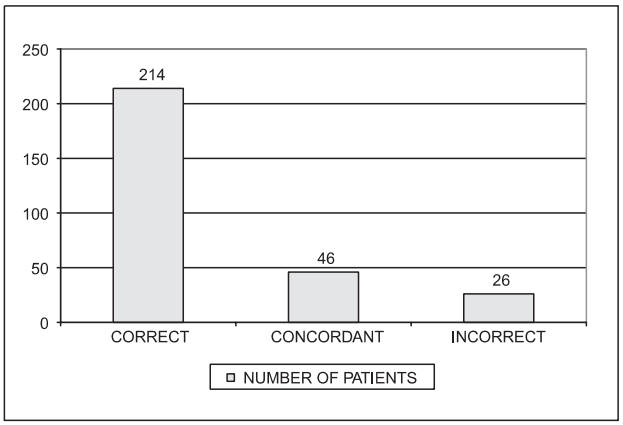
FALSE POSITIVE FNA CYTOLOGY AMONG BENIGN LESIONS.

Final histology	**False positive fna cytology**			**Total**
	Carcinoma	Malignant pleomorphic adenoma	Adenoid cystic carcinoma	
Pleomorphic adenoma	**2**	**3**	**2**	**7**
Warthin's tumor	**2**			**2**
Chronical sialoadenitis	**2**			**2**
Cyst	**1**			**1**
Basal cell adenoma	**1**			**1**
Total	**8**	**3**	**2**	**13**

Table 2.

FALSE NEGATIVE FNA CYTOLOGY AMONG MALIGNANT TUMORS.

Final histology	**False negative fna cytology**				**Total**
	Pleomorphic adenoma	Warthin's tumor	Cyst	Proliferation of ductal epithelium	
Adenoid cystic carcinoma	**1**	**1**	**1**	**1**	**4**
Malignant pleomorphic adenoma	**2**				**2**
Mucoepidermoid carcinoma	**1**	**1**			**2**
Adenocarcinoma			**1**		**1**
Anaplastic carcinoma	**1**				**1**
Acinic cell carcinoma		**1**			**1**
Liposarcoma	**1**				**1**
Malignant myoepithelioma	**1**				**1**
Total	**7**	**3**	**2**	**1**	**13**



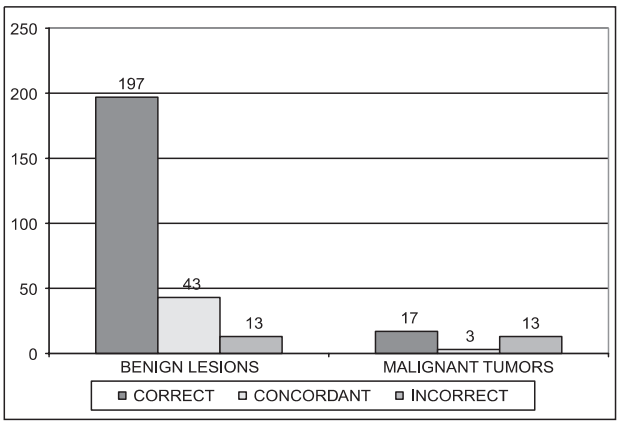


Figure 6. Analysis of FNA cytology reports.

DISCUSSION

The results reported in the current literature and our own experience indicate that FNA cytology of salivary gland lesions is a safe and effective diagnostic technique. The present series was completely free of complications. In literature, in a series of 652 aspirations, one hematoma was reported (9)

The parotid gland is the most frequently involved, while the minor salivary glands and the submandibular glands are less commonly affected (1). In our study, the parotid gland was also most frequently involved (85%), followed by the submandibular (12%) and sublingual gland (0.3%). There is a small proportion of affected small salivary glands (1.4%).

According to literature, the most common benign tumor is pleomorphic adenoma (60-70%). Warthin's tumor represents approximately 15% of all benign epithelial tumors, while oncocytoma, basal cell and other adenomas are rare (10,11). In our series, the most frequent benign tumor was also pleomorphic adenoma (57%), followed by Warthin's tumor (29%). The commonest malignant tumor in large published series is adenoid cystic carcinoma (10%), followed by mucoepidermoid (5%), acinic cell and epithelial-myoepithelial carcinomas (10,11). There was a low incidence of malignant tumors in our series, with similar incidence data adenoid cystic carcinoma being the most frequent malignant tumor (4%).

Using histology as the "gold standard", the sensitivity of FNA cytology for malignant tumors was 61%, with a specificity of 95%. The accuracy was 91%, and the positive predictive value 61%, negative predictive value 95%. Several large published series have documented the accuracy and limitations of salivary gland FNA cytology. The overall accuracy has been reported to be 87% to 100% in distinguishing benign from malignant lesions; FNA cytology also has a reported sensitivity of 87% to 100% and specificity of 90% to 100% (12-19). In our study, the low sensitivity and positive predictive value can be explained with the low incidence of malignant tumors with high morphological diversity.

Cytological diagnosis of malignancy is based on well-established cytological criteria: nuclear enlargement, pleomorphism, chromatin pattern, nucleoli, cytoplasmic differentiation, cell cohesiveness and arrangement and presence of background stromal material as well as on the clinical history and presentation (2). A number of problems were encountered in interpreting some cases, not only in differentiating benign from malignant ones but also in the specific classification of this neoplasm. Cytological smears lack the architecture that is particularly important in differentiating some of the tumors. Some tumors are so rare that a cytologist may not have come across the entity before, either during training or in practice. It is easily noticed in cystic lesions, pleomorphic adenoma, lesions with high proportion of lymphocytes, chronic inflammation and lesions with high proportion of epithelial cells (20). Problems may also be encountered in differentiating hematopoietic from non-hematopoietic lesions and with the interpretation of spindle cell neoplasms, acinic cell carcinoma, adenoid cystic carcinoma, lymphoproliferative disorders and

postirradiation changes (14). We had similar difficulties in FNA cytology of salivary gland lesions in our study.

A cystic lesion of salivary glands must be considered a possible tumor until proven otherwise. Many neoplasms can appear clinically like cystic nodule (Warthin's tumor, acinic cell carcinoma and mucoepidermoid carcinoma). Therefore, an accurate cytologic examination must include material collected from the adjacent pericystic area. In our study, we had 2 false negative results when FNA cytology revealed only cystic fluid and final histological analysis showed malignant tumors (adenoid cystic carcinoma and adenocarcinoma).

Pleomorphic adenoma and adenoid cystic carcinoma may present cytologically some pseudocylindromatous and, respectively, pseudotrabecular stromal fibrillated aspect, which are for an overdiagnosis of adenoid cystic carcinoma in the first case and an underdiagnosis of pleomorphic adenoma in the second one (21). Portions of the aspirated material in some pleomorphic adenomas may exhibit stromal spheres with features very similar to those obtained from an adenoid cystic carcinoma, and adenoid cystic carcinoma may demonstrate a rectangular pseudotrabecular myxoid stroma (22).

A prominent lymphoid component is a characteristic feature in smears of Warthin's tumors, but the stroma of acinic cell carcinoma may also contain abundant lymphoid tissue which may obscure the epithelial cells causing diagnostic problems (23, 24).

Atypical cells in pleomorphic adenoma can be seen frequently: the smears may contain single cells of stromal type that have very large, irregular, often multiple or multilobate, bizarre nuclei which can mimic malignant cells (25).

In sialolithiasis or other situations in which a cystic mass results from obstruction of a salivary gland duct, the FNA cytology findings may closely mimic those of low grade mucoepidermoid carcinoma (26). In these cases, the smears can demonstrate immature squamous metaplastic elements that strongly resemble the ''intermediate'' cells of low grade mucoepidermoid carcinoma. It is suggested that when FNA cytology findings consistent with a low grade mucoepidermoid carcinoma are encountered, the possibility of sialolithiasis should be considered.

A spectrum of neoplastic and non-neoplastic lesions of the salivary glands may contain squamous cells. These may be a defining feature of the lesions or an occasional and thus unexpected finding, with a consequent potential for misdiagnosis. When atypical squamous cells are encountered in needle aspirates from the neck region, squamous cell carcinoma must always be considered in the differential diagnosis. There are, however, several other lesions in which atypical squamous cells may be identified, and consideration of these entities will help to avoid a false positive diagnosis of carcinoma (27). Squamous metaplasia, may be seen in chronic sialoadenitis, lymphoepithelial cysts, ''inflamed'' Warthin's tumor or infracted pleomorphic adenoma (28).

CONCLUSION

FNA cytology of SGT is safe, easy to perform, and accurate. The low incidence of SGT enables us to collect representative cytology series, resulting in unfamiliarity of clinicians and lack of experience of cytologist. Some SGTs are so rare that the cytologist may not have come across the entity before, either during training or in practice and accurate interpretation may be difficult even for the most experienced cytologist. The most frequently misdiagnosed lesions are pleomorphic adenoma, mucoepidermoid carcinoma, chronic sialoadenitis and malignant lymphoma. There are no complications except for few reported in literature. Salivary gland FNA cytology presents difficult interpretation challenges; the cytologist should be aware of potential false-positive and false-negative interpretation that can occur in FNA cytology from the organ site in order to minimize the possibility of diagnostic errors.

FNA cytology should define whether or not the lesion is neoplastic. In the case of neoplasm, FNA cytology indicates whether it is a high or low-grade malignancy.

However, the main concern is whether the needle interference with the SGT will eventually lead to a higher recurrence rate in some tumors, but there is no evidence in many long-term follow-up studies of patients who have had preoperative FNAC, that it influences recurrence of tumors.

FNAC is a useful step in diagnostic process and in planning treatment of salivary gland lesions.

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