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Reliability of fine needle aspiration and *ex tempore* biopsy in the diagnosis of salivary glands lesions

Pouzdanost aspiracije tankom iglom i biopsije *ex tempore* u dijagnostici lezija pljuvačnih žlijezda

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Abstract

Background/Aim. Interpretation of cytological material obtained by fine needle aspiration (FNA) of salivary glands is one of the most challenging areas in cytopathology. FNA is performed easily, it is minimally invasive, inexpensive, fast, reliable and provides valuable information to clinicians about the nature of the lesion and therapeutic modalities. *Ex tempore* diagnosis, frozen section (FS) is a diagnostic tool that is essential in determining the modalities of surgical treatment of lesions of the salivary glands. Today this method is used in determining the status of resection margins and infiltration of adjacent anatomical structures. The aim of this study was to present our experiences in the application of FNA and FS in the diagnosis of salivary gland lesions and to determine the sensitivity, specificity, predictive value, and diagnostic reliability of these methods. **Methods.** The study included 36 patients. In all the patients, cytological analysis was done before surgery and histological analysis of the surgical material. In 23 of the patients the FS diagnostics was done. Then we compared FNA and FS findings with histopathological findings. **Results.** Correlation of cytological and histological diagnosis showed sensitivity of 83.3%, specificity 96.67%, positive predictive value 83.3%, negative predictive value of 96.77% and diagnostic accuracy of 97.2%. Based on the relationship between FS diagnosis and histopathological diagnosis, the sensitivity was 100%, specificity 96.67%, while positive predictive value and diagnostic accuracy were 100% each. **Conclusion.** The study confirmed that FNA is a sensitive, reliable diagnostic method for differentiation of lesions of the salivary glands. In cases with no posibility to definite differentiation in FNA samples, and with the need to assess the resection margins and invasion of anatomical structures, it is recommended to use FS diagnostics.

Key words:
biopsy, fine needle; frozen sections; salivary glands; histological techniques; sensitivity and specificity.

Apstrakt

Uvod/Cilj. Citološka interpretacija materijala dobijenih aspiracijom tankom iglom (*fine-needle aspiration* – FNA) pljuvačnih žlijezda predstavlja jedno od najzahtjevnijih područja u citopatologiji. FNA se izvodi lako, brzo, pouzdano, minimalno invazivno, jeftino, pružajući značajne informacije kliničarima o prirodi lezije i terapijskim modalitetima. *Ex tempore* dijagnostika (*frozen section* – FS) je dijagnostička metoda koja je bitna pri određivanju modaliteta hirurškog liječenja lezija u pljuvačnim žlijezdama. Danas se ova metoda koristi za određivanje statusa resekcionih rubova i infiltracije susjednih anatomskih struktura. Cilj istraživanja bio je da se prikažu sopstvena iskustva u primjeni FNA i FS u dijagnostici lezija pljuvačnih žlijezda, te da se utvrdi osetljivost, specifičnost, vrijednost predviđanja i dijagnostička pouzdanost ovih metoda. **Metode.** Ispitivanjem je obuhvaćeno 36 bolesnika. Kod svih je urađena citološka analiza prije operativnog zahvata i histološka analiza operativnog materijala. Kod 23 bolesnika urađena je dijagnostika FS. Izvršeno je poređenje FNA i FS nalaza sa patohistološkim nalazima. **Rezultati.** Korelacijom citoloških i patohistoloških dijagnoza osetljivost je iznosila 83,3%, specifičnost 96,67%, pozitivna vrijednost predvi-

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đanja 83,3%, negativna vrijednost predviđanja 96,77% i dijagnostička pouzdanost 97,2%. Na osnovu odnosa FS dijagnoza i patohistoloških dijagnoza osjetljivosti je iznosila 100%, specifičnost 96,67%, a pozitivna vrijednost predviđanja i dijagnostička pouzdanost iznosili su 100%. **Zaključak.** Istraživanje je potvrdilo da je FNA osjetljiva i dijagnostički pouzdana metoda za diferencijaciju lezija u pljuvačnim žlijezdama. U slučaju nemogućnosti definitivne diferencijacije u FNA uzorcima, te potrebe da se izvrši procjena resekcionih rubova i invazija anatomskih struktura, preporučuje se FS dijagnostika.

Ključne reči:
biopsija tankom iglom; zamrznuti isečci tkiva; pljuvačne žlezde; dijagnoza; histološke tehnike; senzitivnost i specifičnost.

Introduction

Cytological interpretation of material obtained by fine needle aspiration (FNA) of salivary glands is one of the most challenging areas in cytopathology. Specifically, it describes a wide range of reactive and neoplastic lesions which can be diagnosed in more than 500 salivary glands present in the human body. Histological and cytological analyses confirmed that tumors of salivary glands were the most heterogeneous group of human tumors. An additional difficulty in cytodiagnostics of salivary glands is cytomorphological overlap of many benign and malignant tumors [1–3].

FNA is currently used worldwide to evaluate palpable and deeply located lesions in most anatomic regions [1, 4].

Salivary gland tumors are uncommon and account for 2% to 6.5% of head and neck tumors, of which 21% to 46 % are malignant tumors [5]. Preoperative diagnosis of lesions of a salivary gland requires clinical examination, analysis of lesion by radiographic techniques and more recently the use of FNA [6, 7].

Patients who are candidates for FNA often have enlargement and/or pain on the face, and upper part of the neck and mouth. Sometimes, they have a clinical presentation as partial paralysis or paresthesia of the face. FNA is performed easily, it is minimally invasive, inexpensive, fast, reliable and provides a valuable information to clinicians about the nature of the lesion and therapeutic modalities for each patient. It can be used to obtain material for further analyses (microbiological, immunocytochemical, molecular). Complications are rare [1, 8].

Ex tempore diagnostic (frozen section – FS) is a diagnostic tool that is essential in determining the modalities of surgical treatment of lesions of the salivary glands. FS is often the first procedure in a definitive histopathological diagnostics. Also, this method is used in determining the status of resection margins, and involvement of the tumor's process of some anatomical structures (blood and lymph vessels, nerves, etc.). In recent years, the importance of FS in the diagnosis of lesions was significantly lower and the share in the evaluation of the margins of the pathological process is much higher. In most cases, FS is used as a diagnostic confirmation of FNA results that have been interpreted as nondiagnostic, benign but clinically suspicious, atypical or cytologically suspicious for malignancy [6, 9, 10].

The goal of this research was to present our experiences in the application of FNA and FS in the diagnosis of salivary gland lesions, and to correlate these methods with definitive histopathological analysis of the operation material and determine their sensitivity, specificity, predictive values and diagnostic reliability.

Methods

The study included 36 patients selected at random with puncture of the salivary glands in the period between October 2010 and October 2011. Data on the patients were obtained from the database of the Department of Pathology, Clinical Center Banja Luka, Bosnia and Herzegovina. Criteria in the selection of patients were: clinically confirmed lesion in salivary gland; lesion verified by imaging techniques [ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI)]; completed preoperative puncture of lesion in salivary gland; cytology report of preoperative FNA performed; definitive histopathological findings.

In most of the patients, FS diagnostics, histological and cytological diagnostics were also done. Punctures were made with a thin needle. In most of the cases, a palpable node was present. In a few cases, a change was observed and puncture was guided by US. After puncture, 2–8 direct smears (conventional preparation) were made. Smears were treated in two ways: air-dried and stained with May-Grunwald-Giemsa (MGG) method, and fixed in 95% alcohol and stained with Papanicolaou method. Interpretation of cytological findings was performed as recommended by the guide on how to categorize the changes in aspiration cytology (The United Kingdom National Health Service Breast Screening Programmes, UK NHSBSP) [1, 11]. FNA reports included confirmation of adequacy of a sample and were placed into the following categories: unsatisfactory, nondiagnostic, negative for malignant cells, atypical, suspicious for malignant cells and positive for malignant cells. In most reports, a specific diagnosis or description were indicated.

Operative treatment was carried out in all 36 patients. In 23 of the patients FS diagnostic was done. FS interpretation was performed on the samples and the clinical behavior of the lesion (benign or malignant) was determined. Out of operating material the representative amount of tissue samples were taken, then fixed in buffered formalin, embedded in paraffin, and analyzed using a light microscope. After the diagnostics was completed, the patient was treated with the appropriate type of therapy according to the results of diagnostic procedures. If cytology and FS diagnostics confirm benign lesion, surgical treatment is finished by resection of the lesion with clear resection margins. In cases in whom cytology and FS diagnostic confirm malignant lesion two approaches are used (depending on the degree of malig-

nancy): resection with negative resection margins or radical extirpation of the salivary gland with regional lymph node dissection.

The determined parameters are recommended by the UK NHSBSP, which are used for assessing the performance of FNA/FS diagnostic methods in lesions of salivary glands (analogous to lesions in other organs): absolute sensitivity, complete sensitivity, specificity, positive predictive value, false negative relationship, false positive ratio, an inadequate ratio and inadequate ratio of cancers [12, 13].

For statistical data processing the statistical program SSPS (version 15.0) was used. The processed data and the results are presented in tabular and graphical forms. In the processing and analysis of data, the following statistical methods were used: descriptive statistics, correlation, χ^2-test and Cramer's V test.

Results

Our study included materials obtained from 36 patients, taken during the surgery at the Clinical Center of Banja Luka during the period from October 1, 2010 to October 1, 2011. In all the patients, a palpable or ultrasonically detected lesion in the salivary gland was punctured, followed by processing and analyzing the material, and interpretation of cytological findings. Subsequently, all the patients were treated surgically, depending on the results of cytological analysis. In 23 of the patients the diagnostics was done during the surgery (FS). After the surgical treatment, processing and histological interpretation of the results was performed. Interpretation of tumor processes was carried out according to the World Health Organization (WHO) classification [14].

The youngest patient was one year old and the oldest 83 years. The average age of the examinees was 52.08 years. Most of the patients were aged 51 to 60 years (30.56%). Most of the patients were male – 20 (56%), while the number of female patients was 16 (44%) (Table 1).

In 33 (91.7%) patients changes were localized in the parotid gland, followed by changes in submandibular gland in 2 (5.5%) patients, and the rest of the changes were localized in the minor salivary glands of the oral cavity, in 1 (2.8%) patient (Table 1).

The obtained cytological material was evaluated with respect to the adequacy of a sample. Of 36 analyzed samples, in three cases (8.3%) material was not optimal for analysis and was classified as nondiagnostic (sufficient for analysis, but with limitations), with the stated reasons for this limitation. In the remaining 33 (91.7%) cases the material was sufficient for analysis.

In three cases there were some restrictions: in the first case, it was stated that there was only blood, and the definitive diagnosis was hemangioma; in the second case, serous content and rare ductal epithelial cells were present, and the final diagnosis was salivary duct cyst; in the third case, the cytological details of normal salivary glands and fatty tissue were described, and the final histological diagnosis was lipomatosis of the salivary gland (Table 1).

Table 1
Characteristics of the patients and general interpretation of changes in salivary glands

Characteristics	Number of patients (%)
Sex	
male	20 (56)
female	16 (44)
Localization	
parotid gland	33 (91.7)
submandibular gland	2 (5.5)
minor salivary glands in oral cavity	1 (2.8)
Adequacy of FNA sample	
satisfactory (no limitations)	33 (91.7)
satisfactory (with limitations)	3 (8.3)
unsatisfactory	0 (0)
General FNA interpretation	
unsatisfactory	/ (/)
nondiagnostic	3 (8.3)
negative for malignant cells	28 (77.8)
positive for malignant cells	5 (13.9)
Specific diagnose in FNA samples	
confirmed	26 (72)
not confirmed (descriptive report)	10 (28)
Interpretation in FS samples	
benign	21 (91.3)
malignant	2 (8.7)
Definitive HP diagnosis	
non tumor lesion	7 (19.4)
tumor lesion (benign)	23 (64)
tumor lesion (malignant)	6 (16.6)

FNA – fine-needle aspiration; FS – frozen section; HP – histopathological.

Interpretation of cytological findings was performed according to the guide UK NHSBSP adapted for aspiration cytology of salivary glands. The general interpretation contains six categories: unsatisfactory (0/0), nondiagnostic [3 (8.3%) patients], negative for malignant cells (a benign lesion) (28/77, 8%), atypical (0/0), suspected for malignant cells (0/0), positive for malignant cells (5/13, 9%) (Table 1).

A specific diagnosis was identified in cytological material in 26 (72%) cases. The following specific diagnoses were confirmed cytologically: tumor mixtus (pleomorphic adenoma) in 20 cases (Figure 1), Warthin's tumor in 3 cases and squamous carcinoma in 3 cases.

Descriptive interpretation was seen in 10 (28%) cases (Table 1). The following conclusions were stated in these interpretations: 5 cases of benign findings-inflammation, 2 cases of high grade malignancy, and 3 cases were described without statement (nondiagnostic).

Rapid diagnosis during surgery was performed in 23 (64%) of the patients. The interpretations were: benign lesions in 21 cases, malignant lesions in two cases (Table 1).

In our samples, benign tumors were diagnosed in 23 (64%) of the cases of histological material. Non-tumor processes were diagnosed less frequently (7 cases or 19.4%), and most rarely malignant tumors, in 6 (16.6%) cases (Table 1).

Analysis showed that benign tumors were detected more frequently in men, 13 (56%) cases. Malignant tumors were twice as common in men, 4 (66.7%) cases, while non-tumor lesions were more common in women, 4 (57.1%) of the cases.

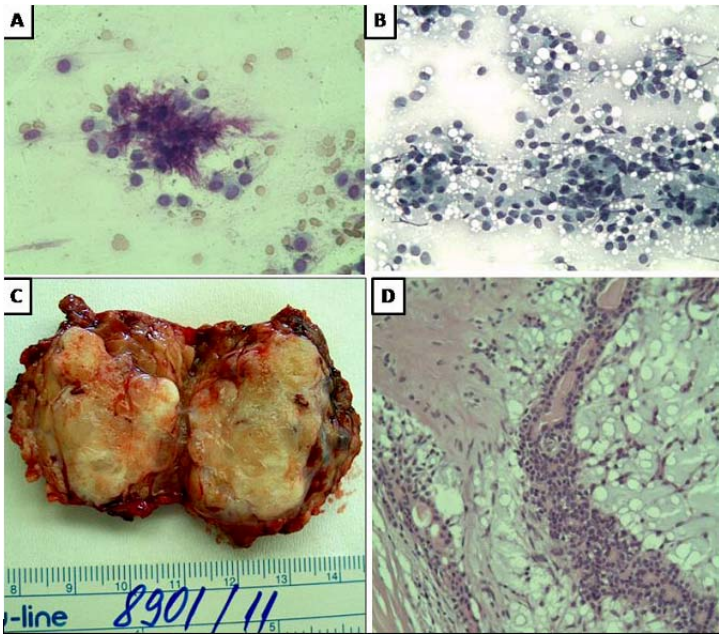

Fig. 1 – Pleomorphic adenoma (tumor mixtus) of the salivary gland.

A) – Myoepithelial cells detected, arranged individually within a gentle fibrillar matrix (MGG ×400); B) – Cellular pleomorphic adenoma. Myoepithelial cells arranged in groups (Papanicolaou ×400); C) – Macroscopic appearance, well-circumscribed, lobular nodule, whitish, glassy surface; D) – Histological appearance: epithelial, myoepithelial component of the tumor and myxoid matrix (HE ×200).

Definitive histological diagnoses of the operative material were established in all the 36 patients. Most frequently diagnosed was tumor mixtus (pleomorphic adenoma) in 16 (44%) of the cases (Figure 1), followed by Warthin's tumor (*cystadenoma lymphomatosum*) in 4 (11.1%) of the cases, squamous cell carcinoma and lymphoepithelial cyst in the 3 (8,3%) of the cases, high grade mucoepidermoid carcinoma (Figure 2), in 2 (5.5%) of the cases. The following histological entities had one case (2.8 %) each: lymphoma, schwannoma, hemangioma, lipomatosis, salivary duct cyst, rupture of epidermal cyst, lymphadenitis and abscessus.

Analysis of reliability of cytological diagnosis and FS diagnosis in terms of general interpretation of benign/malignant in relation to a definitive histopathological diagnosis was determined using the χ^2 test or Cramer's V-test. Based on statistical data, we can safely conclude that FNA and FS diagnostics are absolutely reliable in general interpretation of the lesion (benign/malignant) in salivary glands. [The value of Cramer's V = 0.898, c = 0.710, c = 1,000 ($p < 0.01$)].

Cytological and histological reports regarding specific diagnoses were the same in 22 (61.1%) of the patients. In 8

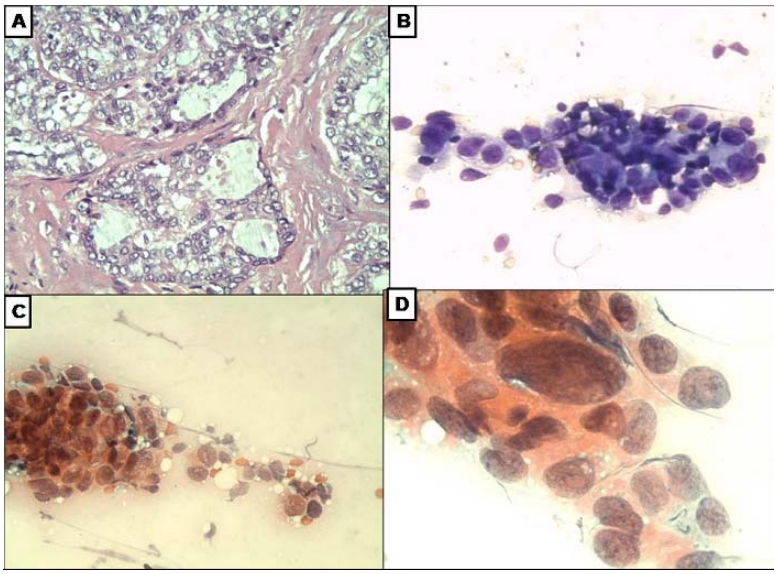

Fig. 2 – Mucoepidermoid carcinoma, high grade.

A) Histologically observed predominantly properly arranged tumor cells with characteristics of epidermoid and intermediate cells. Focally present glandular formations lined with mucinous cells (HE ×400); B) Cytologically, cells with squamoid appearance, sporadically vacuolated cytoplasm, large, polymorphic nuclei were found (MGG ×400); C) Cytologically observed cells with squamoid appearance, large polymorphic nuclei (Papanicolaou ×400); D) Cytologically, cells with squamoid appearance, large, polymorphic nuclei, prominent nucleoli were found (Papanicolaou ×1,000).

(22.25%) of the patients lesions were cytologically and histologically interpreted as benign, but specific diagnoses were different. In 2 (5.55%) of the patients lesions were interpreted cytologically and histologically as malignant, but specific diagnoses were not the same. Malignant cytological reports, which were not confirmed by histological diagnosis, were not present (false positives were not present). In one (2.8%) case, the lesion was interpreted as benign cytologically and as malignant histologically. Three (8.3%) of the cases were nondiagnostic in cytology (Table 2, Figure 3).

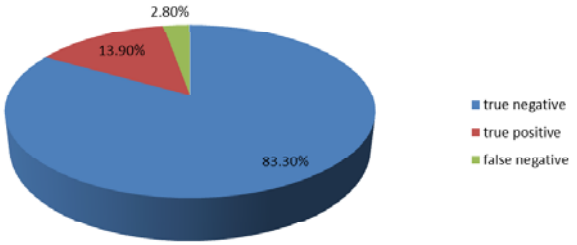

Fig. 4 – Presentation of examinees according to true positive (TP); true negative (TN); false positive (FP); false negative (FN) findings.

Table 2

Representation of matching of specific diagnoses in cytological and histological material

FNA diagnosis	Number of patients (n)	Histopathological diagnosis (n)	
		Congruous	Incongruous
Tumor mixtus	20	16	4 (1 lymphoepithelial cysts [1],1 schwannoma [1], 1 abscess [2], 1 Warthin's tumor [1])
Warthin's tumor	3	3	
Squamous carcinoma	3	3	
Description: benign – inflammation	5		5 (3 lymphoepithelial cysts [1], 1 reactive lymphadenitis, 1 mucoepidermoid carcinoma [3])
Description: malignant high grade	2		2 (1 mucoepidermoid carcinoma [1], 1 lymphoma DLBCL [1])
Description: nondiagnostic	3		3 (1 hemangioma [1], 1 lipomatosis [1], 1 salivary duct cyst [1])
Total	36	22	14

[1] – Minimal (insignificant) difference (n = 12); [2] – Difference of medium significance (n = 1); [3] – Huge (significant) difference (n = 1); DLBCL – Diffuse large B cell lymphoma.

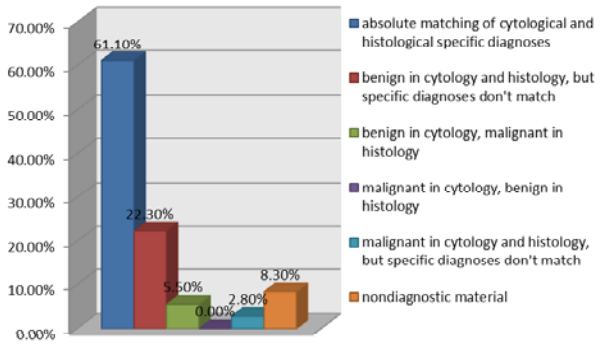

Fig. 3 – Representation of matching of cytological and histological specific diagnoses.

Findings of FS diagnostics and definitive histopathological diagnosis were absolutely matched, given that the interpretation was carried out in terms of clinical behavior of the lesion: benign or malignant. Specific diagnosis was not determined by FS diagnostics.

In the examined material, there were 30 (83.3%) true negative cytological findings, five (13.9%) true positive cases and one case (2.8%) was false negative. False positive cases were not present in our material (Figure 4).

Based on the ratio of cytological and histopathological diagnoses, calculated sensitivity was 83.3%, specificity 96.67%, positive predictive value of 83.3%, negative predictive value of 96.77% and diagnostic accuracy of 97.2%.

Based on the relationship of FS diagnosis and histopathological diagnosis, the calculated specificity was 96.67%, while the positive predictive value and diagnostic accuracy were 100% each.

Discussion

FNA is an effective and important diagnostic method for the diagnosis of diseases of various organs. If the method is correctly performed, cytological material adequately processed and the results interpreted by an experienced cytopathologist, FNA provides reliable information about the disease before surgical treatment [12, 13]. FNA of salivary glands is technically a simple procedure that is usually well-tolerated by the patient, and increasingly popular among clinicians and cytopathologists. Additional advantages of this method are rapid diagnosis and minimal opportunity for spreading of the tumor. To ensure more reliable and specific diagnosis in FNA, ongoing collaboration between clinicians, radiologists and cytopathologists is necessary [1].

One of the earliest analysis of the effectiveness of FNA in the diagnosis of salivary gland disease was published by Frable and Frable [15] in 1991. These authors analyzed 552 aspirates of salivary glands in a 15-year period and showed high sensitivity and specificity of FNA in the diagnosis of tumors of the salivary gland [15]. FNA in salivary glands may provide a saving of 8,000–24,000 dollar per 1,000 FNA of salivary gland tumors [16].

In our study, the average age of the patients was 52 years. Salivary gland tumors occur at all ages. Some of the most common tumors (pleomorphic adenoma, mucoepidermoid carcinoma) occur most frequently in the third and fourth decade of life. Most benign and malignant tumors occur between the fifth and seventh decade of life, and the average age is 46–47 years [1, 14, 17].

In our material, men had more frequently changes localized in the salivary glands and the ratio men : women was 1.25 : 1. Similar results were obtained by Das et al. [18], who analyzed the reasons for enlargement of salivary glands in 712 cases. In salivary glands, most commonly diagnosed are benign tumors, which were, in our samples, diagnosed in 23 (64%) of the cases. Non-tumor processes were seen in 7 (19.4%) of the cases, and malignant tumors in 6 (16.6%). Both benign and malignant tumors were more often seen in men – benign in 56% and malignant in 66.7% of the cases. Non-tumor processes were more common in women (57.1% of the cases). A similar distribution of benign and malignant tumors and non-tumorous processes was shown by other authors who were doing research on a larger number of patients [6, 18–21]. Salivary gland tumors are more common in women, but the differences are present with respect to the histological type (eg. Warthin's tumor and high grade cancers are more common in men) [1, 14, 17, 20].

In most of our patients (91.7%), the changes were seen in the parotid gland. Madani et al. [19] analyzed 169 patients who underwent FNA and subsequent histological analysis. In their samples, most of the changes are localized in the parotid gland – 152 (89.94%) of the cases.

Interpretation of cytological analyses was performed as recommended by the guide on how to categorize changes in aspiration cytology UK NHSBSP. Analysis showed that 77.8% of cases in the group were negative for malignant cells (benign lesion), followed by positive for malignant cells in 13.9% of the cases and nondiagnostic in 8.3% of the cases. In the examined material, three samples were named as nondiagnostic (8.3%). In these samples the final histopathologic diagnosis was lipomatosis of the salivary glands in one case, in the second hemangioma, and in the third case was a cyst of the salivary duct. The number of inadequate samples in FNA salivary glands differs and ranges from 2 to 8.5% [6, 18–20].

A precise criterion for assessing the adequacy of aspiration cytology of salivary gland does not exist. Evaluation of the adequacy is a job of a cytopathologist, who based on the present material determines whether the definitive diagnosis and interpretation can be made. Unsatisfactory FNA samples of salivary glands are usually acellular or hypocellular samples. Such samples are usually the result of various factors such as: abundant blood, inflammation, necrotic debris, artifacts of fixation, staining, and preparation of smears ("crush artifacts"). The exact number of cells required for analysis of salivary gland FNA has not been established, so the estimates based on this parameter are still subjective. Making statement that the sample is "satisfactory" instead of "unsatisfactory" or "nondiagnostic" may be the reason for false negative results in clinically verified changes in the glands. The presence of atypical cells should be stated in the report and provide guidance for further processing (testing). Hypocellular samples that the cytopathologist declared as "unsatisfactory" may be seen in cystic lesions, benign tumors, and so on. In such cases, the correlation of clinical and radiological images and the content of the sample can help to reduce the number of "unsatisfactory" samples [1, 13, 22].

FNA was positive in 5 (13.9%) cases. Postoperative histopathological analysis in all five cases confirmed malignancy of the lesions. Correspondence of specific diagnosis is absolute in the diagnosis of squamous cell carcinoma in cytology and histology. There were three cases with the same specific diagnosis of squamous cell carcinoma. In two cases the cytological findings were interpreted as positive for malignant cells and matched the high grade tumor. In histology, in one case, high grade mucoepidermoid carcinoma was diagnosed, and in the second case non Hodgkin's lymphoma (diffuse large B cell lymphoma). In the literature, the percentage of FNA positive for malignant cells varies and ranges from 10 to 25% [8, 19, 21, 23, 24].

In our study one (2.8%) case was false negative, while we did not find false positive cases. Numbers of false negative and false positive cytology findings are different. Madani et al. [19] had 10.65% of false negative findings and 5.91% of false positive. Rajwanshi et al. [21] in a study on 172 FNA cases had 4 false negative cases and 5 cases of false positive results of cytological analyses. Hughes et al. [8] presented 8 cases of false positive and 32 cases of false negative results.

The range of false negative results is from 1% to 15%, and in most cases negative interpretation is present in low grade tumors, hypocellular cysts. Most common false negative cytological interpretations were observed in mucoepidermoid cancer, low grade of malignancy, lymphomas, acinocellular carcinoma, and adenoid cystic carcinoma. The reason for this is hypocellularity of smears, containing only the content of a cyst, and besides that, epithelial cells appear cytologically without atypia or with minimal atypia, and mucinous cells can be interpreted as histiocytes (muciphages) [1, 3, 8].

False positive results were present in 5% to 8% of cases, mostly due to the presence of benign lesions with reactive and metaplastic changes especially present in inflammation. In the report of the College of American Pathologist Interlaboratory Comparison Program in Nongynecologic Cytology, most common false positive FNA findings are monomorphic adenoma, intraparotid lymph node, oncocytoma and granulomatous lymphadenitis [1, 8, 19, 21, 25].

Specific diagnosis on cytological material in our samples was determined in 26 (72%) of the cases. Matching between specific cytological and histological diagnosis was present in 22 (84.6%) of the cases. The difference was present in the specific diagnosis in four (15.4%) of the cases. In all four cases the interpretation was tumor mixtus and histology found the following entities: Warthin's tumor, lymphoepithelial cyst, chronic abscess, and schwannoma. So, in terms of general interpretation of benign changes there was no difference. Descriptive interpretation was seen in ten cases and the conclusions were: 5 cases of benign findings-inflammation, 2 cases of malignant lesinous-high grade, and in 3 of the cases de-

scription with no statement (nondiagnostic). For cytological statements benign – inflammation, in definitive histological report there were the following diagnoses: three samples were branchial lymphoepithelial cyst, reactive lymphadenitis in one case and one case interpreted as mucoepidermoid carcinoma, high grade (the only false negative cytological finding). The results of various studies indicate a low correlation of specific cytological and histological diagnosis of salivary gland material. Mihashi et al. [26] found that the sensitivity of FNA in the diagnosis of malignant tumors of the salivary glands was 88.2% and an extremely low (30%) matching of cytological and histological specific diagnoses. Jain et al. [27] had a correlation of histological and cytological diagnosis of malignant tumors of salivary glands in 64.2% cases.

Based on the results, the parameters of efficacy of FNA and FS in the diagnosis of salivary gland lesions were derived. Absolute and total sensitivity amounted to 83.3%, specificity of 96.67%, false positive ratio of 0%, false negative ratio of 16.6%, diagnostic accuracy of 97.2%, positive predictive value 100%, and negative predictive value of 96.77%.

Hughes et al. [8] analyzed 6,249 cases of salivary gland tumor and showed the sensitivity of the method of 73% and specificity of 91%. Our results are similar, but minimal differences are due to the sample size. Other studies show the reliability of the method in the range between 81% and 98%, accuracy benign/malignant between 81% and 100%, accuracy in specific diagnosis from 48% to 94%, false negative index from 1% to 15%, false positive index of 5% to 8%, sensitivity 86% to 100% and specificity of 90% to 100% [8, 18, 25–30].

histopathological findings is absolute. Specific diagnosis was not determined at FS samples. Seethala et al. [6] found that of 57 cases analyzed by this method 12% were false negative and no false positive findings. FS is a method that can provide a definitive diagnosis in cases where previous diagnostic methods are not sufficient (FNA). The authors noted that the sensitivity of FS was 77%, specificity 100%, and diagnostic accuracy 88%. The combination of FNA and FS increases sensitivity up to 90%, specificity to 100% and diagnostic accuracy to 95% [10, 31, 32].

FNA was compared with FS diagnosis. FNA had a similar accuracy as the FS diagnosis and the advantage of FNA is in providing preoperative diagnosis, in contrast to FS where the diagnosis is reached during the operation. FNA tends to be a more sensitive diagnostic method than FS and FS has a higher specificity and the advantage in possible evaluation of resection margins [1]. In the study of Seethala et al. [6], FNA and FS are complementary methods, and FS is most useful for assessing nondiagnosticly interpreted cases of FNA, as well as to confirm malignancy in some cases and evaluation of resection margins. According to our results, both diagnostic methods are important in the diagnosis of lesions of the salivary glands. Based on the literature data and experiences in our sample, the diagnostic algorithm for lesions in salivary glands requires clinical examination, radiological examination and FNA [1, 8]. In cases where FNA was interpreted as atypical, suspicious, or in cases of discrepancy between the findings of FNA and clinical and/or radiological findings the FS is indicated. A proposal for the treatment of patients with verified lesions in salivary glands is shown in Figure 5.

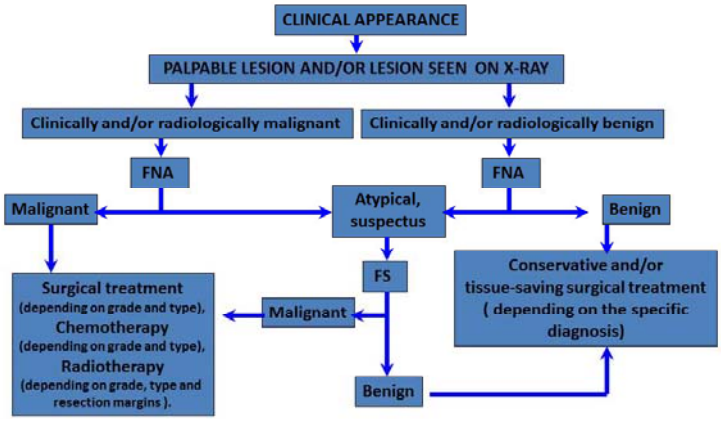

Fig. 5 – The diagnostic algorithm of the salivary glands lesions – treatment of palpable or radiologically detected lesions in the salivary glands [22].

The differences in the presented overall accuracy of FNA of salivary glands are consequences of classification of lesions in the salivary glands, the quality of the sample and the experience of the cytopathologist. FNA is very accurate in determining the diagnosis of certain neoplasms (e.g, tumor mixtus, Warthin's tumor, etc.), but is less effective in the definitive determination of other neoplasms (e.g, basal cell carcinoma, epithelial-myoepithelial carcinoma) [8, 27].

Rapid diagnosis during surgery (FS) was performed in 23 (64%) of the patients. The interpretations were: benign lesions in 21 of the cases, and malignant lesions in two cases. Matching of FS reports in terms of the nature of the lesion and definitive

Conclusion

The obtained results confirm that fine needle aspiration is a sensitive, reliable diagnostic method for differentiation of lesions in the salivary glands. Fine needle aspiration is highly accurate in distinguishing benign from malignant lesions in the salivary glands, and less accurate in determining the specific diagnosis. It be applied in the process of diagnosing of palpable or otherwise visualized lesions in the salivary glands. Fine needle aspiration in combination with clinical and radiological data will enable the establishment of a specific diagnosis in most of salivary gland lesions.

In cases where a definite differentiation in FNA samples is not possible, where there is a need to assess the resection margins and invasion of anatomical structures, frozen section diagnosis is recommended.

Both methods, fine needle aspiration and frozen section diagnostics, are important in evaluating lesions in the salivary glands.

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