A retrospective review of 139 major and minor salivary gland tumors

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ABSTRACT

Aim To describe demographic and histomorphological characteristics of 139 patients with epithelial salivary gland tumors in the Southeastern Serbia population.

Methods A total number of 139 patients with epithelial tumors arising in major and minor salivary glands in the period 2010-2012 was evaluated. After standard tissue proceeding, the routine haematoxylin-eosin (HE) and histochemical alcian blue-periodic acid-Schiff (AB-PAS) methods were used for histomorphological examination.

Results Among 139 patients, 102 (73.38%) had benign, and 37 (26.62%) malignant tumors. The majority of tumors were localized in the parotid gland, in 117 (84.17%) patients. Among benign tumors there were 50 (49.02%) pleomorphic adenoma, 48 (47.06%) Warthin’s tumor, two (1.96%) myoepithelioma, and two (1.96%) oncocytoma. In the group of malignant tumors the most common was mucoepidermoid carcinoma, in 12 (32.43%) patients, carcinoma ex pleomorphic adenoma in six (16.22%), adenoid cystic carcinoma in five (13.51%), and oncocytic carcinoma in three (8.11%) patients.

Conclusion Benign tumors were more common than malignant ones, with predominance of pleomorphic adenoma. Malignant tumors are less common than benign in the large salivary glands, and more common in the minor salivary glands. Histochemical AB-PAS method helps in the diagnosis of mucinous salivary gland carcinoma.

Key words: benign, carcinoma, epidemiology, histopathology.
INTRODUCTION

Salivary gland tumors can show a striking range of morphological diversity among different tumor types and sometimes within an individual tumorous mass. In addition, hybrid tumors, dedifferentiation and propensity for some benign tumors to progress to malignancy can confound histopathological interpretation. These features, together with the relative rarity of a number of tumors (1), can sometimes make diagnosis difficult. There is some geographic variation and among different ethnic groups according to the place of residence (2-5). Therefore, the global annual incidence, when all salivary glands tumors were considered, varied from 0.4–13.5 cases per 100,000 population (6). The frequency of malignant salivary neoplasm range from 0.4–2.6 cases per 100,000 population (7). Between 64% and 80% of all primary tumors occur in the parotid gland, 7%–11% in the submandibular glands, and 9%–23% occur in the minor glands (6,8). Females are more frequently affected (2). The mean ages of patients with benign and malignant tumors is 46 and 47 years, respectively (3,9).

The aim of this study was to investigate both demographic and histomorphological characteristics of epithelial salivary gland tumors of 139 patients over a period of three years, and to compare findings with results of other studies. The purpose of this paper is to contribute to more accurate diagnosis of a lesion of salivary glands.

PATIENTS AND METHODS

The study included 139 patients with epithelial salivary gland tumors arising in the major and minor salivary glands, selected from the medical files of the University Hospital, Department of Maxillofacial Surgery, and the Institute of Pathology of the University Medical Center Niš, Serbia, from the beginning of 2010 to the end of 2012. The following parameters were analyzed: patient age and gender, distribution of tumors in relation to malignancy (benign or malignant), as well as the localization in salivary glands (minor glands, parotid gland, submandibular glands, sublingual glands).

After standard tissue proceeding, routine hematoxylin-eosin (HE) and histochemical alcian blue-periodic acid-Schiff (AB - PAS) methods were used for histomorphological examination. The results were statistically analyzed using descriptive and quantitative analysis, the arithmetic mean (X) and standard deviation (SD). The difference in the average values was calculated using the t-test for two independent samples. The association between the two marks was measured using the $\chi^2$ test. The Pearson’s rank correlation test was used to determine a relation between the associated parameters. The threshold for statistical significance was taken at $p \leq 0.05$.

RESULTS

During the span of 3 years, 139 cases of salivary glands tumors were diagnosed. Among these, 73 (52.52%) patients were females (56 benign and 17 malignant), and 66 (47.48%) were males (46 benign and 20 malignant); 102 (73.38%) were benign and 37 (26.62%) malignant tumors (Tables 1-3). The mean age of the patients was 51.2 ± 13.97 years for benign tumors, and 58.97 ± 10.35 years for malignant tumors. In the group of benign tumors, the youngest patient was a 16-year-old female with pleomorphic adenoma in the right parotid gland. The oldest patient was 80-year-old male with pleomorphic adenoma of the left parotid gland. In the series of malignant tumors, the youngest patient was also female, 43-year old, with mucoepidermoid carcinoma of the right submandibular gland. The oldest patient was a 81-year-old male, who was diagnosed with adenoid cystic carcinoma of the right submandibular gland.

Localization of tumors in the major (parotid, submandibular and sublingual glands) and minor salivary glands is presented in Table 1.

Examining the correlation between types of tumors (benign or malignant) and their localization in the salivary glands (minor glands, parotid gland, submandibular glands, sublingual glands) a statistically significant difference was found ($p<0.0001$) (Table 1).

<table>
<thead>
<tr>
<th>Type of tumor</th>
<th>Minor glands</th>
<th>Parotid gland</th>
<th>Submandibular glands</th>
<th>Sublingual glands</th>
<th>Total</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign</td>
<td>3 (2.94%)</td>
<td>97 (95.10%)</td>
<td>2 (1.96%)</td>
<td>0</td>
<td>102</td>
<td>73.38%</td>
</tr>
<tr>
<td>Malignant</td>
<td>11 (29.73%)</td>
<td>6 (54.05%)</td>
<td>6 (16.22%)</td>
<td>0</td>
<td>23</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total</td>
<td>14 (10.07%)</td>
<td>117 (84.17%)</td>
<td>8 (5.76%)</td>
<td>0</td>
<td>139</td>
<td>37</td>
</tr>
</tbody>
</table>

Table 1. Distribution of tumors in the salivary glands
The most frequent tumors originated from the parotid gland (97 benign and 20 malignant), followed the submandibular gland (2 benign and 6 malignant) and minor salivary glands (benign 3 and malignant 11). The majority of tumors, both benign and malignant, was localized in the parotid gland, 117 (84.17%). The most frequent tumors in minor salivary glands were malignant, 11 (78.57%). Benign lesions were localized in parotid gland, in 97 (95.10%) patients (69.78% of all tumors), and only 20 (54.05%) malignant lesions (14.39% of all tumors) were localized in the parotid gland. No tumor was implicated from sublingual major salivary gland.

There was no statistically significant association between tumor type and gender (p>0.05). Patients with malignant tumors were significantly older than patients with benign tumors (p<0.05). In both, benign and malignant tumors, there was no significant difference considering the localization (right/left) (p>0.05).

Among 102 (73.38%) benign tumors, there were 50 (49.02%) pleomorphic adenoma, 48 (47.06%) Warthin’s tumor, and myoepithelioma and oncocytoma, two (1.96%) of each (Table 2). The ma-
jority of the benign tumors were located in the parotid glands, in 97 (95.10%) cases.

The most common histological types (overall prevalence was 62.16%, e.g., 23 cases) were mucocoeptidermoid carcinoma which were reported in 12 (32.43%) cases, carcinoma ex pleomorphic adenoma in six (16.22%) cases, adenoid cystic carcinoma in five (13.51%) cases, followed by oncocytic carcinoma, in three (8.11%), myoepithelial carcinoma in two (5.41%), cystadenocarcinoma in two (5.41%), squamous cell carcinoma in two (5.41%), basal cell adenocarcinoma in two (5.41%), squamous cell carcinoma in two (5.41%) cases. Small cell carcinoma, salivary duct carcinoma, and mucinous adenocarcinoma were uncommon, in one (2.70%) case each, respectively. Most of the tumors in the minor salivary glands were malignant, 11 (78.57%) (Table 1 and 3).

The most common histologic appearance of benign and malignant tumors is presented in Figure 1 and 2.

**DISCUSSION**

This paper describes the epidemiological and histomorphological features of 139 epithelial tumors of the salivary glands, with reference to their surgical treatment. Our results are similar to other reports in relation to age, sex and localization of the tumors (2,9,10).

In this series, the most common benign tumor was pleomorphic adenoma, localized mostly in the parotid glands, mostly affecting women. Pleomorphic adenoma is a benign tumor, but recurrence appears very often (10). Recurrences can be explained by the growth of the tumor around the facial nerve, which complicates its surgical extirpation (11,12), or they arise as complications of multicentric growth of pleomorphic adenoma (1). The recurrence increases the risk to malignant alteration of pleomorphic adenoma (11,13). Warthin’s tumor was more common in our series, localized in the parotid gland without malignant alteration. In some reports, this is one of rare variants of epithelial salivary gland tumors (14). The discrepancy in the frequency could be explained by geographical, racial factors, as well as aggravated differential diagnosis with metastatic adenocarcinoma tumors in the lymph nodes, that is induced by its mixed lymphoid-glandular structure (3,4,15-17).

Cancers of the salivary glands are less common than benign forms in this study. A higher incidence of malignant tumors, compared to the results of other authors (14,18), could be explained by the profile of patients treated in our institution of tertiary level, as pointed out by the others (19).

The microscopic pattern of malignant salivary gland tumors is sometimes very similar to benign tumors, therefore, the differentiation is difficult (6,8,20). The specific criteria of malignancy include anaplasia, infiltration of the capsule to surrounding tissue or the absence of a capsule, multiple foci of necrosis and hemorrhage, lymphangio invasion, as well as perineural invasion inside the tumor. The most important characteristic of malignant tumor is the involvement of the regional lymph nodes, that we found in our malignant salivary gland tumors (7).

According to the results of this study, the most common was mucoepidermoid carcinoma, reported in 12 cases. Contrary to the literature that
mucoepidermoid carcinoma is frequently located in the minor salivary glands (20), we have found that the mucoepidermoid carcinoma is more frequently presented in the parotid gland and submandibular glands. Carcinoma ex pleomorphic adenoma was second in frequency, which is directly related to the long-standing pleomorphic adenoma and its recurrences. Inexplicable manifestation of metastasizing benign mixed tumor with local or distant metastasis ("metastasizing pleomorphic adenoma") has been described in the new WHO histological classification of tumors of the salivary glands (1). Differential diagnosis of the metastatic adenocarcinoma of surrounding organs from primary salivary gland adenocarcinoma is very difficult (21,22). Due to these characteristics, it is emphasized that pathognomonic finding of primary adenocarcinoma of the salivary gland is the presence of polymorphic adenoma or healthy salivary gland tissue in its vicinity (23). Adenoid cystic carcinoma reported in this study was localized in the small salivary glands, oncocytic carcinoma in the parotid glands, and in the minor salivary glands. In terms of localization and frequency, this is in accordance with data from the literature (24,25).

Other cancers, myoepithelial carcinoma, cystadenocarcinoma, squamous cell carcinoma and basal cell carcinoma were far less frequently found in this study. Myoepithelial carcinoma and cystadenocarcinoma were discovered in the minor salivary glands, while squamous and basal cell adenocarcinoma were found in the parotid gland (5,25).

In conclusion, this study is the first epidemiological study on salivary gland tumors performed on the population from Southeastern Serbia, based on the 2005 WHO tumor classification. The findings of this study contribute significantly to the awareness of clinical and pathological features of salivary gland tumors in our region and can improve our understanding of significant differences in the global distribution of salivary gland tumors which have been reported. Although, the reason for these differences remains unclear, further investigations specifically searching for the possible causes, are greatly encouraged.

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**TRANSPARENCY DECLARATIONS**

Conflict of interest: none to declare.


Retrospektivni pregled 139 tumora malih i velikih pljuvačnih žlezda

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SAŽETAK

Cilj Opisati demografske i histomorfološke karakteristike 139 slučajeva epitelijalnih tumora pljuvačnih žlezda u populaciji jugoistočne Srbije.


Rezultati Studija je obuhvatila 139 slučajeva, odnosno 102 (73,38%) benigna tumora i 37 (26,62%) malignih lezija. Većina tumorâ bila je lokalizovana u parotidnim žlezdama, u 117 (84,17%) slučajeva. Među benignim tumorima bilo je 50 (49,02%) slučajeva pleomorfnog adenoma, 48 (47,06%) Warthino-vog tumora i po dva slučaja (1,96%) mioepitelioma i oncocitoma. U grupi malignih tumora najčešći je bio mukoepidermoidni karcinom, u 12 (32,43%) slučajeva, carcinom ex pleomorphic adenoma u šest (16,22%), adenoidni cistični karcinom u pet (13,51%) i adenocytic carcinom u tri (8,11%) slučaja.

Zaključak Benigni tumori pljuvačnih žlezda su češći nego maligni, uz dominaciju pleomorfnog adenoma. Maligni tumori su se ređe od benignih javljali u velikim pljuvačnim žlezdama, a češće su bili lokalizovani u malim pljuvačnim žlezdama. Histohemijska AB-PAS metoda pomaže u diagnozi mucinous karcinoma pljuvačnih žlezda.

Ključne reči: benigni, maligni, epidemiologija, histopatologija.