

# Histopathological features of salivary gland tumors: A single-center experience

 Fatma Senel,  Hatice Karaman

Department of Pathology, Kayseri City Hospital, Kayseri, Turkey

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## Abstract

**Aim:** This study's goal was to retrospectively evaluate cases who were diagnosed with primary salivary gland tumors in our center, to examine the histopathological features of these tumors, and to reveal difficulties in the differential diagnosis.

**Material and Methods:** Sixty-four patients who applied to our center with complaints of pain and swelling in the salivary gland region between January 2016 and February 2020 and who were diagnosed with salivary gland tumor in our pathology clinic were analyzed retrospectively. The age and sex of the patients, the salivary gland where the tumor was located, and the histopathological examination results were recorded.

**Results:** The age range of the patients was 13-89 years, and 57.8% and 42.2% of 64 patients in total were female and male, respectively. While 86% of the patients had tumors located in the parotid gland, 14% of them had tumors located in the submandibular gland. According to the histopathological examination results, 89% and 11% of the patients had benign and malignant tumors, respectively. While the most common tumor among benign tumors was a pleomorphic adenoma at a rate of 57.8%, the most common tumor among malignant tumors was a mucoepidermoid carcinoma at a rate of 4.7%.

**Conclusion:** In the present study, salivary gland tumors were more common in females. The majority of salivary gland tumors were located in the parotid gland, and the majority of them were benign. The majority of tumors located in the submandibular gland were malignant.

**Keywords:** Histopathology; salivary gland; tumor

## INTRODUCTION

Salivary gland malignancies are rare entities that contribute to approximately 5% of head and neck malignancies (1). These tumors are most commonly observed between the ages of 20 and 60 years (2).

Although the etiology of salivary gland tumors is not fully known, infections, smoking, traumatic and obstructive cause, radiation, and genetic factors are considered to be responsible for their etiology (3,4).

Patients with salivary gland tumors usually consult the doctor due to a noticeable swelling in front of the ear or under the chin. Pain and peripheral nerve involvement are rare symptoms (5).

The most common benign salivary gland tumor is a pleomorphic adenoma, and the most common malignant salivary gland tumor is a mucoepidermoid carcinoma (6). Chronic non-specific or specific sialadenitis takes an essential place in non-neoplastic salivary gland masses (7).

Large behavioral patterns of salivary gland tumors, a difficult preoperative histopathological diagnosis, and

the direct association of the frequency of recurrence with surgical interventions customize the treatment of these tumors (5).

In this study, 64 patients who were diagnosed with primary salivary gland tumor in our clinic were analyzed retrospectively. This study is important because it reflects the histopathological situation of salivary gland tumors in Turkey.

## MATERIAL and METHODS

Sixty-four patients diagnosed with primary salivary gland tumor in our center between January 2016 and February 2020 was included in the study. Patients who were diagnosed with chronic sialadenitis and sialolithiasis were not included in the study. The histopathological examination results of 64 patients were evaluated. The parameters of patients, such as the patients' age, sex, tumor localization, histopathological diagnosis, lymph node metastasis, and recurrence, were recorded.

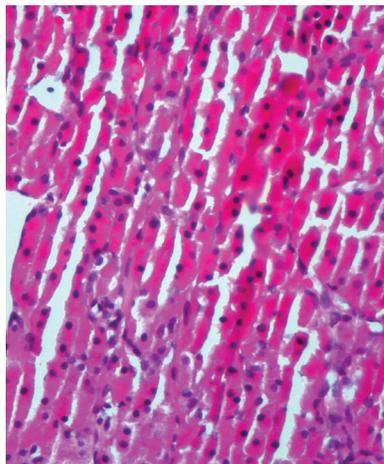
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**Corresponding Author:** Fatma Senel, Department of Pathology, Kayseri City Hospital, Kayseri, Turkey

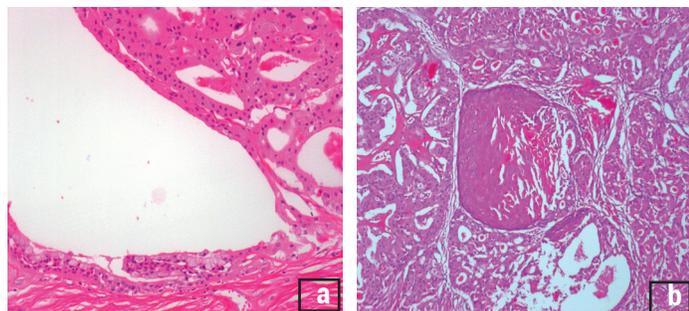
**E-mail:** drfatmasenel2@gmail.com

## RESULTS

The age range of the patients was 13-89 years, and 37 (57.8%) and 27 (42.2%) of 64 patients in total were female and male, respectively. While 55 (86%) of the patients had tumors located in the parotid gland, 9 (14%) of them had tumors located in the submandibular gland. According to the histopathological examination results, 57 (89%) of tumors were benign. While the most common tumor among benign tumors was a pleomorphic adenoma in 37 patients (57.8%), other benign tumors were a Warthin tumor at a rate of 29.7% (19 cases) and an oncocytoma at a rate of 1.5% (1 case) (Figure 1), respectively. While 7 of the patients (11%) had malignant tumors, the most common tumor among malignant tumors was a mucoepidermoid carcinoma in 3 cases (4.7%) (Figure 2a, b). Other malignant tumors were an adenocarcinoma, NOS at a rate of 1.5% (1 case) (Figure 3), epithelial-myoepithelial carcinoma at a rate of 1.5% (1 case) (Figure 4), acinic cell carcinoma at a rate of 1.5% (1 case) (Figure 5), and small cell neuroendocrine carcinoma at a rate of 1.5% (1 case) (Figure 6 a, b, c), respectively (Table 1).



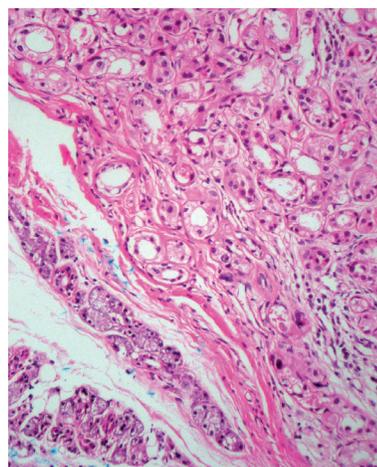
**Figure 1.** Oncocytoma consisting of eosinophilic or clear monotonous cells (HEX40)



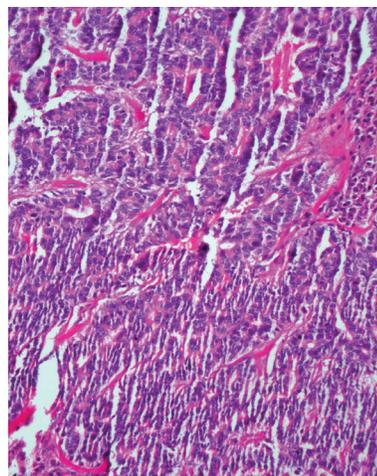
**Figure 2.** a) Mucocytic cells in mucoepidermoid carcinoma (HEX40), b) Squamous cell island in mucoepidermoid carcinoma (HEX40)

The patient with small-cell neuroendocrine carcinoma, one of the malignant tumors, underwent left neck dissection simultaneously with tumor surgery, and twenty-seven metastatic lymph nodes were detected. Radiotherapy was administered to this patient because the tumor

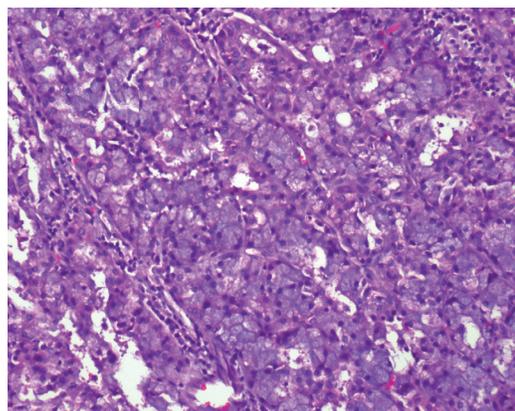
surgical margin was positive. A lymph node metastasis was detected in the neck lymph node dissection of one mucoepidermoid carcinoma case. One patient with a Warthin tumor, one of the benign tumors, was re-operated due to recurrence after 1.5 years. All of the patients are alive.



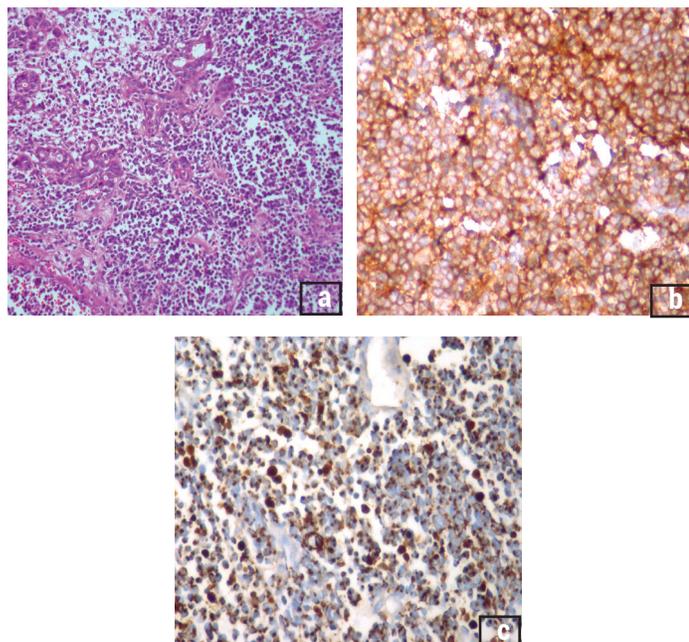
**Figure 3.** Adenocarcinoma, NOS case with adenoid structures (HEX40)



**Figure 4.** Epithelial- myoepithelial carcinoma forming spindle cell islands and nests



**Figure 5.** Acinic cell carcinoma consists of cells similar to the acini of the salivary gland (HEX40)



**Figure 6.** a) Small cell neuroendocrine carcinoma consists of solid tumor tumor islands that infiltrate the salivary gland (HEX20) b) NSE positivity in immunohistochemistry in small cell neuroendocrine carcinoma (IHCX40) c) Pancytokeratin positivity in immunohistochemistry in small cell neuroendocrine carcinoma (IHCX40)

Table 1. Histopathological characteristics of salivary gland tumor cases	
	Total (n=64) (%)
<b>Age, (range) (13-89)</b>	
<b>Sex</b>	
Female	37 57.8 %
Male	27 42.2 %
<b>Tumor localization</b>	
Parotid gland	55 86 %
Submandibular gland	9 14 %
<b>Benign</b>	57 89 %
<b>Malign</b>	7 11 %
<b>Tumor types</b>	
Pleomorphic adenoma	37 57.8 %
Warthin tumor	19 29.7 %
Oncocytoma	1 1.5 %
Mucoepidermoid carcinoma	3 4.7 %
Adeno carcinoma, NOS	1 1.5 %
Acinic cell carcinoma	1 1.5 %
Epithelial-myoeplithelial carcinoma	1 1.5 %
Small cell neuroendocrine carcinoma	1 1.5 %

## DISCUSSION

Salivary gland tumors histopathologically have a very wide range. Different biological behaviors may be observed even in the same tumor type (8).

The most common malignant tumor in the salivary gland is a mucoepidermoid carcinoma (9). In this study, the most common malignant salivary gland tumor was a mucoepidermoid carcinoma at a rate of 4.7%. The most common benign salivary gland tumor was a pleomorphic adenoma, and it constituted 69% of all salivary gland tumors (10). In this study, the most common benign salivary gland tumor was a pleomorphic adenoma at a rate of 57.8%. In the literature, the incidence of Warthin tumors is reported to be between 15 % (11). In this study, the incidence of Warthin tumors was 29.7%, which was quite high compared to the literature.

A general rule in clinical practice is that the smaller the salivary gland is, the more likely the tumor is malignant. Of tumors in the parotid gland, 20-25% is malignant. The malignancy rate is 40% for submandibular gland tumors and more than 90% for sublingual gland tumors (12,13). In the current study, 12.3% of benign tumors and 28.6% of malignant tumors were located in the submandibular gland.

The correct differential diagnosis of salivary gland tumors is a prerequisite for the determination of their prognosis.

Cases with pleomorphic adenoma with pronounced epithelial differentiation should be separated from adenoid cystic carcinoma cases (14). The presence of squamous metaplasia along with mesenchyme-like areas shifts the diagnosis to pleomorphic adenoma, and the presence of perineural invasion shifts the diagnosis to adenoid cystic carcinoma.

The differential diagnosis of solid-type adenoid cystic carcinoma from basal cell adenocarcinoma should be made. The presence of peripheral palisation, the rarity of squamous metaplasia and ductus-like structures, and the presence of the basement membrane-like material surrounding the tumor islands should be interpreted in favor of basal cell adenocarcinoma. In the immunohistochemical examination, epithelial cells that are present in adenoid cystic carcinoma are cytokeratin, EMA, and CEA-positive. Myoepithelial cells are S100, actin-positive (15). CK7 is positive, while CK20 and actin are negative in basal cell adenocarcinoma (16). Oncocytoma, mucoepidermoid carcinoma, kidney and thyroid carcinoma metastases should be considered in the differential diagnosis of acinic cell carcinoma. Acinic cell carcinoma consists of cells that are similar to the acini of the salivary gland. Immunohistochemically, they are cytokeratin-positive. They may be vimentin, S100-positive (17). Clear cell-rich tumors such as clear-cell carcinoma, sebaceous carcinoma, mucoepidermoid carcinoma, acinic cell carcinoma, and renal cell carcinoma should be kept in mind in the differential diagnosis of epithelial-myoeplithelial carcinoma. In epithelial-myoeplithelial carcinoma, epithelial cells are stained with keratin, and myoepithelial cells are stained with actin (18). Oncocytoma can also be confused with epithelial-myoeplithelial carcinoma, but there is no biphasic cell population in oncocytoma (19).

Adenoid cystic carcinoma, pleomorphic adenoma, and basal cell adenocarcinoma should be considered in the differential diagnosis of polymorphous adenocarcinoma. While adenoid cystic carcinoma shows significant nuclear hyperchromasia, it is minimal in polymorphous adenocarcinoma (20).

Small-cell neuroendocrine carcinoma is quite rare in the salivary gland, and it is a high-grade tumor with poor prognosis. In the histopathological examination, solid tumor islands were observed to consist of atypical cells without nucleolus forming trabecular structures. Mitosis and necrosis are common. Immunohistochemically, they are NSE, synaptophysin, chromogranin, and cytokeratin-positive. Adenoid cystic carcinoma, lymphoma, melanoma, and metastasis from the lung should be considered in the differential diagnosis (19).

Mucoepidermoid carcinomas should be differentiated from squamous cell carcinoma and acinic cell carcinoma. Cytokeratin expression is observed in mucoepidermoid carcinoma, which is mucicarmen-positive in mucoid areas (21). Mucoepidermoid carcinoma can also be confused with adenosquamous carcinoma. Adenosquamous carcinoma has high-grade nuclear properties (22).

There were three patients with mucoepidermoid carcinoma in our study. One of these patients was a case of mucoepidermoid carcinoma with diffuse oncocytic differentiation. This tumor can be confused with oncocytic carcinoma. In our case, oncocytic areas were dominant, and a mucoepidermoid carcinoma was suspected in a small area. Therefore, numerous macroscopic sampling was performed from the tumor, and focal mucoepidermoid carcinoma areas were detected. Thus, macroscopic sampling should be performed well, and it is important to take a large number of macroscopic samples, especially in malignant tumors.

In our cases, superficial parotidectomy was applied to the masses in the parotid superficial lobe, and a total parotidectomy was applied to the masses in the deep lobe. The patients with submandibular gland location underwent submandibular gland excision. One mucoepidermoid carcinoma case with palpable lymph nodes in the neck and one case with small-cell neuroendocrine carcinoma underwent neck dissection.

## CONCLUSION

In the present study, salivary gland tumors were more common in females. The majority of salivary gland tumors were located in the parotid gland, and the majority of them were benign. The majority of tumors located in the submandibular gland were malignant.

The final diagnosis of salivary gland tumors is made by a histopathological examination. Accordingly, the most appropriate treatment should be selected, and patients should be closely monitored if necessary. It is necessary to be careful in the differential diagnosis of salivary gland tumors, and macroscopic sampling should be performed well, especially in malignant salivary gland tumors.

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