Salivary Gland Tumors: a Ten-Year Retrospective Analysis in a Brazilian Teaching Hospital

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Tumores de Glândulas Salivares: Análise Retrospectiva de Dez Anos em um Hospital Escola Brasileiro

Tumores de las Glándulas Salivales: Análisis Retrospectivo de Diez Años en un Hospital de Enseñanza Brasileño

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ABSTRACT

Introduction: The tumors affecting salivary glands have a wide morphological diversity. **Objective:** This study aimed to examine the prevalence of salivary gland tumors in patients treated at São Lucas Teaching Hospital at the Pontifical Catholic University of Rio Grande do Sul (HSL-PUCRS), in Porto Alegre (RS), Brazil, from 2007 to 2016. **Method:** A retrospective study analyzing 201 files from the Department of Pathology at the HSL-PUCRS was carried out, by revising the medical records. **Results:** Seventy-three cases of salivary gland tumors were found, and their electronic and physical medical records were analyzed. Of the 73 cases, 56 (76.7%) were benign tumors and 17 (23.3%) were malignant tumors. The age group with the highest number of cases was between 41 and 60 years of age and the highest prevalence was found in females, with 54.8% of the cases. The parotid gland presented the highest prevalence, accounting for 72.6% of the cases. The predominant neoplasia was the pleomorphic adenoma, accounting for 53.4% of the tumors. The standard of distribution of neoplasms of salivary glands was similar to the encountered in other Brazilian regions**. Conclusion:** The largest salivary glands were the most affected by neoplastic processes. Pleomorphic adenoma and adenoid cystic carcinoma were the most frequent benign and malignant tumors, respectively, and parotid gland was the most affected site. In the light of previous literature data, the results allow to infer that some demographic characteristics (for example, sex and age) vary among the different geographic regions.

Key words: Salivary Gland Neoplasms; Salivary Glands, Minor; Parotid Gland; Adenoma, Pleomorphic; Head and Neck Neoplasms.

RESUMO

Introdução: Os tumores que afetam as glândulas salivares apresentam vasta diversidade morfológica. **Objetivo:** Identificar a prevalência de neoplasias de glândulas salivares em pacientes atendidos no Hospital São Lucas da Pontifícia Universidade Católica do Rio Grande do Sul (HSL-PUCRS), em Porto Alegre (RS), no período de 2007 a 2016. **Método:** Estudo retrospectivo por meio da análise de 201 arquivos do Departamento de Patologia do HSL-PUCRS. **Resultados:** Foram encontrados 73 casos de neoplasias de glândulas salivares e os prontuários eletrônicos e físicos dos casos selecionados foram analisados. Dos 73 casos, 56 (76,7%) eram de neoplasias benignas e 17 (23,3%) de neoplasias malignas. A faixa etária com maior número de casos foi entre 41 e 60 anos e o sexo feminino apresentou a maior prevalência com 54,8%. A glândula parótida apresentou maior prevalência, perfazendo 72,6% dos casos. O tipo neoplásico mais prevalente foi o adenoma pleomórfico, com 53,4%. O padrão de distribuição das neoplasias de glândulas salivares foi semelhante ao encontrado em outras Regiões do Brasil. **Conclusão:** As glândulas salivares maiores foram as mais afetadas pelos processos neoplásicos. Adenoma pleomórfico e carcinoma adenoide cístico foram os tumores benignos e malignos mais frequentes, respectivamente, e a glândula parótida foi o local mais acometido. Com base na literatura prévia, esses resultados permitem inferir que algumas características demográficas (por exemplo, sexo e idade) variam entre as diferentes Regiões geográficas.

Palavras-chave: Neoplasias das Glândulas Salivares; Glândulas Salivares Menores, Glândula Parótida; Adenoma Pleomorfo; Neoplasias de Cabeça e Pescoço.

RESUMEN

Introducción: Los tumores que afectan a las glándulas salivales tienen una amplia diversidad morfológica. **Objetivo:** Identificar la prevalencia de neoplasias de glándulas salivales en pacientes atendidos en el Hospital São Lucas da Pontifícia Universidade Católica do Rio Grande do Sul (HSL-PUCRS), en Porto Alegre (RS), desde 2007 hasta 2016. **Método:** Estudio retrospectivo mediante el análisis de 201 registros del Departamento de Patología de HSL-PUCRS. **Resultados:** Se encontraron 73 casos de neoplasias de glándulas salivales y se analizaron los registros electrónicos y físicos de los casos seleccionados. De los 73 casos, 56 (76,7%) fueron de neoplasias benignas y 17 (23,3%) de neoplasias malignas. El grupo de edad con mayor número de casos fue el de 41 a 60 años, y la mayor prevalencia en mujeres, con 54,8%. La glándula parótida tuvo una mayor prevalencia, constituyendo 72,6% de los casos. El tipo neoplásico más prevalente fue el adenoma pleomorfo, con 53,4%. El patrón de distribución de las neoplasias de glándulas salivales fue similar al encontrado en otras regiones de Brasil. **Conclusión:** Las glándulas salivales mayores fueron las glándulas más afectadas por procesos neoplásicos. El adenoma pleomórfico y el carcinoma adenoide quístico fueron los tumores benignos y malignos más frecuentes, respectivamente y el sitio más afectado fue la glándula parótida. Con base en la literatura previa, estos resultados permiten inferir que algunas características demográficas (por ejemplo, sexo y edad) varían entre las distintas regiones geográficas.

Palabras clave: Neoplasias de las Glándulas Salivales; Glándulas Salivales Menores; Glándula Parótida; Adenoma Pleomórfico; Neoplasias de Cabeza y Cuello.

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INTRODUCTION

The salivary glands are organs of exocrine function, with the unique objective of producing saliva. They comprise three pairs of larger glands, namely, parotid, submandibular and sublingual, in addition to the smaller salivary glands, which are numerous and widely distributed through the mouth and oropharynx[1]. The neoplasms that affect these glands can show a great morphological diversity among the various types of tumors[2-4]. They present an annual incidence ranging from 0.5 to 7 cases per 100,000 individuals[5-8], comprehending less than 9% of head and neck neoplasms[3,9-11]. The tumors affecting these glands are of great relevance, considering the variations in clinical, histological and biological behavior[12-14]. The prognosis of salivary gland tumors correlates directly with the clinical stage of the disease; early diagnosis contributes for a better prognosis[2]. The outcomes depend on the gland affected, the histological changes, and the degree of malignancy. It is also relevant to consider whether the tumor involves the facial nerve, has a fixation on the skin or deep structures, or spreads into the lymph nodes or distant sites[4].

Information on the population profile such as sex age, skin color and kind of salivary gland affected by each type of tumor is of utmost importance for an adequate prevention and treatment planning. To analyze the distribution and characteristics of these tumors in a specific population, local registries are required[15-17]. Therefore, the present study aimed to review the cases of salivary gland tumors at Hospital São Lucas of PUCRS (HSL-PUCRS), from 2007 to 2016. The data obtained might contribute for a better definition of these tumors in the population of Rio Grande do Sul, the southernmost state of Brazil by focusing on specific niches.

METHOD

The present retrospective study was carried out in the case records (convenience sample) of salivary gland tumors at HSL-PUCRS, a teaching hospital located in Porto Alegre, Rio Grande do Sul, Brazil, over a period of 10 years (2007-2016). All cases with a microscopic diagnosis of salivary gland neoplasm were included in the analysis except for recurrent neoplasms, metastases in salivary glands and neoplasms from other primary sites (even when affecting the salivary gland). The cases were derived from biopsies and surgical excisions. The Institutional Review Board of the Pontifical Catholic University of Rio Grande do Sul (protocol number 119754/2016) approved this study. The files of the Department of Pathology and the patient's medical records were analyzed. The search was performed using the records in the following topographies: "parotid gland" and "salivary gland", with the SisHos - Hospital Management System (version: 3.11.19.3). The diagnosis was confirmed by the histology reports. When necessary, the immunohistochemical reports were also analyzed using the ikap.exe system (SS computation; version: Hospital São Lucas 2.141). All records with salivary gland neoplasms had the electronic records reviewed using the SisHos - Hospital Management System, in the field "medical records" and "hospitalization" or, the Liquid Client System (version: 4.4.5). Subsequently, the histopathological reports were analyzed.

The inclusion criteria were histopathological diagnosis of primary salivary gland neoplasms. Exclusion criteria were histopathological diagnosis of non-tumoral pathologies (such as sialoadenitis, cysts, mucocele and other inflammations), recurrences, metastasis in salivary glands and tumors in other primary sites.

The variables of the present study were: diagnostic age; sex; skin color; habits (tobacco, alcohol and/or *mate* tea use); marital status; treatment provided by the Unified Health System – SUS or covered by private health insurance; health general status (presence of comorbidities or history of allergies); clinical features of tumors (histological type, anatomic location); clinical stage (TNM); treatment and city of residence (Porto Alegre – RS, countryside or coastal cities). An Excel spreadsheet was created to perform the descriptive analysis of the data and for purposes of comparison with studies that had already been performed in different Brazilian regions. The variables *mate* tea intake and clinical staging (TNM) were not classified due to the lack of information in the medical records.

RESULTS

Two-hundred-one records from the search carried out on the topographies "salivary gland" and "parotid gland" were found. After histopathological review of the reports, 73 cases were included in the sample. Sixty-seven cases were diagnosed as salivary gland tumor, according to the World Health Organization (WHO)[18] and six cases were from non-WHO classification of salivary gland tumors (Monomorphic adenoma, Undifferentiated carcinoma, Epidermoid carcinoma, and Chondrosarcoma grade II).

Among the 73 cases of salivary gland tumors, the most frequent location was the parotid gland (72.6%), followed by the submandibular gland (21.9%). Tumors in smaller glands were found in 4.1% of the cases, while 1.4% were identified in the sublingual gland. The benign tumors affected parotid (75%), submandibular (21.4%) and minor glands (3.6%). For malignant tumors, 64.7%

of the cases affected the parotid gland and 23.5% affected the submandibular gland; only one case (5.9%) was found in the sublingual gland, as well as in the minor salivary glands (Table 1). The minor salivary glands affected were located at the palate (a myoepithelioma and an adenoid cystic carcinoma) and at the buccal mucosa (pleomorphic adenoma).

Of the 73 cases of salivary gland neoplasms, 56 (76.7%) were benign, whereas 17 (23%) were classified as malignant. Considering the benign tumors, 39 (69.6%) were pleomorphic adenomas and 10 (17.8%) were Warthin tumors. Among the 17 cases of malignant tumors, the most common tumor was the adenoid cystic carcinoma, accounting for six cases (35.3%). Of the 73 cases, 40 occurred in women (54.8%) and 33 in men (45.2%), the male to female ratio was 1:1.21. When analyzing benign and malignant tumors separately, the number of women affected was 30 (53.5%) and 10 (58.8%), respectively. For men, the numbers of benign and malignant tumors were 26 (46.5%) and seven (41.2%), respectively. Most tumors occurred in patients aged between 41 and 60 years. Young adults (21-40 years) were the second group most affected by benign tumors. The most affected group by malignant tumors was older adults (> 61 years), followed by the group aged 41-60 years (Table 2).

For pleomorphic adenomas, 36 of the 39 cases had a record on whether the gland affected was on the right side or the left side, the right side being the most found for the parotid gland. Sixteen cases (41%) of pleomorphic adenoma affected the right side while 10 cases (26%) affected the left side of the parotid gland. Conversely, there was no difference for the submandibular gland, where both sides had 5 cases (13%) each (Figure 1).

The majority of the patients were residents of Porto Alegre (71.2%); the others from countryside cities, coastal cities or even out of the state. The number of patients from SUS (49.3%) was similar to private health-insured patients (50.7%). Regarding the skin color, the majority of patients were Whites (79.5%) followed by

Table 1. Histological types of salivary gland tumors per primary location

	Parotid		Submandibular		Sublingual		Minor	
	n	%	n	%	n	%	n	%
Benign tumors								
Pleomorphic adenoma	28	50	10	17.8	0	0	1	1.8
Basal cell adenoma	1	1.8	1	1.8	0	0	0	0
Myoepithelioma	1	1.8	0	0	0	0	1	1.8
Warthin's tumor	9	16	1	1.8	0	0	0	0
Oncocytoma	1	1.8	0	0	0	0	0	0
Hemangioma	1	1.8	0	0	0	0	0	0
Monomorphic adenoma	1	1.8	0	0	0	0	0	0
Total	**42**	**75**	**12**	**21.4**	**0**	**0**	**2**	**3.6**
Malignant tumors								
Adenocarcinoma NOS	2	11.8	0	0	0	0	0	0
Adenoid cystic carcinoma	1	5.9	3	17.6	1	5.9	1	5.9
Carcinoma ex pleomorphic adenoma	1	5.9	0	0	0	0	0	0
Mucoepidermoid carcinoma	2	11.8	0	0	0	0	0	0
Diffuse large basal cell non-Hodgkin's lymphoma	1	5.9	0	0	0	0	0	0
Undifferentiated carcinoma	1	5.9	0	0	0	0	0	0
Follicular lymphoma grade I	1	5.9	0	0	0	0	0	0
Epidermoid carcinoma	1	5.9	1	5.9	0	0	0	0
Chondrosarcoma grade II	1	5.9	0	0	0	0	0	0
Total	**11**	**64.7**	**4**	**23.5**	**1**	**5.9**	**1**	**5.9**

Caption: Adenocarcinoma NOS = Adenocarcinoma not otherwise specified.

Table 2. Frequency of different types of salivary gland tumors by age group and sex

	n = 73	Female		Male		0-20 years		21-40 years		41-60 years		61-99 years	
	n	n	%	n	%	n	%	n	%	n	%	n	%
Benign tumors													
Pleomorphic adenoma	39	22	39.2	17	30.4	2	3.6	15	26.8	17	30.3	5	8.9
Basal cell adenoma	2	1	1.8	1	1.8	0	0	0	0	1	1.8	1	1.8
Myoepithelioma	2	1	1.8	1	1.8	0	0	0	0	2	3.6	0	0
Warthin's tumor	10	3	5.3	7	12.5	0	0	1	1.8	6	10.7	3	5.3
Oncocytoma	1	1	1.8	0	0	0	0	0	0	1	1.8	0	0
Hemangioma	1	1	1.8	0	0	0	0	0	0	0	0	1	1.8
Monomorphic adenoma	1	1	1.8	0	0	0	0	1	1.8	0	0	0	0
Total	**56**	**30**	**53.5**	**26**	**46.5**	**2**	**3.6**	**17**	**30.4**	**27**	**48.2**	**10**	**17.8**
Malignant tumors													
Adenocarcinoma NOS	2	2	11.8	0	0	0	0	0	0	0	0	2	11.8
Adenoid cystic carcinoma	6	4	23.5	2	11.8	0	0	2	11.8	1	5.9	3	17.6
Carcinoma ex pleomorphic adenoma	1	0	0	1	5.9	0	0	1	5.9	0	0	0	0
Mucoepidermoid carcinoma	2	1	5.9	1	5.9	0	0	0	0	2	11.8	0	0
Diffuse large basal cell non-Hodgkin's lymphoma	1	0	0	1	5.9	0	0	0	0	1	5.9	0	0
Undifferentiated carcinoma	1	0	0	1	5.9	0	0	0	0	0	0	1	5.9
Follicular lymphoma grade I	1	1	5.9	0	0	0	0	0	0	0	0	1	5.9
Epidermoid carcinoma	2	1	5.9	1	5.9	0	0	0	0	1	5.9	1	5.9
Chondrosarcoma grade II	1	1	5.9	0	0	0	0	0	0	1	5.9	0	0
Total	**17**	**10**	**58.8**	**7**	**41.2**	**0**	**0**	**3**	**17.6**	**6**	**35.3**	**8**	**47.1**

Caption: Adenocarcinoma NOS = Adenocarcinoma not otherwise specified.

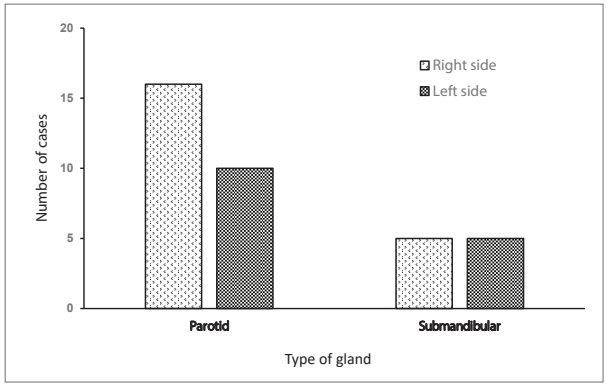

Figure 1. Prevalence of the affected side in cases of pleomorphic adenoma

Blacks (6.8%). As for the records found on habits, eight patients (11%) were smokers and one (1.4%) claimed to intake alcohol beverages daily. Twenty-four patients had some comorbidities, systemic arterial hypertension being the most common (20.6%), and nine patients had a history of allergy (12.3%). The treatment performed for benign tumors was surgical excision of the tumor. For the malignant tumors, only four cases had a record of the treatment, with radiotherapy (2 cases) and chemotherapy (1 case) used alone or combined (1 case). Data are shown in Table 3.

DISCUSSION

Tumors of the salivary glands have a wide morphological diversity[2,15]. The present study analyzed 73 cases of salivary gland tumors diagnosed in a teaching hospital in the city of Porto Alegre. Most of the cases were of benign tumors, in concurrence with other studies[12,13,15,19-26], and different of another study of minor salivary gland tumors[27].

Among the cases analyzed, females were predominant, corroborating previous data of the literature showing a man to woman ratio ranging from 1:1.05 to 1:2[13,20–24,26,28–31]. The major salivary glands were the most affected, mainly the parotid gland, presenting results similar to those described by other Brazilian studies[12,13,15,20-22]. Another similar fact that those studies have with this article is the absence[12,13,15,20,21] of benign tumors affecting the sublingual gland. According to the literature, the sublingual gland is rarely affected by neoplasms, and, when affected, it is usually by malignant neoplasms[32,33], as shown in one

Table 3. Sociodemographic and clinical characteristics of the sample

Variable	n = 73	
Diagnostic age	Mean	SD
	50	16.442
Sex	**n**	**%**
Female	40	54.8
Male	33	45.2
Residence		
Porto Alegre – RS	53	71.2
Countryside or coastal cities – RS	19	26.0
Countryside or coastal cities – SC	1	1.4
Health treatment		
Unified Health System (SUS – Brazil)	36	49.3
Private health insurance	37	50.7
Skin color		
White	58	79.5
Black	5	6.8
Brown	2	2.7
Not informed	8	11.0
Habits		
Smoking	8	11
Alcohol intake	1	1.4
Marital status		
Single	19	26.0
Married	30	41.1
Divorced	4	5.5
Widower/Widow	3	4.1
Not informed	17	23.3
Treatment		
Benign tumor		
Surgical excision	56	100.0
Malignant tumor		
Radiotherapy	2	11.1
Radiotherapy + Chemotherapy	1	5.5
Chemotherapy	1	5.5
Not informed	15	83.3
Comorbidities		
Systemic arterial hypertension	15	20.6
Cardiopathy	3	4.1
Other neoplasm	3	4.1
Allergy	9	12.3
Endocrine disorder	7	9.58
HIV	2	7.7
Asthma	1	1.4
Psychiatric disorder	3	4.1

Captions: SD = standard-deviation; HIV = immunodeficiency virus; SC = State of Santa Catarina.

case. The age ranged from nine to 82 years, with mean of 50 years. The highest incidence for benign tumors was between 41 and 60 years, and over 61 years for malignant tumors. These results are quite dissimilar from the data found in another study, where the greater incidence of salivary gland tumors was seen in younger patients for both benign and malignant tumors, where their majority was diagnosed between 20 and 41 years of age[31], and found in another study conducted with individuals with malignant tumors aged 41-60 years[13]. On the other hand, the results presented are in accordance with a recently published epidemiological study[8].

The pleomorphic adenoma is a mixed benign tumor formed by epithelial and myoepithelial cells arranged in a wide variety of morphological patterns (myxoid, mucoid or chondroid)[2,3]. It was found that the pleomorphic adenoma was the most frequent type of salivary gland tumor, accounting for 53.4% of all tumors and 69.6% of benign tumors. Other studies involving tumors of salivary glands reported similar results, with pleomorphic adenoma representing the most frequent tumor type[8,15,19-22,24-29,31,34-36] and commonly found on the right side. Interestingly, this distribution was observed in the parotid tumors evaluated. The reasons for this remain unknown and new studies are needed to assess whether there was a relationship between the affected side and the masticatory preferred side of the individual.

Cystic adenoid carcinoma was the most prevalent malignant salivary gland tumor (6 cases), representing 8.2% of all tumors and 35.3% of malignant tumors, compatible with what was found in other studies[12,14,15,17,20,22,24,28,30,34]. However, the mucoepidermoid carcinoma, another malignant tumor, was the most prevalent[8,12,14,21,31,35,36] in other studies. Mucoepidermoid carcinoma and adenocarcinoma not otherwise specified (NOS) after cystic adenoid carcinoma, were the second most common tumors found. Another divergence of the results presented was the proportion of glands affected by malignant tumors, where parotid was the most affected followed by submandibular. The sublingual and minor glands were the least affected where each one was only affected once. Previous literature data report that minor salivary glands show a higher prevalence of malignant tumors compared to the major glands[8,12,33-36]. Nevertheless, another study also showed greater involvement of the parotid gland in both malignant and benign tumors[37]. According to Mahomed and Meer[28] discrepancies in studies about the proportion of malignant and benign neoplasms could be attributed to sample characteristics (such as tobacco and drug use, occupational exposure, and immune suppression).

Regarding the treatment choice, all the cases of pleomorphic adenoma reported were treated by surgical excision, in accordance with what is recommended for benign tumors of the salivary glands[3,27]. From the 17 cases of malignant tumors analyzed, the prevalent treatment was radiotherapy, with three registries; nonetheless, there was no description of treatment in most of the cases. This lack of information probably occurred in cases where the patient was referred to another hospital since HSL-PUCRS is not a reference unit for the treatment of head and neck tumors in the city of Porto Alegre.

Because it is a single-center study, this limitation should be highlighted. However, as the low prevalence of salivary glands neoplasms demands long periods of investigation in prospective studies, this could be an obstacle for future clinical trials. In addition, data was collected from medical records and histopathological reports prior to WHO new classification of head and neck tumors[2], therefore, the data comply with the third edition[18], similar to another recent paper[28] published. The latest classification brings new entities like secretory carcinoma which is a neoplasm previously called as mammary analogue secretory carcinoma due to similarity with secretory carcinoma breast that was probably diagnosed as adenocarcinoma NOS or acinic cell carcinoma. In view of that, a review of the histological slides of the two cases of adenocarcinoma NOS, as well as other non-WHO six tumors, would be interesting, but unfortunately it was not possible.

According to data gathered from the literature, it is possible to observe that there are few studies published by Brazilian groups addressing the characterization of cases of salivary gland tumors. Conducting such studies is quite relevant for Dentistry professionals and a better knowledge of these lesions and their presentations may be useful to allow a more effective diagnosis and management. The lack of information in medical records was an obstacle for the analysis conducted, compromising the registration of the data and interpretation of the results. It is relevant to highlight the limited information on habits, base diseases and TNM, among others. The implementation of electronic medical record systems with mandatory fields to be filled out could help to resolve these issues.

CONCLUSION

Considering the data obtained, it is possible to conclude that the largest salivary glands were the most affected by neoplastic processes. Pleomorphic adenoma and adenoid cystic carcinoma were the predominant benign and malignant tumors, respectively, and the most affected site was the parotid gland. In the light of previous literature data, the results allow to infer that some demographic characteristics (for example, sex and age) vary among the different geographic regions.

CONTRIBUTIONS

All the authors approved the final version of the manuscript. Alice Ribeiro designed the study, collected, and analyzed the data, interpreted the results, drafted, and reviewed the manuscript. Ana Luisa Saraiva Homem de Carvalho and Maria Martha Campos designed the study, analyzed the data, interpreted the results, drafted and reviewed the manuscript. Valesca Sander Koth analyzed the data, interpreted the results, and reviewed the manuscript.

DECLARATION OF CONFLICT OF INTEREST

There is no conflict of interests to declare.

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