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OPEN ACCESS JOURNALS

Clinical Case Reports: Open Access

Case Series | Vol 6 Iss 3
ISSN: 2582-5038
https://dx.doi.org/10.46527/2582-5038.263

An Institutional Study of the Salivary Gland Neoplasms: A Case Series and Review of Literature

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Received: June 13, 2023; **Accepted:** June 30, 2023; **Published:** July 07, 2023

Abstract

Objective: Different geographic areas show different frequency and incidence of salivary gland tumors (SGTs) and understanding such a demographic data is useful in knowing the nature of the salivary gland neoplasms worldwide. Not only the demographic data but also the clinical site of occurrence of the tumor, radiological features, staining and IHC are helpful in improving the comprehension of the clinicopathologic characteristics of the SGTs. The aim of the study was to determine the distribution and demographic features of the SGTs in West Godavari, Andhra Pradesh population, India.

Study design: Retrospectively analysis of the clinico-pathological features of all the histologically diagnosed salivary gland tumors of the past 20 years (2002-2022) from the institutional archives with demographic data and site of occurrence was retrieved. This will add information on the diagnosis in the upcoming neoplasms. The study design presents the demographic details which may provide insight of the SGTs worldwide.

Cases presentation: All the relevant demographic and histopathological information regarding the diagnosed cases of salivary gland tumors were retrieved from archival files of the Department of oral pathology, Vishnu Dental College, Bhimavaram, West Godavari, Andhra Pradesh and correlated for clinico-pathological findings. The histological features were re-examined for the assessment of the grade and necessary special staining were performed. The present study analyzed 43 SGTs among them 12 were pleomorphic adenoma, 15 were MECs, 7 were ACCs, 2 myoepitheliomas, 2 adenocarcinomas (of which one was metastatic carcinoma of the mandible), 1 epithelial myoepithelial carcinoma, 1 intra osseous carcinoma, 1 salivary duct carcinoma, 1 depicting both the features of PLGA and adenoid cystic carcinoma and 1 depicting both the features of adenoid cystic carcinoma and epimyoepithelial carcinoma.

Citation: Ranga Raju P, Manyam1 R, Pasupulati S, et al. An Institutional Study of the Salivary Gland Neoplasms: A Case Series and Review of Literature. Clin Case Rep Open Access. 2023;6(3):263.

Aims: 1) To study the frequency of SGT based on the tumor type. 2) To correlate gender, age and anatomic location in different tumor type 3) To analyze benign and malignant tumor location and 4) To recognize various histomorphological patterns of the SGTs.

Results: Among the 43 SGTs 14 were benign constituting 32.56% and 29 were malignant constituting 67.44% with a ratio of 0.48:1. The mean age of occurrence of benign tumors was 40 years where in pleomorphic mean age of occurrence was 42 years and that of myoepithelioma was 28 years. The mean age occurrence of malignant tumors was 45 years where in MEC mean age of occurrence was 41 years and that of Adenoid cystic carcinoma was 41 years. Out of the 43 SGTs 21 were males and 22 were females accounting to male: female ratio 0.95. While benign occurred in the age range of 23 to 62 years malignant occurred in between 14 to 77 years.

Conclusion: Analysis of Salivary gland neoplasms vary in presentation of the demographic details from place to place and region to region. The present data confirms that the PA and MEC are the most common benign and malignant tumors respectively.

Keywords: ***Salivary gland tumors (SGTs); Mucoepidermoid carcinomas (MEC); Pleomorphic adenoma (PA); Adenoid cystic carcinoma (ACC); Polymorphous low-grade adenocarcinoma (PLGA); Immunohistochemistry (IHC)***

1. Introduction

The acinar cells(mucous or serous), the ductal cells(straited duct cell, intercalated duct cell, small excretory duct cell, large excretory duct cell, terminal excretory duct cell), the basal cells(basal cells and basaloid cells), myoepithelial cells (plasmacytoid or hyalin, epithelial or clear, spindle shaped or myoid cells, stellate or myxoid cells) sebaceous cells, oncocyte cells, fat cells and clear cells all of these make the histological diagnosis of salivary gland neoplasms a complicated dilemma when superadded by crystals and various stromal patterns.

The myoepithelial/basket cells gaining various shapes with actinomyosin microfilaments, containing glycogen, lipofuscin and pinocytotic vesicles secrete basement membrane matrix and non-basement membrane matrix making the diagnosis of SGTs furthermore difficult and complicated. The myoepithelial cell identification can be by phosphotungstic acid, hematoxylin and iron hematoxylin, levanol fast cyanine (coomasie blue), silver impregnation or by 12 IHC markers like S100, p63, ki67, ck 14, Glial fibrillary acidic protein, vimentin, h caldesmin, calponin, maspin, metallothioprotein, smooth muscle actin or smooth muscle myosin.

Salivary gland tumors account for 2%-6.5% of all neoplasms of the head and neck region but pose problems due to the rarity, broad morphologic spectrum and histologic overlap among the different tumor types. Hence it is important to understand the basic cytoarchitectural features of each tumor type, in particular whether the tumor shows dual luminal-abluminal cell differentiation, so that the diagnosis can be made logically through the analysis of the cellular components, cell arrangement and the extracellular components. This is achieved by the histology which is considered as the gold standard utilizing various stains like Hematoxylin and eosin, Periodic Acid Schiff, Diastase, Alcian blue, and Mucicarmine and also with IHC markers like Pan cytokeratin, epithelial membrane antigen, carcinoembryonic antigen, calponin, vimentin, p63, Ki67, S100, Glial Fibrillary Acidic protein(GFAP),Smooth muscle actin and others will help to delineate whether there is two cell type

differentiation in tumors with complex architecture. The present study adds salivary gland neoplasms demographic data to the available data in the world wide and may further aid in the diagnosis of SGTs.

SGTs occur in lesser frequency but depict more histopathologic diversity and patterns as shown in Table 1 and 2. Here are the reasons for the continuous change in the classification of SGTs.

1. Periodic redefinition of the nature of the tumors like acinic cell carcinoma and mucoepidermoid carcinoma,
2. The divergence of the new subtypes in histopathology as in oncocytic, oncocytic sebaceous, apocrine, double clear subtypes of epithelial myoepithelial carcinoma and others,
3. The recognition of potentially recent entities like mammary analogue secretory carcinoma, hyalinizing clear cell carcinoma, IgG4 related chronic sclerosing sialadenitis and cribriform carcinoma of tongue.
4. Newer molecular techniques, clinical data and updated clinicopathological correlations will lead to a current classification of SGTs. An extensive and vast impressive increasing knowledge of the cytogenetics, etiopathogenesis, diagnostic variabilities, clinical behavior, various treatment modalities of both the benign and malignant SGTs has emerged in the last few decades.

The epidemiology of the SGTs is not well established though there are many retrospective studies as these studies have been frequently restricted to the specific population of a geographic area, an anatomical location, or a specific tumor type. Various studies have been done on the incidence and histological types of salivary gland tumors from various countries such as Finland and Israel [1], U.K. [2], Tanzania [3], Southern Brazil [4-6], Spain [7,8], Japan [9], Southern Iran [10,11], Bangladesh [12]. Here is one such attempt made in India adding to other series in India. The location of the hospital is in the South India, and which is completely ethnically Indian. Hence the study population is thought to be representative of the Indian population as a whole with minimal bias.

2. Methodology

Clinical data concerning age, gender, and tumor location were gathered from the requisition forms. Histopathological slides of all the cases were reviewed by three independent oral pathologists and if new sections needed, were prepared, and stained with Hematoxylin and Eosin, Periodic Acid Schiff or mucicarmine. The available cases were classified according to 2005 WHO Histologic typing of salivary gland tumors. Analysis of the data available was done to identify the incidence of the SGT type and compile the data on the age and the gender of the patient as well as the distribution of the site of each tumor. Chi-square test and unpaired t test were used for the analysis of the gender and age respectively in the study.

2.1 Pleomorphic adenomas

PAs are the most common benign tumors of the salivary gland in the present study similar to other studies worldwide.

Both the mean and median age of occurrence of PAs is 36 years in the study. The present study indicates that the most common benign and malignant tumors were pleomorphic adenoma and mucoepidermoid carcinomas. Most common site of the pleomorphic lesions was in the hard palate and most commonly seen in the 3rd and the 4th decade.

3. Discussion

Among the 43SGT cases, 21 were male (48.84%) and 22 were female (51.16%)14 were benign among them 6 males and 8 females constituting 42.86% and 57.14% respectively, 29 were malignant among them 15 males and 14 females constituting 51.72% and 48.28% respectively. In the 19-year present study SGTs were among the age range of 14 and 77 years, with mean age of occurrence of 46 years. Benign tumors were noted in the age range of 23 to 62 with the mean age of 43 years and mostly in the second and fourth decade of life. Malignant tumors were noted in the age range of 14 to 77 with the mean age of 46 years and most common in the second and fifth decade of life. The below table represents Pleomorphic adenoma and MEC for more female predilection while Male predilection in the Adenoid cystic carcinoma. Myoepitheliomas and adenocarcinomas have equal predilection for both the sex in the study. The table clearly reveals that in the study MEC is the major tumor to occur with 34.88% and salivary duct carcinoma, epithelial myoepithelial carcinoma, intraosseous carcinoma are the minor tumors to occur with 2.33%. Here is a TABLE 8 presenting the sex predilection of all the 43 SGTs.

TABLE 1.

Benign SGTs	**Histological variants/growth patterns**	**Appearences/Special characteristic features to the tumor**
Pleomorphic adenoma	Recurrent Pleomorphic adenoma, Salivary gland anlage tumor (congenital pleomorphic adenoma)	Swarm of bees,tyrosine crystals in characteristic daisy head pattern by mayers hemalum and tartrazine stain,collagenous crystalloids and intraductal corpora amylacea like condensations
Myoepithelioma	Non myxoid(solid) Myxoid (pleomorphic adenoma type) Reticulartype (canalicular type) Mixed	Spindle shaped cells forming neurilemmoma-like pattern (spindle cell myoepithelioma) Plasmacytoid myoepithelioma.
Basal cell adenoma	Solid, Trabecular, Tubular, Membranous, Stromal rich, Cribriform.	Squamous eddies, whorling pattern Cell nests arranged in large lobules (jigsaw puzzle pattern)
Warthin’s tumor	Coexistent separate tumor,metasis to lymphoid tissue in Wartin’s tumor, Carcinoma ex Wartin’s tumor, maliganant Wartin’s tumor.	concentrate sodium pertechnetate amenable to scintigraphic examination,

Oncocytoma (Mahogany brown) (Concentrate sodium pertechnetate)	Typical oncocytoma Clear cell oncocytoma Hybrid oncocytoma Multifocal nodular oncocytic hyperplasia Diffuse oncocytosis	Serpentine pattern, alveolar pattern,ghost shadow pattern,Organoid pattern of cell clusters that form cords or dough net circular pattern/ configuration. Stippled nuclei
Canalicular adenoma		Tramtrack like double rows of cells, tumor strands are so loose as if appear to be floating in the air. Maize like tubular pattern, Bead on a string form.
Sebaceous adenoma	Microcystic,microcystic+solid,Solid	
Lymphadenoma	Multicystic or solid	
Ductal papillomas	Sialadenoma papilliferum Inverted papilloma Intraductal papilloma	
Cystadenoma and keratocystoma are the other benign tumors of salivary gland.		

TABLE 2.

Malignant SGTs	**Histological variants/growth patterns**	**Appearences**
Acinic cell carcinomas (Peculiar self-destructive with secondaryhemorrhage, lipogranulomatous reaction & cystic degeneration) ostensible capsule	Solid Microcystic Papillary cystic Follicular	Lattice like pattern Hobnailing Serous acinar differentiation with cytoplasmic zymogen secretory granules and salivary ductal cells (Regimented nuclei with reticulated or foamy cytoplasm with violaceous color)

Mucoepidermoid carcinoma	Low grade Intermediate grade High grade	Mucous cells with copious mucin imparting frosted glass appearance cytoplasm
Adenoid cystic carcinoma	Solid Cribriform Tubular	Swiss cheese pattern Lace like pattern, tubules apparently coiled upon themselves producing necklace appearance
Polymorphous low-grade adenocarcinoma	Simple tubules, complex or fused tubules, trabeculae, single cell files, targetoid swirls, solid nests, fasciles, cribriform, papillary or papillary cystic	Indian file arrangement, concentric whirling of cells creating a target like appearance (slate gray blue stroma is characteristic)
Epithelial myoepithelial carcinoma		Verocay like palisading, Double layered duct like structures separated by dense acellular fibrous tissue into theques or nests
Clear cell carcinoma, not otherwise specified	Monomorphic epithelial-myoepithelial carcinoma Glycogen rich squamous cell carcinoma, and Hyalinizing clear cell carcinoma.	
Basal cell adenocarcinoma	Solid, Trabecular, Tubular Membranous	Solid subtypes show mosaic growth patterns
Cystadenocarcinoma	Papillary and nonpapillary	
Salivary duct carcinoma	Sarcomatoid, Mucin rich Invasive micropapillary	Roman-bridge architecture Inside-out staining pattern
Sebaceous carcinoma, Sebaceous lymph adenocarcinoma, Mucinous adenocarcinoma and Oncocytic carcinoma are the other malignant carcinomas of salivary gland origin.		

TABLE 3.

	HP NO.	Age	Sex	Area /site of lesion
1	258/06	35	F	Swelling in the right junction of hard and soft posterior palate
2	274/06	37	F	Swelling in the left neck region (submandibular region)
3	893/10	23	M	Swelling in the left posterior palatal region
4	1572/11	50	F	Swelling in the posterior hard palate
5	4870/11	28	F	Swelling in the right posterior hard palate
6	1611/12	44	F	Swelling in the hard palate i.r.t.14,15,16,17
7	11697/17	62	M	Swelling in the superficial lobe of the right parotid gland
8	12072/17	49	F	Swelling in the posterior hard palate
9	13115/18	48	F	Swelling in the right neck region (submandibular region)
10	13975/19	31	M	Swelling in the right posterior palatal region
11	14005/19	43	M	Swelling in the deep lobe of the left parotid gland
12	14112/20	56	M	Swelling in the midline of the hard palate

TABLE 4. **Mucoepidermoid Carcinomas.**

HP No.	Age	Sex	Type	Site of occurrence
42/04	36	F	Intermediate grade	Intermediate grade
167/06	58	M	High grade	Right lower back tooth region
260/06	45	M	High grade	Left post. Part of palate
545/09	24	F	Low grade	Right max. post palatal region
1710/12	23	M	Clear cell variant low grade	Left max. post palatal region
2367/13	26	F	Intermediate grade	Rt.max.palatal region of 14 to 17
3480/13	26	F	Low grade	Left max post.
3942/13	65	F	Low grade	Rt.post.mand i.r.t. 46,47,48
6254/14	53	M	High grade	Rt.post.mandibular region

7141/15	25	F	High grade	Rt.post.mandibular region
7346/15	45	F	High grade	Lower Right buccal mucosa and alveolar ridge
8530/16	37	F	Low grade	Right maxillary posterior region
	60	M	Low grade	Lower Left retro molar region
	63	M	Intermediate grade	Anterior mandibular alveolar ridge and vestibule
14239/21	25	F	Low grade	Right maxillary palatal region

TABLE 5. **Adenoid cystic carcinomas.**

HP NO.	**Age**	**Sex**	**Area /site of lesion**
234/06	30	F	swelling on left side of palatal area
305/07	25	M	Multiple ulceration in the right patal vault
336/07	45	F	Swelling in the left side buccal mucosa
349/07	55	M	Swelling in the right cheek region
412/08	33	F	Ulceration on the palatal side opposite to 26,27 and also buccal side
607/09	50	M	Swelling in the right middle one third of face
14155/21	65	M	left side of hard palate irt 21 to 27 regions

TABLE 6. **Myoepitheliomas.**

HP NO.	**Age**	**Sex**	**Area /site of lesion**
1435/11	29	F	Swelling in the right posterior palate
802/10	26	M	Swelling in the paraauricular region

TABLE 7. **Other Salivary gland tumors**.

HP NO.	Age	Sex	Area /site of lesion	Type of lesion
541/09	53	M	left posterior 1/3rd of palate	Epithelial Myoepithelial carcinoma
499/08	14	F	Junction of hard and soft palate	PLGA/Adenoid cystic carcinoma
1367/11	77	F	Right parotid gland	Adenocarcinoma
478/08	55	M	swelling in the left region of the mandible	Intraosseous carcinoma
306/07	72	M	left mandibular molar region	Metastatic carcinoma of the mandible/probably adenocarcinoma
11620/17	62	M	unknown	Salivary duct carcinoma
14186/21	49	M	unknown	Epimyoepithelial carcinoma/Adenoid cystic carcinoma

TABLE 8.

Salivary gland tumors	Total no of males	Total no of females	% Of males	% Of females	Total no of cases	% Of tumors
Pleomorphic adenoma	5	7	41.67%	58.33%	12	27.90%
Mucoepidermoid carcinoma	6	9	40%	60%	15	34.88%
Adenoid cystic carcinoma	4	3	57.14%	42.86%	7	16.28%
Myoepitheliomas	1	1	50%	50%	2	4.65%
Adenocarcinomas	1	1	50%	50%	2	4.65%
Epithelial myoepithelial carcinoma	1	0	100%	0	1	2.33%
Salivary duct carcinoma	1	0	100%	0	1	2.33%
Intraosseous carcinoma	1	0	100%	0	1	2.33%

PLGA and adenoid cystic carcinoma	0	1	0	100%	1	2.33%
Epimyoepithelial carcinoma and adenoid cystic carcinoma	1	0	100%	0	1	2.33%

Gender distribution among the groups and chi-square test applied. The chi-square statistic is 0.2971. The p value is 0.585705. Not significant at p<.05. The chi-square statistic with Yates correction is 0.0482. The p value is 0.826228. Not significant at p<.05.

TABLE 9.

Gender	**Type**		
	Malignant	**Benign**	**Total**
Male	15(14.16) [0.05]	6(6.84) [0.1]	21
Female	14(14.84) [0.05]	8(7.16) [0.1]	22
Total	29	14	43

Mean age distribution among the groups and unpaired t test applied. P-value and statistical significance: The two tailed P value equals 0.3717. By conventional criteria, this difference is considered to be not statistically significant. Confidence interval: The mean of benign minus malignant equals -4.62. 95% confidence interval of this difference: From -14.95 to 5.71. Intermediate values used in calculations: t=0.9031, df=41 standard error of difference=5.114

TABLE 10.

Group	**Benign**	**Malignant**
Mean	40.07	44.69
SD	12.01	17.16
SEM	3.21	3.19
N	14	29

The present study states that malignant tumors were more when compared to the benign in the ratio of 29:14 respectively similar to Jimsha Vannathan Kumaran et al [13], Yuichiro Hayashi et al [9]. But the other Indian study's Satish Babu et al [14], Krishnaraj Subashraj et al [15], Shilpa V Uploankar et al [16] showed more benign lesion when compared to the malignant lesions similar to study's [1-4,17], [5,6,8-12,18] suggesting that the geographical and racial factors influence the incidence and

distribution of benign and malignant tumors in the world. Palate was the most common site involved followed by buccal mucosa, floor of mouth, tongue, and alveolar mucosa [19-21].

4. Conclusion

Complex salivary gland lesions sharing common histological features make the diagnosis more difficult. Malignant tumors were more when compared to benign in the present study similar to the study in Puducherry, India.[1] Among the benign tumors pleomorphic was the most common type followed by myoepitheliomas while mucoepidermoid carcinoma was most common in the malignant tumors followed by adenoid cystic carcinomas similar to the other demographic survey.[2] The study concludes that conducting epidemiological surveys based on the latest WHO classification provides clinicopathological co-relations on SGTs that seem to be characteristic even in a small geographic area and conducting further such surveys in India and other Asian countries will be able to help in better understanding of the disease. Though the number of the SGTs presented in the study is small, the age, the sex and the site distribution can help in better understanding of the disease. The demographic details presented in the article can help the surgeons, pathologists, oncologists and those involved in the diagnosis and management of SGTs in determining the optimal treatment approach. The clinical characteristics of this SGT Indian study is similar to those found elsewhere in the world.

Vishnu Dental College Ethical Committee/ Vishnu Dental College Institutional Board has approved the study.

5. Acknowledgement

I thank the faculty members, post graduates, interns and students of Vishnu Dental College, Bhimavaram, Andhra Pradesh, India for the help in the study.

6. Conflict of Interest

None.

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