



Original Research Article

Diversity and diagnostic challenges in salivary neoplasms

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ABSTRACT

Introduction: Salivary gland lesions exhibit a wide spectrum of clinical and morphological diversity. The aim of this study was to evaluate the relative frequencies, types, site, distribution and histomorphological features of salivary gland lesions.

Materials and Methods: A retrospective study for a period of two years was done on 40 cases of salivary gland lesions in the department of pathology at KAPV medical college, Trichy a Tertiary care centre. Cases were analysed based on demographics, anatomical locations and histopathological types. Specimens were fixed in 10% formalin, processed and embedded in paraffin. Sections were stained by hematoxylin and eosin. Histopathological examination was done by microscopy. Special immunohistochemical stains were used for certain rare cases of interest.

Results: Out of 40 cases, 35 cases (87.5%) were neoplastic and 5 cases (12.5%) were non neoplastic. The mean age of presentation was 38.925 (13-67yrs) with equal gender distribution. Regarding the site distribution, Parotid was the common site for location of salivary tumours (18 cases, 45%). Most common benign tumour was pleomorphic adenoma (22 cases, 78.5%) followed by basal cell adenoma (4 cases, 14.2%). Among malignant tumours, mucoepidermoid carcinoma ranks the first (4 cases, 57.1%). One case of Acinic cell carcinoma, adenoid cystic carcinoma with dedifferentiation, and a rare recently described variant mammary analogue secretory carcinoma were also observed.

Conclusion: Histopathology remains the gold standard for diagnosing salivary gland lesions. They have broad morphological spectrum and overlaps between tumour types. Immunohistochemistry serves as an adjunct tool to support histopathological diagnosis. It helps in planning treatment protocols to reduce morbidity and mortality.

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1. Introduction

Salivary gland tumours have limited documented epidemiology and distinct morphological variants. It constitutes 3-10% of head and neck neoplasms.¹ The global incidence of these tumours is 0.4-13.5 per 100000 persons annually.² Salivary gland tumours can occur in any age, more common in adults with slight female predominance.³ Approximately 65-80% of salivary gland tumours are found in parotid gland followed by submandibular (10-15%) and minor salivary glands.⁴ Over all benign tumours outnumber malignant

tumours in salivary gland. The aim of this study was to evaluate the demographic and histomorphologic profile of salivary gland lesions.

2. Materials and Methods

A retrospective study for a period of two years was done on 40 salivary gland specimens in the department of pathology in a tertiary care centre. Specimens were immediately fixed in 10% formalin and processed by paraffin embedding. Sections were stained by hematoxylin and eosin stain. Microscopic examination was done for morphological analysis. Immunohistochemistry was done using the panel

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of markers such as S 100, Smooth muscle Actin (SMA), DOG -1, C- kit, Cytokeratin, Mammoglobin and Ki- 67 in paraffin embedded sections for certain rare cases with diagnostic difficulties.

3. Results

Out of 40 cases, 35 cases (87.5%) were neoplastic and 5 cases (12.5%) were non neoplastic. Chronic sialadenitis was the only non neoplastic lesion observed. Among 35 neoplastic cases, 28(80%) were benign and 7(19.4%) were malignant. The mean age of presentation was 38.925 (13-67 years range) with equal sex distribution. Benign tumours peak in 2nd to 4th decades. Malignant tumours have equal distribution in 2nd, 3rd and 6th decades. Majority of tumours occurred in parotid gland(18,45%) and the rest in submandibular gland (14,35%) and minor salivary gland (8,20%). Most common benign tumour was pleomorphic adenoma (22 cases,78.5%) followed by basal cell adenoma (4 cases, 14.2%). Warthin tumour and myoepithelioma each constitutes 3.57% (1 case) of benign tumours. Most common malignant tumour of salivary gland was mucoepidermoid carcinoma (4 cases, 57.1%). One case of Acinic cell carcinoma, adenoid cystic carcinoma with dedifferentiation and a rare recently described variant mammary analogue secretory carcinoma were also observed.

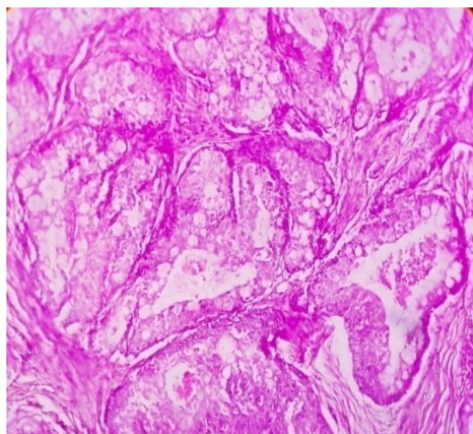


Fig. 1: Mucoepidermoid carcinoma – Cystic spaces lined by mucinous and intermediate type of tumor cells

4. Discussion

Salivary gland disorders represent a wide spectrum of disorders. It ranges from inflammatory disorders to developmental disorders and also neoplasms. In the present study among the salivary lesions there were 12.5% (5 cases) of non neoplastic cases and 87.5% (35 cases) of neoplastic cases with equal gender distribution as shown in the Table 1. Sialadenitis was the only inflammatory lesion observed

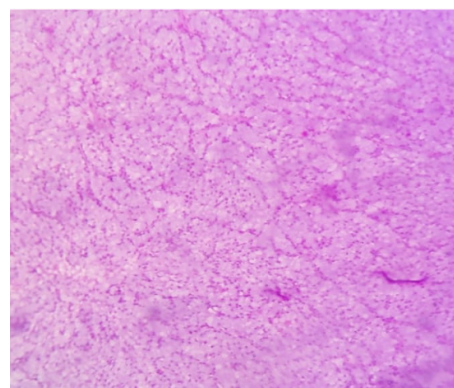


Fig. 2: Acinic cell carcinoma – Tumor cells with basophilic granular cytoplasm in organoid sheets traversed by ramifying delicate blood vessels

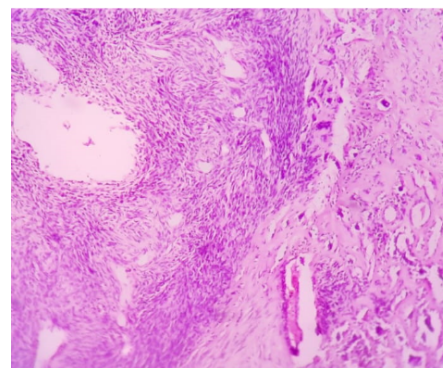


Fig. 3: Adenoid cystic carcinoma showing basaloid cells in tubules in a sclerohyaline stroma and sheets of dedifferentiated spindle cells.

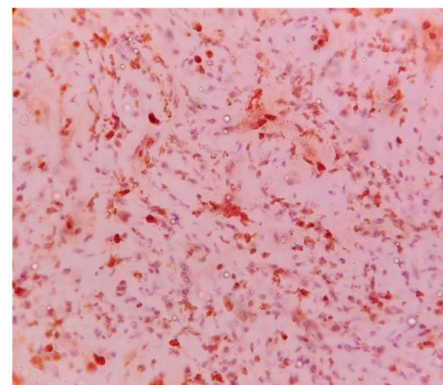


Fig. 4: Adenoid cystic carcinoma with dedifferentiation – spindle cells showing immunoreactivity for Ki - 67

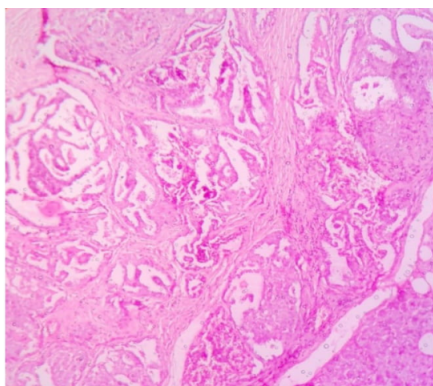


Fig. 5: Mammary analogue secretory carcinoma showing tumor cells arranged in tubulocystic glands and in papillary cystic structures

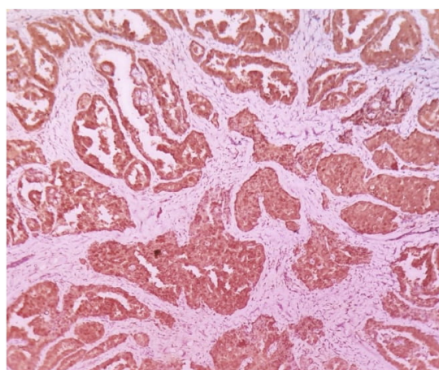


Fig. 6: Mammary analogue secretory carcinoma – Tumor cells showing mammaglobulin positivity.

among non neoplastic cases in our study whereas cystic lesions were predominantly noted in the studies of Teeda et al.⁵ Deepak et al also noted an increased prevalence of sialadenitis in their studies.⁶

In neoplastic lesions benign tumours (28,80%) predominate over malignant tumour(7,20%) in the present study in correlation with other previous studies.⁴⁻⁷ Comparison of incidence of salivary gland neoplasms in various studies is shown in Table 2. Benign tumours are usually more prevalent but they are under reported in poverty stricken areas of Africa because of less comprehensive health care and poor affordability. People with less morbid conditions are least bothered to seek medical care. Only malignancy with increased morbidity compels them to look for medical treatment. Hence a relatively large proportion of malignancies have been accounted in certain African studies.⁸ Similarly Shrestha et al also have noted 62.5% of salivary gland neoplasms to be malignant.⁹ This could be attributed to the fact that their study was conducted at a tertiary care cancer hospital where all diagnosed malignant cases were referred for further management. This led to the increased reporting of malignant tumours in their study in

contrast with developed western world contributing to less than 20% of malignant neoplasms.¹⁰ In the Middle East, Eastern Europe and Far East the proportion of malignancy was intermediate between African and Western studies ranging from 26-30%.¹¹

In this study the mean age of presentation was 38.925 with the range of 13-67 years. Similarly Jude et al also have observed a comparable mean age of 39.34 ± 17 in their study.¹² The age wise distribution of salivary gland tumours is shown in Table 3. Regarding benign salivary gland tumours, 8 cases(28.5%) occurred in 21-30 years followed by 7 cases (25%) in 41-50 years and 6 cases (21.4%) in 31-40years. This is in accordance with the distribution of Jude et al.¹² In case of Malignant tumours in our study, there is equal distribution of 2 cases (28.5%) in age groups of 21-30 years, 31-40 years and 61-70years. In general the age profile of our study is comparable with the African studies involving the younger age group more.⁸ In contrast in the western literature benign lesions appeared predominantly in the 5th to 7th decade and malignancies a decade or two later.¹⁰ This shows that racial origin and many other environmental factors play a significant role in the incidence of salivary gland tumours.

Regarding the anatomical site, the incidence of salivary gland tumours in Parotid, submandibular and minor salivary glands accounted for 46%, 31% and 23% respectively in our series. This predominance of parotid tumours is also evident in other published reports.⁴⁻⁷ A comparison of site-wise distribution of salivary gland tumours is shown in Table 4. The magnitude of Parotid dominance varies markedly across the world. A slight higher incidence in minor salivary gland is observed in our study in correlation with Mohammed et al.⁴

Pleomorphic adenoma was overwhelmingly the commonest tumour in this study constituting 62.8% of all salivary neoplasms and 78.5%(22 cases) of benign tumours. This correlates with the results of other studies.^{4-7,9} The peak age incidence was 21-50 years with female preponderance and parotid dominance (10,45.45%) as in the studies of Deepak Soni et al.⁶ Factors that contribute to the risk of malignant transformation in Pleomorphic adenoma are older age, long standing duration of the tumour, large tumour size, location in submandibular gland, prominent zones of hyalinization and atleast moderate mitotic activity.¹³ In our study 9% (2 cases) of pleomorphic adenomas have occurred in the elderly age group of 5th to 6th decade and 40%(9 cases) of the tumours are located in submandibular gland. Features of prominent zones of hyalinisation are seen in nearly 48% (10 cases) of cases. But features of associated malignant transformation has not been observed in our study. Surgical procedures like enucleation of tumour alone, rupture during removal, extensions beyond the main tumour, abundance of chondromyxoid stroma and young age are associated with higher recurrence rate. In

our study, 13% (3 cases) are seen in younger age group of 1st to 2nd decade. They need a careful follow up since recurrence may also increase the possibility of malignant transformation. All pleomorphic adenomas observed in our study are initially diagnosed cases and no recurrent tumour has been noted.

Basal cell adenoma was the second common benign tumour (14.2%, 4 cases) encountered in our study similar to other previous studies.^{4,12} Females (75%, 3 cases) outnumber males (25%, 1 case) as per literature. Age distribution is equal in all ages ranging from 2nd to 6th decades. Studies of Teeda et al and Shrestha et al point out the location of basal cell adenoma predominantly in parotid gland as 5.66% (3 cases) and 3% (2 cases) respectively in accordance with literature.^{5,9} In our study, location of the tumour in both parotid and minor salivary gland has been equally shared (50%, 2 cases each). Similar site distribution has been observed in the study at a tertiary health institution of Kano, Nigeria.⁸ Regarding the histomorphological features, membranous subtype of basal cell adenoma needs to be given importance because rate of transformation to malignancy is higher upto 28%.¹⁴ In our study no case of membranous subtype has been reported.

One case of Warthins tumour in parotid has been noted in a 67 yr male in our study whereas increased prevalence has been observed in the studies of Deepak soni et al and Shrestha et al as 15.1% (10 cases) and 9.6% (5 cases) respectively.^{6,9} Parotid is observed as the site of predilection in the above mentioned studies also.

A 22 yr old male presented with myoepithelioma in our study. Similarly Mohammed et al, Teeda et al and Shrestha et al also have observed only one case of Myoepithelioma in their studies.^{4,5,9} It is most frequently encountered in parotid gland but in our study it is seen in submandibular gland. Similar to pleomorphic adenoma recurrences of this tumour also leads to malignant transformation.¹⁵ Hence a careful follow up is needed.

Among malignant neoplasms, Mucoepidermoid carcinoma was found to be the most common tumour comprising of 57.1% (4 cases) (Figure 1) similar to the observation of other studies.⁵⁻⁹ In contrast, studies of Jude et al¹² and Zaman et al¹⁶ mark adenoid cystic carcinoma as the commonest malignant tumour. Mucoepidermoid carcinoma has the peak incidence in 6th to 7th decade with male predominance and predilection for parotid as in the studies of Deepak et al.⁶

One case of Acinic cell carcinoma, Adenoid cystic carcinoma with dedifferentiation and mammary analogue secretory carcinoma, each accounting for 14.2% of all malignant salivary gland tumours were observed in our study. Acinic cell carcinoma most frequently occurs in parotid gland. It is an indolent tumour that has a delayed local recurrence and metastasis even after 30 years. Hence life long follow up is imperative. According to Ellis, acinic cell

carcinoma arising from minor salivary glands are associated with better prognosis.¹⁷ In our study acinic cell carcinoma (Figure 2) is reported in minor salivary gland.

A special case of interest observed in our study is Adenoid cystic carcinoma with dedifferentiation (Figures 3 and 4). It is a recently recognised phenomenon indicating transformation into high grade neoplasm. The process of dedifferentiation has also been described in acinic cell carcinoma, epithelial- myoepithelial carcinoma, polymorphous low- grade adenocarcinoma, mucoepidermoid and myoepithelial carcinoma. Genetic event underlying this histological progression needs to be studied more. Few cases have shown evidence of TP53 mutations and deletions.¹⁸ The most useful tool in identifying the transformed component is the combination of morphology and proliferative index aided by Ki67. In our case the basaloid myoepithelial cells showed positive immunostaining for S100 and Smooth muscle Actin (SMA). Ductal epithelial cells showed positivity for Cytokeratin (CK) and C- Kit. Ki- 67 showed more than 50% expression in spindled cells indicating the progression of adenoid cystic carcinoma to dedifferentiation as sarcomatoid carcinoma. Prognostically, dedifferentiation is associated with features of frequent local recurrence, metastasis and rapidly fatal outcome.¹⁸

Another significant entity of rarity is the recently described Mammary analogue secretory carcinoma of salivary gland. It recapitulates histomorphology and molecular features of secretory carcinoma of breast. It also has morphologic overlaps with acinic cell carcinoma making it unclear to be distinct entity or subtype of acinic cell carcinoma. Though both entities have identical growth pattern, Mammary analogue secretory carcinoma lacks basophilic granules that is specific for acinic cells. Moreover Immunohistochemistry aids as an adjunct tool in diagnosing this tumour with mammaglobulin positivity. DOG-1, a marker for gastro intestinal stromal tumour is recently used as an acinar cell marker. It shows complex mixture of intense apical membranous, cytoplasmic and complete membranous staining in acinar cell carcinoma and is negative in mammary analogue secretory carcinoma. In our study one case of mammary analogue secretory carcinoma was diagnosed with positivity for mammaglobulin (Figures 5 and 6), S100 protein and negativity for P63 & DOG1. Chromosomal translocations of t (12:15), (p13q25) and gene fusion of ETV6-NTRK3 are the molecular genetic profiles associated with this tumour. Regarding survival, no statistical significance has been noted between Acinic cell carcinoma and Mammary analogue secretory carcinoma. But higher frequency of regional lymph node metastasis has been observed in Mammary analogue secretory carcinoma.¹⁹ In contrast Oliver et al state that mammary analogue secretory carcinoma is a tumour with a low grade malignant potential in majority of cases reported till date.²⁰

Table 1: Gender wise distribution of salivary lesions

	Male	Female	Total
Non Neoplastic	3	2	5
Benign	12	16	28
Malignant	5	2	7
	20	20	40

Table 2: Comparison of incidence of salivary neoplasms

	Mohammed et al	Shrestha et al	Deepak Soni et al	Ochicha et al	Present Study
Benign	84.61%	37.5%	69.33%	56.4%	80%
Malignant	15.38%	62.5%	30.66%	43.6%	20%

Table 3: Age wise distribution of salivary tumours

Types	11-20 yrs	21-30 yrs	31-40 yrs	41-50 yrs	51-60 yrs	61-70 yrs
Benign						
Pleomorphic Adenoma	3	6	5	6	2	
Basal Cell Carcinoma		1	1	1	1	
Warthins Tumour						1
Myoepithelioma		1				
Malignant						
Mucoepidermoid Carcinoma		1	1			2
Adenoid Cystic Carcinoma			1			
Acinic Cell Carcinoma					1	
Mammary Analogue Secretory Carcinoma		1				
	3	10	8	7	4	3

Table 4: Comparison of site-wise distribution of salivary gland tumours

Location	Mohammad et al	Teeda et al	Deepak Soni et al	Mallepogu et al	Present Study
Parotid Gland	61.53%	65%	73.34%	65%	45.71%
Submandibular Gland	14.10%	25%	20%	25%	31.42%
Minor Salivary Gland	24.37%	10%	6.66%	10%	22.85%

5. Conclusion

Salivary gland neoplasms inspite of having simple histomorphology gives rise to a broad spectrum of benign and malignant neoplasms. Morbidity and mortality are high in salivary gland tumours because of its anatomical location. Histopathology is the mainstay for diagnosis of salivary tumours. Immunohistochemistry though limited serves as an adjunct tool to support histopathological diagnosis and helps us to identify newer variants. A more population based survey with follow up studies will help us to view more into diverse nature of salivary tumours, typing them and predicting their prognosis. This will guide us to improve our treatment protocol.

6. Source of funding

None.

7. Conflict of interest

None.

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