"HISTOMORPHOLOGICAL STUDY OF SALIVARY GLAND NEOPLASMS: A 2 YEAR STUDY"

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ABSTRACT: BACKGROUND: Of all the tissues in the human body, perhaps the salivary glands have the most histologically heterogenous group of tumors and the greatest diversity of morphologic features among their cells and tissues. This diversity combined with the fact that most surgical pathologists have limited opportunity for experience with salivary glands is the primary reason behind the difficulty caused by these diseases for many pathologists. Therefore, present study was undertaken to study the relative incidence and spectrum of histomorphological features of various salivary gland neoplasms. **AIMS**: The aim of this study was to evaluate the relative frequencies, types, site distribution and the histomorphology of salivary gland neoplasms. **MATERIAL AND METHODS**: The material for this study comprised of incisional biopsies and resected specimens of salivary gland neoplasms received in the department of pathology, J.J.M.Medical College, Davangere. In cases of parotid gland lesions, superficial parotidectomy and total parotidectomy without neck dissection was done and specimens were sent for histopathological examination. Gross examination and subsequent microscopic examination was done after staining with hematoxylin and eosin. 53 cases diagnosed histopathologically as salivary gland neoplasms were included in this two year prospective study. **RESULTS**: During the two years of study period 53 salivary gland neoplasms were seen. 38 cases were benign neoplasms and 15 cases were malignant. Among all neoplasms, pleomorphic adenoma was the commonest. Mucoepidermoid carcinoma was the most common malignant neoplasm. The mean age of presentation of all neoplasms was 42.74 years. The male to female ratio was 1:1.2. Most common site of occurrence was parotid gland. No intraparotid lymph nodes were observed. In all the neoplasms studied, typical histomorphological features were seen. Surgical margins were free in all the cases. **CONCLUSION**: It is concluded that some of our results are in harmony with those of other authors.. On the other hand, some of our results are different from published literature. Further nationwide population based survey is needed to define the epidemiology of salivary gland neoplasms.

KEY WORDS: Parotid gland, Pleomorphic adenoma, Mucoepidermoid carcinoma.

INTRODUCTION: Salivary gland neoplasms are a relatively uncommon group of neoplasms that seem to present a disproportionate degree of diagnostic uncertainty relative to their actual numbers. They can show a striking range of morphological diversity between different tumor masses. In addition, hybrid tumors, differentiation and the propensity for some benign tumors to progress to malignancy can confound histopathological interpretation [1,2].

Salivary gland neoplasm are quite uncommon, but they do elicit considerable medical interest because of their multifaceted clinical presentation, varied histologic appearances & the associated difficulties in predicting the diagnosis [3].

However there are no reliable criteria to differentiate on clinical grounds the benign from the malignant lesions and morphologic evaluation is necessary [4].

The present study was undertaken to study the spectrum of histomorphological features of various salivary gland neoplasms

AIMS:

1. To study the age, sex and site incidence of salivary gland neoplasms
2. To study the histomorphological features of salivary gland neoplasms

MATERIAL AND METHODS: The present histomorphological study of salivary gland neoplasms is a two year prospective study done at J.J.M medical college, Davangere. The material for the study comprised of specimens received in the department of pathology J.J.M. medical college, from patients admitted to chigateri general hospital, Bapuji hospital and Women & children hospital attached to J.J.M medical college, Davangere.

The specimens consisted of incisional biopsies and resected salivary gland lesions with or without the draining lymph nodes of that region.

The details of the specimens noted include dimensions, appearance of the external surface and the cut surface and involvement of surgical margins. They were fixed in 10% neutral buffered formalin for 24 to 48 hours. Large specimens were cut serially at a distance of 1cm before fixing.

After fixation, representative areas were selected for paraffin embedding, including the tumor proper and the margin of the tumor with surrounding tissue. Sections of 3 – 5 micron thickness were cut and stained with hematoxylin and eosin. Microscopic examination of the stained sections was performed.

OBSERVATIONS AND RESULTS: There were 53 cases of salivary gland neoplasms. Out of these 38 were benign neoplasms and 15 were malignant neoplasms.

Benign neoplasms consisted of 24 pleomorphic adenomas, four cases of basal cell adenoma, two cases each of warthin tumor, myoepithelioma, schwannoma & inflammatory pseudotumor & one case each of hemangioma & lipoma were seen.

Malignant neoplasms consisted of six mucoepidermoid carcinomas, four adenoid cystic carcinomas, and one case each of acinic cell carcinoma, malignant myoepithelioma, carcinoma ex pleomorphic adenoma, salivary duct carcinoma and undifferentiated carcinoma.

GENDER AND AGE: Fifteen benign neoplasms were seen in males and 23 benign neoplasms were reported in females. Among malignant tumors, ten were seen in males and the remaining

five were reported in females. In the present study, the salivary gland neoplasms presented over a wide range of age from five months to 79 years. The mean age was 42.74 years. Mean age for benign neoplasms was 41.64 years and mean age for malignant neoplasms was 45.53 years

Parotid gland was the commonest site for various tumors, notable exception being adenoid cystic carcinoma, which showed predilection for the minor salivary glands and submandibular glands.

In our study, 24 pleomorphic adenomas were reported. They accounted for 45.27% of all salivary gland tumors & 63.2% of the benign tumors. They presented as painless slowly growing swellings. Most of them occurred in the parotid gland with submandibular gland being the second most common site.

Grossly, these tumors ranged in size from 0.5 to 6cm in their greatest dimension. The shape of the tumors varied from irregular to globular & lobulated. Most of the tumors were firm in consistency & showed partial to complete capsulation. Cut section revealed solid, grey white homogenous areas. Cystic changes hemorrhage & mucoid areas were seen in a few cases. No intralesional lymph nodes were seen.

Microscopically, majority of the tumors consisted of myxoid and chondromyxoid areas with epithelial & myoepithelial cells arranged in various patterns. The tumors had a capsule of varying thickness & completeness. In some tumors the epithelial components were predominant & the tumor cells were arranged in the form of ducts, solid sheets, tubules & strands. In few tumors either myxoid or chondroid areas were predominant. Hyaline areas were seen in a few cases along with areas of pseuodocartilage and mucin. One case of pleomorphic adenoma showed large areas of infarction, with adjacent myxoid areas.

Two cases of warthin's tumor were reported. Cut surface was grey white with variable sized cysts. Microscopically the tumors revealed the classical histopathological features of warthin tumor.

Two cases of myoepithelioma were encountered in our study. One case was seen in hard palate. Grossly both the tumors were well delineated & grey white, measuring 2-4cm in greatest dimensions. Cut surface was grey white. Microscopy of both the tumors showed tumor cells composed of elongated spindle to oval cells having scanty to moderate clear to eosinophilic cytoplasm. The cells were arranged in bundles with focal microcystic areas in one case. One case showed plasmacytoid cells having eccentric nuclei & eosinophilic cytoplasm. Stroma was scanty with focal areas of hyalinization, myxoid change & fibrosis.

Four cases of basal cell adenoma were encountered in our study. They were of size ranging between 2-6cm in the greatest dimension. Microscopically tumors were well encapsulated, bordered by normal salivary tissue. The tumor cells were small, round to oval in shape having scanty basophilic cytoplasm & hyperchromatic nuclei. The tumor cells were arranged in solid groups, nests, cords, trabeculae & sheets with peripheral palisading in some of the cell nests. Stroma was scanty with areas of fibrosis & hyalinization.

Two cases of schwannoma were reported in the present study. The tumors were globular to irregular in shape & varied in size from 2-6cm in the greatest dimension.

Microscopy showed tumor tissue composed of bundles of elongated spindle shaped cells, having plump nuclei & verocay bodies with nuclear palisading. One case of hemangioma was noted in this study. Cut surface showed spongy, lobular mass infiltrating the glandular tissue.

Microscopy showed lobules of salivary gland tissue with intervening fibrofatty stroma having multiple thin walled vascular spaces containing red blood cells.

A case of lipoma ms 6x4x3 cm was encountered in our study which showed classical microscopic features of a lipoma. We encountered two cases of inflammatory pseudotumor which were also included in our study. The two tumors were firm, nodular swellings measuring 2cm to 5cm in their greatest dimensions. Cut surface was grey white, well delineated & whorled in one case. Microscopy showed spindle cells intimately mixed with collagen fibres & variable amounts of plasma cells, lymphocytes, polymorphs & foamy histiocytes. One case showed spindle cells forming vague fascicles.

Malignant tumors: Fifteen cases of malignant neoplasms were encountered is our study. The most common malignant tumor was mucoepidermoid carcinoma, accounting for six cases. Grossly, these tumors varied in size from 2-6cm in greatest dimension. Cut surface of the tumors was grey white to grey brown with cystic spaces containing mucinous fluid. Definitive capsule was not appreciated in majority of the tumors.

Microscopy: All tumors were poorly delineated & consisted of mucous secreting cells lining the cystic spaces. Epidermoid cells were in the form of clumps or strands or as multilayered masses beneath the mucous secreting epithelium along with a group of intermediate type of cells were seen between these two layers. The three cellular components varied in population. Stroma showed lymphocytic infiltration. Few cases showed clear cells & epithelial pearl formations.
These tumors were graded into high grade mucoepidermoid carcinoma, intermediate grade mucoepidermoid carcinoma & low grade mucoepidermoid carcinoma. Low grade tumors show predominance of mucous secreting cells with formation of cystic spaces lined by mucus cells. Nuclear atypia & mitoses were not observed. Cystic spaces in low-grade tumors were filled with mucin & also showed mucin pools in which the tumor cells were floating. Intermediate grade tumors showed a greater tendency to form solid nests of squamous pearls & intermediate cells with less prominent cystic spaces. Same degree of nuclei atypia and mitotic activity were seen.

High grade tumors were predominantly solid consisting of epidermoid cells with occasional pearls & these tumors showed increased degree of nuclear atypia & mitotic activity.

Four cases of adenoid cystic carcinoma were reported in our study. Two cases were seen in intraoral minor salivary glands and two cases were reported in the submandibular gland. Grossly the tumors presented as ill defined infiltrative growths, measuring 0.5to 4cm in their greatest dimension. Cut surface was grey white to grey brown with cystic areas.
Microscopy showed tumor tissue composed of basaloid cells. These tumor cells were small, round to oval having scanty cytoplasm with hyperchromatic nuclei. They were arranged in solid groups, cords, trabeculae & in cribriform patterns separated by hyaline stroma. One tumor showed atypical mitotic activity. Hyaline cylinders & mucoid areas were seen in one tumor. A case of acinic cell carcinoma was reported which was 4x3x2 cm in greatest dimensions macroscopically. Microscopy showed tumor tissue arranged in the form of small nests, sheets & papillary fronds. It was composed of small round to polygonal cells having pale blue or clear cytoplasm. A few cells showed vacuolated cytoplasm. Nuclei were uniform, small & situated either centrally or eccentrically. These tumor cells were arranged in papillary cystic pattern & separated by fibrovascular septa. A single case of malignant myoepithelioma was reported in the present study. The tumor was grey white, nodular & measured 3x3x2cm.Microscopy showed lobules of tumor cells. The tumor cells were short, spindle shaped having clear to pale eosinophilic cytoplasm with pleomorphic nuclei. Mitoses were frequent. Stroma was scanty & showed areas of hemorrhage & necrosis. One case of carcinoma ex pleomorphic adenoma was

seen in our study. Macroscopically, the tumor was irregular & grey brown with infiltrating areas, but the surgical margins were free. Microscopically the malignant component was characterized by widespread cellular pleomorphism & a high mitotic count. Large areas of necrosis were present. The malignant component was poorly differentiated carcinoma. Markedly hyalinized areas were seen adjacent to the carcinoma. Small area of pleomorphic adenoma was also present.

A case of salivary duct carcinoma was reported showing cribriform & solid pattern with prominent comedo necrosis. Histologically it resembled intraductal carcinoma of breast. Also seen were cords, nests and single cells. The tumor cells had abundant eosinophilic cytoplasm, large pleomorphic vesicular nuclei & prominent nucleoli. The stroma was densely fibrous. A case of undifferentiated carcinoma was reported which showed polygonal to spindle cells having abundant cytoplasm with mitosis along with areas of hemorrhage & necrosis

DISCUSSION: The various benign & malignant neoplasms of the salivary glands encountered in our study have been compared with similar neoplasm in other studies

Our study showed an overall mean incidence of 26.5 cases per year for all neoplasms. Jones et al[5] & Bhargava et al[6] have reported a slightly higher incidence than our study where as Sousa et al[7] & Gupta et al [8] showed a lower incidence. The frequency of benign & malignant neoplasms was almost similar to other studies. In our study the mean age for benign tumors was lower than the mean age for the occurrence of malignant tumors.

Our study showed a female preponderance similar to that recorded by Vargas et al[9], Jones et al[5], Sengupta et al[10], Sharkey et al[11] & Budhraja et al[12]. However Renehan et al[13] observed a male preponderance and Sousa et al[7] found an overall equal sex distribution. The site distribution of the salivary gland tumors in the present study is in agreement with the results obtained in other series, with a predilection for the parotid gland.

The commonest benign tumor in our study is pleomorphic adenoma, which showed a peak incidence in the 5th decade & predilection for parotid gland. Our finding was in accordance with the results of other studies. However Vargas et al[9], Gupta et al[8] & Sharkey et al[11] noted a lower age incidence.

Among the malignant tumors, mucoepidermoid carcinoma was the commonest with a male preponderance and a peak age of incidence being 30-69 years.Similar observations were reported by Gupta et al[8] & Sharkey et al[11].

Parotid gland is the most common site for mucoepidermoid carcinoma in over study. Present study did not encounter any case in minor salivary glands as reported by other studies. The age, sex, & site distribution of our cases were similar to the findings of other studies for all other types of tumors.

HISTOMORPHOLOGY: In our study majority of pleomorphic adenomas consisted of myxoid & chondromyxoid areas with the epithelial & myoepithelial cells arranged in various patterns. Similar findings have been reported by Mendenhall w.m et al[14]. One case showed necrosis in a hyalinized area. Alves FA et al[15] also reported similar findings. In our study all pleomorphic adenomas had focally thin capsules. A similar observation made by Stennert et al[16].The microscopic observations made in all other benign neoplasms in our study were similar to the findings reported by other authors.

Malignant tumors: Among the six mucoepidermoid carcinomas, predominant type was of intermediate grade. Similar results were reported by Healey et al[17] & Acceta et al[18].
However Eneroth et al [19] have found a preponderance of high grade tumors & Renehan et al[13] have found a preponderance of low grade tumors. This discrepancy may be due to the subjective differences in the grading of the tumors. The microscopic findings observed were similar to the findings reported by other authors. In the present study adenoid cystic carcinoma constituted 7.55% of all tumors and 26.7% of all malignant tumors. Our findings are similar to the findings of other authors except the findings of Nascimento et al[20] where there was a slightly higher incidence. In our study, tumors measured between 0.5cm to 4cm in greatest dimension, which is similar to that observed by Evans and Cruikshank [21], Batsakis JG [22] and Ellis, Auclair and Gnepp. The microscopic findings we observed were similar to the observations made by Evans and Cruikshank[21], Lucas RB [23] and Ellis, Auclair and Gnepp . One case of acinic cell carcinoma which was encountered in the present study was papillary cystic type microscopically with typical histology. Similar findings were reported by Calmenero C et al.[24]

In our case of Carcinoma ex pleomorphic adenoma the tumor showed irregular grey brown infiltrating areas, with areas of necrosis & hemorrhage. The malignant areas consisted of epithelial cells with an increased nuclear to cytoplasmic ratio, prominent nucleoli & frequent mitoses. Small area of pleomorphic adenoma was seen. The histologic pattern in our case was that of a poorly differentiated carcinoma. Similar observations were made by Wenig & Gnepp[25].
One case of undifferentiated carcinoma was reported in our study which showed polygonal to spindle cells. They were arranged in sheets & thin cords separated by fibrovascular stroma.

A case of malignant myoepithelioma is reported in our study which showed spindle shaped cells having clear to pale eosinophilic cytoplasm with pleomorphic nuclei. Frequent mitoses were present. Stroma showed areas of necrosis. Similar observations were made by Ellis, Auclair, & Gnepp[26] & Savera et al[27]. We also encountered a case of salivary duct carcinoma. Histologically it resembled ductal carcinoma of breast. It showed cribriform & solid pattern with central comedo type necrosis. A case of undifferentiated carcinoma was also reported in our study which showed polygonal to spindle cells arranged in thin cords separated by fibrovascular stroma. Cellular pleomorphism & mitosis were present. There were areas of necrosis & hemorrhage. Similar cases were reported by Eversole & Gnepp[28].

CONCLUSION: It is concluded that some of our results are in harmony with those of other authors.. On the other hand, some of our results are different from published literature. Further more population based surveys are needed to define the epidemiology of salivary gland neoplasms.

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TABLE 01: TYPE OF BENIGN AND MALIGNANT NEOPLASMS AND THEIR GENDER DISTRIBUTION

Neoplasms	No.	Male (%)	Female (%)
Benign			
Pleomorphic adenoma	24	09 (37.3)	15 (62.5)
Warthin tumor	02	02 (100)	00
Basal cell adenoma	04	01 (25)	03 (75)
Myoepithelioma	02	00	02 (100)
Schwannoma	02	00	02 (100)
Hemangioma	01	01 (100)	00
Lipoma	01	01 (100)	00
Inflammatory pseudotumor	02	01 (50)	01 (50)
Malignant			
Mucoepidermoid carcinoma	06	04 (66.6)	02 (33.3)
Adenoid cystic carcinoma	04	02 (50)	02 (50)
Acinic cell carcinoma	01	01 (100)	00
Malignant myoepithelioma	01	01 (100)	00
Carcinoma ex pleomorphic Adenoma	01	00	01 (100)
Salivary duct carcinoma	01	00	00
Undifferentiated carcinoma	01	01 (100)	00
Total	53 (100%)	25 (47.16)	28 (52.83)

TABLE 02: AGE DISTRIBUTION OF SALIVARY GLAND NEOPLASM

NEOPLASMS	**AGE GROUP (YEARS)**								
	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	TOTAL
BENIGN									
PLEOMORPHIC ADENOMA	0	1	4	5	9	4	0	1	24
BASAL CELL ADENOMA	0	0	0	0	2	1	1	0	04
WARTHIN TUMOR	0	0	0	0	0	0	1	1	2
MYOEPITHELIOMA	0	0	0	1	0	1	0	0	2
SCHWANNOMA	0	1	0	0	0	0	1	0	2
HEMANGIOMA	1	0	0	0	0	0	0	0	1
LIPOMA	0	0	0	0	0	1	0	0	1
INFLAMMATORY PSEUDOTUMOR	0	0	0	1	0	0	1	0	2
MALIGNANT									
MUCOEPIDERMOID CARCINOMA	0	1	1	0	2	0	2	0	6
ADENOID CYSTIC CARCINOMA	0	0	1	0	2	1	0	0	4
ACINIC CELL CARCINOMA	0	0	0	0	0	0	1	0	1
MALIGNANT MYOEPITHELIOMA	0	0	0	0	1	0	0	0	1
CARCINOMA EX PLEOMORPHIC ADENOMA	0	0	0	0	0	0	0	1	1
SALIVARY DUCT CARCINOMA	0	0	1	0	0	0	0	0	1
UNDIFFERENTIATED CARCINOMA	0	0	0	0	0	1	0	0	
TOTAL	1	3	7	7	16	9	7	3	53

TABLE 03: SITE DISTRIBUTION OF SALIVARY GLAND NEOPLASMS

NEOPLASMS	NO. OF CASES	PAROTID GLAND	SUBMANDIBULAR GLANDS	MINOR SALIVARY GLANDS
BENIGN				
PLEOMORPHIC ADENOMA	24	20	04	00
BASAL CELL ADENOMA	04	03	00	01
ARTHIN TUMOR	02	02	00	00
MYOEPITHELIOMA	02	01	00	01
SCHWANNOMA	02	01	01	00
HEMANGIOMA	01	01	00	00
LIPOMA	01	01	00	00
INFLAMMATORY PSEUDOTUMOR	02	02	00	00
MALIGNANT				
MUCOEPIDERMOID CARCINOMA	06	06	00	00
ADENOID CYSTIC CARCINOMA	04	00	02	02
ACINIC CELL CARCINOMA	01	01	00	00
MALIGNANT MYOEPITHELIOMA	01	01	00	00
CARCINOMA EX PLEOMORPHIC ADENOMA	01	01	00	00
SALIVARY DUCT CARCINOMA	01	01	00	00
UNDIFFERENTIATED CARCINOMA	01	01	00	00
TOTAL	53	42(79.25%)	07(13.21%)	04(7.54%)