Histopathological study of salivary gland tumors

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INTRODUCTION

Salivary gland tumors (SGTs) are rare and their annual incidence is <1/100,000 inhabitants, without noticeable geographical gap, and they represent <5% of head and neck tumors.[1] These tumors show a striking range of morphological diversity between different tumor types and sometimes within an individual tumor mass. In addition, hybrid tumors, dedifferentiation and the propensity for some benign tumors to progress to malignancy can confound histopathological interpretation.[2]
In India, overall incidence of SGTs can be ascertained from the cancer registry established by Indian Council of Medical Research. However, the geographic area and population covered by these registries are small and perhaps unrepresentative of the Indian population. In addition, there is a limited published literature on SGTs in Indian population.

This study proposed to examine the histopathological features of various SGTs, aimed at understanding the epidemiological pattern of these tumors and to compare our findings with reports done elsewhere.

SUBJECTS AND METHODS

This is a 3-year (2009–2012) retrospective study of all SGT biopsies received at our referral teaching hospital in Bagalkot, Karnataka, India. The hospital is the major tertiary health institution offering histopathology services to the entire district. Biodata (age, sex and site) were obtained from laboratory records derived from information provided on histopathology request forms. All specimens were fixed in 10% formalin, then processed into paraffin-embedded sections and stained with hematoxylin and eosin. Special stains (e.g., for mucin) were occasionally employed. All the slides were reviewed by the authors and classified according to the World Health Organization histological typing of tumors (2005).

RESULTS

A total of 9757 specimens were received in 3-year duration (2009–2012). Out of these, SGTs accounted for 0.6% (59) of all. In this study, 35.59% of affected patients were male (n = 21) and 64.40% were female (n = 38). The age of patients in this study was between 18 and 68 years (mean age 43 years). The mean age of affected patients by malignant SGTs was 45 years while it was 35 years for patients with benign SGTs. The frequencies of salivary gland neoplasms according to age and sex are shown in Table 1.

Most of the tumors were located in the major salivary glands (96.61%) among which parotid was the most common site (84.21%) with $\chi^2 = 12.26$, df = 1 and $P = 0.0004$ which is statistically highly significant. Minor salivary glands were involved in 3.39% of cases.

Out of 59 salivary gland neoplasms, 43 (69.16%) cases were classified as benign tumors and 16 (22.39%) cases as malignant tumors. Pleomorphic adenoma (PA) was the most common benign tumor (60.71%), and adenoid cystic carcinoma was the most common malignant tumor (14.94%). The frequencies of salivary gland neoplasms according to histopathological features are shown in Table 2.

DISCUSSION

In this study, SGTs constituted a meager 0.6% of all tumors, which is much smaller than 2% of tumors in the Western world. The relatively low frequency of SGTs is the most likely reason in our review. Only a few recorded analysis of SGTs based on significantly large number of cases are published from India as very little information is available on the tumors of the head and neck over the last two-three decades.

In this 3-year study, SGTs were found in patients between the ages of 18 and 68 years (mean: 43 years) with slight overall female predominance, male to female ratio of 1:1.8, this finding is similar with the other reports. However, few studies have reported more male predilection in SGTs. The incidence of benign neoplasms was more in the fifth decade whereas malignant neoplasms were seen more common in sixth and seventh decades. In the present study, benign tumors were more common than malignant ones in all the salivary glands. Furthermore, the results have shown that patients with malignant SGTs are older...
than patients with benign tumors which agree with most published reports.[8,11]

Parotid gland was the most common site of SGTs, followed by submandibular gland and the minor salivary gland in the palate and floor of the mouth.

The present study has indicated that the most common benign and malignant tumors of parotid gland and submandibular gland were PA and adenoid cystic carcinoma [Figures 1 and 2]. However, Warthin's tumor [Figure 3] and schwannoma were exclusively seen in the parotid gland. None of the benign tumors occurred in minor salivary glands, and only two cases of malignant tumors, i.e., mucoepidermoid carcinoma [Figure 4] in palate and polymorphous low-grade adenocarcinoma (PLGA) in the floor of mouth were noted.

PA was the most common SGTs, which consists of 60.71% of all tumors and 86.04% of benign SGTs. All epidemiological studies on the SGTs have shown a pronounced predominance of 42%–80% PA.[1,6,7] Histopathological feature shows both epithelial and mesenchymal differentiation. Epithelial component includes the well-formed ductal structures formed of inner epithelial and outer myoepithelial cells with associated features of spindle, squamous, basaloid, cuboidal, oncocytoid, mucous, sebaceous, round, plasmacytoid, polygonal or clear cells. Squamous differentiation with keratin pearls (positive CK19) was noted in four cases, and in one of the tumors, there was predominant adipose tissue. Cytologic features of epithelial cells were bland, and the mesenchymal component consisted myxoid, hyaline, cartilaginous or osseous differentiation. Variants include cellular with predominant epithelial element and myxoid type having myxochondromatous mesenchymal elements. Thickness of fibrous capsule varied, often absent in predominantly myxoid tumors. Special stains and immunohistochemistry (IHC) are noncontributory,
however, show positive for epithelial membrane antigen, secretory component, carcinoembryonic antigen (CEA), gross cystic disease fluid protein-15, interleukin-6 and steroid C-21 hydroxylase. Cyogenetic studies show clonal chromosomal rearrangements, 8q12 (typically young patients) and 12q13–15. Differential diagnosis (DD) includes PLGA and carcinoma ex PA.\(^\text{[5]}\)

The second most common benign tumor of salivary gland was Warthin’s tumor (5.07%), which was found only in the males and occurred exclusively in the parotid gland. Smoking habits are the main etiological factor for Warthin’s tumor mainly affecting the elderly patients and rarely occurs in <30 years of age, with a peak incidence in the sixth decade of life.\(^\text{[8]}\) The differences in results could be affected by racial, behavioral, geographical and unknown environmental factors. Microscopically, epithelial tall columnar (IHC-somatostatin) with basaloid oncyotic cells lining cysts form prominent papillae, the cystic spaces are filled with lymphoid stroma and few show lymphoid follicles. Other techniques for diagnosis are noncontributory.\(^\text{[2,12]}\)

The results of the present study showed that malignant SGTs consist of 27% of all SGTs. Adenoid cystic carcinoma (14.94%) was the most common malignant SGT, followed by the mucoepidermoid carcinoma (5.08%). Sando and Subhashraj et al.\(^\text{[1]}\) also found adenoid cystic carcinoma the same occurrence 25% and 6.6%, respectively.\(^\text{[1,4]}\) However, Kalburge et al. and Ochicha et al. found the mucoepidermoid carcinoma as the most frequent malignant tumor (58.53% and 5.12%) ahead of adenoid cystic carcinoma (33.33% and 1.28%).\(^\text{[7,18]}\) Classically, the histopathological features of adenoid cystic carcinoma include cribriform (50%), tubular (20%-30%) and solid patterns (10%-15%) with most tumors having mixtures of cytoarchitectural patterns. Stroma is eosinophilic, hyalinized or collagenous. The diagnostic feature of this malignancy includes the propensity for perineural invasion, found in >50% of cases in the present study. DDs are PLGA, basolaid squamous cell carcinoma and epithelial-myoepithelial carcinomas. IHC markers are positive for keratin, CEA, lysozyme, lactoferrin, S-100 protein and CD117.\(^\text{[2,12]}\)

Mucoepidermoid carcinoma on microscopy is composed of varying proportions of mucous, epidermoid and intermediate-type cells with cystic or papillary mucin-filled cystic lumens, often have pools of extravasated mucin in surrounding tissue which are strongly positive for mucicarmine stain (IHC positive for simple mucin-type carbohydrate antigens, i.e., T, Tn and sialosyl–Tn). These carcinomas may also have clear cells with clear cytoplasm mainly glycogen and less mucin. This carcinoma is reported on a grading system of low (Grade I - Predominant cystic), intermediate (Grade II - Cystic and cellular) and high (Grade III - Predominant solid pattern). DDs include sialometaplasia and cystadenocarcinoma.\(^\text{[10,12]}\)

Cyogenetic balanced translocation involving 6q regions and C-kit expressions is shown in AdCCa and translocation of (11; 19) with resultant fusion gene transcript, CTRC1/MAML2 in MECa.\(^\text{[10,12]}\)

Single cases of acinic cell carcinoma and PLGA occurred in males whereas ex carcinoma PA, basal cell adenoma and schwannoma were noticed in females. While these single reported cases do not have any impact on the presented data as no consistent data were found in the literatures.

**CONCLUSIONS**

The present study was a single institutional experience where analysis of 59 SGTs was carried out. The findings of age, sex, site distribution and pathologic features encountered in our study were in agreement with those studies reported from India and other parts of the world. Although the number of SGTs discussed in this study is small, the findings should contribute in better understanding of the disease. Only a few SGTs based on significantly large number of cases are published from India as very little information is available on the tumors of the head and neck over the last two-three decades and hence prospective studies need to be carried out on bigger samples to better discriminate the influencing factors.

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**Conflicts of interest**

There are no conflicts of interest.

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