MANAGEMENT OF SALIVARY GLAND TUMORS IN A NIGERIAN TERTIARY INSTITUTION

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Abstract

Background: The salivary glands consist of three major paired glands (the parotid, submandibular and sublingual) as well as numerous minor salivary glands, situated mostly in the oral cavity but also found in the pharynx, larynx, trachea, and sinuses. Tumours of salivary glands show a wide variety of pathologic types varying from benign to malignant. More salivary gland tumours are benign than malignant.

Patients and Methods: Data for this study were obtained from retrospective survey of case notes of all patients with Salivary gland tumours seen at the Maxillofacial Unit, Ahmadu Bello University Teaching Hospital, Shika, Zaria between January 2003 and August 2013. **Results:** There were 135 patients 73 (54.1%) females and 62 (45.9%) males within the age range of 2.5 to 80 years (41.85 years). Thirty nine (28.9%) were benign while 96 (71.1%) were malignant. Major salivary glands were involved in 60.7% of tumours; the rest 39.3% involved

minor salivary glands. Pleomorphic adenoma (86.7%) formed the bulk of benign tumours while adenoid cystic carcinoma (47.5%) was the predominant malignant tumour of salivary glands. Of 135 patients (n=,57.1% had surgery in our institution and were followed up. Those with malignancy also benefited from radiotherapy, chemotherapy or palliative oncology treatment. **Conclusion:** Management of salivary glands tumours in our environment is a challenge due to late presentation and the size of the tumour.

Abstract in French

Résumé
Contexte: Les glandes salivaires se composent de trois principales glandes appariées (la parotides, sous-maxillaire et sublinguales) mais aussi de nombreuses glandes salivaires, situées principalement dans la cavité buccale mais aussi trouvé dans le pharynx, larynx, trachée et sinus. Tumeurs des glandes salivaires montrent une grande variété de types pathologiques variant entre bénignes et malignes. Plus de tumeurs des glandes salivaires sont bénignes que malignes. Patients et Méthodes: Données pour cette étude proviennent de l'enquête rétrospective sur les notes de cas de tous les patients atteints de tumeurs des glandes salivaires, vus à l'unité maxillo-facial, Shika, Ahmadu Bello University Teaching Hospital, Zaria entre janvier 2003 et août 2013.
Résultats: Il y avait 135 patients 73 (54,1%) femmes et 62 hommes de (45,9%) dans la tranche d'âge de 2,5 à 80 années (41,85). Trente neuf (28,9%) étaient bénignes tandis que 96 (71,1%) étaient malignes. Les glandes salivaires principales ont participé à 60,7% des tumeurs; le reste de 39,3% impliqué des glandes salivaires. Adénome pléomorphe (86,7%) ont formé la majorité des tumeurs bénignes, tandis que le carcinome adénoïde kystique (47,5%) était la principale tumeur maligne des glandes salivaires. De 135 patients (n=,57.1% a été opéré dans notre institution et ont été suivis. Ceux qui ont une tumeur maligne aussi retombées ted de soins palliatifs, la chimiothérapie ou la radiothérapie traitement d'oncologie.
Conclusion: Gestion des tumeurs des glandes salivaires dans notre environnement est un défi en raison de la présentation en retard et la taille de la tumeur.
Mots-clés: Bénigne, maligne, glandes salivaires, tumeur

Keywords: Benign, malignant, salivary glands, tumor

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Introduction

The salivary glands consist of three major paired glands (the parotid, submandibular and sublingual) as well as numerous minor salivary glands, situated mostly in the oral cavity. [1] Salivary gland tumors (SGTs) are rare, accounting for 2-10% of all head and neck tumors in studies. [2] They have different benign and malignant pathologic types. In studies, benign SGTs are said to be more common than malignant ones with a ratio between 1.2:1 and 3.5:1. About 65-80% of SGTs arise within the parotid, 10% in the submandibular gland and the remainder in sublingual and minor salivary glands. The likelihood of a SGT being benign is directly proportional to the size of the gland of origin. [2]

Salivary gland tumors are a heterogeneous group of neoplasms in the maxillofacial area with complex morphologic appearance and differences in clinical behavior. However, they are important in head and neck pathology due to the relative difficulty in their diagnosis, management and unpredictable clinical course. [3] While etiologic factors of this group of neoplasms have not been specifically recognized, sunlight, chemotherapy, diet, smoking and Vitamin A deficiency have been associated. [2],[3],[4] Other factors such as genetic predisposition, viral infections, rubber manufacturing, plumbing, some types of woodworking, as well as asbestos mining, exposure to nickel compounds, and cellular phone use have also been suspected. The only well-established risk factor is exposure to ionizing radiation. [4]

Salivary gland tumors have inconsistent characteristics in different countries, and it seems that the geographic location and ethnic factors may affect their clinicopathologic profiles. [3] The purpose of this report is to present the characteristics of SGTs seen at our center with a view to contributing to existing literature on these interesting lesions.

Patients and Methods

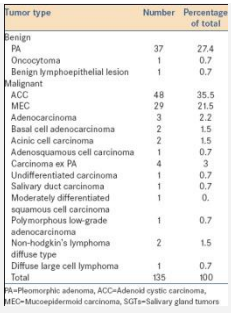
Data for this study were obtained from retrospective survey of case notes and histopathology results of all patients with maxillofacial tumors seen at the maxillofacial unit, Ahmadu Bello University Teaching Hospital, Shika, Zaria between January 2003 and August 2013. Of these, patients with SGTs were selected for recording of demographics, clinical history, diagnosis, investigations and treatment. As the oldest referral center in Northern Nigeria, our center receives patients from the North West and North Central geopolitical zones of Nigeria. The WHO classification (2005) was the basis for histopathologic diagnosis of SGTs.

Results

Out of 1688 cases of maxillofacial tumors seen within the study period, 135 patients (8%) had SGTs of which 62 were males and 73 were females, male to female ratio was 1:1.2. The age range was 2.5 years to 80 years (mean 41.8 years). Most patients (n = 109, 80.7%) were between 21-60 years old. Fewer SGTs (n = 39, 28.9%) were benign than malignant (n = 96, 71.1%). The most common SGT was adenoid cystic carcinoma (ACC) with a relative prevalence of 35.5% followed by pleomorphic adenoma (PA) (27.4%) and mucoepidermoid carcinoma (MEC) (21.4%). The relative prevalence of various SGTs seen in this study is shown as [Table 1]. The

major salivary glands (parotid and submandibular) accounted for 82 SGTs (60.7%) while the rest 53 (39.3%) occurred in minor salivary glands. There was no tumor recorded in the sublingual salivary gland. Site distribution of 135 SGTs is at [Table 2]. All patients with benign SGTs presented with complaint of swelling (100%) while the malignant cases presented with swelling (90%) followed by pain (70%) and inability to chew food properly (30%). Details of clinical features of SGTs seen in this study are in [Table 3]. The age range of patients with benign SGTs was from 18 to 70 years (mean 38.6 years ± 14 years standard deviation [SD]) while for patients with malignant tumors, the age range was 2.5-80 years (mean 44.5 years ± 15.1 years SD) with the mean difference of 5.9 years. From the descriptives [Table 4], people with benign tumors have an average age of 38.6 years with a SD and standard error of 14.0 and 2.24 respectively. On the other hand, people with malignant tumors have an average age of 44.5 years with a SD and standard error of 15.1 and 1.54 respectively. Distribution of SGTs on basis of age groups is at [Table 5]. Of the 135 patients, 75 (55.5%) had surgery, 36 (26.6%) had surgery combined with radiotherapy and chemotherapy, and 52 (38.5%) had radiotherapy and chemotherapy [Table 6].

Statistical independent *t*-test [Table 7] shows that the mean difference in age of both benign and malignant tumors is statistically significant ($P < 0.05$).



Tumor type	Number	Percentage of total
Benign		
PA	37	27.4
Oncocytoma	1	0.7
Benign lymphoepithelial lesion	1	0.7
Malignant		
ACC	48	35.5
MEC	29	21.5
Adenocarcinoma	3	2.2
Basal cell adenocarcinoma	2	1.5
Acinic cell carcinoma	2	1.5
Adenosquamous cell carcinoma	1	0.7
Carcinoma ex PA	4	3
Undifferentiated carcinoma	1	0.7
Salivary duct carcinoma	1	0.7
Moderately differentiated squamous cell carcinoma	1	0.
Polymorphous low-grade adenocarcinoma	1	0.7
Non-hodgkin's lymphoma diffuse type	2	1.5
Diffuse large cell lymphoma	1	0.7
Total	135	100

PA=Pleomorphic adenoma, ACC=Adenoid cystic carcinoma, MEC=Mucoepidermoid carcinoma, SGTs=Salivary gland tumors

Table 1: Relative prevalence of SGTs in Northern Nigeria

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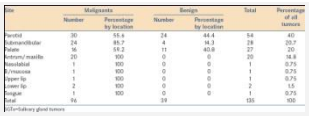

Table 2: Anatomical site distribution of benign and malignant SGTs

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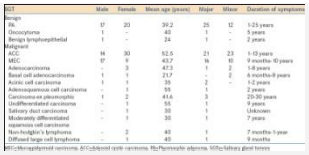

Table 3: Clinical details of SGTs

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Cancer status	*n*	Mean	SD	SE
Benign	39	38.6	14.0	2.24
Malignant	96	44.5	15.1	1.54

SD=Standard deviation, SE=Standard of error

Table 4: Descriptives of ages of benign and malignant cases

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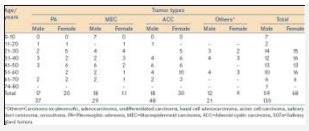

Table 5: Age group distribution of SGTs

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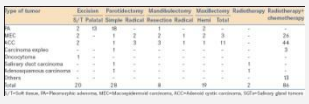

Table 6: Treatment of SGTs

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From the independent sample *t*-test [Table 7] above, since $P = 0.040 < 0.05$, it was, therefore, concluded that there is a significant difference in the mean ages between patients with benign and malignant tumors. In other words, using the descriptives [Table 4], we, therefore, conclude that malignant cases have older people (mean = 44.5 years) than benign cases (mean = 38.6 years). This is further depicted by the following bar chart [Figure 1].

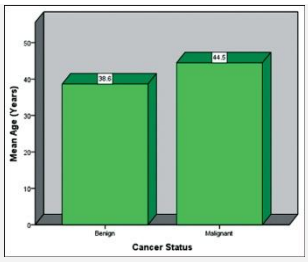

Figure 1: Ages of benign and malignant cases

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T	df	Significant (2-tailed)	Mean difference	SE difference
2.077	133	0.040	5.9	2.80

SE=Standard of error

Table 7: T-test of ages of benign and malignant cases

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{Figure 1}

Discussion

Salivary gland tumors probably are the most complex human neoplasia, accounting for 2-10% of head and neck or maxillofacial tumors. Between 2003 and 2013, we recorded 135 SGTs accounting for 8% of maxillofacial tumors. This is lower than 6.3% of oro-facial tumors and tumor-like lesions reported by Ladeinde *et al*. [5] from Lagos in Southern Nigeria but quite comparable to 9.3% from Uganda/Tanzania based on histopathologic reports according to Kamulegeya and Kalyanyama. [6] In view of the differences in the definition of head and neck, oro-facial, maxillofacial tumors and tumor-like lesions, the actual rate of SGTs remains unclear.

The ratio of benign to malignant SGTs varies from 1:1 to 6:1 in African and European reports respectively. [3],[7] In Nigeria, reports indicate more malignant than benign SGTs. [2],[8] Our study found the benign to malignant ratio was 1:2.3 with predominant involvement of major glands. The reason for the high number of malignancies could be that since most Nigerian reports are from tertiary referral centers like ours, they receive a disproportionate number of malignant lesions from outlying centers. There is no categorical proof of higher predilection of Africans especially Nigerians to malignant SGTs.

Generally, there is greater involvement of major glands in SGTs than minor salivary glands. In Croatia, 72.8% of SGTs were in the major glands. [9] This is slightly higher than 60.7% recorded in our study. This is however contrary to Gonzalez-Alva *et al*. [10] who reported 62.2% of involvement of minor salivary glands. The parotid gland is the site of the majority of SGTs (40%) in our study. This is similar to the findings of other African and Asia workers. [3],[11],[12] The sublingual gland was not involved in our study possibly due to the sample size. It accounted for 0.9-1.7% in the report by Lukšic *et al*. [9] and Lawal *et al*. [13] from Croatia and Nigeria respectively.

The minor SGTs of the lips, oral cavity, pharynx, larynx, trachea, nasal mucosa, and paranasal sinuses are uncommon sites (9-23%) for SGTs. [14] In our survey, minor salivary glands were the second most common site accounting for 36.3% of SGTs. This is double the Ghanaian report of 18% by Oti *et al*. [12] Among the minor salivary glands, most tumors occur in the palate (55.1-87.5%) according to previous reports from West Africa. [12],[15] This is in agreement with our finding with 55.1%. In Poland Wyszynska-Pawelec *et al*. [16] and USA Jansisyanont *et al*. [17] they found that the palate was also the commonest site with 47.6% and 53.8% respectively.

In this study, the age range of patients with SGTs was between 2.5 and 80 years with a mean of 41.8 years. Patients in the third to sixth decades made up 80.7% of total patients that is in conformity with other studies. [7],[12] The mean age of patients in benign neoplasms was 38.6 years. This is similar to other studies. [3],[10]

Malignant tumors occurred showed a mean of 44.50 years which was 5.9 years higher than benign tumors, and this was statistically significant ($P < 0.05$). The difference between the means of malignant and benign tumors has been reported to vary from 3 years in the Chinese to 10 years in the African population, but some authors have found an almost equal average age in malignant and benign tumors. [3],[10]

Most studies have shown that more females than males have SGTs as in our study, but others have shown a predominance in the male group. [3],[7],[8],[10],[15],[17],[18],[19] There was no discrepancy in the occurrence of tumors between females and males in the Croatian report by Lukšic *et al*. [9]

Pleomorphic adenoma undoubtedly is the most common SGT although it accounted for only 29.36% in our study. According to Malik, [20] Gonzalez-Alva *et al*. [10] and Jaafari-Ashkavandi *et al*., [3] PA account for 40.4-89.9% of all SGTs.

Adenoid cystic carcinoma was the most common SGTs in this study and also the commonest malignancy (34.9%) followed by MEC with 20.6%. These findings are consistent with researches in Brazil, India Africa and Bratislavia. [3],[10]

Pleomorphic adenoma is typically a slowly growing, asymptomatic, discrete nodule most often located in the superficial lobe of the parotid gland. It is usually mobile with palpation and rarely causes facial paralysis due to extrinsic compression of the VII cranial nerve. [4],[21] Majority seen between fourth and sixth decades of life and more commonly in females. [20],[22] Our study agrees with their finding.

In the major salivary glands, MEC usually presents as a solitary, painless lesion. Similarly, to other malignant neoplasms, over 50% of patients have been aware of the tumor for <6 months. Two-thirds of individuals are asymptomatic. Some patients report rapid growth of the mass; others experience pain, dysphagia, trismus, and facial paralysis. In minor salivary glands, 40% of patients are symptomatic, suffering from pain, numbness of teeth, dysphagia, ulceration, and hemorrhage. [4],[21]

Adenoid cystic carcinoma manifests as a slowly growing mass often accompanied by pain and in some cases, facial paralysis. [4],[21],[22] Some also experience fixation to the deeper structures and

local invasion. Some of the lesions, particularly the intraoral ones, exhibit surface ulceration. [22]

Adenoid cystic carcinoma is an epithelial malignancy composed of epithelial and myoepithelial cells variably arranged in tubular, cribriform, and solid patterns. The cribriform pattern, which is the most common, is characterized by nests of cells containing small, circular cyst-like spaces. The solid pattern is associated with a poor prognosis compared to the tubular and cribriform architecture. Neural invasion is a hallmark of this entity and often extends beyond the main tumor mass. Infiltration of adjacent soft tissues is also characteristic of ACC. [4]

Computed tomography (CT) and magnetic resonance imaging (MRI) are important in the evaluation of clinically palpable masses involving parotid and adjacent and their relationship to the facial nerve. The relationship of a mass to the facial nerve will dictate the surgical approach to be used for its removal. On axial CT examination, the relationship of the parotid mass to the facial nerve can be inferred by noting the relationship of the mass to the retromolar vein. Lateral displacement of retromolar vein is indicative of a lesion arising medial to the facial nerve, whereas, lack of, or medial displacement of retromolar vein is indicative of a lesion arising lateral to the facial nerve. MRI, by the virtue of its greater soft tissue resolution, is capable of directly visualizing the facial nerve, as well as, showing possible early perineural spread in case of a malignancy. MRI also provides better delineation and definition of soft tissue masses. [20]

T2-weighted images provide an insight into the cellularity of SGTs. Highly cellular masses, e.g., high-grade malignancies tend to have low to intermediate intensities on images; whereas masses with lesser degrees of cellularity, e.g., benign tumors or low-grade malignancies, tend to be bright on T2-weighted sequences. [20]

The submandibular gland and larger portion of the parotid gland, because of their superficial location, can be readily examined with high-resolution ultrasound. [20]

In this study, 59% of patients had surgery with parotidectomy (37.33%) being the commonest followed by excision (26.66%) and maxillectomy (25.33%). The extend of surgery was determined by the tumor size rather than histology type. Advance cases [Figure 1] were considered for radiotherapy and chemotherapy. Response of ACC to radiotherapy remain controversial. [23] It is the belief in our center that radiotherapy is useful in unresectable, inaccessible cases and also postoperatively to prevent local recurrence.

Because of the risk of recurrence and malignant transformation, radical surgical excision is required. Still, whether to perform superficial parotidectomy or extra- capsular dissection remains debated. Additional surgery in case of recurrence exposes to an increased risk of facial nerve injury. [4]

Mucoepidermoid carcinoma is treated by wide local surgical excision, followed by radiation therapy in case of inadequate surgical margins or pejorative microscopic features (e.g. neural invasion). Classification into high-grade and low-grade tumors guides treatment but the behavior of intermediate-grade neoplasms remains difficult to predict. [4]

Treatment of ACC consists of wide local and radical surgical resection with or without radiation therapy, but the disease is usually relentless. [4]

The prognosis of PA is excellent if completely removed. Recurrence rates at 5- and 10-year follow-up are 3.4% and 6.8%, respectively. [4] Most patients (80-90%) with ACC die of the disease within 10-15 years. The solid pattern is associated with a worse prognosis compared to the tubular or cribriform architecture. The prognostic value of neural invasion is debated. [4] The 5- and 10-year survival rates of MEC are about 35% and 10-20%, respectively. Presence of distant metastases portends a poor prognosis. [4]

Suprahyoid neck dissection in conjuction with primary surgery is advocated only for cases with positive lymph nodes. [23] In this study, our patients who presented with positive lymph node were immediately referred for chemotherapy and radiotherapy. We lost a patient postoperatively after a course of chemotherapy. We had one case of recurrence for a benign tumor. Ajike *et al*., [23] had no recurrence and believe wide circumscribing incision with about 3-5 mm margin of apparent normal mucosa was the treatment philosophy.

In this study, some of our patients experience transient facial nerve paresis which resolved within weeks postoperatively. Those with delayed recovery were placed on neurobion.

Conclusion

Management of SGTs remains a challenge due to the late presentation.

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