



Research Article

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Maxillary Alveolar Carcinoma: Risk of Recurrence and its Relation with Prognostic Indicators

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Abstract

Background: Maxillary Alveolar carcinoma is a relatively uncommon entity with occurrence reported between 3.5 to 10% of all oral cancers. Recurrence when occurs locally are particularly difficult to treat due to the close proximity of this region to the infratemporal fossa and the base of skull. There is also a debate when to perform elective neck dissection in these patients.

Objectives: The aim of this study was to identify cases with recurrence and correlate its association with various prognostic factors and disease free survival in these patients.

Methodology: Overall, 15 cases were identified with maxillary alveolar carcinomas that were treated between 2011 to 2015. Eight of these cases were Squamous cell carcinomas, 5 Adeno carcinomas and 2 Adenocystic carcinomas. T stages, N stage, grade of tumor, surgical margin involvement by the tumor, presence of perineural and lymphovascular invasion were identified as prognostic indicators. The chi-square and Pearson correlation tests were applied to analyze the association between recurrence and these prognostic factors.

Results: Recurrence developed in 3 SCC (37.5%) and 1 ADC (20%) patient during the three years period following the treatment. Among the SCC patients, 2 recurrences were local and 1 regional. Recurrence was found to have a strong positive correlation with T stage ($r=0.330$, $p=0.271$), surgical margin involvement ($r=0.575$, $p=0.566$) and three years disease free survival ($r=0.959$, $p=0.000$). A weak positive correlation was also established with tumor grade ($r=0.155$, $p=0.0613$) and perineural invasion ($r=0.149$, $p=0.725$).

Keywords: Oral squamous cell carcinoma; Maxillary alveolus; Hard palate; Prognostic factors; Survival rates; Recurrence

Introduction

Background

Oral carcinoma is one of the ten most frequently occurring cancers around the world and when grouped together with pharyngeal cancer, it is the sixth most common cancer in the world [1]. In the Asian and South east population the prevalence of oral cancer is on the rise. The unique cultural practices in the Asian population such as snuff dipping, smoking, use of alcohol and areca nut are the main predisposing factors for the development of this cancer. The incidence of OSCC restricted to the hard palate and maxillary ridge is very low, with an estimated 3.5 to 10 % of

all OSCC [2,3]. Because of the anatomical proximity of the upper alveolar mucosa with the maxillary gingivo-buccal sulcus, cancer of the maxillary alveolus may spread to the nearby spaces thus making it difficult to locate the actual initiation point of the disease [4].

Various prognostic factors have been suggested that could affect patients overall survival and disease specific survival in oral cancer. Of the known prognostic factors, the TNM stage, histological grade, and tumor thickness are widely recognized [5]. Other prognostic factors like lympho-vascular invasion (LVI) and peri-neural invasion (PNI), extracapsular spread and involvement of surgical margin by

tumor cell are also known to play a role in recurrence and overall poor prognosis [6-9].

Objectives

The aim of this study was to identify cases of recurrence and correlate its association with various prognostic factors and disease-free survival in these patients.

Methodology

A retrospective cohort study was planned to identify patients who had undergone surgical resection for maxillary alveolar carcinoma over a period of 4 years from 2011 to 2015. Data was collected through clinical and pathological records of the patient. A total of 26 Maxillectomies were performed during this period. Out of these, 15 cases were maxillary alveolar carcinomas while the rest were either non-malignant lesions or the sarcomas of maxillary alveolus. The 15 carcinomas were then classified according to their type. Gender, age distribution, T stage, N stage, histological grade, perineural and lymphovascular invasion and involvement of surgical margin by the tumor was determined. The cases which had received Adjuvant Radiotherapy and those who had developed recurrence were identified. Disease free survival was measured at three years following completion of treatment.

4 cases with recurrence were then categorized separately. Various prognostic indicators that might have played a role in recurrence were correlated with risk of recurrence and their significance determined using chi-square and Pearson correlation. These prognostic indicators were tumor grade, T stage, N stage, Perineural invasion (PNI), lymphovascular invasion (LVI) and involvement of surgical margin by tumor. Recurrence was then evaluated for its impact upon disease free survival.

Results

The distribution of the 15 carcinomas according to its type was

as following: 8 squamous cell carcinomas (SCC), 5 Adenocarcinomas (ADC) and 2 Adeno-cystic carcinomas (ACC). Gender wise, SCC had affected 8 females, ADC 5 males and ACC 1 male and 1 female. SCC had occurred between the ages of 35 to 76, ADC between 35 to 58 while the 2 ACC cases were found in 43 and 53 years old. Mean age for SCC was 51.1 years, median 50 years and modal 45 years with standard deviation of 12.35 years. 7 cases of SCC were well to moderately differentiated while 1 was poorly differentiated. 4 ADC cases were well differentiated and 1 was poorly differentiated while there was 1 each in well and poorly differentiated category for ACC. Only 1 SCC presented at T1 stage, 5 SCC and 2 ADC presented at T2 stage, 1 SCC, 3 ADC and 1 ACC presented at T3 stage while 1 SCC and 1 ACC presented at T4 stage. On histopathological evaluation perineural invasion and lympho-vascular invasion was found in 2 case of SCC only. 5 SCC and 2 ADC had microscopically margin involved on surgical resection specimen. Adjuvant Radiotherapy was given to 5 SCC cases, 1 ADC and 2 ACC cases (Table 1).

5 SSC (62.5%), 4 ADC (80%) and 2 ACC (100%) patients were disease free at 3 years following treatment. 3 SCC (37.5%) and 1 ADC (20%) patient had developed recurrence. Of the three recurrences in SCC cases, 2 were local and 1 regional. The impact of various prognostic factors on 4 cases of recurrence was then evaluated. Recurrence was found to have strong positive correlation with T stage ($r=0.330$, $p=0.271$) and surgical margin involvement ($r=0.575$, $p=0.566$) while a weak positive correlation was identified with tumor grade ($r=0.155$, $p=0.0613$) and perineural invasion ($r=0.149$, $p=0.725$). Since none of the recurrence cases had either clinical or radiological nodal involvement or lymphovascular invasion found in them, it was designated as not having any relationship with recurrence. Recurrence was also found to have a strong positive relation with three years disease free survival ($r=0.959$, $p=0.000$) (Table2).

Table 1: Cancer Cases.

S no.	Age years	Gender	H.P	T Stage	N Stage	LVI	PNI	Maxillectomy Type	Margin	Adj.RT	Recurrence	Further Tx	DFS
1	55	Female	SCC (MD)	T2	NO	+ve	-ve	Ila	Clear	Yes	Nil	RT	Disease free
2	76	Female	SCC(MD)	T2	NO	-ve	-ve	Ila	Close (1mm)	Nil	Yes (neck)	Palliation	Ad- vanced disease
3	45	Female	SCC(MD)	T2	NO	-ve	-ve	IIIb	Superior involved	Yes	Yes	Chemo-RT	Disease con- trolled
4	40	Female	SCC(MD)	T2	NO	+ve	+ve	Ila	Clear	Yes	Nil	Nil	Disease free
5	60	Female	SCC(MD)	T4	NO	-ve	+ve	IVb + eye + skin	Clear	Yes	Yes	Nil	Ad- vanced disease
6	45	Female	SC- C(WD)	T3	NO	-ve	-ve	Ilb + SND	Deep involved	Yes	Nil	Nil	Disease free
7	50	Female	SC- C(WD)	T2	NO	-ve	-ve	Ila	Close (<5mm)	Nil	Nil	Nil	Disease free

8	55	Female	SC-C(WD)	T1	NO	-ve	-ve	Ia	A-Med involved	Nil	Nil	Nil	Disease free
9	65	Male	ADC(PD)	T3	NO	-ve	-ve	IIa	Involved	Yes	Yes	Nil	Advanced disease
10	35	Male	ADC(PD)	T2	NO	-ve	-ve	IIa	Clear	Nil	Nil	Nil	Disease free
11	51	Male	AD-C(WD)	T3	NO	-ve	-ve	IIb	Clear	Nil	Nil	Nil	Disease free
12	38	Male	AD-C(WD)	T2	NO	-ve	-ve	IIa	Clear	Nil	Nil	Nil	Disease free
13	58	Male	AD-C(WD)	T3	NO	-ve	-ve	IIb	Clear	Nil	Nil	Nil	Disease free
14	43	Male	ACC(PD)	T4	NO	-ve	-ve	IIa + infratemporal fossa contents	Clear	Yes	Nil	Nil	Disease free
15	40	Female	AC-C(WD)	T3	N[i]0	-ve	-ve	IIb	Clear	Yes	Nil	Nil	Disease free

SCC: Squamous Cell Carcinoma; ADC: Adenocarcinoma; ACC: Adenoid cystic carcinoma; WD: Well Differentiated; MD: Moderately Differentiated; PD: Poorly Differentiated; Adj. RT: Adjuvant Radiotherapy; LVI: Lympho-vascular Invasion; PNI: Perineural Invasion; DFS: Disease Free survival; HP: Histopathology

Table 2: Recurrence Cases.

	Gender	Age	Histo-diff	T stage	N stage	LVI	PNI	MT	Margin	Recurrence	Outcome
SCC	Female	76 yrs	Mod diff	T2	N ⁰	-ve	-ve	II	Close (1mm)	Neck	Advance Disease
SCC	Female	45 yrs	Mod diff	T2	N ⁰	-ve	-ve	III	Involved	Local	Advance Disease
SCC	Female	60 yrs	Poorly diff	T4	N ⁰	-ve	+ve	IV	Clear	Local	Advance Disease
ADC	Male	65 yrs	Poorly diff	T3	N ⁰	NK	NK	II	Involved	Local	Advance Disease

ADC: Adenoid Cystic Carcinoma; SCC: Squamous Cell Carcinoma; LVI: Lymphovascular Invasion; PNI: Perineural Invasion; MT: Maxillectomy Type; T Stage: Tumor Stage; N Stage: Nodal Stage/ Lymph node involvement

Discussion

The biology of oral cancer varies with site of its presentation. The tongue carcinoma, for example, is a much aggressive entity as compared to lip carcinoma. Similarly maxillary alveolar carcinoma differs from Mandibular alveolar carcinoma in terms of biological behavior. The rarity of maxillary alveolar carcinoma, its location in oral cavity and the limited information about its biology has led to debate about its optimum management.

Lin, et al. [10] in a case series of 725 cases of maxillary alveolar and hard palate carcinoma, found cervical metastasis in 4.1% in T1, 14.9% in T2, 10.3% in T3 and 24.7% in T4 cases. They also found significant effect of T stage and Nodal stage on mean overall survival [10]. Dalal, et al. [11] found 23% cervical metastasis in 25 of the 30 cases of T4 squamous cell carcinoma at initial presentation. Hence recommending Elective neck dissection for all T4 maxillary alveolar carcinomas [11]. Joosten et al reported that in a group of 77 patients out of 95, 14.3% (11/77) had occult metastasis. In T2-T4 patients, this number increased to 19.0% while in T4 alone it was 24.1%. 45.5% of the occult metastasis developed in the contralateral neck. Their salvage rate for recurrence cases was 40%. Based upon these findings, they recommended elective neck dissection for all T2-T4

cases [12]. Similar recommendation was also made by Morris et al, based upon their analysis of 139 patients of maxillary alveolar and hard palate carcinoma. Regional failure in their study was 28.4%, ranging from 18.7% (pT1) to 37.3% (pT4) [13].

The other peculiarity of maxillary alveolar carcinoma is its anatomical location. Anterior alveolus is superiorly related to nasal cavity, middle alveolus is closely associated with maxillary sinus and then to orbital cavity and the posterior alveolus carcinomas tend to infiltrate to the infratemporal fossa. McMahon, et al. [14] in a review of 50 patients reported recurrences in 16, out of which 11 were local. Of these 11, 8 were in superior and posterior direction that included orbit, infratemporal fossa, pterygopalatine fossa, the traversing canals of sphenoidal bone, the gasser an ganglion and the dura of the middle cranial fossa. Hence they concluded that the advance cancer of mid face often equated with disease of the skull base [14]. Wang, et al. [15] in a 10-year review of survival outcome for hard palate and maxillary alveolar carcinoma found involvement of soft palate or infratemporal fossa as poor outcome indicators. Ulcerative tumor features, tumor volume larger than 10 ml and local disease that could not be salvaged had poor survival outcome [15]. Li, et al. [16] in-case series of 155 cases stated that the 5-year

disease specific survival rates N+ and N- patients was 21.54 % and 47.36% respectively. They also reported that cervical metastasis was found in as high as 49.03% of all cases with 40% presenting at initial consultation and 9.03 % presenting after therapy [16]. Likhterov, et al. [17] in a study of 75 cases reported 19 out of total of 22 recurrences occurred locally. Additionally they identified recurrence was associated with T4 disease, positive margins and surveillance imaging. Furthermore in cases where reconstructive flap was used to repair the defect, it needed flap mobilization to obtain biopsy. In 13 of the 19 cases salvage surgery was attempted and was successful in 6 (42%) cases [17].

Conclusion

Based upon the literature search, it seems the consensus is developing that Elective neck dissection is indicated for lesions between T2-T4 (SCC). The most important prognostic factors are T stage, N stage and surgical margin involvement. Tumor grade and perineural invasion may be weaker indicators but play a role in recurrence and disease free survival. Recurrence can occur in the form of nodal metastasis but local is more common. Surgical salvage probably offers the best chance to the patient for clearance but the overall survival for these patients remains poor.

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Conflict of Interest

No conflict of interest.

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