"Lymphatic Mapping to Tailor Selective Lymphadenectomy in Squamous Cell Carcinoma of Oral Cavity"

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Objective: The purpose of this study was to determine the distribution of cervical lymph node metastases in the Squamous cell carcinoma of oral tongue and or floor of mouth; hence to improve the pretreatment evaluation of these patients.

Study design: Descriptive study.

Setting: Department of Oral and Maxillofacial Surgery, King Edward Medical University/ Mayo Hospital Lahore. From 1st July 2008 to 31st December 2009.

Methods: This study was carried out on 50 consecutive patients who were having Squamous cell carcinoma of oral tongue and or floor of the mouth with $T_1 – T_4$ lesions.

Results: Neck lymph node levels I and II were the most common sites of cervical lymph node metastases that was, 30%. Levels IV and V were involved very rarely. The overall metastases to cervical lymph node levels I – III combined was seen in 90% cases of oral tongue or floor of the mouth.

Conclusion: The most common region for cervical lymph node metastases in Squamous Cell Carcinoma of oral tongue and floor of mouth is levels I – III in the ipsilateral neck, so based on pattern of metastases, supraomohyoid neck dissection for cN0 and functional neck dissection for cN+ necks are suggested.

Key Words: Oral Squamous cell carcinoma (OSCC), cervical lymph node metastasis, cN0 (clinically lymph node negative), cN+ (clinically lymph node positive) ($N_1 – N_3$), pN+ (pathologically lymph node metastases found), elective neck dissection, occult metastasis, radical neck dissection (RND).

Introduction

Squamous cell carcinoma is the most common cancer of head and neck region in Pakistan. Higher incidence rates, i.e. 150/100,000, have been reported in Asia.[1] More than 90-95% of oral cancers are SCC or one of its variants.[2,3] The two most common subsites of the oral cavity involved by the SCC are mobile oral tongue and the floor of the mouth. Tumors arising from each of these structures, including those found in patients with early ($T_1 – T_2$) disease, have a significant propensity to metastasize to the regional lymph nodes. Also the early staged tongue and floor of the mouth cancers have a significant incidence of occult cervical metastasis.[4]

Oral cavity has abundant blood supply and lymphatic drainage hence chances of cervical metastases are very high. The biological behavior of oral SCC is uncertain; many of these tumors have an aggressive biological behavior at initial stages with early regional metastases and cause death. On the other hand, advanced tumors may metastasize slowly, and these patients may remain disease – free for long periods after surgery. Regardless of the site of the primary tumor, the presence of a single lymph node in either the ipsilateral or the contra lateral side of the neck reduces the 5 – year survival rate by 50%.[5,6]

At present, there are three options for neck treatment of neck disease in patients with cN0 SCC of the tongue / floor of the mouth.[7] The first one is Functional neck dissection (FND) or elective radiotherapy.[8] Second option is supra-omohyoid neck dissection (SOHND), the lymph nodes with suspicious metastases are examined by frozen sections to decide whether more extensive neck dissection should be performed or not. The third treatment option is wait and watch policy.[9] Salvage surgery is not performed until the metastatic lymph nodes are observed so that overtreatment for cN0 patients / undertreatment of cN+ patients can be avoided. In the present condition, no clinical/ radiographical examinations or biochemical indicators can be used to assess the metastatic condition of the cervical lymph node accurately. Hence, the hotspots are to provide the evidence for neck dissection in management of cN0/ cN+ patients with SCC of the tongue or floor of the mouth by analyzing the distribution characteristics of cervical lymph node metastases and it will also guide for post operative follow up by exploring the emergence time of metastases.[10]

Radical neck dissection (RND) has been the standard surgical procedure for cervical lymphadenectomy that includes removal of at-risk lymph node groups (levels I – V) along with sternocleidomastoid muscle, submandibular gland, internal jugular vein and spinal accessory nerve. It is widely used as an elective procedure for occult neck disease and as a therapeutic procedure for clinically manifested nodal metastases. Clinical and pathologic studies have

supported the concept that functional neck dissection (level I – V) comprises unnecessary overtreatment in the elective management of the OSCC.[11] While dissection of level IV may expose the patients to some risk of chyle fistula or even phrenic nerve injury. Hence, such neck dissections have significant morbidity.

At present, however, despite the high incidence, poor prognosis and abundance of reports, the correct management still does not seem to have been adequately established. Also very limited research work has been done in our country in this aspect.

The endless search into histological samples of OSCC as one means of assisting in the evaluation of prognosis and in the planning of adequate therapy for the patient has led us to conduct this study.

The goal of our study was to provide grounds for an appropriate and optimal type of neck dissection in patients of SCC of oral tongue / floor of the mouth. Therefore, prediction of the distribution of cervical nodal metastasis will help us to reduce the morbidity associated with over or undertreatment in cN0 / cN+ patients and consequently contributing towards the greater goals of better treatment options and in due process to benefit the concerned patients.

Patients and Methods

The study was conducted in the Department of Oral and Maxillofacial Surgery King Edward Medical University/ Mayo Hospital Lahore. This was a descriptive study of 50 patients of Squamous cell carcinoma of oral tongue or floor of the mouth presented in the department from 1st July 2008 to 31st December 2009. Their age range was 15 – 75 years, mean 47.28 ± 10.5 years. Thirty five (70%) patients were male while fifteen (30%) patients were female. The method of sampling was purposive.

All OSCC were staged according to the American Joint committee on cancer (AJCC)/ UICC 2002 TNM classification. Cases with SCC of Oral tongue and or floor of the mouth, previously untreated, T_1 to T_{4a} cases, cN0 or cN+ necks with or without fixed nodes were the inclusion criteria. T_{4b} cases were not included in the study. Each patient was evaluated by two Oral and Maxillofacial consultants in the department and stage of the disease was confirmed.

In all of the cases CT scan was done. Patients whose tumors were crossing the midline were excluded.

Among all patients there were 29 cases of tongue and 21 cases of SCC of floor of the mouth. All patients underwent excision of the primary tumor with 1 – 1.5 cm safe margin and with ipsilateral functional neck dissection in cN0 / cN+ (but unfixed node) patients and RND in the cN+ with fixed nodes. The lymph node specimens were sent as separate groups with clear markings for histopathology review.

The results were analyzed using statistical package for social sciences (SPSS) 13 and percentages and frequencies were calculated.

Results

According to T – classification most of the cases were of T_3 n = 15 (30%) and T_4 n = 19 (38%). The overall rate of cervical lymph node metastases was 60% (30 / 50) which included 59% (17 / 29) metastases in cases of SCC of oral tongue, while 62% (13 / 21) cases of SCC of floor of the mouth. No metastases were observed in T_1 sized lesion of floor of the mouth. The overall highest cervical lymph node metastasis was found in T_4 lesions that was 79% (15/19). Metastases in T_3 size lesions were at second number 60%.

Table 1: *Distribution of cases by T – Classification and Metastasis of primary tumor site n =50.*

T – Classification	Lymph Node Metastasis		
	Tongue	Floor of Mouth	Total (%)
T_1	2 / 4	0 / 1	2 / 5 (40)
T_2	2 / 7	2 / 4	4 / 11 (36)
T_3	4 / 7	5 / 8	9 / 15 (60)
T_4	9 / 11	6 / 8	15 / 19 (79)
Total (%)	**17 / 29 (89)**	**13 / 21 (62)**	**30 / 50 (60)**

Table 2: *Distribution of cases by Tumour site and clinical lymph node status (cN+/ cN0) n = 50.*

Tumor site	Lymph Node Palpable	
	No (cNo)	Yes (cN+)
Tongue	9 / 29 (31%)	20 / 29 (69%)
Floor of mouth	5 / 21 (24%)	16 / 21 (76%)
Total (%)	**14 / 50 (28)**	**36 / 50 (72)**

The rate of tumor free nodes were highest 60% (n = 3) in case of T_1 sized lesions.

Clinical examination reveals 69% cases were cN+ in cases of carcinoma of the tongue out of which 59% cases had pN+ and similarly 76% cases of floor of the mouth were cN+ however only 62% were found pN+.

Out of 30 (60%) positive metastatic lymph nodes (pN+) cases of oral tongue and floor of the mouth, Level I and II were the most frequently involved 30% (n = 9) cases. While isolated level II was the second highest 23% (n = 7) and Level I, II, III combined were the third most frequently involved metastatic groups. 17% (n = 5). Metastasis to level IV and level V were very rare and no metastasis was found at level V in case of floor of the mouth tumor site.

Overall individual level count remained n = 62 total levels (total number of each pathologically positive metastatic lymph node level) in ipsilateral necks among 30 (60%) pN+ patients. The most common region with highest

rate of metastases was level II and it was 42% (26 / 62). The second highest was level I and the percentage was 31% (19 / 62). The third most common was level III, in 18% (11 / 62) cases. Hence the over all percentage of metastases in levels I to III was 90% (56 / 62). Metastases in level IV were found in 5 patients 8% (5 / 62) and only one, 2% (2 / 62) patient was found to have metastases at level V.

Table 3: *Distribution of pN+ cases by lymph node levels and tumor site n = 50.*

Level of Nodes	Metastatic Nodes		Total (%)
	Tongue	Floor of Mouth	
Level – l	1	2	3 / 30 (10)
Level – ll	4	3	7 / 30 (23)
Level – III	1	0	1 / 30 (3)
Level – IV	0	0	0
Level – V	0	0	0
Level I and II	5	4	9 / 30 (30)
Level l, ll and lll	3	2	5 / 30 (17)
Level l, ll, lll and IV	1	1	2 / 30 (7)
Level II, III and IV	1	1	2 / 30 (7)
Level II, III, IV, V	1	0	1 / 30 (3)
Total	**17**	**13**	**30 / 50 (60)**

Table 4: *Total individual level metastatic count n = 62 levels.*

Primary Tumor Site	Levels (No. of Cases)				
	I	II	III	IV	V
Tongue (n = 36)	10	15	7	3	1
Floor of Mouth (n = 26)	9	11	4	2	0
Total (n = 62)	**19**	**26**	**11**	**5**	**1**

Discussion

In cases of OSCC, metastases in the cervical lymph nodes may occur even in T_1 or T_2 cases of primary tumor as described by Okada Y et al,[12] Robins KT et al.[13] The incidence of occult cervical lymph node metastases in OSCC is high that was reported 6-46% as reported by Capote et al,[14] which is a problem when establishing a therapeutic regimen. However, a possible predicting factor has not been established which can accurately determine the cervical lymph node metastases. In the present study, metastasis in the cervical lymph nodes was examined clinically and histopathologically in patients with Squamous cell carcinoma of oral tongue and flour of the mouth.

The percentage of cervical lymph node metastases in oral cavity Squamous cell carcinoma is variable and different for different subtypes in oral cavity. The overall rate of cervical lymph node metastasis in oral Squamous cell carcinoma was reported 34% - 50%[15,16] and by others 35 – 60%, in addition the rate according to the site of the primary lesion it was reported to be 37 – 55% for oral tongue, as said by Woolger et al[9] and for floor of the mouth it is said that one third to one half (10 – 65%) of the patients present with regional metastases, as described by, Sharma Pk et al,[17] as in our studies the overall cervical lymph node metastases in cases of tongue and floor of the mouth were 59% and 62% respectively. We have found the almost same results but it is also a very small data to comment on.

In the present study we have also found a significant metastasis even in cases of T_1 40% or T_2 36% lesions. And 50% of the cases of carcinoma of the tongue at T_1 showed metastases at some level. It shows that even a smaller lesion of tongue has very high potential of metastasis. The same results were shown by Robins KT et al[13] in their study on similar lines.

According to some authors[18] the tumor stage has been shown to be an independent prognostic value by them and not by others.[19] Relationship of tumor stage and metastases further explained by DiTroia,[20] who described that there is difficulty for the tumor emboli to form in small caliber lymphatics of the superficial areas, compared with wider lymphatics of deeper tissues. The same was true in our study that the tumors at late stages were having more metastases. The highest rate of metastasis was found in T_4 lesions which were 79% and 60% for T_3 lesions.

The overall rate of cervical lymph node metastases remain 60% (30 / 50). Same results were described by Dias FL and Lima D et al[21,22] that when comparing with other oral cancers, SCC of the tongue and floor of the mouth has great predisposition to produce metastases in lymph nodes (15 – 75%). In our cases this was due to the fact that the time of presentation most of the cases were at their late stages i.e most of cases were T_3, 30% (n = 15), T_4, 38% (n = 19), this was in contrast to the previous studies by S Manuel et al and Y Okada et at[3,12] which shows presentation of the cases at their early stages. This might be due to other factors high illiteracy rate, ignorance about the disease, poor referral system and limited dental professional screening in our country.

As for the site of metastasis in the cervical lymph nodes a high rate of metastases was reported in the submandibular lymph nodes and superior internal jugular nodes, which is also confirmed in our results for both single and multiple types. This finding was well in agreement with the anatomical running pattern that lymph flow in the cervical region enters predominantly into the submandibular nodes and then descends from superior internal jugular nodes. As the present study also indicates that there is a law for the cervical lymph node metastases in SCC of the tongue or floor of the mouth. The most common regions of involve-

ment were levels I and II 30% in the ipsilateral neck, the second highest were, isolated level II 23%, and the third most common were level I – III in combination 17%. To the contrary Jin Wu – long[23] according to which the most common site of cervical lymph node metastases was level II, second most common one was level III and the third most common one was level I and IV. While in our study level IV was involved very rare of only, 8% and same was true for level V, 2% metastases only. Kafif et al,[10] described that only 2% metastases at level IV in $T_1 – T_3$, N0. While in our cases T_4 and N+ were also included even though very low rates of metastases were found at these distant levels.

Elective neck dissection is the useful treatment for oral cavity SCC as it allows accurate neck staging and also helps to determine adjuvant therapies. Clinical and pathological studies show that modified radical neck dissection (level I – V) is responsible for overtreatment if opted as elective modality and claimed to have equal results for supraomohyoid neck dissection and modified radical neck dissection, Dias FL.[22] While dissection of level IV may cause injury to phrenic nerve and chyle fistula formation. But according to some authors the inclusion of level IV in the dissection appears justified for the patients with oral tongue cancer in view of known lymphatic drainage of the tongue and higher incidence of "skip" metastasis.[24] Byers et al[25] reported a high incidence (15.8%) of either level III or IV metastasis as the only manifestation of disease in the neck, without disease in levels I and II, among 277 patients with oral tongue carcinoma. However in our study we have never found isolated levels III or IV without the involvement of level I or II (except one case of tongue with isolated level III). We concluded that level IV need to be included only in the dissection when there is intraoperative suspicion of metastases to levels II or III.

In our cases, 90% nodal metastases occur in level I-III. Same was described by Shah JP and candela FC that the nodal involvement usually occurs in levels I – III.[26,27] Clearly, these lesions require a neck dissection; but just which dissection depends on the characteristics of the lesion. Metastasis to level IV and level V were very rare and no metastatic node was found at isolated level IV or V. This is in agreement with Dias FL et al.[22] This indicates a more conservative, approach like a selective supraomohyoid neck dissection (level I – III) should be performed, if at all, where there is no other indication for radical neck dissection. Same described by Dias FL and Hamakawa H.[22,28]

Conclusion

Supraomohyoid neck dissection (level I – III) should be done as elective treatment in $T_1 – T_4$, N0 for tongue or floor of the mouth SCC cases and level IV should be included only when there is peroperative suspicion of level II or III nodal involvement.

For cN+ neck modified radical neck dissection type III (functional neck dissection, level I – V) should be carried out as therapeutic treatment modality if there are no findings of extracapsular spread, which would need a more extensive neck dissection (modified radical I or II) and post operative radiotherapy according to the lymph node status.

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