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Original Article

A Study on Secondary Neck Nodes from Squamous Cell Carcinoma

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Abstract

Introduction: Head and neck squamous cell carcinoma also carries a high rate of occult nodal metastasis. It is important to detect lymph node development in its early stages for improving the prognosis. The mechanisms by which malignant tumors, invade lymphatics, and metastasize to regional lymph nodes are complex and interrelated, the exact mechanisms have only recently been the subject of intense interest and sophisticated experimentation.

Aim: The aim of the study was to correlate the incidence of cervical node metastases by the site of primary in squamous cell carcinoma of the head and neck region and to correlate individually the size of the tumor and its degree of histopathological differentiation.

Materials and Methods: The present prospective study of 60 patients with proven squamous cell carcinoma at various sites of head and neck was undertaken to study the possible tumor factors which influence the incidence and the pattern of regional nodal metastases.

Results: A progressive increase in the incidence of node metastases was observed with increasing tumor size 55.55% for lesions smaller than 2 cm, 75% for lesions between 2 and 4 cm, and 100% for lesions larger than 4 cm. A progressive increase in the incidence of node metastasis was observed with increasing histological undifferentiation of the tumor (4.3% for well-differentiated primaries and 75% for moderately differentiated primaries).

Conclusion: Large primaries (more than 4 cm) and those with higher histologic grade (moderate to poorly differentiated) especially when situated in the oropharynx or the oral tongue, have a greater propensity for developing regional nodal metastasis compared to the rest.

Key words: Cervical node metastases, Head and neck, Squamous cell carcinoma

INTRODUCTION

Squamous cell carcinoma of the head and neck, especially those arising in the oral cavity and oropharynx accounts for more than 50% of all cancers in India compared to 2–3% in the U.K. and U.S.A. More than 30% of these patients have clinical evidence of cervical node metastases when the first seen.[1]

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The presence of an enlarged node proven histological positive for metastases is an ominous sign and as a general rule decreases the 5-year survival rate by at least 50%. When the nodal involvement becomes multiple and extends low in the neck, few patients get cured regardless of the treatment given.[2]

No definite conclusions about the efficacy of treatment of the neck in the absence of palpable nodal disease can be drawn from studies from the literature. However, many indicate improved survival for those undergoing therapeutic neck treatment for occult disease versus those undergoing therapeutic neck treatment for clinically positive nodes. Spiro and strong reported significantly better survival for patients undergoing elective neck treatment for oral and oropharyngeal cancers who had clinically negative

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but histologically positive nodes, compared to patients undergoing therapeutic neck dissection for clinically positive nodes.[3]

Since there is currently no way to identify occult disease in the cervical nodes other than removing and examining them histopathologically, various features of the primary tumor (namely, site, size, gross appearance thickness, and differentiation) have been correlated with the incidence of nodal disease in the neck by different workers.[4]

In the present study, an attempt has been made to determine the tumor factors increase the propensity for regional metastases in squamous cell carcinoma of the head and neck, so as to help, identify the cluster of high-risk patients who are likely to harbor occult nodal disease in the absence of clinically negative nodes and for whom elective neck treatment may prove beneficial.

Nine areas of the head and neck including five primary sites in the oral cavity, three in the oropharynx, and the maxillary antrum have been considered under the preview of this study, as these were the sites involved in the patients presenting with squamous cell carcinoma of the head and neck in the surgical department of our hospital.

Aim

The aim of the study was to correlate the incidence of cervical node metastases by the site of primary in squamous cell carcinoma of the head and neck region and to correlate individually the size of the tumor and its degree of histopathological differentiation.

MATERIALS AND METHODS

This prospective study was conducted in patients with carcinoma arising in the oral cavity, oropharynx, or maxillary antrum in the surgical units of Kilpauk Medical College and Hospital and Government Royapettah Hospital, Chennai. A total of 60 patients were ultimately included in the study and all had histologically proven squamous cell carcinoma of varying degrees of differentiation. The patients who were not included in this study were seven for want of one reason or other, for example, biopsy report one case reported as pseudoepitheliomatous hyperplasia without any evidence of malignancy, one case reported as adenocarcinoma arising from ulcer in the lower lip, and another case involving the buccal mucosa were adenoid cystic carcinoma.

A detailed history was obtained regarding the nature and duration of presenting complaints as well as of all other associated complaints particular attention being paid to factors increasing the likelihood of malignancy, for example, white or red patch in the oral cavity, non-healing ulcer, throat pain more than 3 weeks duration, non-tender enlarging neck mass, pressure symptoms or obstructive symptoms, or addiction to tobacco, alcohol, betel leave chewing, snuff dipping, irradiation to head and neck in the past, and past treatment of other head and neck carcinomas.

Complete physical examination including an indirect laryngoscopy in selected cases was done to note characteristics of the primary in terms of site, extent, size (in cm), macroscopic appearance (exophytic, endophytic, or mixed), degree of local infiltration, presence of other synchronous lesions, and T stage of the tumor.

Attention was then paid to the neck to detect any palpable nodes. The criterion for "a clinically positive node" as defined by Lindberg was used to differentiate metastatic from nonmetastatic nodes throughout the study. Any palpable node more than 1 cm in size, spherical rather than ovoid in shape, hard in consistency, and situated in the drainage area of a histologically proven primary was considered as metastases.

The note was made of the side and triangle of the neck involved, the total number of palpable nodes, the groups involved, size (in cm), consistency, presence of tenderness, fixity to the skin as well as node, and N stage of the nodes.

When nodes belonging to deep cervical chain were enlarged, they were included in the anterior cervical triangle with regard to their position, as the classical description of the cervical triangle excludes the nodes deep to sternocleidomastoid muscles from either of two major triangles. Midline nodes were considered as homolateral nodes. In evaluating the size of the nodal mass, allowances made for the intervening soft tissue.

Biopsy from the primary site was obtained in all the cases included in the study to obtain histological proof regarding its nature as well as to note its degree of differentiation. The latter was expressed in terms of three grades, well differentiated, moderately differentiated, and poorly differentiated.

RESULTS

Of 60 patients with histologically proven squamous cell carcinoma arising from various primary sites in the head and neck who were ultimately included in the study. Thirty-five (58%) were males and 25 (42%) were females. Palpable neck nodes were detected on admission in 30 males (68%) and 14 females (32%). The overall incidence of patients with head and neck squamous cell carcinoma (HNSCC) was in the age group of 30–70 years [Figure 1]. Incidence

of cervical node metastases on clinical examination was 73%. [Figure 2].

The most frequent site of the primary in the present series was the buccal mucosa (18 patients) which accounted for 30% of the head and neck cancers [Table 1]. Next in frequency was the anterior 2/3rd of the tongue 11 patients (18.3%) and alveolus 7 patients (11.6%). Posteriorly situated cancers arising in the oropharynx showed a comparatively lower frequency with the base of tongue having the highest 7 patients (11.6%). Overall the least frequent site was maxillary antrum 3 patients (5%). Irrespective of sex, patients had clinical evidence of cervical node metastases on admission. Bilateral nodes were present in 2 patients. Sixteen were negative for adenopathy.

Among the primaries, tonsils accounted for the higher incidence of node metastases. All 4 patients with tonsillar carcinoma had palpable nodes on admission, accounting for 100% nodal involvement. Other posteriorly situated cancers also showed a similar pattern of behavior as compared to the anteriorly situated cancers with the base of the tongue and soft palate having 85.71% and 50%,

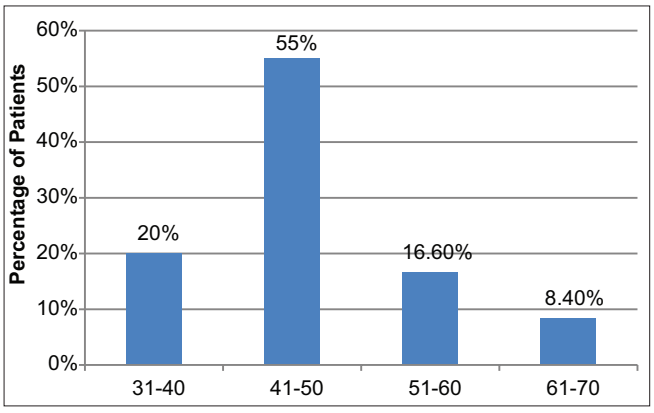

Figure 1: Age of incidence of primary

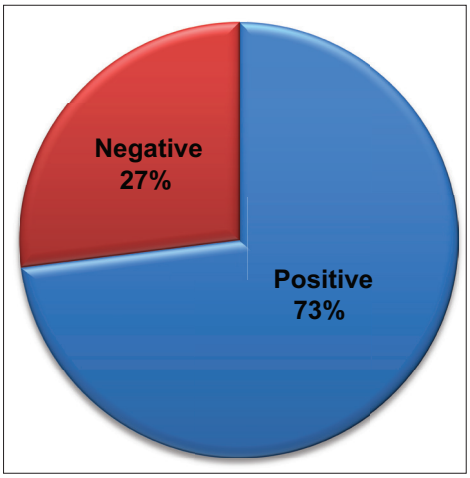

Figure 2: Incidence of cervical node metastases

respectively. The least incidence of nodal metastases was from lesions of the hard palate and maxillary antrum.

Carcinoma of the buccal mucosa predominantly metastasized to the submandibular nodes. Only when very advanced (T4 with retromolar extension), they involve the upper deep cervical nodes. Submental node involvement was totally absent. Carcinoma of the alveolus predominantly metastasized to submandibular nodes. Submental node involvement was infrequent.

Carcinoma of hard palate infrequently metastasized. The only one patient, in whom this happened, had involvement of the ipsilateral submandibular node. The lower incidence of cervical metastases in patients with cancer of the hard palate has been ascribed in the literature to a less extensive lymphatic network in the immobile palate mucosa. Although the number of patients with hard palate cancer was small in the present series, our findings appeared to confirm with this explanation.

Carcinoma of the anterior two-thirds of the tongue most commonly involved the upper deep cervical group followed by the submandibular group of nodes. In only one instance, the middle deep cervical nodes involved. The involvement of nodal groups at a lower level in the neck was not seen. As none of the primaries involved the tip of the tongue, predictably submental node involvement was absent. Bilateral nodal involvement was present in one instance with the involvement of the contralateral submandibular nodes.

Carcinoma of the floor of the mouth predominantly metastasized to the ipsilateral submandibular nodes, in spite of the anterior location of the tumors and their proximity to the midline, submental node involvement was infrequent and contralateral nodes were uninvolved at all.

Carcinoma of the soft palate commonly metastasized to upper deep cervical nodes. Although it is a midline structure, the incidence of the bilateral nodal involvement was nil, possibly of the small numbers of patients involved in the present study [Tables 2 and 3].

Going by individual sites all the patients who had tumors larger than 4 cm in diameter with primaries situated in the buccal mucosa, alveolus, and anterior two-third of the tongue and the maxillary antrum had clinically palpable nodes on admission. Conversely, the majority of patients having tumors smaller than 2 cm with primaries in the same sites had a clinically negative node on admission [Figure 3].

The degree of differentiation of the primary varied according to the tumor site. The majority of the

Table 1: Incidence of cervical node metastases by site of primary

Primary	No. of patients	%	No. palpable nodes (N0) on admission	Palpable nodes (N+) on admission	% of (N+) patients
Buccal mucosa	18	30	3	15	83.33
Alveolus	7	11.60	3	4	57.14
Hard palate	3	5	2	1	33
Floor of mouth	4	6.60	1	3	75
Soft palate	3	5	1	2	66
Tongue ant 2/3rd	11	18.30	3	8	72.72
Tongue post 1/3rd	7	11.60	1	6	85.71
Tonsil	4	6.60	0	4	100
Max. antrum	3	5	2	1	33

Table 2: Topographical distribution of cervical nodal metastases from ipsilateral nodes only

Ipsilateral nodes only	N0	N1	N2a	N2b	N2c
Buccal mucosa – submandibular node (main)	3	9	4	2	-
Alveolus (submandibular node)	3	2	1	1	-
Hard palate (submandibular node)	3	1	-	-	-
Floor of mouth – submandibular (main)	1	2	1	-	-
Soft palate (upper and middle cervical nodes)	1	2	-	-	-
Tonsils (jugulodigastric nodes)	0	2	1	1	-

Table 3: Topographical distribution of cervical nodal metastases from ipsilateral nodes and contralateral nodes

Ipsilateral nodes and contralateral nodes	N0	N1	N2a	N2b	N2c	N3
Tongue anterior 2/3rd (upper deep cervical nodes)	3	4	2	1	-	1
Tongue posterior 1/3rd (upper deep cervical nodes)	1	2	1	1	-	2
Maxillary antrum (submandibular node)	2	-	1	-	-	-

anteriorly situated tumors, i.e., those arising in the oral cavity, were well or moderately differentiated (55.55 and 26.66%, respectively), whereas the bulk of those situated posteriorly, i.e., in the oropharynx was moderately or poorly differentiated (26.66 and 53.33%, respectively) [Table 4].

The degree of differentiation, in turn, was found to influence the incidence of regional nodal metastases. Overall tumor differentiation showed an inverse relationship with the incidence of nodal metastases. Decreasing tumor differentiation was associated with increasing nodal spread (64.29%, 75%, and 87.5% in cases of well, moderately, and poorly differentiated tumors, respectively). Conversely, the number of patients who had a clinically negative neck on admission showed a decline with increasing tumor grade 35.7%, 25%, and 12.5% with well, moderately, and poorly differentiated, respectively [Table 5].

When both tumor differentiation and its site were considered together in relation to the incidence of node metastases, it was observed that the majority of

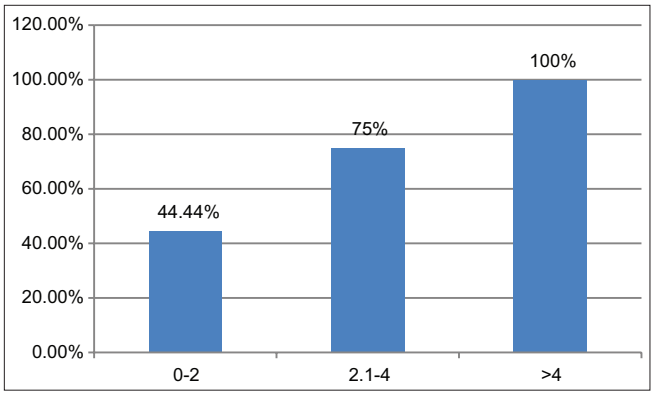

Figure 3: Correlation between tumor size and cervical nodal metastases

the anteriorly situated tumors were histologically well differentiated, and 33–83% of these tumors produced regional metastases. This was in contrast to the posteriorly situated tumors, the majority of which were histologically moderate to poorly differentiate and gave rise to a high regional metastatic rate of 66–100%.

DISCUSSION

Squamous cell cancer of the head and neck is one of the most common cancers worldwide, with incidences of more than 30/100,000 population in India (oral cancer) and in France and Hong Kong (nasopharyngeal cancer). It constitutes about 4% of all cancers in the United States and 5% in the United Kingdom. A total of 2940 new cases of lip, mouth, and pharyngeal cancer in men were reported in the United Kingdom in 1996: An incidence of 10.2/100,000 population.[5] People in their 40s and 50s are most susceptible. The 3:1 ratio of prevalence in men to women is decreasing: In the past 10 years, the incidence in Scotland has risen by 19.4% in men and 28.7% in women. In the United Kingdom, incidence and mortality are greater in deprived populations, most notable in carcinoma of the tongue.[6]

Depending on the site of the primary, 73% of these patients already have palpable nodes in the neck when first seen. A significant percentage, in addition (20% according

Table 4: Tumor site and its histologic differentiation

Site	Total number	Well-differentiated (%)	Moderately differentiated (%)	Poorly differentiated (%)
Anteriorly situated tumors (buccal mucosa, alveolus, hard palate, tongue ant 2/3rd, floor of mouth	45	25 (55.55)	12 (26.66)	8 (17.77)
Posteriorly situated tumors (soft palate, tonsils, tongue post 1/3rd, maxillary antrum	15	3 (20)	4 (26.66)	8 (53.33)

Table 5: Correlation between tumor differentiation and cervical nodal metastases

Degree of differentiation	No. of patients	Total N0 (%)	Total N+ (%)	N1 (%)	N2 (%)	N3 (%)
Well	28	10 (35)	18 (64.29)	16 (57.15)	2 (7.14)	-
Moderately	16	4 (25)	12 (75)	4 (25)	6 (37.5)	29 (12.5)
Poorly	16	2 (12.5)	14 (87.5)	4 (25)	9 (56.25)	1 (6.25)

to one estimate), harbor occult nodal disease which manifests clinically at a later date often after the primary has been treated adequately.

The presence of the palpable regional lymph nodes markedly alters the prognosis of patients with HNSCC by reducing the 5-year survival rate to less than half. Therefore, treatments of the neck before regional nodes become clinically palpable may help to improve the local-regional control rate and the overall survival in these patients.

However, in view of the morbidity imposed by any form of additional treatment to the neck at the time treating the primary, especially when surgery is chosen as the modality. Its blanket use in all patients with head and neck primary has not been considered justifiable.

Kuperman *et al*. revealed the relationship between the risk of distant metastasis and tumor site, size, and nodal status.[7] The size of the cervical lymph node remains an important factor in the interpretation of a clinically suspicious lymph node metastasis; however, it remains controversial regarding the significance of the size of the cervical node.

The accuracy of staging depends on the status of the cervical node. Many methods have attempted to detect the node status but no gold standard exists, except the histopathologic examination. Some studies have reported that the size of the cervical node was an inaccurate predictor of nodal metastasis and could not be regarded as an accurate means of staging in patients with clinically negative nodes.[8,9] Neck dissection is both a therapeutic and staging procedure and has evolved to include various types with standardized level designations (I–VI) for lymph node groups. Neck dissection is still a challenging treatment among patients with clinically negative nodes.

Ozer *et al*. suggested therapeutic neck dissection among patients with clinically negative nodes because pathologically positive nodes might be found in some patients.[10] Some reports have shown pathologically identified neck node metastasis occurred 34–51% in prophylactic neck dissections.[11,12]

Di *et al*. reported the significance of the size of the lymph node and recurrence. The size of the cervical node metastasis is the key risk factor in determining the development of cervical recurrence. Patients presenting extracapsular nodal spread and invasion of non-lymphatic structures have a high risk of developing cervical recurrence.[13]

CONCLUSIONS

Squamous cell carcinoma at various sites of head and neck was undertaken to study the possible tumor factors which influence the incidence and the pattern of regional nodal metastases. That large primaries (more than 4 cm) and those with higher histologic grade (moderate to poorly differentiated), especially when situated in the oropharynx or the oral tongue, have a greater propensity for developing regional nodal metastasis compared to the rest. These data could help to define the group of patients who are likely to harbor occult disease in their neck in the absence of clinically detectable nodes and for whom elective treatment of neck at the treatment of the primary may prove to be beneficial.

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