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GCC Cancer Treatment Protocol Guidelines for Breast and Colorectal Cancer

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Introduction

Head and neck (H&N) cancer is the sixth most common type of cancer in the world, representing about 6% of all cancer cases (1). Overall, 57.5% of global H&N cancers occur in Asia, especially in India for both sexes (2). Risk factors associated with squamous cell carcinoma (SCC) include betel quid chewing, tobacco and alcohol consumption, and due to the differences in etiology and species, there are significant differences in pathology, clinical presentation, treatment outcomes and survival between Western and Asian countries (3). Surgery or radiotherapy (RT) as a single modality is currently considered a suitable method for the treatment of early stage SCC, whereas postoperative radiotherapy (PORT) with/without chemotherapy combined with surgical excision is recommended for advanced tumours (4). Loco regional failure has been documented to be the major cause of death for squamous buccal mucosa (BM) cancers managed with surgery and RT (3).

Approximately 300 lymph nodes (LN) are located in the H&N comprising 30% of the total 800 LN in the human body. Cervical metastasis has a major impact on the prognosis in patients with carcinomas of the H&N and the frequency of such spread is greater than 20% for most SCC (5).

This study was undertaken in an attempt to correlate the incidence of cervical (neck) LN metastasis in...
carcinoma BM and compare the survival outcome with the node negative patients.

Patients and methods

Ninety-nine patients of carcinoma BM, treated with PORT were analyzed in the study. Patients in this study were advised PORT based on the pathological findings that indicated adjuvant RT. Pathological report was used to determine the nodal involvement and staging. Patients were classified into three groups as (A) No nodal involvement, (B) Up to three LN positive and (C) >3 LN positive. All patients received PORT to face and neck region using cobalt—60 gamma rays or a 6 MV linear accelerator with standard treatment portals to a total mean dose of 60 Gray (range 54–62 Gray) at 1.8–2 Gray/fraction and spinal cord shielding at a dose of 46 Gray. Appropriate steps were taken during planning and implementation of treatment. Hospital case records were assessed to evaluate the follow up duration and status of the patients after completion of the treatment. Overall survival was calculated from the duration between the dates of diagnosis to the last recorded follow up and was calculated in months. Online Graph Pad software was used for statistical analysis. P value was calculated using unpaired t test and a value of p < 0.05 was considered significant.

Results

Ninety-nine patients of carcinoma BM were evaluated retrospectively. Of these, 79.79% were males (n=79) and 20.20% were females (n=20). The male: female ratio was 3.95:1. The mean age of the patients was 45.71 years (range 27–70 years). According to T classification, majority of the cases were T4 (n=40, 40.40%), closely followed by T2 lesions (n=35, 35.35%). T3 lesions constituted for 19.19% cases (n=19) while there were five cases (5.05%) of T1 lesions with positive neck nodes or positive surgical margin.

Sixty-two patients (62.62%) had positive neck nodes, with/without adverse pathologic features mandating PORT while 37 patients (37.37%) did not have any neck nodal involvement but were advised PORT in view of other adverse pathologic features.

The total number of positive LN was 158 (minimum 01 to maximum 11). Between T status and metastatic node, cross tabulation showed the following incidence of LN metastases (Table 1)

<table>
<thead>
<tr>
<th>Stage</th>
<th>N</th>
<th>Number of node positive</th>
<th>%</th>
<th>Total number of nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>T4</td>
<td>42</td>
<td>29</td>
<td>69.04</td>
<td>80</td>
</tr>
<tr>
<td>T3</td>
<td>16</td>
<td>09</td>
<td>56.25</td>
<td>25</td>
</tr>
<tr>
<td>T2</td>
<td>36</td>
<td>21</td>
<td>58.33</td>
<td>50</td>
</tr>
<tr>
<td>T1</td>
<td>05</td>
<td>03</td>
<td>60</td>
<td>03</td>
</tr>
</tbody>
</table>

Table 1: Cross tabulation between T status and lymph node metastases.

N= number of patients, %=percentage.

the node positive patients (group B+C) was 10.82 months (range 01–35 months). On statistical analysis, this value was found to be significant (p=0.0335),

In comparing survival between groups B (up to 3 LN metastases) and C (>3 LN metastases), no statistically significant difference was noted (p=0.1167).

Independent comparison of Group A with group B revealed a statistically insignificant difference (p values 0.1089), however the difference in survival between group A and group C (>3 LN positive with PNE) was statistically significant (p=0.0483).

Discussion

Oral cancer has emerged as a global health problem with its particular relevance in certain parts of Europe and South–Eastern Asia especially in Sri Lanka, Pakistan, Bangladesh, and India. The Indian National Cancer Control Programme estimates the total cancer burden in India for all sites nearing 1.4 million new cases by 2026. Oral cancer is the sixth most common cancer worldwide with 575,000 new cases each year and 200,000 deaths annually of which carcinoma BM is a major concern owing to the widespread tobacco chewing habit prevalent in the Indian subcontinent.

Carcinoma BM usually presents as an indolent mass on the BM. Small lesions are usually asymptomatic but often noted on general oral examination. Pain commonly occurs at enlargement of lesion and development of ulceration. Deficient oral intake leads to malnutrition and dehydration. Associated symptoms include bleeding, facial weakness associated with sensory changes, dysphagia, odynophagia, and trismus. An in depth history is required to determine the patient’s candidacy for surgery or RT. Usually, the patient has a history of betel nut chewing associated with some form of tobacco and alcohol use. An appropriate management of the neck in patients with squamous H&N cancers is critically
Neck nodal involvement and survival in buccal mucosa cancers, Vivek Tiwari, et. al.

important because the presence of cervical metastasis is the most powerful independent indicator of locoregional recurrence and overall survival rate. Incidence of neck metastasis in oral SCC is reported to be 34% to 50% (9).

Ninety-nine patients were retrospectively evaluated during the course of this study. Of these, 79.79% were males (n=79) and 20.20% were females (n=20). The male:female ratio was 3.95:1. A male preponderance of cases was noted consistent as per literature (9). It also stems from the fact that in India, Bhopal (the place where the study was conducted), has the world’s highest age-standardized incidence of both tongue (10.9) and mouth cancers (9.6) in males (10). However, gender of the patient is not an influencing factor in the survival rate. Among the 99 patients in our study, mean age was 45.71 years, similar to the reported trend in literature that shows carcinoma BM to be a disease of middle age from the third to fifth decades (9).

Of all the subsites in oral cavity, BM is a very common presenting site of oral SCC in India and especially in Bhopal. The widespread practice of smokeless chewable tobacco appears to be a major causative agent. The presentation of cases in our series differed from the previous studies in the sense that although the majority patients presented in T4 stage (n=40, 40.40%), the incidence of T2 lesions exceeded that of T3 lesions (35.35 versus 19.19%).

In cases of oral SCC, metastasis in the cervical LN may occur even in T1 or T2 cases of primary tumor (11). In our series, we found 3 out of 5 (60%) T1 lesions with pathologically positive LN involvement.

Cervical node metastasis is an important prognostic factor for H&N SCC. (12) Literature review demonstrates that regional LN metastases in BM carcinoma occurred less frequently than other oral cavity subsites at about 25–30% (9). However, in the present study, we found 62.62% patients presenting with positive cervical LN. Our findings correlate with those of DeConde et al (13) who reported 54% of the patient sample to be positive for neck LN metastasis. These findings may be explained by the differences in distribution according to tumor differentiation as well as different geographical and tobacco chewing habits.

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 (14). Stage of the disease at presentation, surgical margin status, and extracapsular spread of cervical nodal disease have been reported as the most important prognostic factors in patients with carcinoma BM (15). In our analysis, there was a statistically significant difference in survival between the patients with pathologically node negative disease versus node positive disease (p=0.0335).

Cervical nodal involvement is an important variable concerning the appropriate treatment and subsequent outcome. An inferior outcome is expected in patients with nodal disease and worsens in the presence of extracapsular spread (16). The incidence of occult LN metastasis in early stage tumours (T1/T2) has been reported to be between 27%–40% (17). However, in our series, the early stage tumours had a higher incidence (nearing 60%) of LN involvement.

Factors influencing tumour spread to the LN include the primary site, thickness, double DNA aneuploidy and poor differentiation. (16) In addition, peri-neural invasion, infiltrating-type invasive front, as well as low E–cadherin are contributing factors for LN metastases (16). In our study, we found >55% pathological confirmation of cervical LN in the cases and the incidence was almost 70% in the T4 lesions.

Shibuya et al (18) have reported that oral SCC having multiple neck metastases (>10) have a poor prognosis when compared node negative cases in view of the proportion of distant metastasis being higher. Our study demonstrates a poor survival in the subgroup of >3 LN.

Surgery remains the mainstay of initial definitive treatment for the majority of oral SCC patients (16). Primary tumour along with dissection and removal of the cervical lymphatic chain, when indicated, is the norm. Along with RT, the survival of oral SCC has increased from 40% to 70%. (19) Elective neck dissection is employed when the risk of cervical involvement is over 15–20% (16). It assists in defining the neck nodal status, removal of undetectable metastasis and determines the need for adjuvant therapy (16). Therapeutic neck dissection is of utmost importance in patients with clinically positive neck as well as beneficial in patients with NO neck (20). Aggressive adjuvant therapy has been recommended for patients with extracapsular spread (21). RT is a key component of the management of early–stage and locally advanced cancer BM, either alone or more frequently combined with surgery and/or chemotherapy (22). In the present study, we analyzed 99 post–operative patients of carcinoma BM who received adjuvant RT.

In H&N SCC, the search for better prognostic factors beyond TNM—stage is ongoing. LN ratio (positive LN/total LN) is gaining interest in view of its potential prognostic significance (23) and has emerged as an independent prognostic factor for overall survival and local failure–free survival in H&N cancer patients (24). However, in contrast, in the study by Mamalle et al. (25), the number of positive LN was found to be a superior predictor of outcome.
for H&N cancer patients. Additional studies (26, 27) have documented a significant likelihood of finding neck LN metastasis with increase in the total number of dissected LN. The criteria of total number of LN to be superior has been further supported in recent studies (23, 28–30). Similar to these studies, our study demonstrates a poor outcome in patients with >3 positive LN.

This retrospective study has some limitation in the sense that the total number of dissected LN depended on disease and physicians’ LN criteria that might have affected the resection outcome. On the other hand, the main advantage of this study was that all patients received surgery plus adjuvant RT and the dose prescribed was fairly homogenous. Compared to other studies, our treatment was more consistent. We recommend further studies to confirm our hypothesis.

**Conclusion**

Carcinoma BM remains a major public health problem in the Indian subcontinent. Advanced disease constitutes a major proportion of patients presenting for treatment. Surgery followed by adjuvant RT is the mainstay of management. The number of pathologically positive neck nodes are an indicator of treatment outcome and in addition to the existing staging systems, holds promise in risk stratification of carcinoma BM patients.

**References**


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