Outcome of Per Oral Wide Excision of T1-2 N0 Localized Squamous Cell Cancer of the Buccal Mucosa—Analysis of 156 Cases

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**Objectives/Hypothesis:** The purpose of the study was to study the outcomes of per oral wide excision of early T1-2 N0 squamous cell cancer of buccal mucosa.

**Methods:** This is a retrospective study of early and localized squamous cell cancer of the buccal mucosa treated with peroral wide excision at a tertiary-care hospital.

**Results:** A total of 156 patients were analyzed. One hundred ten patients (70.5%) had no recurrence, whereas 15 (9.6%) had a local recurrence, 24 (15.4%) had regional metastasis, three (1.9%) had locoregional recurrence, and four (2.6%) developed second primary tumors over a median follow-up of 48 months. Most patients with local recurrences (14 patients, 93.3%) and regional metastases (24 patients, 100%) could be salvaged with treatment. In contrast, all three cases with locoregional could not be salvaged. Most of the cases with recurrences, 36 (78%) in this study group, occurred within 2 years of primary treatment. Out of 143 cases with a habit of tobacco/beetel quid chewing, premalignancy was seen in 62 (43.4%) cases, showing a statistically significant association with P-value of 0.012. Fifteen (21.4%) cases with stage T2 developed regional neck nodes, while only 9 (10.5%) cases with stage T1 developed regional neck nodes with P-value of 0.032. Three-year overall survival rate and disease-free survival rates were 91.7% and 70.5%, respectively.

**Conclusions:** Peroral wide excision seems to be an adequate procedure for T1-2N0 localized squamous cancer of buccal mucosa. Prophylactic selective neck dissection should be considered in only T2 N0 cases as only T stage of the disease could be significantly correlated with the development of the metastatic neck nodes.

**Key Words:** Buccal mucosa, squamous cell cancer, oral cavity.

**Level of Evidence:** 2c.

**INTRODUCTION**

Squamous cell carcinoma of the buccal mucosa is the most common form of oral cancer, especially in India and other Southeast Asian countries. The high incidence of cancer of the buccal mucosa in India is due to the habitual tobacco/betel quid chewing, which exposes the buccal mucosa to high doses of carcinogens. Traditionally, treatment for stage I and II lesions has been either surgery or radiation therapy as a single modality. It has been our policy to treat all early and limited T1 to T2 cancers by peroral wide excision, providing that the mouth opening is adequate.

There are few reports in the literature analyzing the outcomes of surgical treatment of early and localized cancer of the buccal mucosa. The aim of this study was to analyze the outcome of per oral wide excision and to evaluate various clinic-pathological prognostic factors. This study represents the largest series of previously untreated patients with early (T1-2 N0) cancer of buccal mucosa treated only with per oral wide excision.

**MATERIALS AND METHODS**

A retrospective analysis of early-stage squamous cancer of buccal mucosa was done from January 2003 to January 2010 in the Head and Neck Unit of Prince Aly Khan Hospital, Mumbai, India. This study was limited to the patients with previously untreated, biopsy-proven, limited T1-2 N0 cancer of buccal mucosa who underwent per oral wide excision. All cases had N0 neck on clinical palpation, USG with color doppler, and guided FNA. Intense follow-up rather than neck dissection was used for clinically negative neck. Only patients with squamous cancer limited to the buccal mucosa were included, and those with extension to commissure, lip, alveolus, and gingiva were excluded. Patients with carcinoma in situ were also excluded from the study. In all of the cases, frozen section was used to check that the margin were free of the tumor. The raw area was either left to heal by granulation or covered by split skin graft. Active jaw-stretching exercises were encouraged postoperatively to avoid oral scarring and trismus. Strict oral hygiene was maintained to avoid secondary infection and bleeding. All of the patients had negative margins and base (deep margin) on histopathologic analysis. Tumors were staged according to the TNM staging system, as proposed by the 2002 American Joint Committee on Cancer (AJCC).

The survival time was measured from the time of histologic diagnosis; and the period of follow-up was calculated as...
the duration between the date of initial diagnosis to the date of death or last follow-up when alive. For disease-specific survival, patients dying from other diseases were censored at the time of death. Survival curves were calculated by the Kaplan-Meier method. Various demographic, clinical, and pathologic factors were analyzed and correlated with the development of regional neck nodes. The prognostic significance of clinicopathologic factors on regional recurrence was assessed using Cox’s regression model with forward selection. SPSS version 12.01 (SPSS Inc., Chicago, IL) was used for the statistical analysis. A \( P \)-value < 0.05 was considered to be significant.

RESULTS

A total of 156 patients with a diagnosis of T1-2 N0 squamous cancer of buccal mucosa were found eligible for the study. The patients were not evenly distributed by gender (142 males, 14 females). The overall male-to-female ratio was 10:1 in this study. At the time of diagnosis, the mean age was 50 years (range, 22–86 years). The prevalence rate of habitual tobacco/betel nut chewing was documented in 143 patients, that is, 91.7%. Premalignant lesions in the form of leukoplakia, erythroplakia, and oral submucous fibrosis were seen in 63 (40.4%) of cases. Out of 143 cases with habit of tobacco/betel nut chewing, premalignancy was seen in 62 (43.4%) cases, showing a statistically significant association with \( P \)-value of 0.012.

The median follow-up time was 48.40 months [standard error, 1.50; 95% confidence interval (CI), 44.35–52.45]. Recurrence developed in 46 patients (29.5%) during follow-up. Among them, 15 (9.6%) had disease recurrences only at the primary site, 24 (15.4%) had recurrences only in the ipsilateral neck, and 3 (1.9%) patients had simultaneous primary and neck recurrences during follow-up. Second primary tumours were seen in four cases (2.6%) (Table I). Thirty-six patients (78.3%) had a recurrence within the first 2 years of primary resection of the disease.

Forty-two (91.3%) out of the 46 that had recurrence could be salvaged. Among four cases that could not be salvaged, one had unresectable recurrence at the primary site, while three other cases had unresectable locoregional recurrence. Second recurrence was seen in four cases after salvage treatment. Only one could be salvaged; this patient had second recurrence in the primary site and also developed neck metastases simultaneously. One more case apart from that of locoregional disease developed multiple pulmonary and skeletal metastases.

At last follow-up, 143 (91.7%) cases were alive and free of disease, four (2.6%) cases were alive but with disease, six (3.8%) cases were deceased because of the cancer-related cause, and three (1.9%) cases were deceased due to other causes (Table II). The prognostic factors analyzed for nodal recurrence were age, sex, T stage, pathologic differentiation, depth of infiltration (< 5 mm and >5 mm), perineural infiltration, and lymphovascular invasion. Univariate analysis of the correlation of the various clinicopathologic factors to the development of the metastatic neck nodes was done.

Only T stage of the cancer showed statistically significant correlation with the development of the neck nodal metastases. Fifteen (21.4%) cases with stage T2 developed regional neck nodes, while only nine (10.5%) cases with stage T1 developed regional neck nodes with \( P \)-value of 0.032. Only 1 (2.5%) case of verrucous carcinoma and 6 (12.5%) cases of WDSCC developed metastatic neck nodes, while 25% cases of MDSCC and 33.3% cases of PDSCC developed neck nodes. Although the number of neck recurrences was much higher in MDSCC and PDSCC and the \( P \)-value (0.06) had a trend toward significance, but it was greater than 0.05, which was taken as cutoff for reporting significance. No other clinic-pathological factor could be correlated with the development of metastatic neck nodes with statistical significance (Table III).

The Kaplan-Meier analysis showed a 70.5% 3-year disease-free survival rate and a 91.7% 3-year overall survival.

DISCUSSION

The literature on the treatment of squamous cell cancer (SCC) of buccal mucosa is dominated by the studies from the tobacco/beetel nut-chewing endemic areas of the world, such as Southeast Asia and India.\(^1\)–\(^{10}\) Surgery is the treatment of choice in case of early (T1-2 N0) SCC of the buccal mucosa. The current study seeks to supplement the literature from one of the endemic areas of tobacco/beetel nut chewing by reporting outcomes of peroral wide excision in early (T1-2 N0) SCC of buccal mucosa. We also studied the correlation of different clinic-pathological prognostic factors on the development of metastatic neck nodes.

In our study, out of the 156 patients, there were 91% males with male-to-female ratio of 10:1. This strengthens the fact that oral SCC has a predilection for males in Southeast Asia, with a rate of 75% to 98%, as reported by various studies from the region.\(^1\)–\(^{10}\) This is significantly more than in North American studies in which males accounted for just 14% to 55%.\(^{11}\)–\(^{14}\)

\[\text{TABLE I.} \]

<table>
<thead>
<tr>
<th>Site of Recurrence</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>No recurrence</td>
<td>110</td>
<td>70.5</td>
</tr>
<tr>
<td>Local</td>
<td>15</td>
<td>9.6</td>
</tr>
<tr>
<td>Regional</td>
<td>24</td>
<td>15.4</td>
</tr>
<tr>
<td>Locoregional</td>
<td>3</td>
<td>1.9</td>
</tr>
<tr>
<td>Second primary</td>
<td>4</td>
<td>2.6</td>
</tr>
<tr>
<td>Total</td>
<td>156</td>
<td>100</td>
</tr>
</tbody>
</table>

\[\text{TABLE II.} \]

<table>
<thead>
<tr>
<th>Status of Last Follow-Up</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive without disease</td>
<td>143</td>
<td>91.7%</td>
</tr>
<tr>
<td>Alive with disease</td>
<td>4</td>
<td>2.6%</td>
</tr>
<tr>
<td>Died of disease</td>
<td>6</td>
<td>3.8%</td>
</tr>
<tr>
<td>Died of other causes</td>
<td>3</td>
<td>1.9%</td>
</tr>
<tr>
<td>Total</td>
<td>156</td>
<td>100.0%</td>
</tr>
</tbody>
</table>
also reflects the fact that the prevalence of tobacco/betel quid chewing is much higher among males than females in the Asian population. The increased incidence of oral cancer in females in North American studies can be explained by the high prevalence of smoking and snuff use. In our study, 143 patients (91.7%) had a history of tobacco chewing/beetel nut in some form. Sixty-two cases (43.6%) with a history of tobacco/beetel nut chewing had premalignant lesions in the form of leukoplakia, erythroplakia, or submucous fibrosis. This association was statistically significant with $P$-value of 0.012.

We found that we had 26% verrucous carcinomas, 31% well-differentiated tumors, 41% moderately differentiated tumors, and only 3% poorly differentiated tumors. This was almost similar to what was reported in the literature from the endemic tobacco/beetel nut chewing areas, which tend to have better-differentiated tumors (41.8% well, 51.6% moderately, and 6.6% poorly differentiated). In their study on early buccal mucosa from endemic tobacco chewing areas, also report similar differentiation (70% well, 26% moderately and 4% poorly differentiated).5

The overall number of recurrences in our study was 46 (29.5%). This is approximately the same as what was reported by Iyer et al., 26.5% for early cancers of buccal mucos. Age group (≤40 or >40 years), sex, depth of infiltration (≤5mm and >5mm), perineural spread, and lymphovascular infiltration did not bear any prognostic significance to the development of the metastatic nodes. Out of 70 cases with T2 disease, 15 (21.4%) developed metastatic nodes, while only 9 (10.5%) of the cases with T1 disease had metastatic nodes. This association had a strong statistical significance with $P$-value of 0.032.

While only 2.5% of verrucous carcinoma and 12% in WDSCC developed metastatic neck nodes, 25% and 33% of MDSCC and PDSCC had nodal recurrences, respectively. Although the number of recurrences were high in MDSCC and PDSCC groups, $P$-value was toward significance (0.06), but it was more than <0.05, which was taken as a cutoff for statistical significance. Most recurrences in this study cohort occurred within 2 years of primary treatment of 36 (78.3%) out of 46 patients. Most patients with local recurrence (14 of 15) and regional metastases (24 of 24) could be salvaged with further treatment. Locoregional recurrences seemed to portend a poorer prognosis, because none of the three cases of locoregional recurrence could be salvaged. Iyer et al., in their analysis of early cancer of the buccal mucosa, also could salvage only four cases out of 10 with locoregional disease.

The management of the N0 neck, natural history of occult neck disease, and its clinical conversion in head and neck squamous carcinoma are still controversial. The combined locoregional and nodal recurrence, that is, the incidence of neck node metastases, was 27 (17.3%) out of 156. In our study, only nodal metastasis with the primary tumor controlled occurred in 24 cases (15.4%). A decision analysis proposed by Weiss et al. concluded that a 20% to 25% risk of occult disease warranted neck treatment.17

On analysis as per stage, only 10.5% cases with T1 stage developed neck nod, as compared to 21.4% cases stage T2 disease in this study. It seems that routine elective neck dissection is not warranted in patients with T1 early cancer of buccal mucosa with N0 neck, but T2 cases should be consideration for prophylactic selective neck dissection. Bloom and Spiro do not advocate elective neck dissection for patients with early-stage (stage I) squamous carcinoma of the buccal mucosa.18 Iyer et al., in their study of 147 cases with early cancer of buccal mucosa, do not recommend elective neck dissection due to only 14.6% occult metastases in their
series. Dhawan et al. do not advise the routine elective neck dissection for carcinoma of buccal mucosa, as they found only 11.7% level I and 9% level II occult nodal metastasis in patients with T3 and T4 cancer of buccal mucosa. Our experience with the per oral wide excision of early and localized cancer of buccal mucosa, it has shown a 70.5% 3-year disease-free survival rate and 91.7% 3-year overall disease-specific survival rate. Iyer et al. also reported a 77% 3-year disease-free survival rate and a 91% 3-year overall disease-specific survival rate in their study of early cancer of buccal mucosa. Forty-two (91.3%) out of the 46 cases with overall recurrences could be salvaged, while all the cases with nodal recurrence were salvaged. Our salvage rate is higher than the 69% reported by Iyer et al., which may be explained by a more vigilant follow-up by both clinical examination and USG, with FNA in the follow-up period. Regional (15.4%) recurrence was the most common, followed by local (9.6%) and locoregional (2%) recurrence in our study. On contrary, local recurrence was most common, followed by locoregional and regional recurrence in the study done by Iyer et al. Strome et al. reported a 100% overall incidence of local disease recurrence for patients with stage I and II tumors treated with wide local excision alone. In their study, 4 of 10 histologic specimens evaluated showed buccinator muscle involvement, and no comment was made on deep margin or base. This may explain the high recurrence rate in this study.

A second recurrence was seen in four cases after initial salvage therapy. Only one case could be re-salvaged. Schwartz et al. in a study of salvage treatment for recurrent oral cavity squamous cancers, found an overall recurrence rate of 28%, with local recurrence being the most common (58%), followed by locoregional (27%) and regional (16%) metastasis. They concluded that patients most likely to benefit from retreatment are those who have primary stage II and I tumors: those with a recurrence developing more than 6 months after initial treatment, and those with recurrences amenable to salvage surgery. We also held the same view, and also stress vigilant follow-up in the first 2 years after surgical treatment as 78% of the recurrences occurred during that period in our study.

Our study may be criticized for the lack of adequate follow-up, but early results are promising. Limited follow-up time, as well as an underpowered sample, inherently limit our ability to draw more conclusions that are statistically significant. These limitations, however, highlight the benefit of single institutions publishing their own clinical experience so that these data can eventually be consolidated and interpreted through meta-analysis.

CONCLUSION

Per oral wide excision is the adequate treatment for early localized cancer of buccal mucosa (T1-2 N0). Prophylactic selective neck dissection should be considered for T2 lesions as that was the only factor which showed statistical significant correlation with the development of neck nodes in N0 necks. N0 necks in case of well-differentiated SCC, especially verrucous carcinomas, can be observed as there were only 12% and 2.5% neck metastases, respectively, in our study. The habit of chewing tobacco/beetel nut was strongly related to the development of premalignant lesions and malignancy in our study population.

BIBLIOGRAPHY