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Local Spread Of Advanced Buccal Mucosa Cancer – A Review With 8 Patients.

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ABSTRACT

Buccal mucosa cancer involving masticator space is classified as very advanced local disease (T4b). The local recurrence rate is very high due to poor understanding of the extent of tumor spread in masticator space and technically difficult surgical clearance. The objective of this study is to understand the extent of tumor spread in masticator space to form basis for appropriate surgical resection. All consecutive patients with T4b-buccal cancer underwent compartment resection, with complete anatomical removal of involved soft-tissue structures. Specimens were systematically studied to understand the extent of invasion of various structures. The findings of clinical history, imaging and pathologic evaluation were compared and the results were evaluated. A total of 8 patients with advanced buccal cancer (T4b) were included in this study. The skin, mandible and lymph nodes were involved in 8, 6 and 4 cases respectively. The pterygoid muscles were involved in 8 cases (medial-ptyergoid in 6 and both pterygoids in 3cases) and masseter-muscle in 8 cases. Average distance for soft-tissue margins after compartment surgery was 2 cm and the margins were positive in 4 cases. The group with involvement of medial pterygoid muscle had safest margin with compartment surgery while it was also possible to achieve negative margins for group involving lateral pterygoid muscle and plates. The involvement of pterygomaxillary fissure was area of concern and margin was positive in 2 cases with one patient developing local recurrence with intracranial extension. At 20 months median follow-up (15-30 months), 3 patients were alive without disease while five developed local recurrence at the skull base. T4b buccal cancers have significant soft-tissue involvement in the masticator space. En bloc removal of all soft-tissues in masticator space is advocated to remove tumor contained within space. The compartment surgery provides an opportunity to achieve negative margins for cancers actually contained within masticator space. It is inappropriate to club all patients with masticator space involvement in one group.

Keywords: Buccal mucosa cancer, gingivobuccal sulcus, infratemporal fossa, masticator space, oral cancer, pterygoid muscles, retromolartrigone

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INTRODUCTION

Squamous cell carcinoma (SCC) of the buccal mucosa and gingivobuccal sulcus (GBS) is the most common oral cancer in India.^{[1],[2],[3],[4],[5],[6]} Many patients present at an advanced stage with involvement of masticator space.^{[1],[3],[7]} Outcome remains particularly poor for this group of patients due to high rate of local recurrence.^{[8],[9]} These cancers are staged as T4b based on American Joint Committee on Cancer (AJCC) classification.^[10] They are conventionally considered very advanced and probably unresectable because of the inability to consistently achieve negative margins in 3-dimension.

The soft-tissue margin status is the most important prognostic factor in patients undergoing curative intent surgery.^{[11],[12]} It is difficult to consistently achieve pathological safety margin of 1cm for involved soft-tissues in masticator space. The major limitation for surgical planning is a poor understanding of the extent of soft-tissue involvement in this area. The pre-operative assessment of the extent of disease spread with the clinical examination and imaging is inaccurate at times. Intraoperative assessment and adequate removal of the soft-tissues is often compromised due associated bleeding. Liao *et al.* first suggested that T4b buccal cancers can be operated with acceptable outcome.^[8] He further showed that tumors above the mandibular notch (tumors involving both medial and lateral pterygoid muscles) have inferior outcome to tumors only occupying the compartment below the mandibular notch (involving medial pterygoid muscle only).^[9] This further substantiates the need to understand the extent of soft-tissue involvement in T4b buccal cancers that can help in the surgical planning.

In this pathology based study, specimens were systematically evaluated after composite resection and the findings of clinical, radiological and pathological examination were compared with understand the extent of soft-tissue involvement in masticator space. This can be of immense help in planning surgical resection for this difficult area.

MATERIALS AND METHODS

This study included all previously untreated, consecutive patients presenting to our center with advanced SCC of buccal mucosa involving masticator space (T4b) from 2012 to 2015. Patients were staged as T4b if they showed recent onset or worsening trismus or radiological evidence of masticator space involvement. The extensive involvement of masticator space (medial and lateral pterygoid muscles and pterygoid plates) and extensive skin involvement were not considered contraindication for surgery. The exclusion criteria were involvement of internal or common carotid artery, pre-vertebral fascia and tumors with intracranial extension. The clinical history and computed tomography (CT) scan findings of all patients were noted.

All patients underwent an en bloc compartment resection.^[13] This included segment of mandible, segment of upper alveolus, skin (if involved), entire masseter muscle, whole of both medial and lateral pterygoid muscles with pterygoid plates and part of temporalis muscle in en bloc fashion. All the soft-tissue structures (masseter and pterygoid muscles) with possibility of involvement were removed completely from origin to insertion. This enabled us to study these structures in detail to evaluate the extent of disease spread. The inferior alveolar and lingual nerves were resected from the skull base. All patients underwent selective neck dissection for level I to IV lymph node clearance.

The surgically resected specimen was systematically evaluated for all the structures involved, their extent of involvement and their margin status. The specimen was immediately taken to the pathologist to understand the anatomy better. The size of the specimen and the size of tumor were noted in three dimensions. The size of the skin paddle was noted in two dimensions and the involvement of skin or subcutaneous tissue was noted separately. The mucosal and skin (if resected) margins were taken from all around. The specimen was cut through its epicenter in retromolar trigone in horizontal direction to know the depth of invasion. The tissue lateral to the ramus of mandible was identified as masseter muscle and the tissue medial to ramus as pterygoid muscles. The sections in full depth were taken through the epicenter of tumor. Further sections were taken from individual soft-tissues at every 5 mm distance above and below to identify the extent of tumor spread. This was also used to calculate the distance of tumor from the resected margin. The masseter muscle margin was taken from the upper most portions, near the zygoma and the distance from

tumor margin in muscle was calculated. Similarly, the pterygoid muscle margin was taken from the skull base, adjacent to pterygoid plates and the distance from tumor margin was calculated. The tissue from pterygomaxillary fissure was taken separately to evaluate the presence of disease. The bone involvement of mandible and upper alveolus was evaluated using standard technique and their margin status was reported separately. Only the bone adjacent to the tumor was sampled and subsequently decalcified and evaluated by examination of continuous sections. The neck dissection specimens were evaluated using standard described technique. The number of nodes involved at each level and the presence or absence of extra-capsular spread (ECS) was noted. All sections were studied using the standard method of histopathological examination, with hematoxylin and eosin staining.

The detailed clinical history, findings of CT scanning and the findings of pathologic evaluation were compared and the results were evaluated.

RESULTS

A total of 8 patients with advanced buccal mucosa cancers (T4b) with masticator space involvement were included in this study. There were 2 female and 6 male patients. The average age at the time of presentation was 40 years (range: 25-65 years). A total of 5 patients had lower GBS cancer while patients had upper GBS cancer and 1 patients had buccal cancer (non-chewer). All patients underwent composite surgery described earlier and the reconstruction was achieved using free flaps and regional flaps. There was no procedure related mortality. Major post-operative complications were seen in 2 cases and could be managed without mortality. A total of 4 patients received adjuvant radiotherapy, with 2 patients receiving concurrent chemoradiotherapy.

On clinical examination, 6 patients had either recent onset or worsening trismus [Table 1]. The skin was involved in 6 cases and the mandible in 5 cases. A significant paramandibular spread was noted in 4 cases. There were palpable nodes in 5 cases. The radiological evaluation was carried out by CT scan [Figure 1] and showed involvement of skin in 4 cases, mandible in 3 cases, pterygoid muscles in 7 cases and masseter muscle in 7 cases and pterygoid plates in 1 cases. The lymph nodes were involved by CT scan criteria (>1 cm, central necrosis) in 3 cases.

Table 1: Pathological involvement of different structures

STRUCTURE	INVOLMENT (no.) N=8
Skin	4
Mandible	3
Maxilla	1
Pterygoid muscle	2
Pterygoid plate	1
Masseter muscle	3
Nodes	3

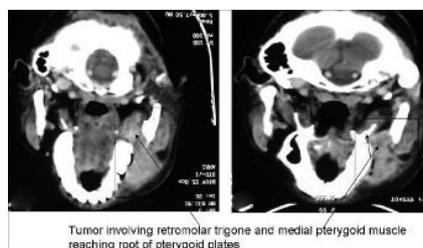


Figure 1: Computed tomography image showing infiltration of masticator space

The average size of resected specimen was 10 cm × 8 cm × 8 cm and average size of tumor was 5 cm × 4 cm × 3 cm [Figure 2]. The average size of skin paddle was 8 cm × 6 cm. [Table 1] is showing structures commonly involved by histopathology and their margin status. The skin and mandible were involved in 4 and 3 cases respectively. The pterygoid muscles were involved in 6 cases while masseter muscle was involved in 5

cases. The pterygoid plates were involved in 1 cases, but margins were tumor free. In 1 case the tumor was involving temporomandibular joint capsule.

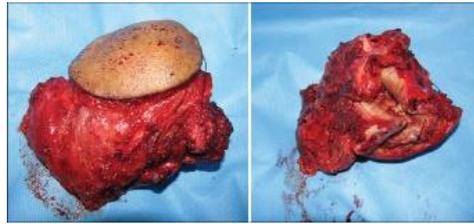


Figure 2: Pathological specimen

The margins were positive in 5 cases. The anterior bone margin was positive in one patient. The pterygomaxillary fissure area showed presence of tumor tissue in 1 cases. The mucosal, skin and soft-tissue margins were negative in all other cases. The average distance of skin and mucosal margin from tumor were 2 cm and 1 cm respectively. The extent of tumor spread in each soft-tissue structure was calculated by counting the number of cut sections above and below the main section showing tumor cells. The average masseter muscle involvement was 2.5 cm and the average pterygoid muscle involvement was 2 cm. The average distance of pterygoid muscle margin at the skull base from the tumor was 2 cm, but it was about 1 cm when tumor was from upper GBS. The average margin for masseter muscle from tumor was 2.5 cm. In 2 cases, the skin was excised on clinical grounds but was not involved by pathology. In all these 2 cases, the tumor was coming up to 6 mm of skin surface.

The lymph nodes were involved in 3 cases. Only one lymphnode was involved in 4 cases (5 cases-level I and in 2 cases-level II). More than one lymph nodes were involved (minimum 3 and maximum 5) in other 3 cases. Positive lymph nodes were not found in level IV in any case. ECS was not seen in any of these cases.

[Table 2] shows comparison of various structures involved by clinical, radiological and pathological examination. Clinically, the skin was involved in 40 cases while CT scan suggested involvement in 32 cases. Pathology confirmed skin involvement in 30 cases. The mandible involvement was overdiagnosed by the clinical examination, but CT scan accurately predicted it in all 24 cases. Recent onset or worsening trismus indicating masticator space involvement was present in 41 cases, but CT scan showed infiltration of masticator space only in 27 cases. Pathology revealed masticator space involvement in 35 cases. The pathological examination upstaged neck disease in 3 cases.

Table 2: Comparison between clinical, radiological and pathological involvement

STRUCTURE (N=8)	CLINICAL	RADIOLOGICAL	PATHOLOGICAL
Skin	2	2	1
Mandible	3	2	2
Maxilla	1	1	3
Infratemporal fossa	2	3	2
Node	4	1	1

The pterygoid muscle involvement is the key area of interest for clinicians. Involvement of lateral pterygoid muscle is considered as sign of inoperability. We tried to identify involvement of both the pterygoid muscles separately. Only the medial pterygoid muscle was involved in 5/8 cases while in other cases both medial and lateral pterygoid muscle were involved. Pterygoid plates were involved only when lateral pterygoid muscle was also involved (5 cases). We did not examined tissue from pterygomaxillary fissure separately for initial cases. We found tumor cells present in 2/8 cases where this area was separately examined. The tumor was coming very close to soft tissue margins when it was involving lateral pterygoid muscle with involvement of pterygomaxillary fissure. This group of patient had close margins compared to group of patients with involvement of medial and lateral pterygoid muscle only.

The main focus of this study is to understand the extent of tumor spread in T4b buccal mucosa cancers. We performed composite resection along with complete anatomical (compartment) removal of involved soft-tissue structures in masticator space irrespective of the extent of their involvement. This

provided us an opportunity to evaluate the specimen completely. As a secondary objective, we evaluated margin control and outcome with early 20 months median follow-up (range: 15-35 months). A total of 2 patients are alive and disease free, one patients are alive with local recurrence while five have died. Three patients have died due to unrelated causes, one died due to opposite side neck recurrence and another died due to distant metastasis. Two patients have developed local recurrence in pterygomaxillary fissure area with gross intracranial extension. One of them had a positive margin while other showed no tumor cells at pterygomaxillary fissure area. The objective functional assessment showed good functional outcome for all the patients , but in depth description of these findings are beyond scope of this paper.^[13]

DISCUSSION

The cancer of buccal mucosa and GBS are the most common oral cancer sub-sites in India.^{[1],[2],[3],[4],[5],[6]} Many patients present at an advanced stage with involvement of masticator space.^{[7],[8],[9]} The masticator space consists of ramus of mandible, masseter and two pterygomuscles and pterygoid plates with various neurovascular bundles. Oral cancer involving masticator space is staged as T4b in AJCC classification and is considered very advanced local disease.^[10] The main reason for poor outcome in this group of patients is due to local recurrence at the skull base.^{[8],[9]} The local recurrence is largely due to inability to achieve negative 3-dimension margins of involved soft-tissues. Surgical clearance with adequate histological safety margin is difficult for this area due to variety of reasons. These patients have associated trismus and clinical evaluation is quite difficult. Imaging modality with CT scan and magnetic resonance imaging scan improves assessment, but has its limitation due to associated edema and involvement of the multiple structures. It is difficult to plan the extent of soft tissue resection in infratemporal fossa solely on imaging findings. Surgery in this area is associated with excessive bleeding and intraoperative assessment of tumor depth is very difficult. These factors make it difficult to achieve negative soft-tissue margins consistently. This was reflected in the study published by Liao *et al.*^[9] The outcome was poorer in a group of patients with involvement of multiple structures in masticator space (supra-mandibular notch) compared to patients with tumor inferior to mandibular notch (probably involving medial pterygoid muscle only). Understanding the involvement of various structures and the extent of their involvement can significantly improve chances of achieving complete tumor clearance. This study systematically evaluates the extent of tumor spread in masticator space.

The study group involved all buccal mucosa complex cancer with potential invasion of masticator space. Recent onset or worsening trismus and radiological evidence of pterygoid or masseter muscle involvement were taken as inclusion criteria for this study. Long standing trismus could be due to associated submucous fibrosis and might not indicate actual masticator space involvement and was not considered in inclusion criteria. Composite resection was performed for all cases in this series. Conventional composite resection includes removal of tumor with the histological safety margin of 1cm. Earlier studies have adopted similar approach.^{[8],[9]} In order to extensively examine all involved soft-tissues, we resected all the structures from origin to insertion irrespective of the extent of their involvement.^[13] This gave us chance to study the extent of disease spread in each structure and their distance from farthest possible margin. We could also evaluate margin control rate after this anatomical compartment resection.

The pterygoid muscles and the pterygoid plates occupy medial and posterior aspect of masticator space while the masseter muscle occupies lateral compartment. The pterygoid muscles were pathologically involved in 6 cases. The CT scan missed the diagnosis of masticator space involvement in 4 cases where minimal infiltration of medial pterygoid muscle was observed by pathology. This may be due to infection and edema associated with these tumors. The clinical finding of recent onset or worsening trismus over-diagnosed masticator space involvement in about 6 cases. The masseter muscle occupies the area lateral to the ramus of mandible and was involved in 2 cases. Removing the entire muscle from the zygomatic arch provided adequate margin control.

The skin was pathologically involved in about two third (6) of cases, but we removed it in 8 cases based on the clinical finding (ulceration, induration, not pinchable). In 2 cases where the skin was pathologically not involved, the tumor was reaching at least within 6 mm of skin surface. This demonstrates that most of these tumors are more infiltrative than exophytic and it may be advisable to resect the skin when in doubt. The mandible was involved only in about half the cases. The clinical evaluation over diagnosed mandibular involvement, but CT scan correctly predicted it. Many of the advanced GBS cancer patients have a

significant paramandibular spread and it is an accepted practice to perform segmental mandibulectomy for them.^{[1],[7]} The segmental mandibulectomy also helps in correcting trismus and in clearing soft-tissues in the masticator space. It is not feasible to perform mandibulotomy for a buccal cancer going into masticator space and performing marginal mandibulectomy would compromise on surgical clearance due to paramandibular spread and inadequate soft-tissue clearance. The lymph nodes were involved only in 4/8 cases; although, primary tumor burden was significantly high in each case. The lymph node involvement was typically low in number and volume. This suggests that these are locally aggressive tumors with extensive local spread, but have less inclination toward regional spread. These patients may benefit from curative intent aggressive local treatment.

The margins were positive in 5 cases. The anterior mandibular marrow margin was positive in 1 case. The pterygomaxillary tissue margin showed presence of disease in 1 cases. There is potential for tumor to spread to intracranial compartment once it reaches the pterygomaxillary fissure. Both patients received adjuvant chemoradiotherapy, but one patient developed local recurrence. The tumors involving pterygomaxillary fissure area are at high risk for local failure and chance for salvage is minimal due to intracranial extension.

The soft-tissue, skin and mucosal margins were negative in all other cases. The average distance of tumor from distal pterygoid muscle margin was about 2 cm while it was 1 cm when upper GBS was involved. The masseter muscle margins were also adequate with this technique. This suggests en bloc removal of the involved soft-tissue structures may be needed to improve the margin control. This approach also eliminates errors in the assessment of disease spread. Thus, surgery becomes a standard one (clearance reaching anatomical limit) for every case and eliminates potential errors. The functional outcome is largely unaffected as only non-functioning soft-tissue in masticator space is removed in addition to conventional approach. The merits and de-merits of this surgical approach can be discussed in depth in another paper. The early results of our clinical data suggest encouraging trend.

There is no other similar study published in the literature for comparison of our results. This is an initial effort to understand the extent of disease spread of buccal mucosa cancers involving masticator space (T4b). It is not advisable to club all cases involving masticator space in one subgroup (T4b) based on the finding of this study. Tumors that involve only medial pterygoid muscle has got the safest margins with compartment surgery. The group with involvement of lateral pterygoid muscle and pterygoid plates without involvement of pterygomaxillary fissure area (truly contained within masticator space) also has potential for negative margin with infra-cranial surgical approach. Tumors spreading to other compartment through pterygomaxillary fissure require more extensive surgical approach and further evaluation is needed.

CONCLUSION

T4b buccal cancers have a significant soft-tissue involvement in the masticator space. The compartment surgery provides an opportunity to achieve negative margins for cancers actually contained within masticator space. It is inappropriate to club all patients with the masticator space involvement in one group

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