COMPARTMENTAL ITF CLEARANCE IN LOCALLY ADVANCED BUCCAL MUCOSA CANCER: A DECADE OF PROGRESS AND HOPE

Abstract

Locally advanced Buccal mucosa carcinoma with infratemporal fossa (ITF) extension is an oncological challenge with poor outcome. Historically it was deemed unresectable and was treated with palliative intent. Better anatomical knowledge has made surgical resection possible in most of the cases. Using multimodal approach, the disease is now treatable with its prognosis nearing to other advanced operable oral cancers. This chapter aims to briefly review the complexities involved in managing these cancers, the evolution of treatment modalities and currently available treatment options with its outcome.

Keywords: Buccal Mucosa cancer, Infratemporal fossa, Tumor

Authors

Dr. Rajshekar Puttaswamy
Senior Resident
Department of Surgical Oncology
Dr. RMLIMS
Lucknow, India

Dr. Ashish Singhal
Proffessor
Department of Surgical Oncology
Dr. RMLIMS
Lucknow, India

I. INTRODUCTION

Oral squamous cell cancer has significant variability in geographic distribution, site susceptibility and risk factors. Though not a forerunner globally, it is the second most common malignancy in the Indian subcontinent forming a significant health concern(1). These cancers contributes to 2% of all new cases worldwide, but 10% of all new cancers in India(2). This variation is largely due to widely prevalent habit of areca nut and tobacco products chewing among south-east Asian population. 90% of them are of squamous histology and it includes wide array of subsites viz oral tongue, Buccal mucosa, lip, gingiva, floor of mouth, RMT etc. Cancers involving tongue is common in western countries while the specific predilection of these cancer to involve buccal mucosa more commonly is due to a unique way of placing the tobacco quid adjacent to buccal mucosa.. Most of the patients present with locally advanced stage of the disease due to lack of awareness, negligence, stigma or inaccessibility to proper healthcare facilities. This is also seen in countries where plenty of resources and accessibility to health care is available. A national cancer data base study in USA revealed that 55% of oral cancers present in advanced stage. Locally advanced buccal mucosa cancers typically manifest as a large proliferative growth with variable ulceration and involve surrounding structures like skin and bone. They can also present as small fibrotic growth involving the area of retromolar trigone resulting in trismus. The patients present with intraoral growth, pain, trismus, bleeding, neck node swelling. Due to the proximity of the buccal mucosa to the masticator space, tumours of this sub-site have high propensity to invade the muscles of mastication and ITF space. This locally advanced oral cancer pose a challenge to head and neck surgeons, particularly when they involve the Infra-temporal fossa(ITF). This chapter aims to present a brief review about staging, updated management options and prognosis of locally advanced oral cancers involving ITF.

II. RELEVANT ANATOMY

Although in the current edition of AJCC T staging for head neck cancers, ITF and MS are used interchangeably, the anatomical definitions are clearly different(3). Masticator space(MS) is a well defined anatomic space formed by the splitting of deep cervical fascia at mandible and extending upto base of the skull. Strictly speaking, the nonfascial lined ITF encompasses the medial MS (MS excluding the masseter), a part of the prestyloid compartment of Parapharyngeal space (the pterygoid plexus containing parapharyngeal fat) reaching up to the lateral pharyngeal wall and the retroantral buccal fat (buccal space). It is situated below the temporal bone bounded laterally by condylar process and ramus of mandible, medially by lateral pterygoid plate, anteriorly by posterior border of maxillary sinus, posteriorly by styloid and condylar process(Figure 1 and 2). The roof is formed by the greater wing of sphenoid and the floor of the fossa is formed by the medial pterygoid muscle. The space contains muscles of mastication, pterygoid muscles, variable length of temporalis muscle, along with soft tissue containing pterygoid plexus of veins. Liao et al(4,5) proposed the concept of dividing ITF into supra-notch and infra-notch tumours by a trans-axial plane crossing at the level of sigmoid notch of mandible. Further Trivedi et al(6,7) proposed subclassification and dividing them in 3 groups. Class I: low masticator space = medial pterygoid and masseter muscles, ascending ramus of mandible (infra-notch). Class II: intermediate masticator space = class I 1 lateral pterygoid and temporalis muscle and lower half of pterygoid plates (low supra-notch). Class III: high masticator space = involvement of pterygomaxillary fissure and intracranial extension (high supranotch). The location of the

infratemporal fossa makes it an area of interest as it communicates with middle cranial fossa through various foramens, with middle ear and paranasal sinus, with parapharyngeal space, orbit and oral cavity. Any tumor in this space spreads easily to surrounding structures and vice-versa. The complex anatomy of ITF and major complex network of neurovascular bundles packed in a closed space makes it very difficult to dissect and achieve adequate margin, resulting most of the time in piecemeal removal of tumor.

III. STAGING AND DIAGNOSIS

The diagnostic process often involves a combination of clinical examination, imaging techniques and biopsy. The American joint committee on cancer staging system(AJCC) eighth edition for oral cancer use anatomic extent of tumor invasion without distinguishing anatomic origin of the tumors(8). The same T-stage criteria is applicable for oral tongue, floor of mouth, gingiva and buccal mucosa cancers . The current staging classifies locally advanced oral cancers into T4a and T4b2 . T4a consists those tumours invading cortical bone of mandible / maxilla or skin of the face. T4b are those tumors that involve masticator space, pterygoid plates or skull base or encases internal carotid artery. This division implies that there is higher incidence of complications, unresectability and poor prognosis in T4b tumors. High quality imaging is necessary to accurately stage, to define proper anatomical extent and plan surgical resection. Contrast enhanced Computed Tomography (CECT) scan with puffed cheek technique is the most commonly used imaging modality. Tumour size, epicenter, its extent and relationship to surrounding structures, bone erosion and its extent(cortical/medullary), perineural spread, nodal staging which include number, size and extra-nodal extension, signs of inoperability including skull base, carotid involvement are predicted well(9). MRI has better soft tissue delineation and is better in predicting perineural invasion and skull base involvement, but has poor specificity for cortical bone erosion(10–12). PET CT is indicated in advanced disease especially with N2 and N3 nodal disease , but rarely done in clinical setting owing to its less yield and high cost and lower availability(13). Synoptic reporting with detailed template should be standardised to ensure uniformity and to avoid any missing data. The histopathological confirmation and defining the subtype is done by most often, by punch biopsy.

1. **Treatment:** Traditionally the tumours of buccal mucosa involving ITF were treated with definitive chemoradiation as surgical resection was deemed impossible with difficult surgical access, increased blood loss from pterygoid plexus, high rates of positive margin and subsequent local recurrence resulting in poor quality of life. Also, according to recent NCCN guidelines the preferred treatment for T4b tumors is either enrolling in a clinical trial or nonsurgical definitive Radio-chemotherapy . But the prognosis and overall survival rates with this approach is poor(14,15). Also, the incidence of these cancers in India and South east population is far more compared to western population. Hence, the treatment recommendation by western literature has been questioned by few authors who have shown that a subset of T4b tumours which involves masticator space that can be resected with clear margins have prognosis comparable to T4a tumours. The subclassification of ITF emphasize that infra-notch, class I /II tumours are resectable and have better prognosis compared to supra-notch and class III tumours. Further the concept of compartmental resection was introduced by Trivedi et al(16) in which they advised to remove the whole ITF as one compartment, resecting along the anatomic planes rather than through the tissue as was done before in traditional approach. This approach

improved the surgical access, avoid excessive bleeding and remove the entire ITF tissue and muscles from their origin, thereby achieving adequate clearance and optimal margin. Compartmental resection is feasible and repeatable with variable but favourable local control. The rates of positive margin was bought down drastically as shown by Trivedi et al(7)(<5%), Katna et al(17) (13%), Mair et al(18) (12%), Pillai et al(19)(6.8%). Reconstruction is by either free flap or pedicled flap. In the current era, surgical resection in the form of composite resection with compartmental ITF clearance and comprehensive neck dissection form the back bone of management. The author in their experience found that compartmental ITF clearance is feasible and repeatable with better oncological outcome. A demonstration of compartmental surgery is available at: https://youtu.be/P8TXzgXRSG8.

The role of adjuvant radiotherapy after surgical excision is as crucial as surgery itself. Advances in radiotherapy including IMRT achieve higher radiation dose to the tumour bed and have shown to improve recurrence free survival. Adjuvant chemotherapy is indicated only in case of close/involved margin and Extracapsular extension. There is a dearth of literature evidence in guiding the management of high ITF cancers. The role of Neo-adjuvant or induction chemotherapy is emerging(20–23). Some studies have shown NACT has helped in downstaging the tumour, converting borderline and unresectable tumours to resectable tumour. Assessing the response to NACT is crucial to select patients either to surgery or palliative chemo-radiation. Presently RECIST criteria or PETCT scans are indicated, though inadequate. In the last decade considerable progress have been made in managing these tumours involving multiple specialities viz head and neck surgical oncologist, medical and radiation oncologist, plastic surgeon, Nutrition, palliation and psychiatric specialist. Compartmental resection, advances in radiotherapy and holistic patient approach are the highlights.

2. **Prognosis, Supportive Care, Rehabilitation And Future:** The patients with locally advanced buccal mucosa cancers with ITF involvement often experience physical and emotional challenges due to the disease and treatment often, resulting in disfigurement, compromised speech, poor dentition and speech. Supportive measures, including pain management, nutritional support, psychosocial counselling are integral to improve the patient's quality of life. Rehabilitation programs, including speech therapy, dental rehabilitation programs, dental prosthetics and physical therapy, aim to restore optimal function and address any functional deficits from surgery or radio therapy. The prognosis of low ITF tumours are similar to that of T4a, while the management of high ITF is controversial and there is dearth of evidence in the current literature. Future studies are required to evaluate the role of NACT, trimodal management- induction chemotherapy followed by dedicated compartmental resection along with chemo-radiation, especially in high ITF cancers. The future studies should also focus on identifying tumour biology, both to target therapy and selecting good prognostic patients for surgical resection.

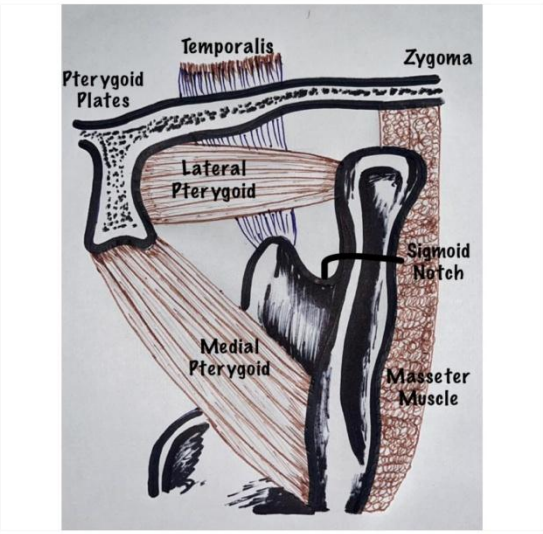

Figure 1 : Anatomical Depiction of ITF showing its Division and Muscles

Figure 2 : Axial and Coronal Section of CT Scan Showing Extent of ITF(red line and shadow) and Differentiating it from Masticator space(yellow lines).

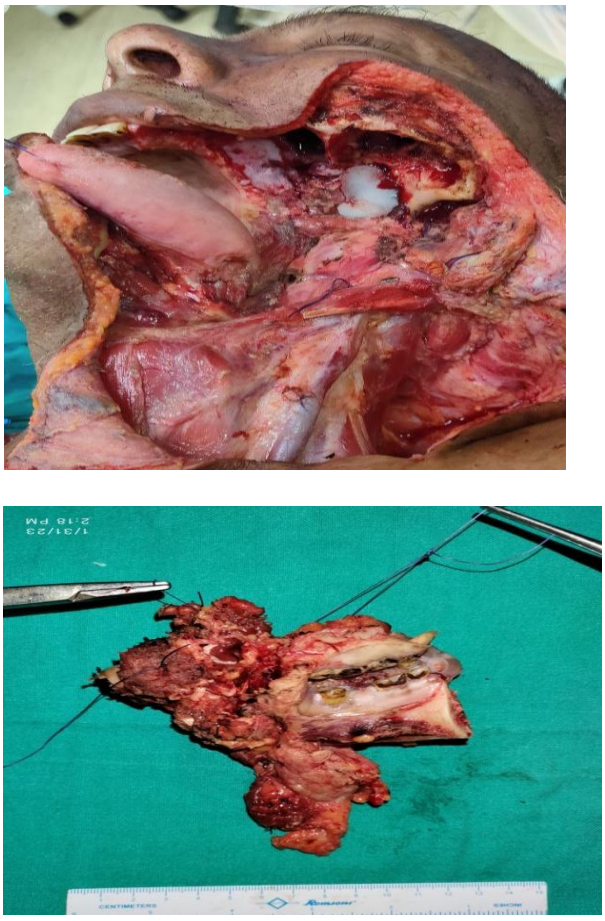

Figure 3: Intra-Operative Picture after Compartment ITF Clearance of Left Buccal Mucosa Cancer and the Resected Specimen

REFERENCES

[1] 1-Lip-oral-cavity-fact-sheet.pdf [Internet]. [cited 2023 Jun 23]. Available from: https://gco.iarc.fr/today/data/factsheets/cancers/1-Lip-oral-cavity-fact-sheet.pdf

[2] Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians [Internet]. 2021 May 1 [cited 2023 Jun 23];71(3):209–49. Available from: https://doi.org/10.3322/caac.21660

[3] Sah A, S. TG, H. CS. Imaging of the Infratemporal Fossa: a Comprehensive Pictorial Essay. Indian Journal of Surgical Oncology [Internet]. 2022 Dec 1;13(4):868–75. Available from: https://doi.org/10.1007/s13193-022-01591-x

[4] Liao CT, Ng SH, Chang JTC, Wang HM, Hsueh C, Lee LY, et al. T4b oral cavity cancer below the mandibular notch is resectable with a favorable outcome. Oral Oncology [Internet]. 2007 Jul 1;43(6):570–9. Available from: https://www.sciencedirect.com/science/article/pii/S1368837506001850

[5] Liao CT, Chang JTC, Wang HM, Ng SH, Hsueh C, Lee LY, et al. Surgical outcome of T4a and resected T4b oral cavity cancer. Cancer [Internet]. 2006 [cited 2023 Jan 29];107(2):337–44. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1002/cncr.21984

[6] Trivedi NP. Oral cancer involving masticator space (T4b): Review of literature and future directions. Head & Neck [Internet]. 2018 Oct 1 [cited 2023 Jan 29];40(10):2288–94. Available from: https://doi.org/10.1002/hed.25211

[7] Trivedi N, Kekatpure V, Shetkar G, Gangoli A, Kuriakose M. Pathology of advanced buccal mucosa cancer involving masticator space (T4b). Indian Journal of Cancer [Internet]. 2015;52(4). Available from:

https://journals.lww.com/indianjcancer/Fulltext/2015/52040/Pathology_of_advanced_buccal_mucosa_cancer.42.aspx

[8] Mb A, Fl G, Sb E, Cc C, Je G, Rk B, et al. The Eighth Edition AJCC Cancer Staging Manual: Continuing to build a bridge from a population-based to a more "personalized" approach to cancer staging. CA: a cancer journal for clinicians [Internet]. 2017 Mar [cited 2023 Jan 28];67(2). Available from: https://pubmed.ncbi.nlm.nih.gov/28094848/

[9] Hansen EK, Yom SS, Chen CP, Schechter NR. Cancer of the Lip and Oral Cavity. In: Hansen EK, Roach M, editors. Handbook of Evidence-Based Radiation Oncology [Internet]. New York, NY: Springer New York; 2010. p. 131–44. Available from: https://doi.org/10.1007/978-0-387-92988-0_8

[10] Ong CK, Chong VFH. Imaging of perineural spread in head and neck tumours. Cancer Imaging [Internet]. 2010 Sep 29 [cited 2023 Jan 28];10(1A):S92–8. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2967145/

[11] Caldemeyer KS, Mathews VP, Righi PD, Smith RR. Imaging features and clinical significance of perineural spread or extension of head and neck tumors. RadioGraphics [Internet]. 1998 Jan 1 [cited 2023 Jan 29];18(1):97–110. Available from: https://doi.org/10.1148/radiographics.18.1.9460111

[12] Paul P, Sable N, Arya S. Imaging of Oral Cancer. In: Panta P, editor. Oral Cancer Detection: Novel Strategies and Clinical Impact [Internet]. Cham: Springer International Publishing; 2019. p. 109–31. Available from: https://doi.org/10.1007/978-3-319-61255-3_5

[13] head-and-neck.pdf [Internet]. [cited 2023 Jan 29]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf

[14] Corry J, Peters LJ, Costa ID, Milner AD, Fawns H, Rischin D, et al. The 'QUAD SHOT'—a phase II study of palliative radiotherapy for incurable head and neck cancer. Radiotherapy and Oncology [Internet]. 2005 Nov 1;77(2):137–42. Available from: https://www.sciencedirect.com/science/article/pii/S0167814005004500

[15] Agarwal JP, Nemade B, Murthy V, Ghosh-Laskar S, Budrukkar A, Gupta T, et al. Hypofractionated, palliative radiotherapy for advanced head and neck cancer. Radiotherapy and Oncology [Internet]. 2008 Oct 1;89(1):51–6. Available from: https://www.sciencedirect.com/science/article/pii/S0167814008003356

[16] Trivedi NP, Kekatpure V, Kuriakose MA. Radical (compartment) resection for advanced buccal cancer involving masticator space (T4b): Our experience in thirty patients. Clinical Otolaryngology [Internet]. 2012 Dec 1 [cited 2023 Feb 6];37(6):477–83. Available from: https://doi.org/10.1111/j.1749-4486.2012.02529.x

[17] Katna R, Kalyani N, Singh S, Bhosale B, On behalf of Mumbai Oncology Group – Head and Neck. Compartmental Clearance of Infratemporal Fossa for T4b Carcinoma of Buccal Mucosa/Alveolus: Clinical Outcomes. Indian Journal of Surgical Oncology [Internet]. 2020 Jun 1;11(2):316–20. Available from: https://doi.org/10.1007/s13193-020-01057-y

[18] Mair MD, Sawarkar N, Nikam S, Sarin R, Nair D, Gupta T, et al. Impact of radical treatments on survival in locally advanced T4a and T4b buccal mucosa cancers: Selected surgically treated T4b cancers have similar control rates as T4a. Oral Oncology [Internet]. 2018 Jul 1;82:17–22. Available from: https://www.sciencedirect.com/science/article/pii/S1368837518301611

[19] Pillai V, Yadav V, Kekatpure V, Trivedi N, Chandrashekar NH, Shetty V, et al. Prognostic determinants of locally advanced buccal mucosa cancer: Do we need to relook the current staging criteria? Oral Oncology [Internet]. 2019 Aug 1;95:43–51. Available from: https://www.sciencedirect.com/science/article/pii/S1368837519301666

[20] Patil VM, Prabhash K, Noronha V, Joshi A, Muddu V, Dhumal S, et al. Neoadjuvant chemotherapy followed by surgery in very locally advanced technically unresectable oral cavity cancers. Oral Oncology [Internet]. 2014 Oct 1;50(10):1000–4. Available from: https://www.sciencedirect.com/science/article/pii/S1368837514002255

[21] Zhong L ping, Zhang C ping, Ren G xin, Guo W, William WN, Sun J, et al. Randomized Phase III Trial of Induction Chemotherapy With Docetaxel, Cisplatin, and Fluorouracil Followed by Surgery Versus Up-Front Surgery in Locally Advanced Resectable Oral Squamous Cell Carcinoma. J Clin Oncol [Internet]. 2013 Feb 20 [cited 2023 Jun 23];31(6):744–51. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5569675/

[22] Posner MR, Hershock DM, Blajman CR, Mickiewicz E, Winquist E, Gorbounova V, et al. Cisplatin and Fluorouracil Alone or with Docetaxel in Head and Neck Cancer. N Engl J Med [Internet]. 2007 Oct 25 [cited 2023 Jun 23];357(17):1705–15. Available from: https://doi.org/10.1056/NEJMoa070956

[23] Vermorken JB, Remenar E, van Herpen C, Gorlia T, Mesia R, Degardin M, et al. Cisplatin, Fluorouracil, and Docetaxel in Unresectable Head and Neck Cancer. N Engl J Med [Internet]. 2007 Oct 25 [cited 2023 Jun 23];357(17):1695–704. Available from: https://doi.org/10.1056/NEJMoa071028

