

# An Unusual Presentation of Squamous Cell Carcinoma of Head and Neck Region

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## Abstract

**Background:** Oral cavity cancer, ranking sixth in global cancer prevalence, primarily manifests as Squamous Cell Carcinoma (SCC), accounting for over 90% of cases. Neoadjuvant chemotherapy (NACT) plays a pivotal role in locally advanced head and neck cancer management, focusing on disease downstaging and distant metastasis reduction. However, little research explores the effects of delayed local treatment post-NACT on oncological outcomes. This report details an exceptional case - a small primary lesion with extensive metastasis. **Case Report:** A 53-year-old chronic smoker and alcoholic presented with a three-month history of a painful ulcer in the left oral cavity. Initially diagnosed with cT3N2bMx squamous cell carcinoma in the left lower gingiva buccal sulcus at another institution, he received one cycle of NACT with Docetaxel, Cisplatin, and 5-Fluorouracil (TPF). After a two-month delay, he sought care at our facility. Clinical examination revealed grade II trismus, a residual lesion in the left lower gingiva buccal sulcus, and unhealthy mucosa in the left retromolar trigone. An enlarged left level Ib lymph node was notable. Slide review confirmed squamous cell carcinoma, and a PET-CT scan disclosed multiple metastatic sites. Subsequently, the patient developed right hemiparesis. A multidisciplinary tumor board recommended palliative systemic therapy and care, which the patient and spouse accepted. **Conclusion:** We present an unusual case featuring widespread metastasis in locally advanced squamous cell carcinoma post-one-cycle NACT. This emphasizes the significance of timely locoregional treatment post-NACT, particularly for non-responders. Further prospective studies are crucial to delineate whether NACT defaulters are prone to widespread metastasis and to establish the optimal NACT-to-locoregional treatment interval.

**Keywords:** Neoadjuvant Chemotherapy, Metastasis, Oral Cancer, Oral Ulcer, PET-CT.

## Introduction

Oral cavity cancers (OCC) represent a significant global health concern, ranking as the sixth most prevalent malignancy. Squamous cell carcinoma (SCC) predominates among the histological subtypes, accounting for over 90% of OCC cases. Traditionally, OCC has been associated with elderly males in their fifth to eighth decades of life. However, a troubling trend has emerged with an increasing incidence in younger individuals. Notably, India bears a substantial burden of OCC, primarily attributed to the widespread use of

tobacco in various forms. In older patients, the primary risk factors remain tobacco and alcohol abuse, contributing to the prevalence of OCC in India, where it ranks among the top five cancer sites in both sexes. Unfortunately, a majority of patients present at an advanced stage, resulting in challenging treatment outcomes. In the context of managing locally advanced head and neck cancer, neoadjuvant chemotherapy (NACT) has become a pivotal strategy for downstaging the disease and mitigating the risk of distant metastasis [1-3]. Remarkably, despite its clinical importance, there is a dearth of comprehensive studies exploring the

impact of delayed local treatment following NACT on oncologic outcomes [4-8].

This case report presents a rare scenario - a small primary lesion with extensive metastasis, in a patient diagnosed with locally advanced squamous cell carcinoma of the left gingiva buccal sulcus following one cycle of NACT. This case underscores the need for timely intervention and prompts further investigation into the ideal timing of local treatment post-NACT.

## Case Report

A 53-year-old male patient presented to our outpatient department with a three-month history of a painful ulcer on the left side of his oral cavity. He had a substantial history of smoking for 30 years and chronic alcohol consumption for 20 years. Prior to coming to our facility, he had undergone evaluation and received a diagnosis of squamous cell carcinoma in the left lower gingiva buccal sulcus, classified as cT3N2bMx, at another hospital. The initial treatment plan there involved Neoadjuvant chemotherapy (NACT) followed by a reassessment for surgical intervention.

The patient had completed one cycle of NACT with a Docetaxel, Cisplatin, and 5-Fluorouracil (TPF) regimen at the previous hospital; however, specific details about the chemotherapy dosage were not available to us. There was a two-month delay between the conclusion of the first NACT cycle and his visit to our outpatient department. Upon examination, the patient presented with grade II trismus, a residual lesion in the left lower gingiva buccal sulcus measuring 3 × 3 cm in the area of the second and third molars, and unhealthy mucosal tissue in the left retromolar trigone (RMT). A significant clinical finding was an enlarged left level Ib lymph node. No other clinically significant neck nodes were detected.

Slide review confirmed the presence of squamous cell carcinoma. Subsequently, a

metastatic workup was initiated, which included a PET-CT scan. The scan revealed a soft density lesion in the left lower gingiva buccal sulcus involving the RMT, with a standardized uptake value (SUV) of 8.51. Multiple nodes in the left neck were involved, encompassing submandibular, level II, level III, jugular group, and the posterior triangle, with an SUV of 11.88. Additionally, multiple irregular hypodense lesions were observed in both lobes of the liver, involving all segments, with an SUV of 11.01. The scan also identified multiple lytic lesions in the axial and appendicular skeleton, affecting various areas such as the skull, bilateral scapulae, clivus, medial ends of the bilateral clavicles, bilateral humeri, multiple ribs, sternum, multiple levels of the cervical, dorsal, lumbosacral spine, pelvis, and bilateral femurs, with an SUV of 12.27 [Fig.1-3]. Furthermore, an intramedullary lesion was noted in the left femur, with an SUV of 5.31. During a subsequent visit to our hospital, the patient developed right hemiparesis. Although an MRI of the brain was recommended, the patient's attendants declined the procedure. Given the extensive nature of the disease and the possibility of brain metastasis, the case was deliberated upon by our multidisciplinary tumor board. It was determined that palliative systemic therapy, in conjunction with palliative care, was the most appropriate course of action.

The patient's condition, advanced disease, and the palliative intent of treatment were thoroughly explained to his wife, who opted for symptomatic and supportive care, which is currently being provided at our institute.

## Discussion

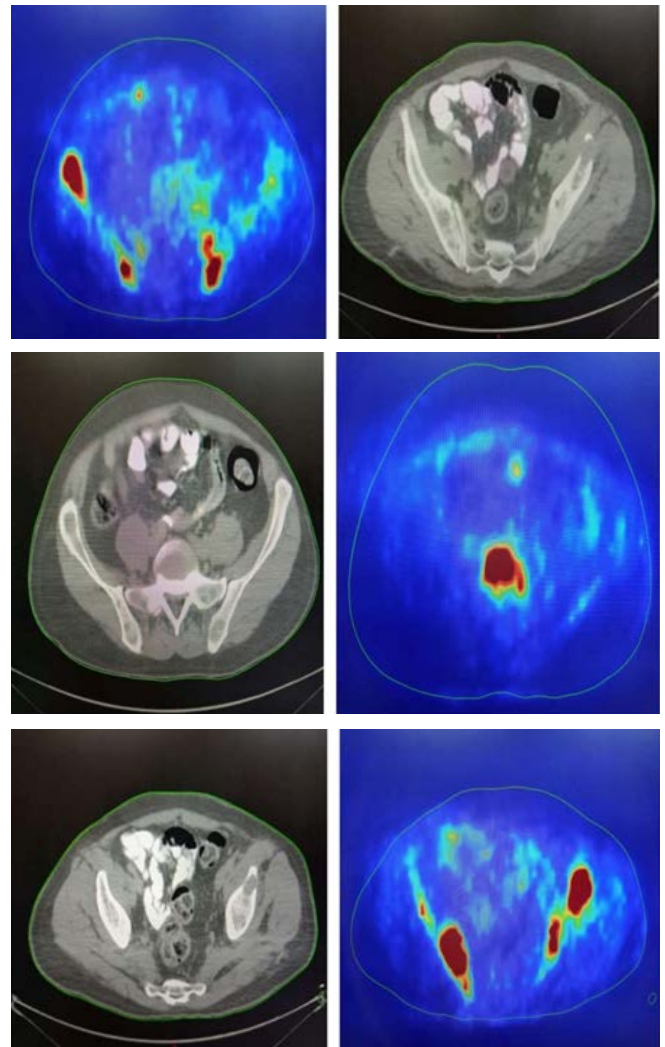
The phenomenon of tumor repopulation following the initiation of radiation therapy for HNSCC (Head and Neck Squamous Cell Carcinoma) is well-documented in the literature. Several randomized controlled trials (RCTs) have corroborated that accelerated radiotherapy yields a locoregional control advantage when concurrent chemotherapy

is not part of the treatment regimen [9-12]. This effect is likely applicable to chemotherapy as well. Prolonging the interval between the completion of Neoadjuvant chemotherapy (NAC) and definitive locoregional treatment may provide a window for micrometastases originating from the primary site to proliferate and disseminate.

The reasons behind delays in surgery post-NAC are multifaceted. Trials utilizing induction chemotherapy have reported up to a 6% incidence of toxic deaths. Even when variations in doses and cycle numbers are taken into account, induction TPF therapy often leads to substantial hematological toxicity, notably leukopenia and febrile neutropenia. Among patients with a lower socioeconomic status, data indicate that 38.2% were unable to complete or receive planned definitive therapy following induction chemotherapy. While alternative chemotherapy regimens may exhibit lower toxicity and better tolerability, adverse events and toxicities remain a concern that can impact subsequent surgical planning. Furthermore, clinicians may intentionally postpone surgery after NAC to allow for recovery, with the aim of minimizing surgical complications. Therefore, efforts should be made to minimize surgical delays, especially for patients showing stable disease or progression after NAC, as these delays have a significant impact on oncologic outcomes. Recognition of significant weight loss before and during NAC may help identify patients at risk of surgery-related delays [13-16]. Beyond the precise administration of chemotherapy and appropriate supportive measures, it is imperative to minimize avoidable logistical delays, as these factors are predictable and amenable to intervention.

## Conclusion

In this report, we presented an unusual case characterized by metastasis in a patient with locally advanced squamous cell carcinoma of the left lower gingiva buccal sulcus, who had undergone treatment with the Neoadjuvant chemotherapy



**Fig.1-3:** Metastasis in bones visualized.

(TPF) regimen. Our findings underscore the importance of prompt initiation of definitive locoregional treatment following NAC, particularly for non-responders. Further prospective studies are essential to determine whether patients who fail to complete NAC are at an increased risk of widespread metastasis and to establish the optimal time interval between NAC and locoregional treatment. Recognizing and addressing these factors can significantly improve the management and outcomes of patients with HNSCC.

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