Case Report

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Oncology Section

Isolated Hepatic Metastasis Following Curative Treatment of Stage II Poorly Differentiated Buccal Mucosa Squamous Cell Carcinoma: A Case Report

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ABSTRACT

Distant Metastasis (DM) in early-stage Oral Squamous Cell Carcinoma (OSCC) is uncommon and is usually associated with advanced locoregional disease. However, intrinsic tumour biology may occasionally overridess conventional prognostic determinants. We report a rare case of early isolated hepatic metastasis following curative-intent treatment of stage II, poorly differentiated squamous cell carcinoma of the right buccal mucosa. A 50-year-old male from central India presented with a non-healing ulcer involving the right buccal mucosa. Diagnostic evaluation included detailed clinical examination, Orthopantomogram (OPG) to assess mandibular involvement, and Contrast-Enhanced Computed Tomography (CECT) of the face, neck, and thorax, which revealed a localised mucosal lesion without bone invasion, extranodal extension, or DM. Ultrasonography of the neck demonstrated enlarged cervical lymph nodes without definitive metastatic features. Incisional biopsy showed severe epithelial dysplasia, while frozen section analysis was suggestive of squamous cell carcinoma. The patient underwent wide local excision with ipsilateral modified radical neck dissection. Final histopathological examination confirmed a poorly differentiated squamous cell carcinoma staged as pT2N0M0, with a Depth of Invasion (DOI) of 5 mm, negative surgical margins, absence of Perineural Invasion (PNI) and Lymphovascular Invasion (LVI), and no nodal metastasis. In view of poor differentiation and dysplasia at the surgical margin, adjuvant Intensity-Modulated Radiotherapy (IMRT) was administered. Despite satisfactory locoregional control, follow-up imaging prompted by abdominal symptoms revealed multiple hepatic revealed multiple hepatic lesions on abdomen CECT, without locoregional recurrence or pulmonary metastasis. Ultrasound-guided liver biopsy confirmed metastatic squamous cell carcinoma. This case highlights the dominant influence of adverse tumour biology in early haematogenous dissemination and underscores the limitations of stage-based prognostication, supporting biologically informed surveillance in selected early-stage OSCC patients.

Keywords: Disease progression, Haematogenous spread, High-grade tumour, Neoplasm metastasis, Prognosis, Postoperative surveillance

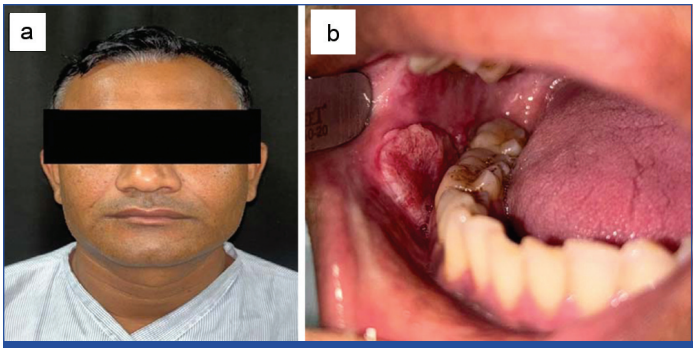
CASE REPORT

A 50-year-old male from central India presented to the Department of Oral and Maxillofacial Surgery with a non-healing intraoral ulcer involving the right buccal mucosa of one month's duration. The lesion had progressively increased in size from a small ulcer to approximately 3×2 cm. There was no history of preceding trauma. The patient denied pain but reported a burning sensation while consuming hot and spicy foods for the preceding 20 days. He also complained of progressively reduced mouth opening over the past six months. The patient denied exposure to smokeless tobacco, betel quid, or areca nut chewing and reported no history of tobacco use or alcohol consumption.There was no history of dysphagia, difficulty in mastication, altered salivation, weight loss, or loss of appetite. The patient also denied any history of spontaneous tooth exfoliation, numbness, or paresthesia. His medical history was unremarkable, except for implant fixation of the right forearm following a road traffic accident one year earlier and hospitalisation for arthritis three years ago. There was also a history of blood transfusion following a road traffic accident one year earlier. On general physical examination, the patient was conscious, cooperative, and oriented with an average build and good nutritional status. His height was 178 cm, weight 74 kg, and body surface area was 1.91 m^2. There was no icterus, pallor, cyanosis, clubbing, pedal oedema, or generalised lymphadenopathy. Systemic examination was unremarkable, and abdominal examination revealed no organomegaly.

On local examination, extraoral assessment revealed no facial asymmetry. Temporomandibular joint movements were restricted, without deviation or clicking. The lips were competent, and examination of the eyes, ears, and nose revealed no abnormalities. Neck examination identified a palpable lymph node in the right submandibular region measuring approximately 2×1 cm. The node was oval in shape, firm in consistency, freely mobile, and non-tender. Intraoral examination revealed restricted mouth opening of approximately 25 mm. An ulceroproliferative lesion measuring approximately 3×2 cm was present on the right buccal mucosa, extending superiorly from 1 cm above the mandibular occlusal plane to the lower gingivobuccal sulcus and anteroposteriorly from the distal aspect of tooth 44 to the mesial aspect of tooth 48. The lesion exhibited a pinkish-white surface with everted edges and ill-defined margins [Table/Fig-1]. On palpation, it was soft to firm in consistency, tender, and associated with underlying induration. The remaining intraoral structures were within normal limits. In view of the restricted mouth opening, the patient was further evaluated for Oral Submucous Fibrosis (OSMF). Bimanual palpation of the buccal mucosa did not reveal any fibrous bands, and other characteristic clinical features of OSMF were absent. Therefore, the restricted mouth opening was considered secondary to tumour-related involvement rather than underlying OSMF.

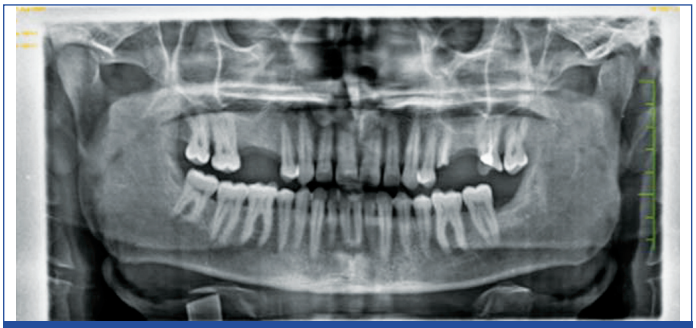
Imaging and Preoperative Evaluation

An orthopantomogram (OPG) was performed, which revealed no evidence of cortical erosion or medullary bone involvement of the



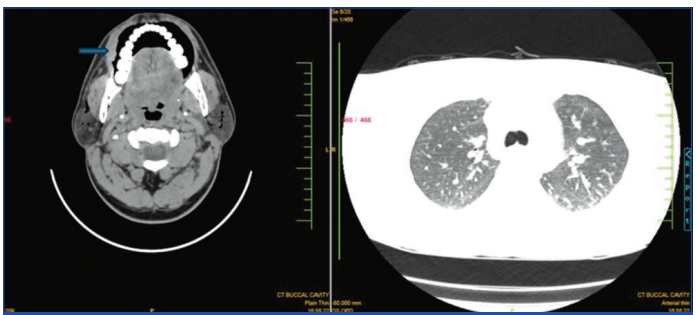
[Table/Fig-1a,b]: Preoperative face and clinical ulceroproliferative lesion of right buccal mucosa.

mandible in the region of the right buccal mucosa and retromolar area. The dentition and overall mandibular architecture were preserved [Table/Fig-2].



[Table/Fig-2]: Orthopantomogram (OPG) showing no evidence of mandibular bone erosion and multiple missing teeth in the maxillary arch.

Ultrasonography of the neck revealed multiple enlarged right submandibular and jugulodigastric lymph nodes, the largest measuring 2.13×1.02 cm, with loss of the fatty hilum. Contrast-enhanced computed tomography (CECT) of the face, neck, and thorax demonstrated mucosal thickening measuring 25×10×7 mm along the right posterior lower gingiva extending into the retromolar region, without evidence of mandibular bone invasion. A single enlarged right jugulodigastric lymph node measuring 24×11 mm was identified, without evidence of central necrosis or extranodal extension. Thoracic imaging was unremarkable [Table/Fig-3]. Preoperative chest radiography revealed no abnormalities, and two-dimensional echocardiography demonstrated normal left ventricular systolic function.

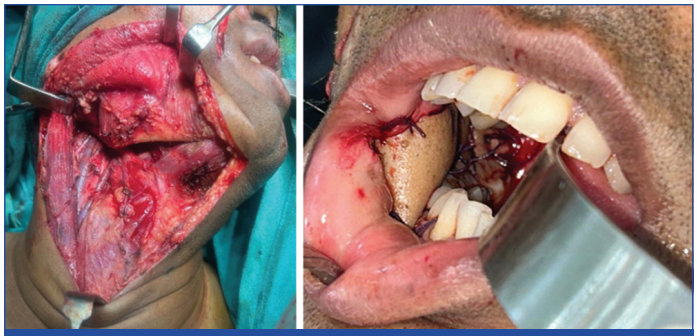


[Table/Fig-3]: Contrast-enhanced computed tomography (CECT) of the face, neck, and thorax showing mucosal thickening involving the right posterior lower gingiva and retromolar region (arrow), with a single enlarged right jugulodigastric lymph node. No evidence of mandibular invasion, extranodal extension, pulmonary metastasis, or mediastinal lymphadenopathy is seen.

Histopathological Diagnosis and Surgical Management

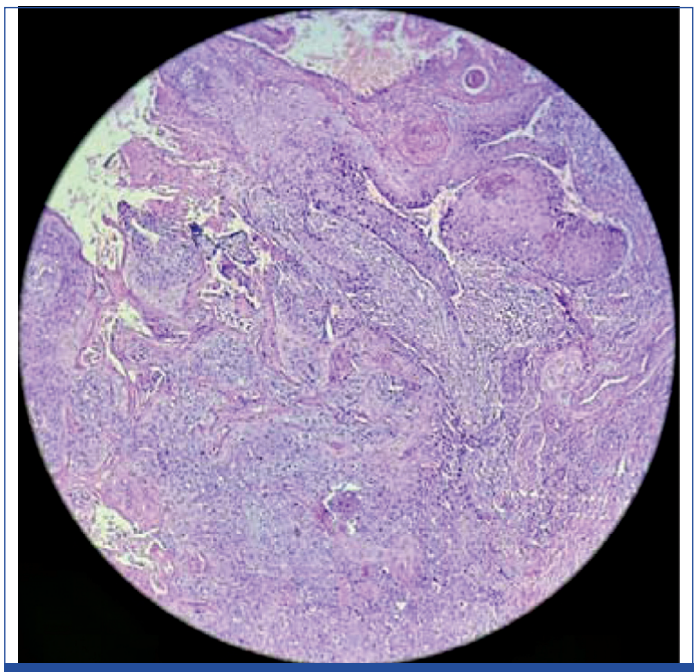
Frozen-section examination of the right buccal mucosal mass was suggestive of verrucous carcinoma or squamous cell carcinoma, whereas the initial incisional biopsy revealed severe epithelial dysplasia. The patient subsequently underwent right segmental mandibulectomy with ipsilateral modified radical neck dissection (Levels I-III) [Table/Fig-4].

Reconstruction was performed using a reconstruction plate and a Pectoralis Major Myocutaneous (PMMC) flap. Final histopathological



[Table/Fig-4]: Intraoperative photograph of the surgical specimen following right segmental mandibulectomy with ipsilateral modified radical neck dissection (Levels I-III).

examination confirmed a poorly differentiated squamous cell carcinoma measuring 3.6×2.0×1.8 cm, with a Depth of Invasion (DOI) of 5 mm [Table/Fig-5].



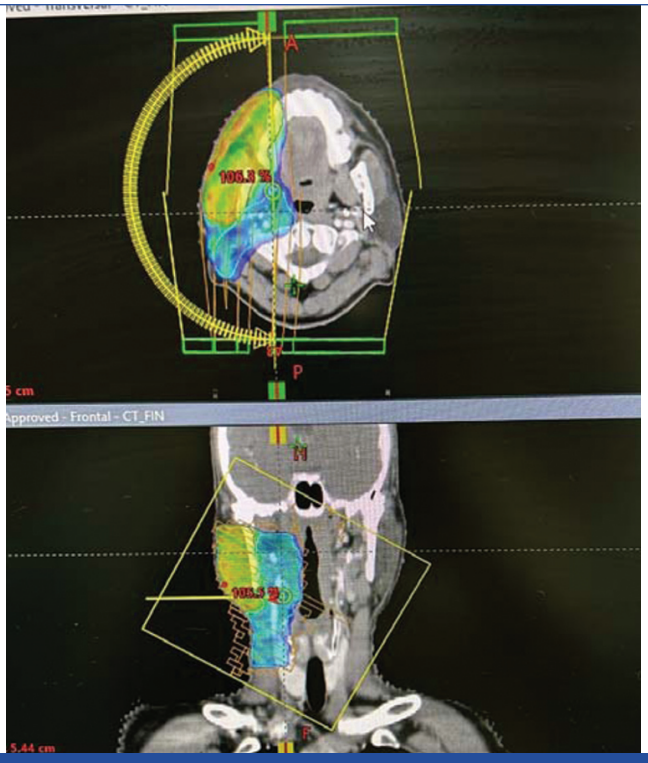
[Table/Fig-5]: Haematoxylin and eosin (H&E)-stained section (20×) showing tumour cells arranged in sheets and cords, exhibiting marked pleomorphism, enlarged irregular hyperchromatic nuclei with prominent nucleoli, a high nuclear-to-cytoplasmic ratio, scant keratin pearl formation, and increased mitotic activity, consistent with poorly differentiated squamous cell carcinoma.

The anterior surgical margin measured 1 cm and demonstrated severe epithelial dysplasia/carcinoma in situ-like changes, whereas all other margins were greater than 1 cm and free of invasive carcinoma. Perineural invasion (PNI) and lymphovascular invasion (LVI) were absent. The worst pattern of invasion was classified as Worst Pattern of Invasion-3 (WPOI-3). All 17 dissected lymph nodes were negative for metastatic involvement, and there was no evidence of bone invasion. Based on these findings, the tumour was staged as pT2N0M0 (Stage II) according to the AJCC 8th edition staging system.

Adjuvant Treatment

In view of poor tumour differentiation and the presence of severe dysplasia at the anterior surgical margin, the patient received adjuvant Intensity-Modulated Radiotherapy (IMRT) to the primary site and ipsilateral neck [Table/Fig-6].

A total dose of 60 Gy in 30 fractions over six weeks was delivered at 2 Gy per fraction. The treatment was well tolerated, with manageable acute toxicities. The patient developed Grade II radiation dermatitis, Grade II oral mucositis, and Grade I dysphagia, graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0. These toxicities were managed conservatively with standard supportive measures,

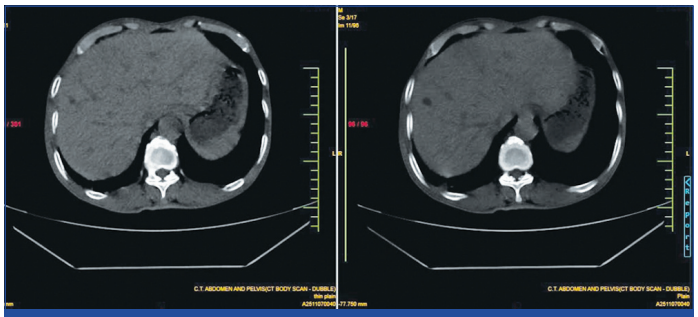


[Table/Fig-6]: Intensity-modulated radiotherapy (IMRT) treatment planning image demonstrating adequate target volume coverage of the primary tumour bed and ipsilateral neck, prescribed to receive 60 Gy in 30 fractions.

including topical agents, analgesics, nutritional supplementation, and meticulous oral hygiene. Body weight remained relatively stable during radiotherapy, decreasing from 72 kg to 70 kg.

Follow-Up and Disease Progression

During routine follow-up, three months after completion of adjuvant radiotherapy, the patient developed vague abdominal discomfort. Contrast-enhanced computed tomography (CECT) of the abdomen revealed multiple arterially enhancing hepatic lesions demonstrating venous washout, the largest measuring 1.5×1.4 cm [Table/Fig-7].



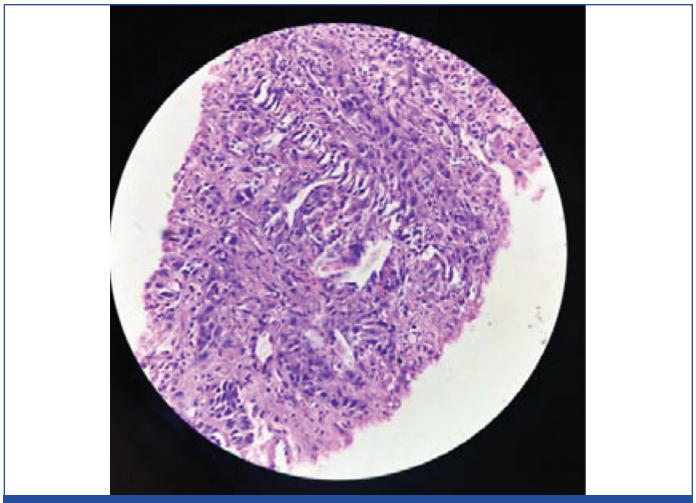
[Table/Fig-7]: CECT of the abdomen demonstrating multiple hepatic lesions with arterial phase hyperenhancement and venous washout, consistent with metastatic disease. No evidenceof locoregional recurrence is identified.

No evidence of locoregional recurrence, pulmonary metastasis, or nodal disease was detected. Ultrasound-guided liver biopsy confirmed metastatic squamous cell carcinoma [Table/Fig-8].

The patient was referred for systemic palliative chemotherapy with weekly paclitaxel (80 mg/m^2) and carboplatin [Area Under the Curve (AUC) 2]. At the time of writing, this report, the patient had completed four cycles of chemotherapy.

DISCUSSION

Distant metastasis (DM) in OSCC has traditionally been considered uncommon, particularly in early-stage disease managed with curative intent [1]. Classical oncological teaching emphasises locoregional lymphatic spread as the predominant pathway of tumour dissemination [2]. Established predictors of distant failure



[Table/Fig-8]: Haematoxylin and eosin (H&E)-stained section at high-power magnification showing tumour cells arranged in cords and nests. The cells are polygonal, with enlarged hyperchromatic nuclei, coarse chromatin, and abundant cytoplasm, consistent with metastatic squamous cell carcinoma involving the liver.

include cervical nodal metastasis, extracapsular spread, tumour thickness, perineural invasion (PNI), lymphovascular invasion (LVI), and advanced T and N stage [3]. However, accumulating clinical evidence challenges the assumption that the absence of these adverse pathological features reliably predicts favourable outcomes [4]. Recent retrospective analyses and systematic reviews have demonstrated that a measurable proportion of patients with early-stage OSCC develop distant metastases despite favourable pathological profiles [5]. Dolens E da S et al., systematically reviewed metastatic patterns in OSCC and confirmed that distant spread can occur across a wide spectrum of clinical stages [6]. The present case, characterised by pT2N0M0 disease, negative surgical margins, absence of PNI and LVI, and yet rapid development of isolated hepatic metastasis, highlights how tumour biology can override classical risk stratification frameworks. Histologic grade serves as a surrogate marker for intrinsic tumour aggressiveness. Poorly differentiated carcinomas exhibit higher proliferative indices (Ki-67), genomic instability, enhanced invasive capacity, and increased metastatic potential. Molecular mechanisms such as Epithelial Mesenchymal Transition (EMT), immune evasion, extracellular matrix remodeling, and resistance to anoikis are now recognised as key drivers of systemic tumour dissemination [7,8]. Despite this, tumour grade often receives less emphasis than nodal status or tumour thickness in prognostic models. In the present case, poor differentiation likely acted as the dominant driver of early hematogenous spread to the liver. Several institutional studies have demonstrated that the risk of DM increases with advanced T and N stage, tumour thickness >1 cm, PNI, extracapsular spread, and locoregional recurrence [5,9]. Nevertheless, many patients with early-stage, node-negative disease still experience distant relapse. This apparent inconsistency reflects biological heterogeneity driven by tumour microenvironment interactions, immune escape, circulating tumour cell survival, and tumour dormancy mechanisms that are not captured by routine histopathological assessment [10]. This case supports the need for risk-adapted surveillance strategies that integrate tumour biology with conventional staging parameters. Selected patients with early-stage disease and aggressive histological features, such as poor differentiation, may benefit from enhanced systemic surveillance and broader imaging strategies to facilitate earlier detection of occult metastatic disease [3]. The lung is the most common site of distant metastasis in OSCC, followed by bone, skin, liver, and brain [11,12]. Isolated hepatic metastasis without pulmonary involvement is distinctly uncommon. The present case illustrates the unpredictable behaviour of biologically aggressive oral cavity squamous cell carcinoma. Poor histological differentiation remains an important yet under-recognised predictor of aggressive disease behaviour in oral cavity cancer [12]. Early-stage, node-negative oral cavity cancer

may still carry a substantial risk of early distant metastasis when adverse biological features are present [13]. Integrated surveillance models incorporating biological and molecular markers are urgently needed [14]. Future guidelines should incorporate biology-driven risk stratification rather than relying exclusively on conventional pathological parameters, including PNI, LVI, extranodal extension (ENE), depth of invasion (DOI), tumour stage, and nodal status.

CONCLUSION(S)

This case demonstrates that early stage, node negative oral cavity cancer of the right buccal mucosa should not invariably be regarded as biologically low risk. Even in the setting of complete locoregional treatment and the absence of established adverse pathological features, poor histological differentiation may serve as an independent predictor of aggressive tumour behaviour and early distant metastasis. The present case highlights its propensity for early and atypical haematogenous spread, as evidenced by the development of isolated hepatic metastasis. These findings expose the limitations of relying solely on stage based prognostic models and reinforce the importance of tumour biology in predicting disease behaviour. Integrating biological risk indicators into post-treatment surveillance protocols may facilitate earlier detection of distant relapse in selected patients with early-stage disease, thereby enabling more timely systemic intervention and truly individualised patient care.

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