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Case Report

A rare presentation of an oral cavity metachronous malignancy: Case Report

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Abstract

Introduction or Background: Head and neck cancers, particularly those involving the oral cavity, are associated with high morbidity and mortality rates globally. Despite advancements in surgical techniques, chemotherapy, and radiotherapy, the development of second primary malignancies (SPMs) remains a critical concern for long-term survivors. The occurrence of metachronous double primary malignancies, where the second primary cancer arises at a different anatomical site and time, poses additional diagnostic and therapeutic challenges.

Case Presentation: We present a rare case of a 42-year-old male with a history of chronic tobacco use, diagnosed with metachronous double primary malignancies involving the left lateral border of the tongue and left buccal mucosa, separated by a disease-free interval of 15 months. The patient initially presented with a non-healing ulcer and left cervical lymphadenopathy. Biopsy confirmed squamous cell carcinoma, and he underwent wide local excision with left radical neck dissection

followed by adjuvant chemoradiation. Following a disease-free period of 15 months, the patient developed a second primary malignancy in the left buccal mucosa. After multidisciplinary discussions, the patient received palliative chemotherapy due to the extensive involvement of critical structures, including the infratemporal fossa.

Discussion and Conclusion: The case highlights the clinical significance of field cancerization in head and neck cancer patients with long-term tobacco exposure, leading to the development of SPMs. It emphasizes the importance of ongoing surveillance, early detection strategies, and multidisciplinary approaches for optimal management. The case also underscores the complexities in distinguishing between recurrence and second primary malignancies, which have different treatment and prognostic implications. This report adds to the literature on SPMs and reinforces the need for vigilance in the follow-up of high-risk patients.

Keywords: Metachronous malignancy, second primary malignancy, head and neck cancer, oral cavity malignancy, field cancerization

Introduction

Head and neck cancers, particularly those involving the oral cavity, present significant clinical challenges due to their high incidence and associated morbidity and mortality. According to GLOBOCAN 2022, the Lip & Oral Cavity tumours entity accounts for the incidence of 389,846 cases and 188,438 deaths per annum globally. ⁽¹⁾

These malignancies are frequently linked to lifestyle risk factors, including tobacco use, alcohol consumption, and betel nut chewing. While advancements in surgical techniques, radiotherapy, and chemotherapy have

improved local control of these cancers, the development of second primary malignancies (SPMs) remains a significant concern in long-term survivorship.

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Metachronous double primary malignancies refer to the occurrence of a second primary cancer at a different anatomical site and at a different time from the initial primary cancer, with an interval of at least six months. Studies have shown that the median time to onset of second primary malignancies (SPMs) in head and neck cancer patients is 72 months, with 87.6% of SPMs occurring after two years. ⁽²⁾

In head and neck cancer patients, this phenomenon is often attributed to the concept of field cancerisation, where the entire epithelial field is exposed to carcinogenic insults like tobacco, predisposing it to multiple independent malignancies. The high incidence of SPMs necessitates rigorous, long-term surveillance and early detection strategies to optimise patient outcomes.

We report the rare occurrence of a case of metachronous double primary malignancy of the left lateral border of the tongue and left buccal mucosa within an interval of 15 months in a tertiary care cancer centre in South India.

Case History:

A 42-year-old male with a history of oral tobacco chewing for 20 years presented with a non-healing ulcer on the left lateral border of the tongue and a swelling in the left neck, both gradually progressive over four months. He also had a loss of weight and appetite for three months. He had no history of bleeding or foul discharge from the lesion, fever, cough, shortness of breath, speech difficulty or nasal obstruction. He had no history of tuberculosis, prior surgeries or dental procedures. No significant family history of any malignancy was noted.

The patient was well built and moderately nourished, with a performance status (ECOG) of 1. On examination, his vitals were stable and the oral cavity showed restricted opening (Grade 2 Trismus), no ankyloglossia and a 3x2 cm ulceroproliferative growth noted along the left lateral border of the tongue with dorsal surface involvement involving the posterior one-third of the tongue. The rest of the oral cavity & oropharynx were normal. A video laryngoscopy revealed normal findings. A hard, immobile, non-tender level II lymph node enlargement of 3x3cm was noted on the left side, with laryngeal crepitus and overlying skin intact.

All routine blood investigations (Complete Hemogram, Liver Function Test, Renal Function Test and Serum electrolytes) were within normal limits, and viral markers were negative. A biopsy confirmed moderately differentiated squamous cell carcinoma of the tongue, and FNAC of the lymph node confirmed metastasis. Contrast Enhanced Computed Tomography (CECT) revealed an ill-defined, heterogeneously enhancing, lobulated soft tissue

density in the anterior aspect of the left lateral border and dorsum of the tongue measuring 3.3x1.5x1.2cm with no obvious bony erosion and an enlarged, well-circumscribed heterogeneously enhancing left level II cervical lymph node with central necrosis measuring 3.7x3.8cm suggesting nodal metastasis. (Figure 1) The clinical staging was determined to be cT2N3bM0.

The patient underwent wide local excision of the tumour along with left radical neck dissection. The surgical specimen revealed a moderately differentiated squamous cell carcinoma with lymphovascular and perineural invasion, a DOI of 9 mm. The margins were 0.4cm superiorly, 0.7cm inferiorly and 0.7cm deep. Anterior & inferior margins were free of tumours. Thirty lymph nodes were dissected, of which one node was malignant with extranodal extension (ENE). The pathologic staging was determined to be pT2N3bM0.

After obtaining dental fitness and assessment for chemotherapy, the patient underwent adjuvant chemoradiation of 64 Gy in 32 fractions, along with concurrent cisplatin 100mg/m² delivered three-weekly. The patient had Grade II dermatitis, mucositis and pharyngitis at the time of completion of the radiotherapy course and was managed conservatively.

On routine follow-up, he was found to have no evidence of disease on clinical examination, and a response assessment of CECT after three months of treatment completion showed negative for malignancy. He started tolerating oral intake with normal oral hygiene, and improvement in weight and nutritional status was noted. He also had persistent grade 2 trismus, for which jaw-opening exercises were advised.

After a disease-free interval of 15 months after treatment, the patient presented with an ulceroproliferative growth over the left buccal mucosa with insidious onset and gradually progressed for one month. The patient had no history of oral tobacco chewing during this period. On examination, the lesion was noted to be 4x3cm over the left buccal mucosa involving left retromolar trigone and upper and lower gingivobuccal sulcus extending anteriorly till first molar associated with grade 3 trismus. (Figure 2) The primary tumour site of the tongue and neck were normal. Biopsy from the lesion was suggestive of moderately differentiated squamous cell carcinoma, the imperative of a metachronous incidence of second malignancy. (Figure 3)

Positron Emission Tomography (PET) scan reveals an FDG-avid (Fluoro-deoxy-glucose) ill-defined heterogeneously enhancing soft tissue dense lesion involving the left gingivobuccal region, contiguous with the infiltration of ramus and body of left hemimandible,

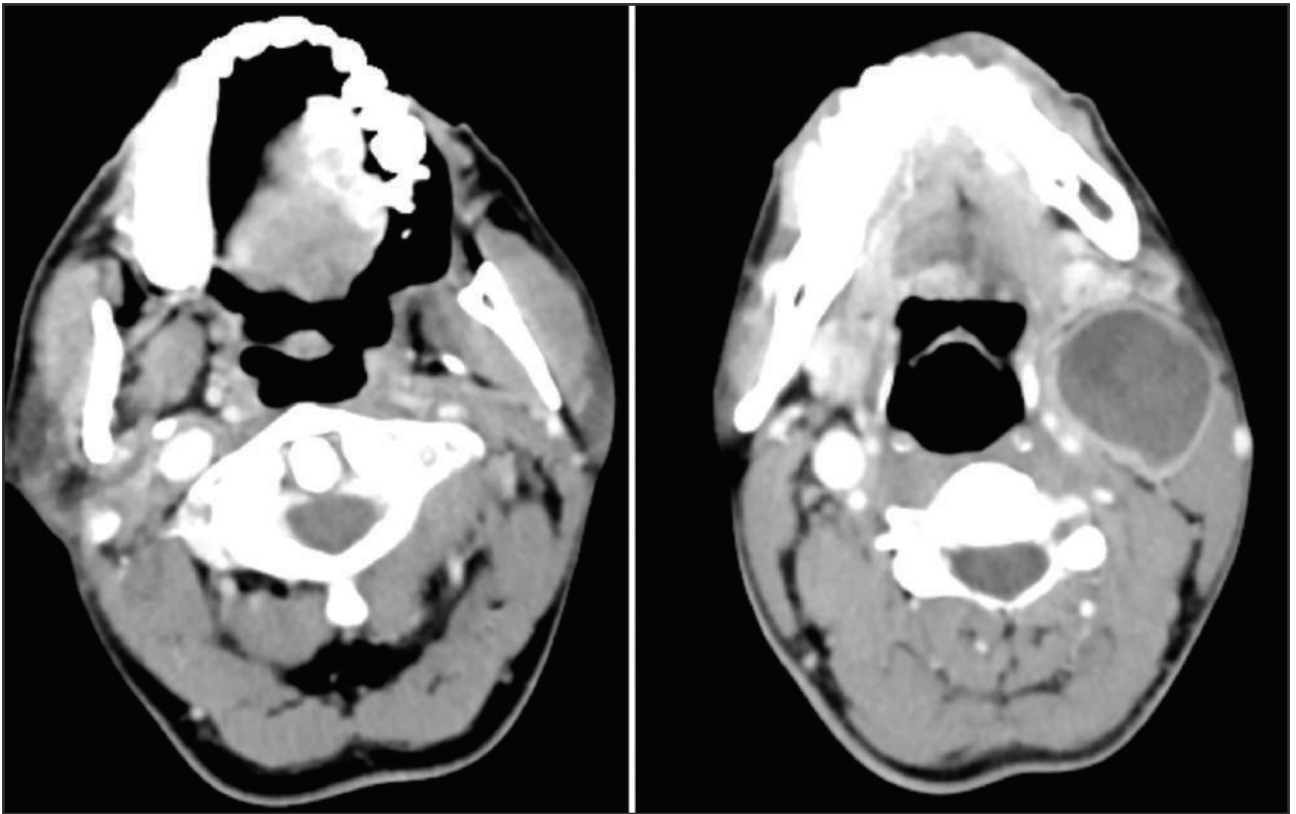


Figure 1. Baseline CECT scan showing the primary malignancy over the left lateral border of the tongue and left cervical lymph node



Figure 2. Clinical photograph of the second primary malignancy in the left buccal mucosa

superiorly involving the hard palate and lower half of left infratemporal fossa and inferiorly reaching the left tonsillar fossa. FDG avid peripherally enhancing right level II cervical lymph nodes with central hypodense areas are noted. (Figure 4)

After confirming the second primary malignancy (SPM) and the large extent of the disease, further management options were discussed in a multidisciplinary tumour clinic. In view of the large extent of the second primary involving the infratemporal fossa, the patient was deemed not suitable for radical surgical excision. After discussing the risks and benefits with the patient and family, we offered the options of salvage radiotherapy and palliative chemotherapy for further treatment. They opted for palliative chemotherapy and the patient was started on 3-weekly Paclitaxel & Carboplatin. After six cycles, the patient had progressive disease and was advised of the best supportive care.

Discussion

Differentiating between a recurrence and a second primary malignancy (SPM) is critical, as it impacts treatment decisions and prognostic expectations. Recurrence of the tumour typically occurs at or near the site of the original tumour (local) or, in the regional lymph nodes (regional), or both (loco-regional). Recurrences usually manifest within the first few years post-treatment,

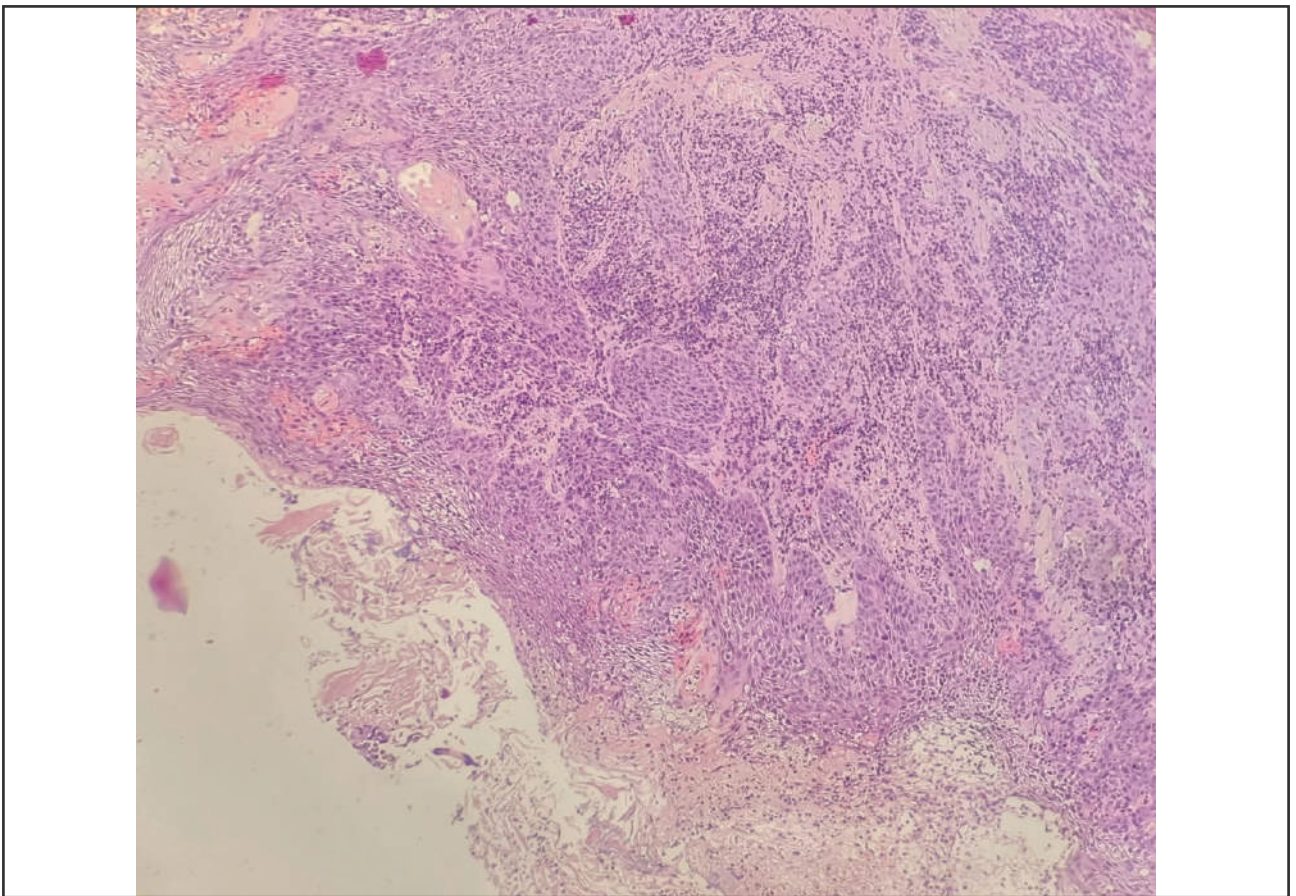


Figure 3. Histopathologic slide depicting moderately differentiated squamous cell carcinoma of the left buccal mucosa

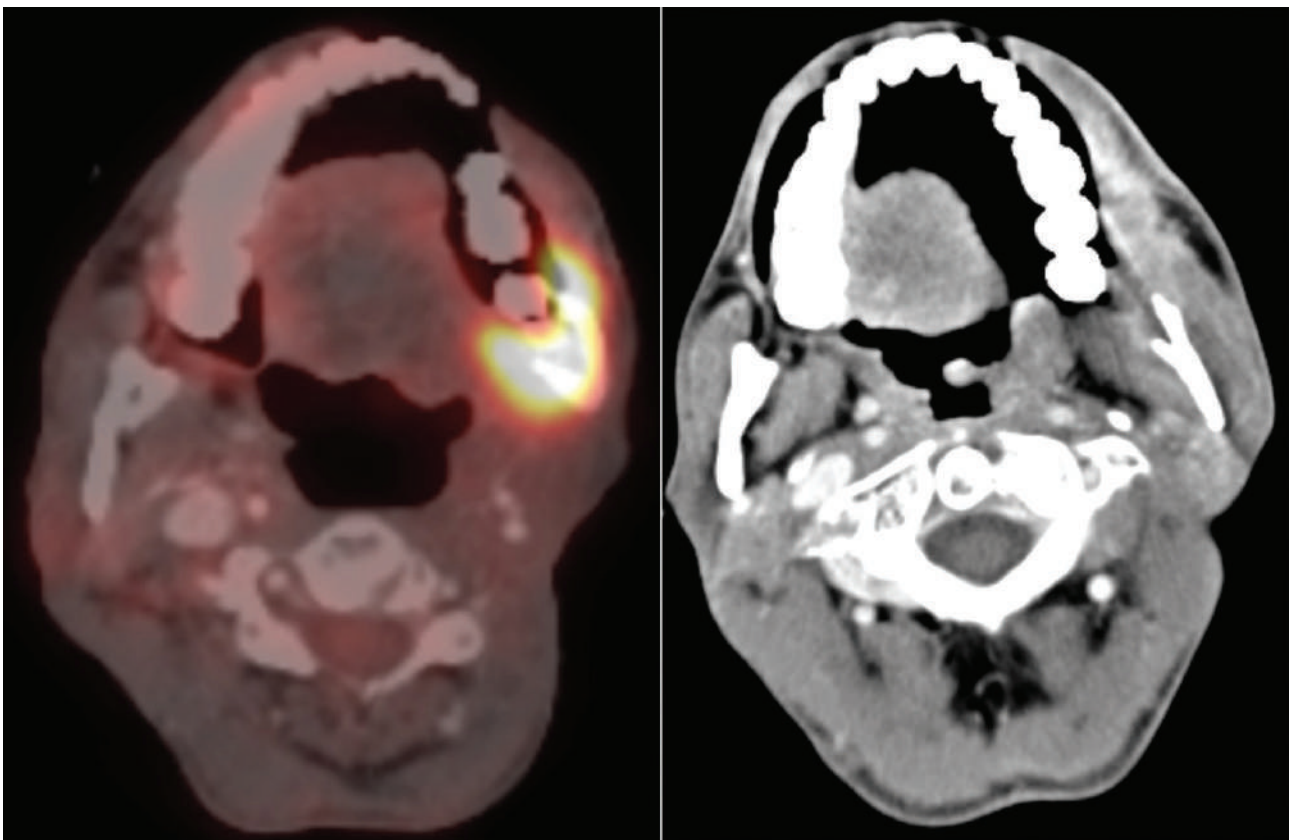


Figure 4. Response assessment PET & CT scan showing the second primary malignancy at the left buccal mucosa

with a median time to recurrence being relatively short. A study by Patel et al. (2023) found that 34.5% of patients with buccal mucosa carcinoma developed recurrence within one year, with neck node metastasis, ENE, and margins of resection less than 5 mm being significantly associated with recurrence. ⁽³⁾

In contrast, SPMs are new primary cancers that occur in different anatomical locations and are histologically distinct from the original tumour. The development of SPMs is often influenced by the field cancerisation effect, shared risk factors such as tobacco and alcohol use, and the carcinogenic effects of previous radiotherapy.

Several studies have documented the incidence of SPMs in head and neck squamous cell carcinoma (HNSCC) patients. The median time to onset for SPMs is typically longer compared to recurrences, often occurring several years after the initial cancer treatment. Ng et al. (2019) reported a median time to onset of SPMs of 72 months in head and neck cancer patients treated with radiotherapy, emphasising the need for extended surveillance. This study also emphasised the increased risk associated with smoking due to field cancerisation, suggesting that patients with a history of tobacco use require particularly careful monitoring. ⁽²⁾ However, in our case, the incidence of a second primary malignancy occurred unusually within 15 months after the treatment of the first primary malignancy.

A retrospective cohort study by Adeel et al. (2018) reported an SPM incidence rate of 8.14% over a median follow-up of 67 months. Notably, 77.7% of these SPMs were located in the oral cavity, with a smaller proportion (11%) occurring in the lungs. This study underscores the significant risk of developing SPMs in the oral cavity, highlighting the need for continued and enhanced vigilance in this patient population. ⁽⁴⁾ On the contrary, in our case, the incidence of SPM was diagnosed within two years of treatment as a result of routine follow-up visits.

The occurrence of SPMs also varies according to the modality of treatment of the first primary malignancy. Hashibe et al. (2005) highlighted that the patients who received radiotherapy alone had a slightly higher risk of second primary cancers compared to patients who received radiotherapy with surgery, but patients who were treated with surgery alone did not have an elevated risk of second primaries within the first decade of treatment. ⁽⁵⁾ However, despite undergoing surgery followed by adjuvant chemoradiation, our patient had developed SPM within two years of treatment.

For patients with SPMs, the prognosis can vary depending on the site and stage of the second malignancy at diagnosis. In a retrospective analysis by Wang et al.

(2022), it was found that most SPMs that occurred after IMRT-based treatment in the past decade were diagnosed at an advanced stage and a shorter interval compared to those treated in the conventional radiotherapy era. The study also showed a correlation between the advanced stage at the diagnosis of the first primary malignancy and the occurrence of an advanced stage for the SPM and poorer prognostic outcomes. ⁽⁶⁾ These findings of this study are consistent with our patient's case, in which the advanced stage of the initial primary malignancy resulted in the rapid onset and progression of the SPM.

Studies indicate that the survival rates for SPMs are generally better, provided they are detected early and treated promptly with a radical intent. Denaro et al. reported that salvage surgery or radiotherapy must be offered as the first line of management for patients with SPM, if feasible. ⁽⁷⁾ However, in our case, the disease was not resectable, and the patient had opted for palliative chemotherapy after a multidisciplinary tumour clinic discussion and shared decision-making.

Fujisawa et al. (2014) analysed the causes of death in patients treated with radiotherapy for early-stage oral cancer. They observed that within the first five years post-treatment, the primary cause of death was the initial oral cancer. However, between five and ten years, the leading causes of death shifted to SPMs, particularly those in the head and neck and oesophagus. Beyond ten years, lung cancer emerged as a predominant cause of death. ⁽⁸⁾ These findings highlight the evolving nature of mortality risks in long-term cancer survivors and the necessity for prolonged follow-up.

A study by Kim-Anh Do et al. suggests that long-term tobacco use in patients with head and neck squamous cell carcinoma significantly increases the risk of developing SPMs by 2.3 times compared to those who quit tobacco. ⁽⁹⁾ This heightened risk is associated with the concept of field cancerisation, where prolonged tobacco exposure leads to widespread genetic changes and predisposes individuals to SPMs. In our case, the time to onset of SPM was 15 months, the location of the second malignancy was different from the first tumour site, and the presence of long-term oral tobacco history supports the theory of field cancerisation rather than radiation-induced carcinogenesis of the second primary malignancy.

Comprehensive follow-up plans should include regular clinical examinations, imaging studies, and targeted screenings for common SPM sites with enhanced vigilance and surveillance. Appropriate psychosocial counselling for cessation of tobacco usage is of paramount importance in the prevention of second primary malignancies. This approach can facilitate early intervention and improve survival rates in this high-risk population. ⁽¹⁰⁾

Conclusion

The occurrence of metachronous double primary malignancies, as demonstrated in this case, underscores the complex interplay of factors such as tobacco-induced field cancerisation in head and neck cancer patients. The early detection and management of second primary malignancies (SPMs) remain critical, as they significantly impact prognosis and overall survival. Long-term surveillance, cessation of tobacco use, and multidisciplinary approaches are essential for optimising patient outcomes, particularly in high-risk populations. This case highlights the necessity of vigilant follow-up and the importance of patient education on lifestyle modifications.

Conflict of Interest:

None

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None

Disclosure:

The manuscript has not been published elsewhere in any journal.

References

1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA A Cancer J Clinicians*. 2024 May;74(3):229–63.
2. Ng SP, Pollard C, Kamal M, Ayoub Z, Garden AS, Bahig H, et al. Risk of second primary malignancies in head and neck cancer patients treated with definitive radiotherapy. *npj Precis Onc*. 2019 Sep 27;3(1):22.
3. Patel P, Singhal PM, Lakhera KK, Chatterjee A, Babu A, Singh S, et al. Predicting recurrence in oral cavity cancers: a review of 116 patients with buccal mucosa carcinoma in northwestern India. *Arch Craniofac Surg*. 2023 Oct 20;24(5):211–7.
4. Adeel M, Siddiqi MI. Metachronous second primary malignancy in head and neck cancer patients: is five years of follow-up sufficient? *J Korean Assoc Oral Maxillofac Surg*. 2018;44(5):220.
5. Hashibe M, Ritz B, Le AD, Li G, Sankaranarayanan R, Zhang ZF. Radiotherapy for oral cancer as a risk factor for second primary cancers. *Cancer Letters*. 2005 Apr;220(2):185–95.
6. Wang SW, Chan LP, Wang LF, Wu CW, Lin SH, Huang TY, et al. Secondary primary malignancy in patients with head and neck squamous cell carcinoma: 27-year experience from the perspective of diagnostic tools. Tornesello ML, editor. *PLoS ONE*. 2022 Feb 15;17(2):e0263773.
7. Denaro N, Merlano MC, Russi EG. Follow-up in Head and Neck Cancer: Do More Does It Mean Do Better? A Systematic Review and Our Proposal Based on Our Experience. *Clin Exp Otorhinolaryngol*. 2016 Dec 1;9(4):287–97.
8. Fujisawa R, Shibuya H, Harata N, Yuasa–Nakagawa K, Toda K, Hayashi K. Chronological shifts and changing causes of death after radiotherapy for early-stage oral cancer. *Int J Clin Oncol*. 2014 Feb;19(1):24–9.
9. Do K, Johnson MM, Doherty DA, Lee JJ, Wu XF, Dong Q, et al. Second primary tumors in patients with upper aerodigestive tract cancers: joint effects of smoking and alcohol (United States). *Cancer Causes and Control*. 2003;14(2):131–8.
10. Karam-Hage M, Cinciripini PM, Gritz ER. Tobacco use and cessation for cancer survivors: An overview for clinicians. *CA A Cancer J Clinicians*. 2014 Jul;64(4):272–90.