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Diagnostic Conundrum: Recurrence or Postoperative Inflammation in A Case of Oral Carcinoma

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Introduction

In the early postoperative period, the reparative mechanism involves inflammation followed by formation of granulation tissue and subsequently, fibrotic changes. Occasionally, these changes can mimic as recurrent tumour in the postoperative bed. Even with the availability of advanced imaging modalities these changes sometimes can lead to a diagnostic dilemma. Although, a positive biopsy is confirmatory, a negative biopsy cannot exclude the disease. Here, we present a case of oral carcinoma treated with surgery who presented with clinic radiological inflammatory changes masquerading as recurrence. The high focal FDG uptake on PET-CT added to the dilemma.

Case presentation: A 39-year-old male patient, reformed chewer, without any comorbidities presented to the head and neck outpatient department with the complaint of ulcer in the left side of the oral cavity. He had undergone an excisional biopsy outside one month back and was reported as squamous cell carcinoma (SCC). On examination, a 1x1 cm ill-defined lesion wasseen involving left buccal mucosa. Retromolar trigone (RMT), upper and lower gingivo-buccal sulcus (GBS) were not involved.

CT scan of Head and Neck showed 1.8x0.5x1.1cm, heterogeneously enhancing lesion seen involving left buccal mucosa. (Figure 1) All muscles of mastication were free and there was no bone erosion. There were no suspicious nodes. An ill-defined nodule of 0.8x0.9x0.9 cm size with a peripheral rim of calcification in the right lobe of the thyroid was detected incidentally. Ultrasound guided fine needle aspiration cytology (FNAC) of thyroid nodule was suggestive of follicular neoplasm of undetermined significance (Bethesda 3).

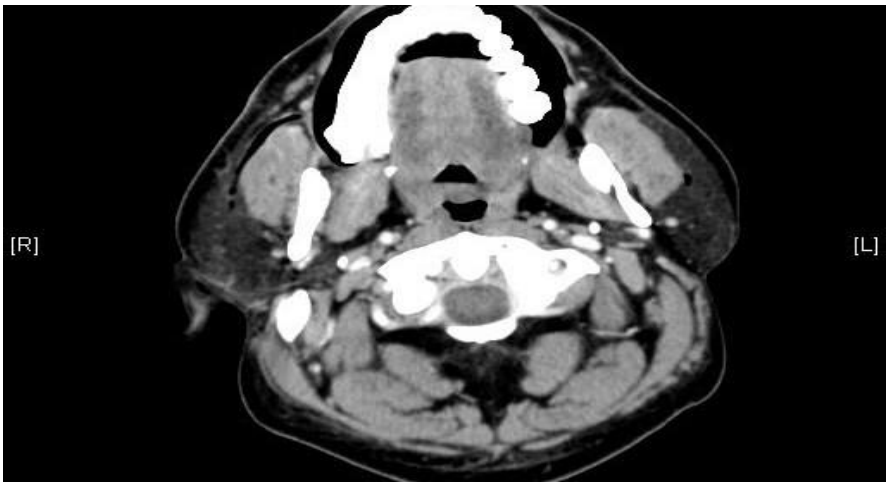

Figure 1: Preoperative CT image

The patient underwent wide local excision of buccal mucosa with left I-III neck dissection and skin graft. In view of papillary carcinoma nodes detected on frozen, total thyroidectomy with right central compartment clearance was done on 5th April 2021. The post-operative period was uneventful. On final histopathology report, no residual tumour was identified in the buccal mucosa and thus the patient was kept under observation. The patient was planned for RAI therapy in view of positive central compartment nodes. The patient was kept hypothyroid for RAI therapy. While waiting for Figure-1 Preoperative CT image RAI, the patient presented to our outpatient department with a suspected lesion in the left buccal mucosa and swelling over the face after 8 weeks of surgery.

On examination, suspicious ulceration wasseen amidst granulation tissue-like lesion with underlying induration. The epicenter was left buccal mucosa extending posteriorly till left RMT and anteriorly reaching till canine region, involving both upper and lower GBS as shown in figure 2. Oedema of the overlying skin reached till zygoma (Figure 3). No palpable neck nodes were found.

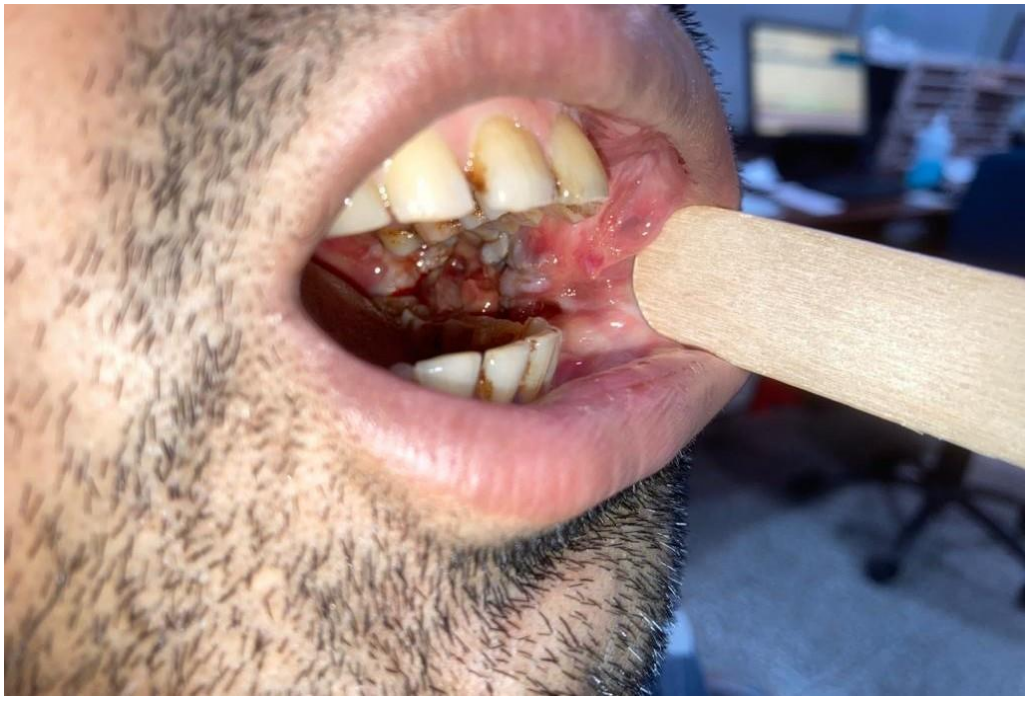

Figure 2: Suspicious lesion on left buccal mucosa

Figure 3: Oedema over the face

PET CT was done which was suggestive of focal FDG avid lesion of size 1.4x1.6 cm (SUV max 14.36) involving upper GBS with subtle cortical erosion along the outer surface of the in background of intense post-operative oedematouschangesin left buccal space (Figure 4a). Knife biopsy was taken from the suspicious ulcerative area and was reported as granulation tissue. MRI was also done which showed an ill-defined 17x11x10mm, T1 isointense, STIR hyperintense enhancing lesion with epicenter in the left buccal mucosa, involving the upper and lower GBS, buccal space, and reaching up to the RMT (Figure 4b). There was early enhancement on dynamic post-contrast imaging and was reported as suspicious for malignancy.

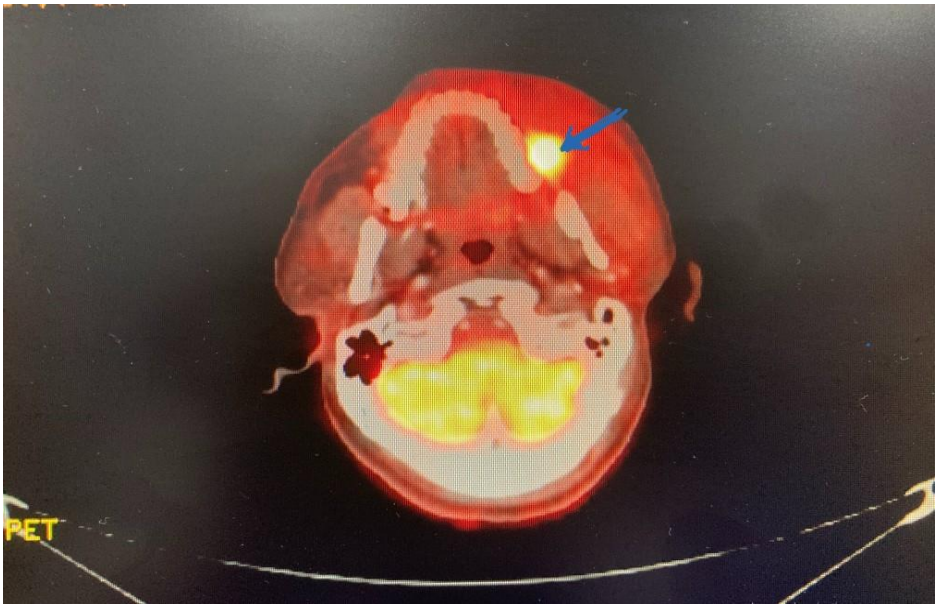

Figure 4a - PET in early post operative period at 8 weeks showing high focal FDG uptake (SUV max 11.43) marked with arrow

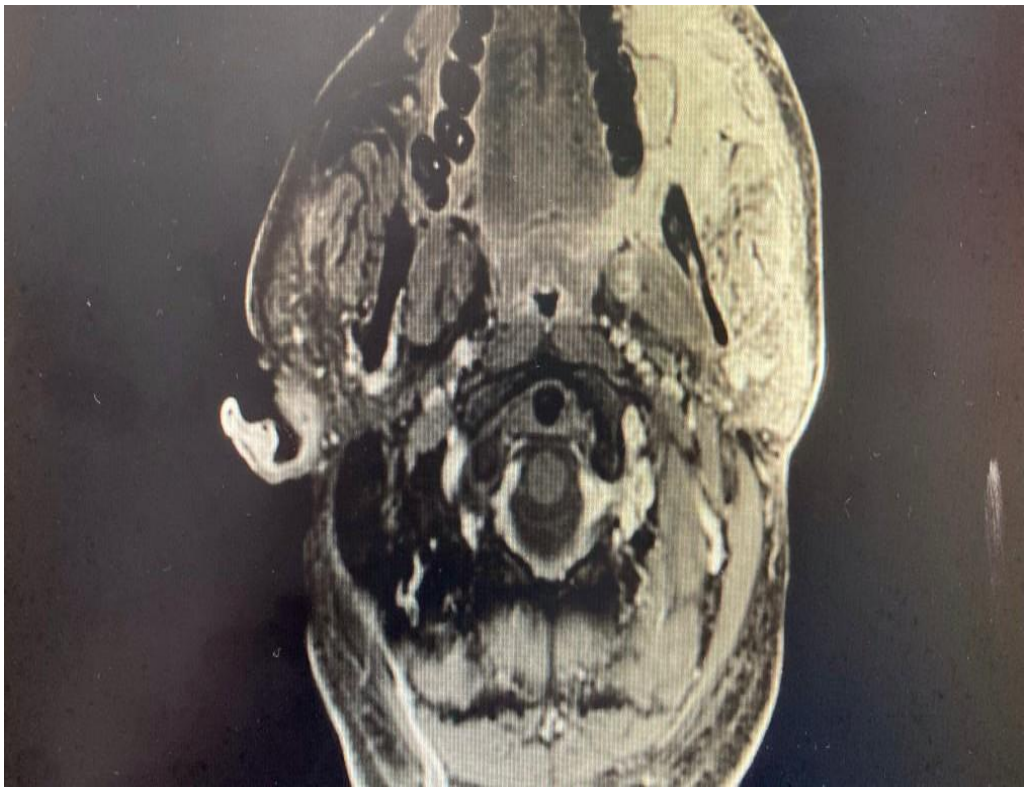

Figure 4b- MRI post-surgery 8 weeks

In view of suspicious clinical and radiological findings (PET CT and MRI), CT guided biopsy was done from a focal enhanced area (SUV max 11.43). Biopsy from the lesion was negative. None the less, in view of strong clinical suspicion and positive radiological findings, the decision for surgery vs observation was discussed with the patient. As the tissue diagnosis was negative twice and an extensive surgical resection was needed, a decision was taken to keep the patient under observation. The patient was started on Tab Clindamycin 600 mg TDS, Tab Trypsin Chymotrypsin TDS, Tab Thyroxine 150mcg OD for 15 days. After 15 days, there was a decrease in oedema over the face. Hence, antibiotics were discontinued, and the patient was kept under observation.

PET CT scan (Figure 5) was repeated after 4 months of surgery, showing a significant decrease in FDG uptake (SUV max 5.5), and clinically significant decrease in oedema and size of lesion at the operated site. Thus, in view of negative biopsy and low uptake on PET, it was considered as postoperative changes. One year follow up showed hypertrophied scar over the operated region and patient was locoregionally controlled (Figure 6).

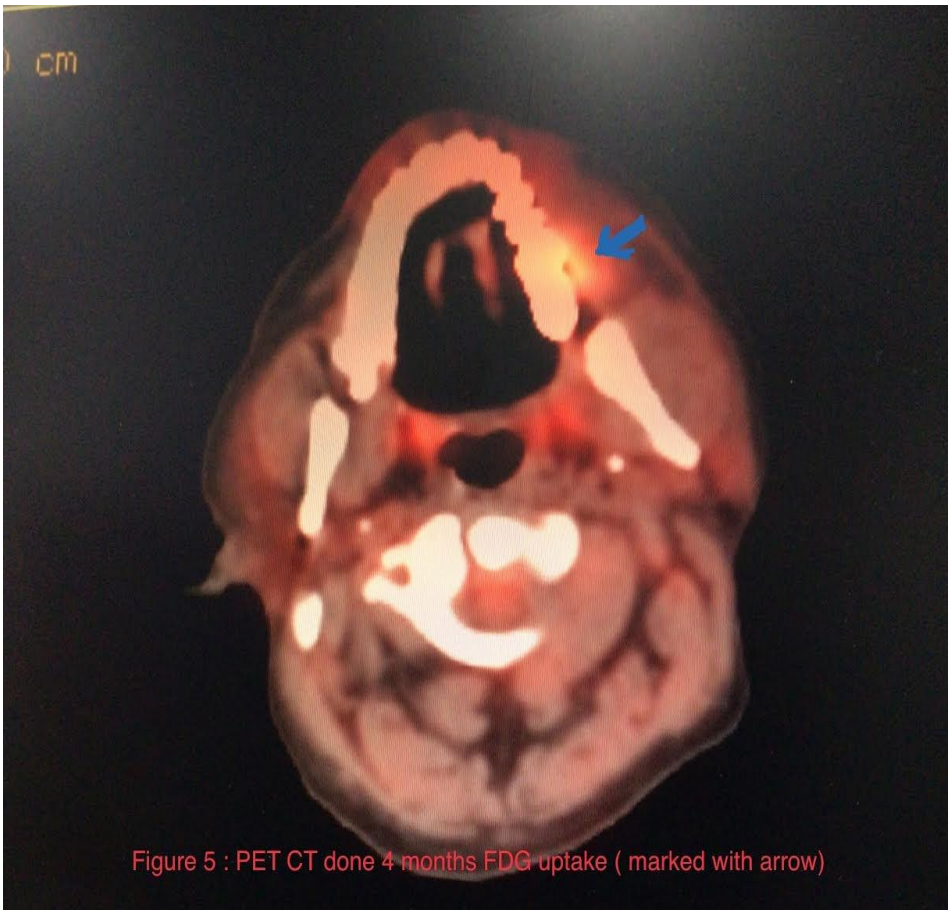

Figure 5: PET CT done 4 months FDG uptake (marked with arrow)

Figure 6- Post operative 1 year follow up showing hypertrophied scar

Discussion

Imaging-based detection of disease recurrence in head and neck squamous cell carcinoma can be performed using various modalities like CT, MRI, PET CT, and ultrasound. While, MRI has good sensitivity (70-100%), the specificity is poor ranging from 41% to 54%. CT has a wider range with moderate sensitivity (50% to 86%) and specificity (33% to 100%).[3] USG is mainly used in surveillance for nodal recurrence in the neck. USG has several advantages over CT and MRI as it is cost effective, there is no radiation exposure and guided FNAB can be done in the same sitting. Reported sensitivity, specificity, positive predictive value, and negative predictive value of USG in detecting nodal recurrence when combined with FNA is 80%,100%,100%, 92.3% respectively. The diagnostic accuracy of ultrasonography guided FNA at detecting residual persistent cancer is 88%.[8] However, it is not an appropriate imaging tool for oral cavity recurrences.

MRI has incremental value over CT scan in assessment of tumor recurrence and differentiation from post-surgery changes.[7] T2 signal intensity within the treated field can be used to distinguish between scar and recurrent neoplasm, although both may demonstrate post-contrast enhancement and an infiltrative pattern. Thus, a scar is generally associated with a lower T2 signal, whereas a recurrent tumor exhibits an intermediate to high signal on T2-weighted images. MRI have low PPV and can overestimate the disease. MRI leads to false positive estimation of post-operative changes as recurrent disease in the present case as well.[6]

To increase the effiicacy of MRI in differentiating recurrence from post treatment changes, the role of Diffusion-weighted MRI images (DWI) is promising.6 DWI is based on the T2 sequence of MRI. The apparent diffusion coefficient (ADC) measures the degree of motion of water molecules and is thought to serve as a surrogate measure for tissue cellularity. Residual or recurrent tumour, due to increased cellularity, typically produces a low ADC, whereas scar composed of large fibroblasts allowing more movement of water molecules results in a relatively higher ADC. Thus, DWI might have been valuable in this case.[6]

PET CT has distinct advantage as it offers information regarding the functional activity of the treated disease along with anatomical details. It is more sensitive than CECT, MRI, ultrasound, and physical examination in detecting recurrent disease.1Systematic review and meta-analysis by Gupta et al showed the role of PET/CT in response assessment and surveillance imaging of head and neck squamous cell carcinoma patients. The study reported a high negative predictive value (NPV)(>94%) and a low positive predictive value (PPV) (<60%) for both primary site and cervical nodes. For patients with a PET-positive result, a biopsy is recommended because of a relatively high false positive rate due to post-treatment inflammation.[4]

In the postoperative period, the first response of the human body in wound healing is the formation of granulation tissue from the connective tissue around the damaged area, which mainly contains inflammatory cells, fibroblasts, myofibroblasts, and small vessels. Over time, the granulation tissue disappears by apoptosis and is replaced by immature and then mature scars in the presence of macrophages, which take place within 2 months of injury.[2] During these initial few months, there is increased FDG uptake seen on PET/CT images, and the FDG uptake tends to decrease gradually over time as the inflammation subsides. Post-surgical anatomical distortion can further increase the diagnostic dilemma in such cases. A review of the literature, by Zimmer et al in 2005, recommended that PET imaging should not be performed before 2 to 3 months after the surgery or chemoradiation therapy to reduce the incidence of false-positive results secondary to inflammation.[5] Similarly, in our

case postoperative Inflammation and Infection led to high FDG uptake in the post-operative sites even after 8 weeks of surgery.

The presence of a clinically suspicious lesion in buccal mucosa along with intense focal uptake of FDG raised the suspicion of recurrence in the present case. This focal uptake can be explained by the fact that localized infection of the bone and granulation tissue can lead to focal FDG uptake. The presence of inflammatory cells (eg, neutrophils, lymphocytes, macrophages) with increased metabolic activity result in increased activity on FDG PET.[9]

Stephanie et al in their study concluded that despite high false-positive rates of PET CT in the immediate postoperative period, it has the potential to prevent overly aggressive treatment thus reducing toxicity and treatment related cost. PET CT application can lead to more aggressive treatment when appropriate (loco-regional persistent or recurrent cancer) and can define radiation therapy treatment fields and doses. But PET CT findings should be confirmed by biopsy as PET has a significantly high false-positive rate in the early postoperative period.[1]

The hypothyroid state of the patient could have contributed to high false positive values on PET CT and MRI. However, no relevant literature is available for the same. It warrants further research on the effect of hypothyroidism on PET uptake.

Conclusion

PETCT is an important imaging modality in the posttreatment surveillance of Head and neck cancers. However, accuracy of PET CT is limited in the early postoperative period due to post treatment changes. The accuracy improves moderately if performed more than 12 weeks of completion of treatment. The role of DWI needs to be explored further as it has shown promising results in differentiating recurrence and inflammation. A positive biopsy is confirmatory, but a negative biopsy does not rule out disease. Moreover, there may be false-negative results due to granulation and fibrosis in the post operative period. A close follow up with thorough clinical examination and appropriate imaging is recommended in such cases.

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