Long-term Survival Following Palliative Chemoradiotherapy in an Elderly Patient with Advanced Squamous Cell Carcinoma in the Right Mandibular Gingiva

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Research Article

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Abstract

Advanced squamous cell carcinoma (SCC) of the mandibular gingiva in elderly patients is difficult to cure. The treatment policy for elderly patients with advanced SCC of the mandibular gingiva has not been clear. We report a case of right mandibular gingival carcinoma that was successfully treated by palliative chemoradiotherapy. An 83-year-old female complained of pain and an ulcer in her right mandibular gingiva. Oral examination revealed a lesion of about 20 mm in size in the right mandibular gingiva. A diagnosis of SCC in the right mandibular gingiva was made by histology. Imaging findings revealed some right neck lymph node metastases. Based on these findings, a clinical diagnosis before treatment was SCC in the right mandibular gingiva (cT4N2bM0, stage IV). She refused to receive definitive surgery or chemoradiotherapy due to concerns about the invasiveness of these definitive therapies and requested palliative chemoradiotherapy. We delivered S-1 (a combination of tegafur, gimeracil, and oteracil) and radiation therapy (RT) to the primary tumor alone with 30 Gy in 10 fractions using 4 megavoltage equipment via a multiple leaf collimator by three-dimensional RT. Although we could not complete the delivery S-1 because of an acute side effect, the palliative chemoradiotherapy resulted in a complete response and the lymph node metastases also disappeared. The patient remains in complete remission 5 years without surgery or chemotherapy. Palliative chemoradiotherapy for elderly patients with mandibular gingival carcinoma is therefore considered to be an effective therapeutic option.

Introduction

Oral cancer is a difficult malignant neoplasm to cure. Squamous cell carcinoma (SCC) is a common type of oral cancer [1]. Approximately 10% of all malignant tumors of the oral cavity occur on the gingiva [2]. Although surgical resection is usually performed [3], the prognosis of advanced SCC of the mandibular gingiva is poor [4].

In the current aging society, not all patients can be treated with surgery because of their clinical condition or complications. However, the treatment strategy for patients of advanced age who cannot receive definitive therapy is unclear.

We herein report the achievement of long-term survival after palliative radiation therapy with S-1 (a combination of tegafur, gimeracil, and oteracil) for SCC of the mandibular gingiva. This is the first report of a patient with long- term survival palliative chemoradiotherapy for SCC of the mandibular gingiva.

Case Presentation

An 83-year-old Japanese women complained of pain and an ulcer in her right mandibular gingiva. Her dentist adjusted her denture, but the lesion in the right mandibular gingiva did not improve and she was recommended to receive an examination in a hospital. The patient had a history of alcohol consumption (approximately 350 mL of beer per day for 20 years) but no smoking. The medical history of the patient was hepatitis C, diabetes mellitus and hyperlipidaemia. Her medications were Metformin, Sitagliptin

Phosphate Hydrate and Rosuvastatin Calcium. Her family history included liver cancer in her father. Oral examination revealed a lesion of 15–20 mm in size in the lower right gingiva (Fig. 1). Computed tomography (CT) revealed a tumor that had spread from the right mandibular gingiva to the right lower mandible. The lesion had destroyed the alveolar bone and there was a possibility of periodontal disease or gingival cancer (Fig. 2). Magnetic resonance imaging (MRI) revealed an irregular tumor in the lower right gingiva and two enraged lymph nodes in the right neck region. The tumor showed lower intensity on a T1-weighted image (WI). The tumor showed intermediate intensity on a T2WI and the mandible bone close to the tumor showed diffuse lower intensity. On a gadolinium-enhanced T1WI, a uniform enhancing tumor extended to the mandible bone (Fig. 3). Positron emission tomography-CT (PET-CT) revealed uptake of 18F-2-fluoro-2-deoxy-D-glucose (FDG) on the right mandibular gingiva (maximum standardized uptake value [SUVmax] of 14.5) and on two lymph nodes in the right neck region (SUVmax of 2.0-2.3) (Fig. 4). we could not confirm pathological diagnosis for lymph node metastases. The diagnosis based on histological examination of biopsy specimens from the lesion were squamous cell carcinoma (SCC). The clinical diagnosis before treatment was SCC in the right mandibular gingiva (cT4N2bM0, stage IV).

Although surgery is the standard therapy for SCC of the mandibular gingiva, the patient refused to receive surgery due to concerns about damage after surgery. She and her family requested palliative dose radiotherapy and oral medication of chemotherapy for her pain of right mandibular gingiva.

We delivered radiation therapy (RT) of 30 Gy in 10 fractions over a period of 2 weeks with S-1 (a combination of tegafur, gimeracil, and oteracil). RT was delivered with 4 megavoltage equipment via a multiple leaf collimator by three-dimensional RT. Gross tumor volume (GTV) was defined as the primary tumor alone based on pretreatment examination of CT, MRI and PET-CT. We existed right cervical lymph node metastases because these metastases did not associate with her pain of right mandibular gingiva. The clinical target volume (CTV) was defined as GTV plus 0.5-cm margins. The planning target volume (PTV) was CTV plus 0.5-cm margins (Fig. 5).

On the 12th day of treatment, we canceled the administration of S-1 because the patient had an acute side effect of grade 3 stomatitis and fatigue according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0. (Fig. 6). As a result of loss of appetite due to the severe stomatitis and abdominal symptoms, the patient was hospitalized for one week.

After treatment, imaging showed no evidence of recurrence and the lymph node metastases that had not been irradiated had also disappeared. The patient remains in complete remission (CR) 5 years after the initial treatment without surgery or chemotherapy.

Conclusion

Carcinomas of the mandibular gingiva are more common than those of the maxillary gingiva [5]. Mandibular gingival carcinoma invades the mandible in an early stage [6]. If it invades the mandible deeply, it cannot be expected to be cured by RT alone because radiation osteoradionecrosis occurs after

high-dose RT [7]. In addition, the transfer of antitumor drugs to bone is poor and surgical resection is performed for carcinomas of the mandibular gingiva [3].

In stage III or IV, locally advanced SCC of the head and neck is usually treated by surgery or concurrent chemoradiotherapy [8–10]. The 5-year overall survival (OS) rate after resection for mandibular gingival carcinoma has been reported to be 38-80.6% [3, 4]. On the other hand, the 5-year disease-free survival rate of patients with cervical metastasis is about 25% [1]. In the present case, good control was achieved without resection. The combination of RT and S-1 might have been good. S-1 is an oral anticancer drug containing gimeracil and oteracil potassium in tegafur that is a prodrug of 5-FU. Gimeracil inhibits dihydropyrimidine dehydorogenase, which is a 5-FU-degrading enzyme, and oteracil potassium has the effect of suppressing gastrointestinal toxicity caused by 5-FU [11]. Gimeracil was reported to exert radiosensitizing effects on oral squamous cell carcinoma cells *in vitro* and *in vivo* [12]. Response rates of 46.2% and 28.3% were reported for early and late phase II clinical trials for advanced and recurrent head and neck cancer, respectively [13]. There are also some reports of CR with administration of a single agent for head and neck cancer and oral cancer [14]. In addition, elderly patients are considered to be tolerant for S-1 [15].

A severe acute complication occurred in our patient. It is desirable to reduce the side effects of chemotherapy as much as possible. Alternate day administration of S-1 may help to reduce side effects. This takes advantage of the fact that the cell cycle in humans is about one day, whereas that of cancer cells is 5–7 days [16–18]. In animal experiments, it was shown that the effects were the same and that side effects were reduced compared to alternate day administration and daily administration [17].

Patients with head and neck cancer who receive cumulative radiation doses of more than 50 Gy are more likely to have oral side effects and they have a higher risk of unplanned breaks in radiation therapy [19]. Our patient was hospitalized for one week due to loss of appetite and an oral side effect, but the low radiation dose of 30 Gy with S1 might have been an effective treatment option.

The abscopal effect is probably associated with our local control for lymph node metastases in the right neck region out of the radiation field. This effect is known that radiation shrinks tumors outside the irradiation field [20]. The biological mechanism underlying this effect remains unclear. To the best of our knowledge, there has been no study on an abscopal effect of mandibular gingival carcinoma. In our case, it is difficult to distinguish between the effects of chemotherapy and the potential for abscopal effects. There are some reports that CR was obtained only with S-1 [14] .In the present case, the combined use of S-1 is only for one week, and the effect of S-1 alone is considered to be limited. In addition, we could not confirm pathological diagnosis for lymph node metastases. It is possible that it was misdiagnosis for nodal clinical staging.

Because this study is a case study, it is difficult to define the indication for palliative chemoradiotherapy in an elderly patient with advanced SCC in mandibular gingiva. However, it is possible that some patients advanced SCC in mandibular gingiva were treated only by surgery, chemotherapy or radiation therapy

although they were potential candidates of palliative chemoradiotherapy. Palliative chemoradiotherapy for advanced SCC in mandibular gingiva is therefore considered to be a therapeutic option.

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee. For this type of study, formal consent is not required.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Availability of data and materials

The data include individual patient data, but the data are available from the corresponding authors upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' Contributions

All listed authors contributed to the original manuscript. YI is the main radiation oncologist of this case and wrote the manuscript draft. UR and KJ coordinated and completed the manuscript. NT, TY, KT and YS supported proton beam therapy management. All authors have read and approved the manuscript of this case report.

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Figures

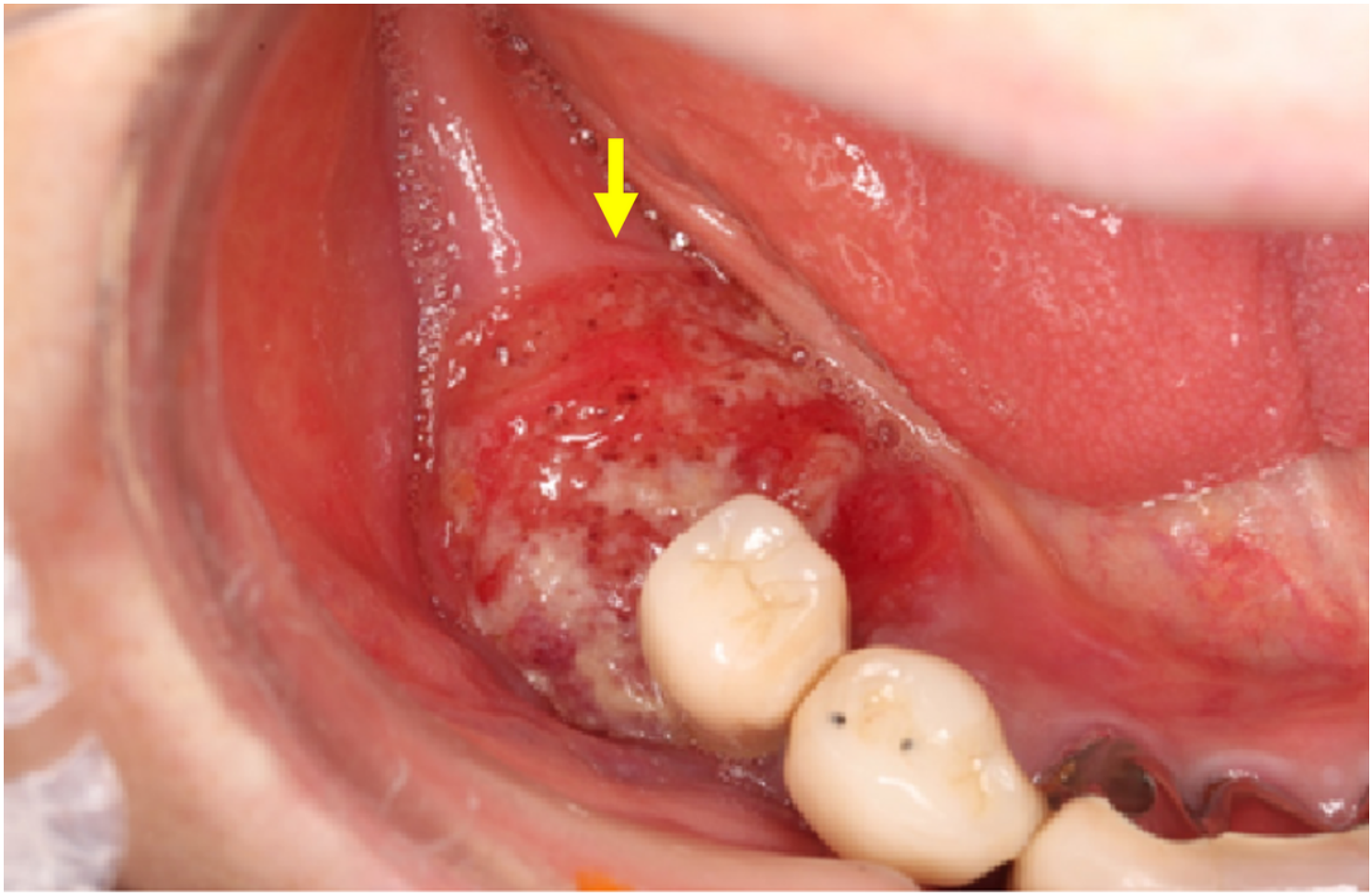

Figure 1

Oral examination revealed a lesion of 15-20 mm in size in the lower right gingiva.

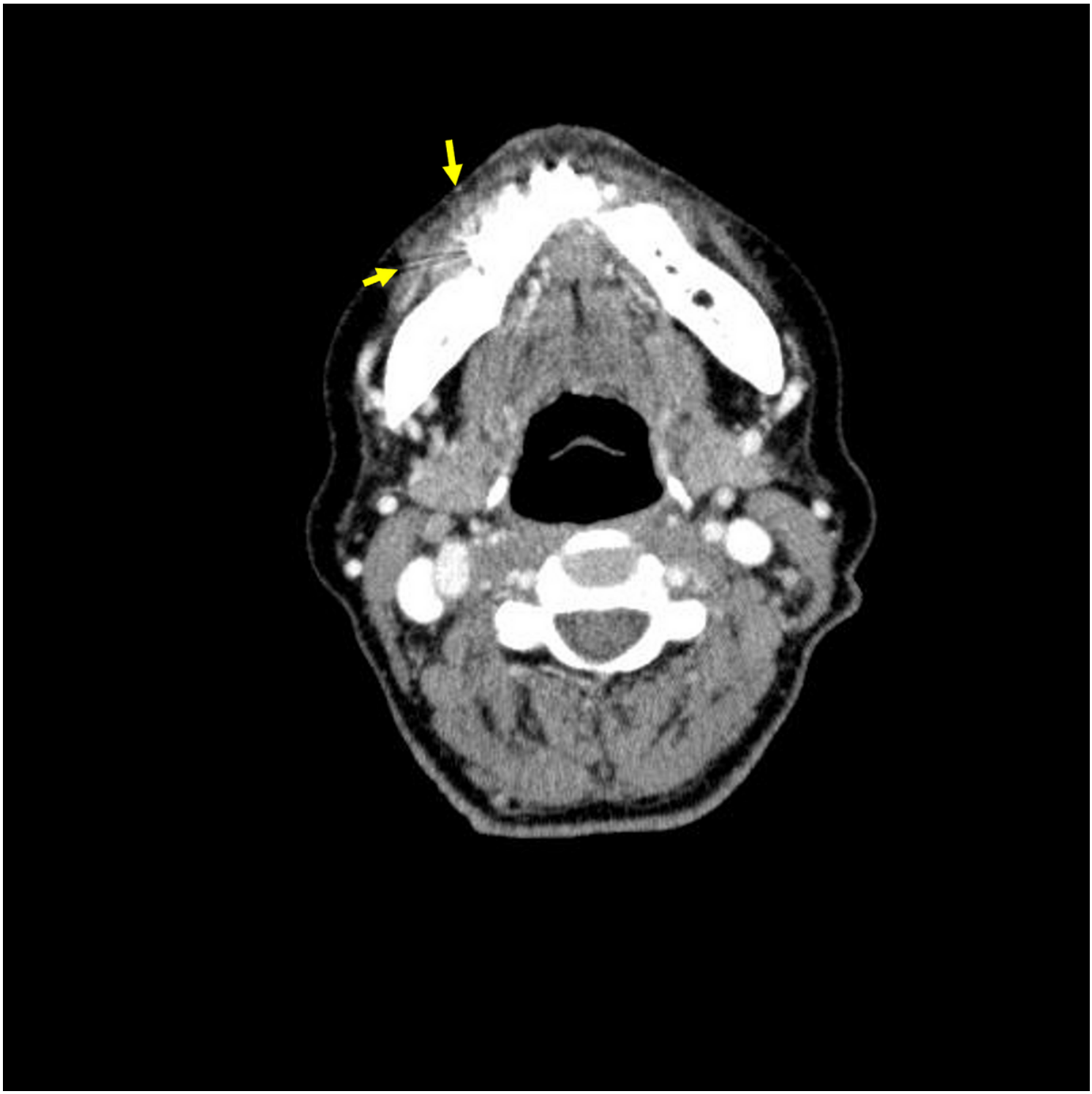

Figure 2

Axial enhanced computed tomography scan images of the head and neck showed a tumor that had spread from the right mandibular gingiva to the right lower mandible. The lesion destroyed the alveolar bone.

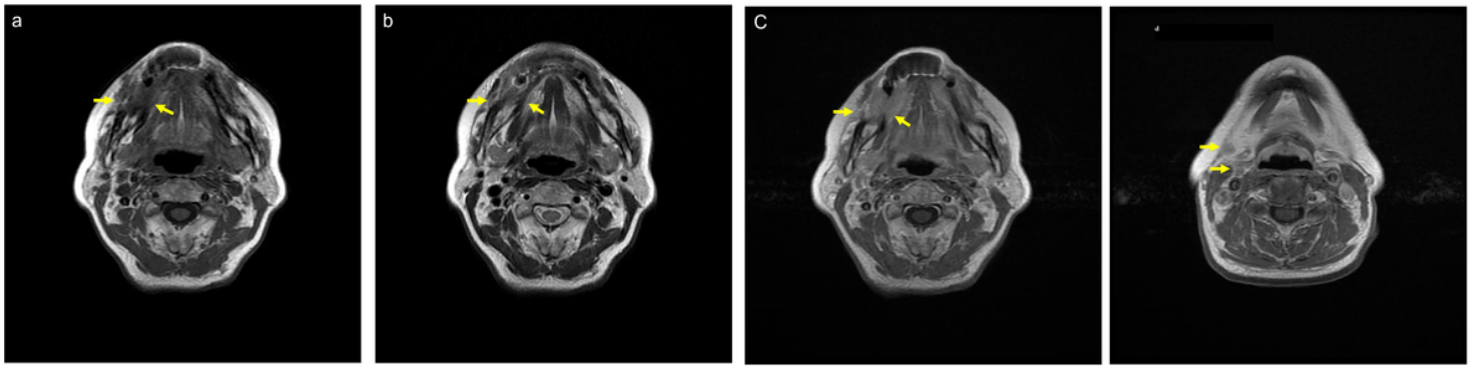

Figure 3

Axial magnetic resonance imaging (MRI) of the head and neck showed an irregular tumor in the lower right gingiva. The tumor showed lower intensity on a T1W1 (a) and intermediate intensity on a T2WI (b). A gadolinium-enhanced T1WI, a uniform enhancing tumor extended and to the mandible bone (c). A gadolinium-enhanced T1WI shows two small lymph node of the right neck (d).

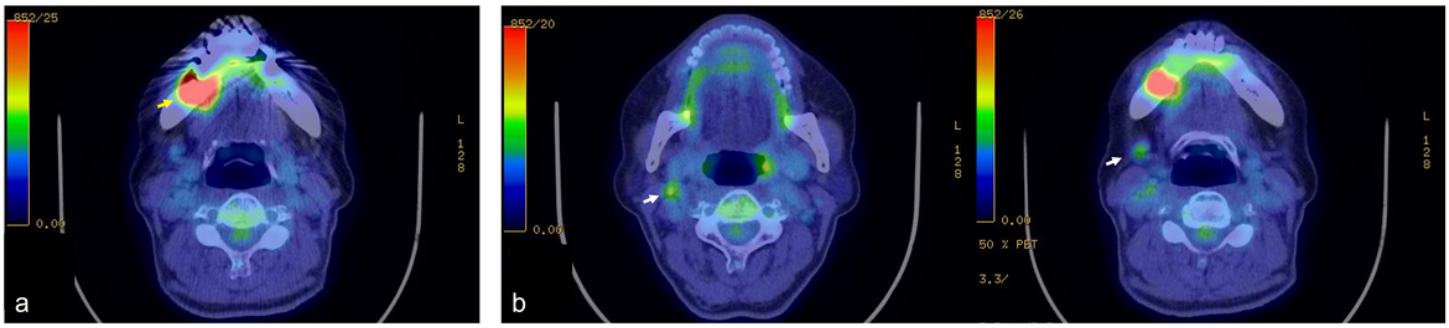

Figure 4

Positron emission tomography-CT showed uptake of 18F-2-fluoro-2-deoxy-D-glucose in the mandibular gingiva with a maximum standardized uptake value (SUVmax) of 14.5 (a). Uptake of FDG of two lymph nodes of the neck had an SUVmax of 2.0-2.3 (white arrow) (b).

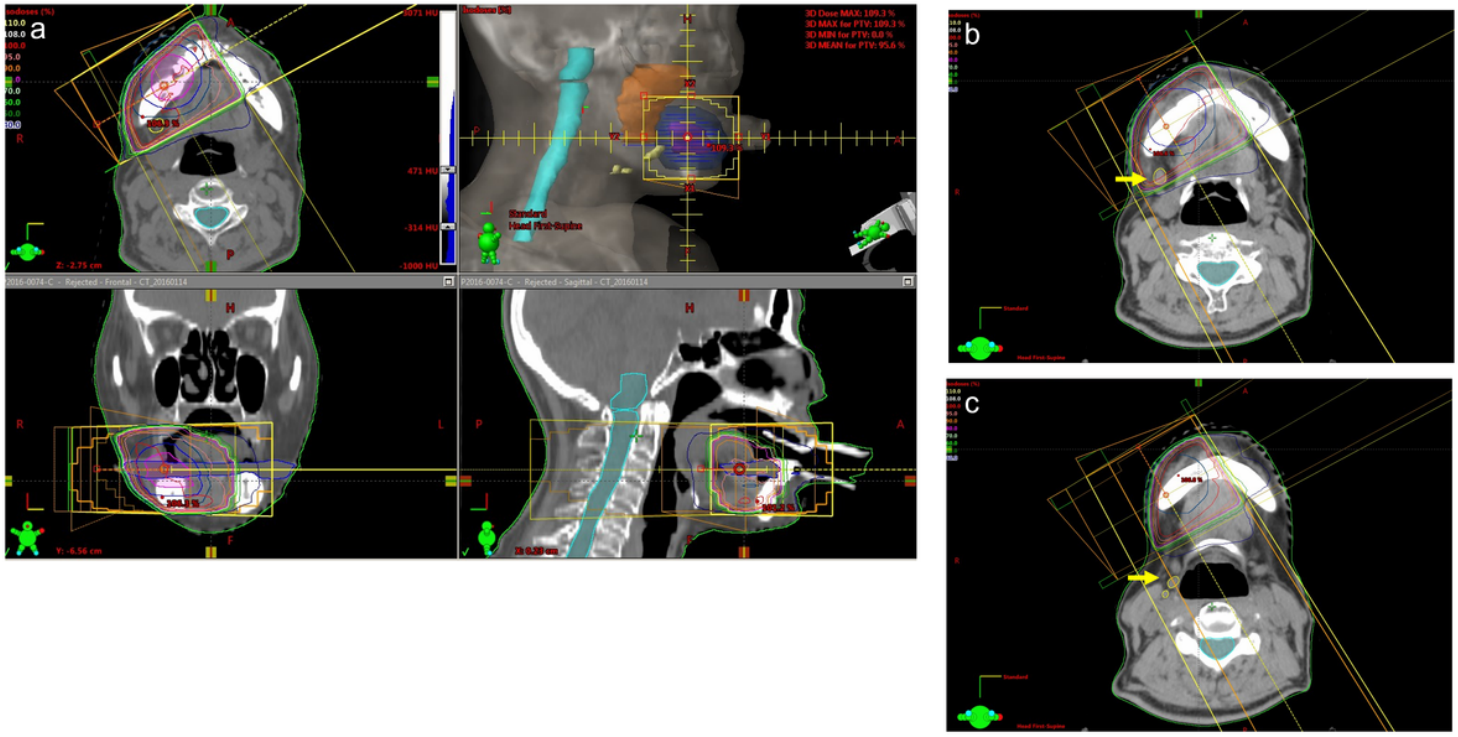

Figure 5

The primary carcinoma of the right mandibular gingiva received 30 Gy (a). A lymph node metastasis received 15-30Gy (yellow arrow) (b), another lymph node did not receive radiation (yellow arrow) (c).

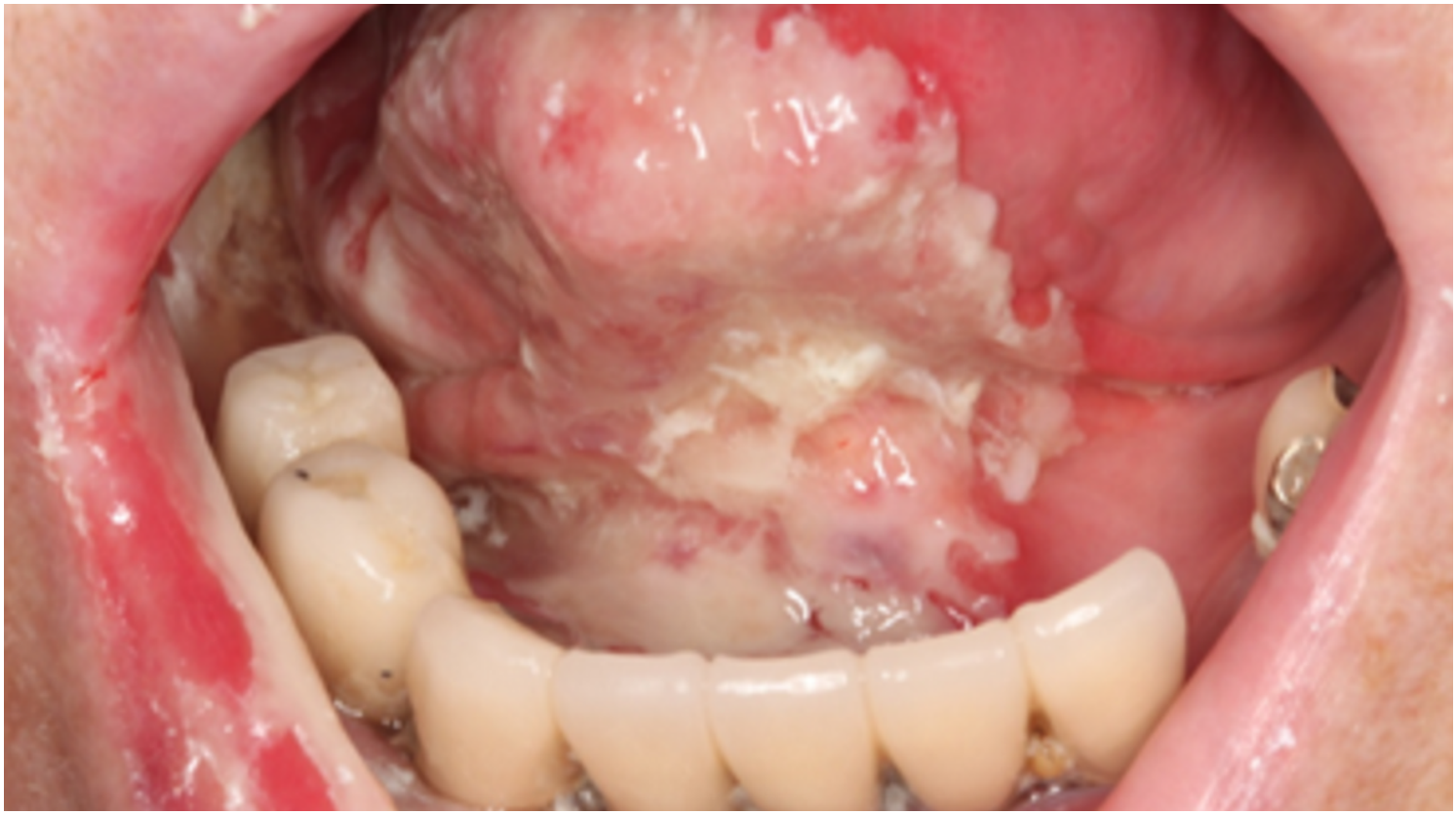

Figure 6

Oral findings: Acute side effect of grade 3 stomatitis according to the National Cancer Institute Common Terminology Criteria for Adverse Events version 4.0.

Supplementary Files

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- CAREchecklistEnglish2013.pdf