Clinical Case Report

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Sarcomatoid carcinoma after radiotherapy for early-stage oral squamous cell carcinoma

Case report

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Abstract

Rationale: Sarcomatoid carcinoma is a rare variant of squamous cell carcinoma (SCC) with poor prognosis. Previous radiation has been reported as one of the etiologic factors.

Patient concerns: We describe a case of a 57-year-old man presented with a painless mass in the left supraclavicular area. Five years before, he was diagnosed with SCC in floor of mouth (FOM) and underwent radiotherapy (RT).

Diagnoses: Sonography-guided biopsy on the supraclavicular lymph node revealed diffuse spindle cell proliferation with a focus of squamous differentiation. Local recurrence on primary site or distant metastasis was not obvious on both computed tomography (CT) of the neck and ^{18}F-fluorodeoxyglucose positron emission tomography CT. The final diagnosis was confirmed as sarcomatoid carcinoma via surgery.

Interventions: The patient underwent surgery including explorative resection of the mouth floor, excision of the submandibular gland, and modified radical neck dissection. Following surgery, the patient received adjuvant radiation therapy.

Outcomes: There were no complications according to the surgery. Six months after adjuvant therapy, distant metastasis to liver was identified. The patient is currently undergoing palliative chemotherapy.

Lessons: This may be the first reported case of sarcomatoid carcinoma arising from early-stage SCC in FOM that was previously treated with RT alone. When RT is performed as a single modality for oral SCC, even in an early stage, rigorous follow-up should be performed.

Abbreviations: CT = computed tomography, FDG = fluorodeoxyglucose, FOM = floor of mouth, PET = positron emission tomography, RT = radiotherapy, SC = sarcomatoid carcinoma, SCC = squamous cell carcinoma.

Keywords: case reports, mouth floor, radiotherapy, sarcoma, squamous cell carcinoma

1. Introduction

Sarcomatoid carcinoma (SC) is a rare biphasic tumor characterized by a dysplastic epithelial element and a stromal element with invasive spindle cells.[1] It shows a poor prognosis with frequent local recurrence and systemic metastasis.[2] The mechanism of its pathogenesis is unclear; however, conversion of existing carcinomas to sarcomatous components is the most robust theory.[1] Radiation, tobacco use, alcohol consumption, and trauma have been reported as etiological factors.[3]

Both surgery and radiotherapy (RT) alone are listed as primary treatments for early-stage oral cavity squamous cell carcinoma (SCC).[4] However, several studies have reported that surgery demonstrated better prognosis than RT alone.[4,5] We report a case of early-stage (T1N0M0) SCC on the floor of mouth (FOM) that was treated with RT alone and recurred as SC 5 years later. Despite rescue treatment, the recurrent SC eventually developed distant metastasis. According to our literature review, there is no previous report of a case with such a clinical course.

The present study was approved by the Institutional Ethics Committee of the institution to which the authors belong (approval no. 2018-10–028). Informed written consent was acquired from the patient for publication of this case report and consequent images.

2. Case report

A 57-year-old man presented with a painless mass in the left lateral neck that had progressively become larger over a few weeks. The patient did not report any associated symptom aside from vague discomfort. Five years ago, he presented with a 0.7 × 0.7 cm sized painful ulcer on the FOM that had persisted for 1 month (Fig. 1A). The tumor was diagnosed as well-differentiated SCC with incision biopsy (Fig. 2A). Additional ^{18}F-fluorodeox-

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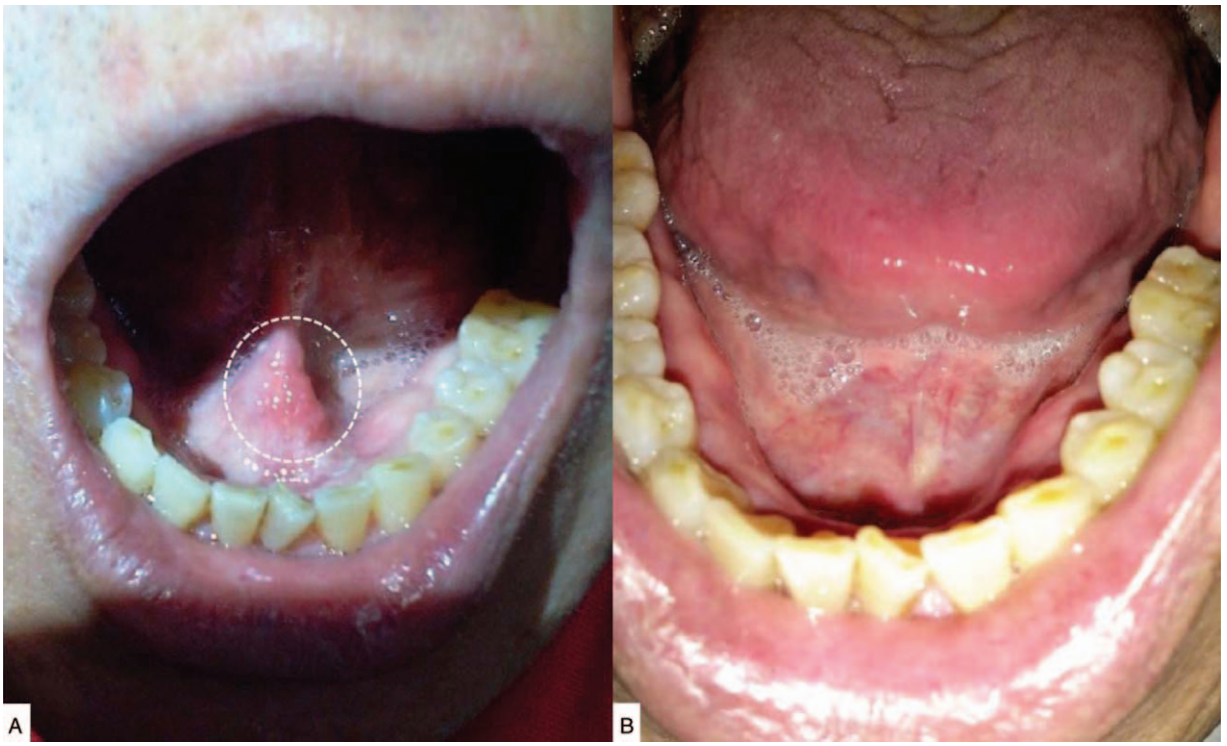

Figure 1. Findings of mouth floor when the patient first visited the otolaryngology department 5 years previous. (A) A reddish mass with irregular surface (dotted circle) is indicated in the middle of the sublingual ligament. (B) The floor of the mouth was free from any prominent mucosal lesion when the patient later presented with a neck mass.

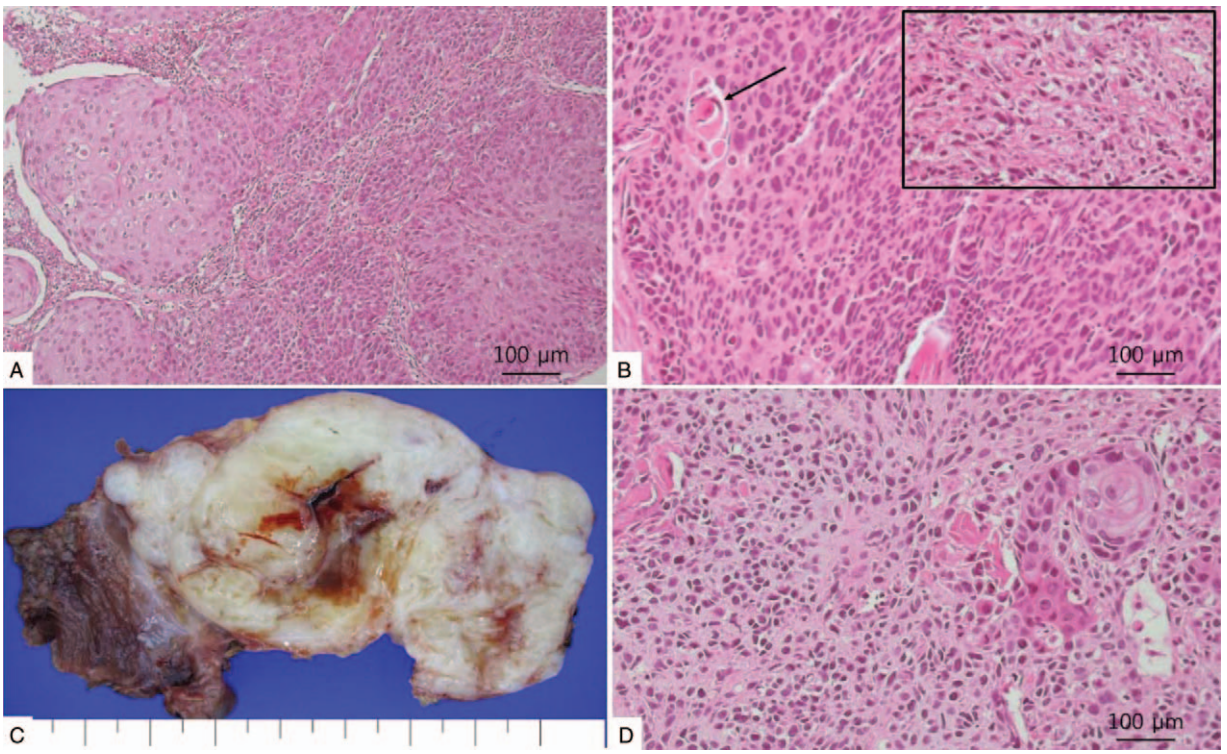

Figure 2. Pathologic findings. (A) Initial squamous cell carcinoma in floor of mouth (FOM) showing squamous cell nests (hematoxylin-eosin; original magnification ×100). (B) Recurred carcinoma in the FOM nodule. Most of the tumor was squamous cell carcinoma showing focal keratinization (arrow). Spindle cell proliferation (inlet) was noted in small foci (hematoxylin-eosin; original magnification ×200). (C) Supraclavicular mass revealed a grayish white solid firm cut surface with central hemorrhage. (D) Diffuse pleomorphic spindle cell proliferation with multifocal carcinoma foci (hematoxylin-eosin; original magnification ×200).

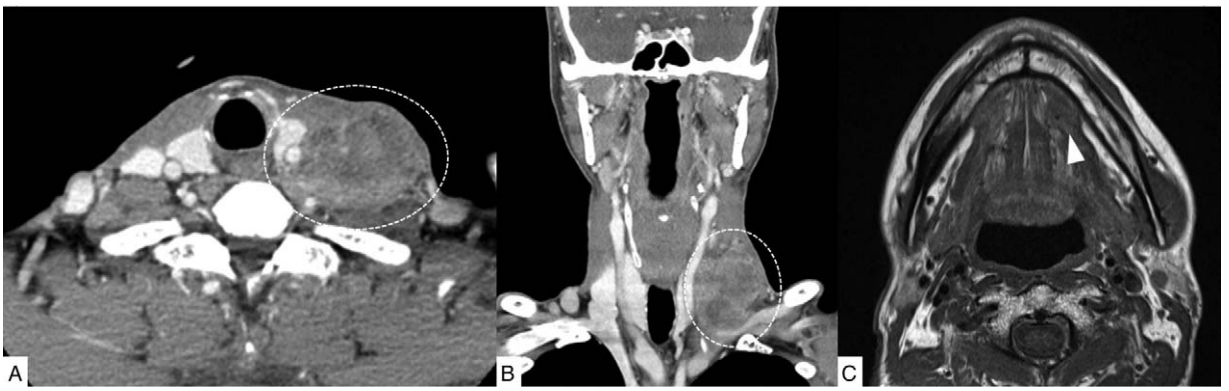

Figure 3. Enhanced CT scan with axial (A) and coronal (B) images shows the 5.7 × 3.8 × 5.7 cm sized, multi-lobulating mass with suspicious internal hemorrhage and peripheral heterogenous enhancement (dotted circle and black arrow). (C) Axial magnetic resonance imaging findings of T1-weighted image show a 1.5-cm-sized ambiguous nodule in the left side of mouth floor (white arrow head).

yglucose (FDG) positron emission tomography (PET) computed tomography (CT) revealed no definite metastasis (cT1N0M0). He was recommended for curative resection but refused surgery. Instead, he received volumetric modulated arc RT at a total dose of 63.0 Gy (1.80 Gy per fraction, 35 fractions). The patient experienced no recurrence for 3 years after treatment; however, he was then lost to follow-up for 2 years until he visited the clinic again. Physical examination revealed a 9 × 5 cm sized, smooth, firm, nontender, supraclavicular mass with no other palpable lymph nodes. In the oral cavity, the mucosa was atrophied and dried, and there was no grossly visible lesion (Fig. 1B). However, on palpation, a hard, round nodule was identified along the path of the left Wharton duct. CT of the neck showed a 5.7 × 3.8 × 5.7 cm sized left supraclavicular lymph node with heterogeneous enhancement with no remarkable finding in the mouth floor (Fig. 3A and B). Additional magnetic resonance imaging of the oropharynx demonstrated a 1.5 cm, ill-defined nodule with low signal on T1-weighted image (Fig. 3C). Sonography-guided biopsy on the supraclavicular lymph node revealed diffuse spindle cell proliferation with a focus of squamous differentiation. Subsequent PET CT showed intense FDG uptake in the supraclavicular lymph node, but definite uptake was not identified at the mouth floor. Distant metastasis was not obvious either. Recurrence of previous SCC was suspected and the patient underwent surgery including explorative resection of the mouth floor, excision of the submandibular gland, and modified radical neck dissection. The nodule of the mouth floor was 1.2 cm in size, whitish yellow, smooth, and hard and was well demarcated from peripheral soft tissues in the mouth floor. Histopathology revealed SCC with keratinization and focal pleomorphic spindle cells (Fig. 2B). Wide surgical resection with a clear margin was performed in the FOM, and the defect was covered with a full thickness skin graft. The supraclavicular lymph node was 7.2 × 4.5 × 3.0 cm in size, gray-tan in color, and encapsulated with a nodular surface (Fig. 2C). There were no complications such as facial nerve or thoracic duct injury during neck dissection. Following surgery, the patient received adjuvant RT including the lateral neck at a total dose of 66.6 Gy (1.80 Gy per fraction, 37 fractions).

Histopathology revealed diffuse pleomorphic spindle cell proliferation admixed with peripheral and multifocal poorly differentiated carcinoma foci (Fig. 2D). Invasion of the tumor cells into blood vessels was also identified (pT1N3M0). The results of immunohistochemical staining were positive for pan-cytokeratin, EMA, vimentin, and p63 and negative for S100 protein, p16, and Her2. The Ki67 proliferation index was 80%. The final pathologic diagnosis was SC.

Followed PET CT performed 6 months after completion of adjuvant RT demonstrated that the primary site and lateral neck lesions were controlled, but new FDG uptake was identified in hepatic segments IV and VIII. Sonography-guided percutaneous liver biopsy was performed, and distant metastasis was confirmed (pT1N3M1). The patient is currently undergoing palliative chemotherapy.

3. Discussion

SC is a rare variant of SCC and displays a biphasic histologic figure with an invasive spindle cell component and various types of surface epithelium ranging from mild dysplasia to invasive carcinoma.[2] The sarcomatous portion usually composes the majority of the tumor with spindle cells, and an epithelioid pattern is present in some regions. Typical growth patterns and presence of traditional invasive or related dysplasia/in situ carcinoma component are important features that distinguish SC from other primary spindle cell sarcomas or melanomas. However, the carcinomatous component can easily dissipate or be obscured because of extensive ulceration, and the relative scarcity of the carcinomatous portion may cause confusion in diagnosis.[6] Immunohistochemistry (IHC) to identify markers for epithelial differentiation (pan-CK, EMA, or p63) may be useful for diagnosis of mucosal SC in head and neck.[7] A negative result of epithelial marker expression, however, does not exclude the possibility of SC because the epithelial differentiation evident within the tumor is highly variable. The epithelial component undergoes progressive phenotypic change, following a mesenchymal pathway of differentiation with conversion to a spindle shape, loss of cellular polarity, generation of mesenchymal matrix, and gain of vimentin with loss of keratin expression.[8,9] Conversion of the tumor cell to mesenchymal differentiation is the most widely accepted hypothesis for pathogenesis of SC.[1] Radiation, trauma, tobacco use, and alcohol consumption are proposed as key factors in this conversion mechanism. Previous radiation on the mouth floor appeared to play a major role in this case.

Newer RT modalities such as intensity-modulated RT have been reported to considerably increase the risk of secondary malignancies.[10] This is probably because normal tissues are

exposed to a low dose of radiation, and the total dose of body exposure is somewhat increased. Tissues surrounding the primary tumor are especially at risk. It still remains uncertain to distinguish radiation-induced malignancy with separate secondary tumor.[11] Cahan et al[12] first presented diagnostic criteria for radiationinduced sarcoma, which included a minimum latency of 5 years from previoys RT; however, some reports have proposed that even shorter periods would be acceptable.[11] The authors suspect that the present case may also be a radiation-induced malignancy, based on its etiology, ipsilateral location, and latency period. Radiation-induced secondary malignancy appears to have a worse prognosis than sporadic malignancy because the diagnosis can be delayed because of the central location, and the choice of treatment is unclear. The primary site has already been irradiated at the tolerance dose during previous RT, and the low vascularization and fibrotic change of the surrounding tissue may reduce the effectiveness of rescue chemotherapy.[13] The choice of treatment strategy should be based on previous RT dose, time elapsed between RT course, amount of overlap between irradiation fields, and application of a high confirmation technique. Surgery is the treatment of choice, although the prognosis depends on whether the location of the lesion is suitable for resection. In addition, size of tumor, depth of invasion, stage, and keratin staining in the spindle cells were also reported as important prognostic factors.[11] Most authors consider RT alone ineffective for radiation induced-sarcoma or SC; however, RT is an acceptable alternative for inoperable patients as well as those with positive surgical margins or nodal metastasis.[7,11] In the present case, adjuvant RT was conducted for nodal metastasis that was not previously included in the radiation field. Despite wide surgical resection, oral SC has a high potential for local recurrence and metastasis.[2]

Although current NCCN treatment guidelines (version 2.2014) accept both surgery and definitive RT as primary therapy for early-stage oral cavity SCC, surgical resection is preferred as the primary treatment, and RT is considered optional.[4,5] Treatment with RT alone is highly associated with T stage, tumor location, and advanced age of patients. The rate of treatment of oral cavity SCC with RT alone has decreased from 8.3% to 6.5% during the last 2 decades; nonetheless, 5% of cases of early-stage oral cavity SCC are still treated with RT alone.[4] The choice of RT alone is presumably because of the difficulty of reconstruction after removal of the bony structure, although medical comorbidities or refusal of surgery by the patient can also be major reasons. SCC in FOM has an especially poor prognosis among oral cavity SCC because of the high possibility of invasion of the mandible. Furthermore, FOM has abundant regional lymphatics and is vulnerable to progression of nodal disease even in early-stage SCC.[14] Surgery fulfills an important role in early-stage SCC for managing local disease and guiding the decision to perform adjuvant RT based on precise staging in accordance with clinicopathological features.[5]

4. Conclusion

Although there have been studies concerning the role of RT in the occurrence of SC,[1,3,11] in our review, there was no case of SC that occurred 5 years after RT alone for early-stage SCC in FOM. The most likely cause of SC in the present case is previous history of RT, and this report might serve as a basis for recommending surgery as an initial treatment for early-stage SCC in FOM. Whenever RT alone is performed for SCC in FOM, close follow-up should be maintained for at least 5 years, even in patients with early-stage cancer.

Author contributions

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