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Case report

Radiation-induced Leiomyosarcoma of the Oral Cavity: A Rare Occurrence Detected on 18F-FDG PET/CT

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Abstract

Radiation-induced sarcomas (RIS) or postirradiation sarcomas have been reported as a rare long-term complication of radiation therapy (RT). The survival benefit offered by radiotherapy has been masked by an increase in the incidence of these sarcomas, thus making radiotherapy a double-edged sword. RIS generally develop with a mean latency period of 10–15 years and encompass different histological types. We report a case of oral leiomyosarcoma with a rather short latency period of 4 years after the radiotherapy of the prior oral squamous cell carcinoma (OSCC) detected on fluorine-18 (18F)-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography/computed tomography (PET/CT). The rarity of occurrence of leiomyosarcoma in the oral cavity is also highlighted.

Keywords: Leiomyosarcoma, oral cavity, radiation, squamous cell carcinoma

Introduction

Radiation-induced sarcomas (RIS) of the head and neck region, although a well-known complication of treatment, remain a rare diagnosis. They usually arise within the radiation field after radiation doses of 45–60 Gray (Gy), with a mean latency period of 10–15 years. Prognosis is poor with a survival rate of 10–30%.[1,2]

RIS can be of variable histological subtypes, the most common being osteosarcoma and malignant fibrous histiocytoma/undifferentiated pleomorphic sarcoma-not otherwise specified (MFH/UPS-NOS). Leiomyosarcomas induced by radiotherapy are very rare, especially in the head and neck region.[1,3] We report a case of leiomyosarcoma arising after radiation therapy (RT) for oral squamous cell carcinoma (OSCC).

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Case Report

A 70-year-old male presented with a growth in the right oral cavity for the past 6 months [Figure 1a]. Fluorine-18 (18F)-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography/computed tomography (PET/CT) scan revealed a hypermetabolic well-defined homogenously enhancing soft tissue mass lesion in the oral cavity with a probable origin from anterior gingivobuccal mucosa with erosion of anterior cortex of mandible [Figure 1b]. Histopathologic examination of biopsy from the swelling revealed an ulcerated mucosa. The submucosa showed a tumor containing markedly pleomorphic ovoid to spindle

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cells arranged in fascicles and bundles. The cells had moderate-to-abundant eosinophilic cytoplasm and raised nucleocytoplasmic ratio. Brisk mitotic activity and areas of necrosis and fibrosis were noted [Figure 2]. A diagnosis of malignant mesenchymal tumor was given. On immunohistochemistry (IHC), tumor cells showed positivity for vimentin, smooth muscle actin (SMA), and desmin and negativity for cytokeratin (CK), rendering the diagnosis of leiomyosarcoma [Figure 3a and b]. Full-body workup did not show any evidence of metastases. The patient's records revealed that he had OSCC 3 years back. At that time, the patient was treated by a radical surgery followed by adjuvant concurrent chemoradiotherapy with a cumulative radiation dose of 66Gy in 33 fractions via external beam RT (EBRT) along with cisplatin. The present case was thus a radiation-induced leiomyosarcoma. As the role of p53 has been implicated in the pathogenesis if RIS, we looked for its expression in the present case. IHC revealed overexpression of p53 with about 30% showing nuclear positivity [Figure 3c]. The patient has now been treated by a margin-negative surgical excision. He has opted out of further radio/chemotherapy and he has been kept under close follow-up.

Discussion

RIS is a well-reported long-term complication of radiotherapy with an incidence rate varying from 0.03% to 0.3%.[4] As radiation carcinogenesis is a stochastic late effect, no "safe" or threshold dose has been reported below which RIS are not seen. Most sarcomas are known to occur after a radiation dose of 55 Gy and above, with a dose ranging from 16 to 112 Gy but there is no consensus on the minimum of cumulative radiation dose or the modality and form of radiation that causes RIS.[1,5] Nonetheless, a higher prevalence has been observed with EBRT.[2] Combined chemoradiotherapy also increases risk of sarcomas especially with anthracycline-based regimens and alkylating agents.[2] Our patient received cisplatin followed by methotrexate along with EBRT.

Criteria for diagnosing malignancy as radiation induced were firmly established by Cahan *et al*., in 1948.[6] These criteria comprised (1) an history of RT; (2) origin of radiation-induced malignancy in previously irradiated field; (3) histological evidence of a sarcoma; (4) latency period of at least 5 years between radiation and presentation of radiation induced sarcoma and exclusion of tumor relapse; and (5) the proof, that primary and secondary tumor are different histological entities. Our patient fulfilled four of these criteria. Murray *et al*., in 1999 included soft tissue sarcomas and a shorter latency period of 5 years to fulfill the criteria for being radiation induced.[7] Although the median latency period in studies

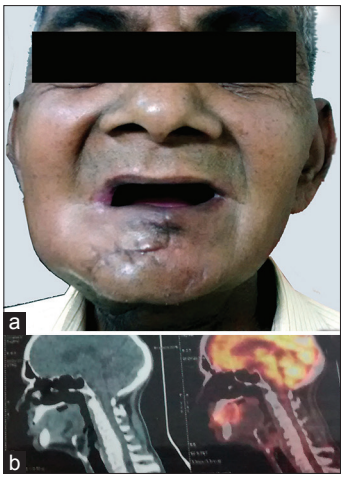

Figure 1: (a) Clinical picture of the patient with swelling in oral cavity (scar mark of previous surgery for OSCC visible); (b) PET scan revealing hypermetabolic homogenously enhancing soft tissue mass lesion in the oral cavity

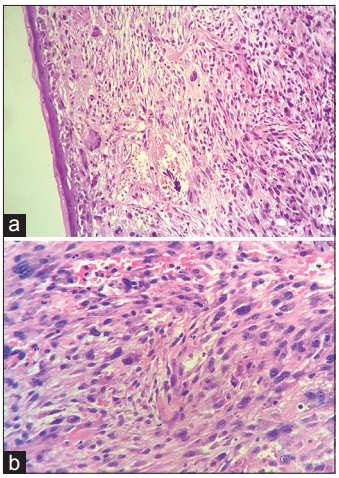

Figure 2: (a) Microphotograph showing attenuated mucosa with underlying tumor in submucosa showing interlacing fascicles and bundles of spindle cells (H and E ×100); (b) nuclear pleomorphism and brisk mitoses in tumor (H and E ×400)

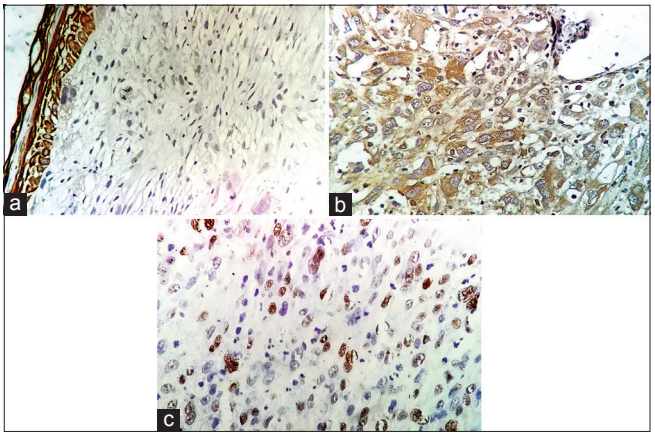

Figure 3: (a) Tumor cells showing negativity for CK; (b) cytoplasmic positivity for SMA; (c) nuclear positivity for p53 (IHC ×400)

reported in the international literature is 10–15 years, technological advances in RT have reduced to this period to months.[1]

The pathogenesis of RIS is still unknown. In regulation of early G1 phase of cell cycle and apoptosis, p53 protein participates. TP53 gene mutations, which are commonly accompanied by immunohistochemical p53 overexpression, appear to play an important role in the causation of postradiation sarcoma as was demonstrated by p53 immunohistochemical positivity in our case. Genetic aberrations in Rb gene have also been implicated. However, recent literature suggests a far more complex pathogenesis warranting more studies.[4,8]

The most common primary tumors associated with RIS include breast carcinoma, Hodgkin lymphoma, cervical carcinoma, and bone and soft tissue sarcomas. Head and neck region is rarely affected with an incidence rate of 1%. RIS can be of variable histological subtypes. MFH/UPS-NOS is the most common subtype followed by osteosarcoma, angiosarcoma, leiomyosarcoma, fibrosarcoma, and rarely liposarcoma.[1,4] The rarity of leiomyosarcoma in head and neck region is attributed to scarcity of smooth muscle here. It may be derived from blood vessels, arrector pili, circumvallate papilla, primitive mesenchyme, and myoepithelial cells of salivary glands.[9] Various imaging modalities that have been used for early detection of these sarcomas include x-ray, magnetic resonance imaging (MRI), and CT scan. Lately, FDG-PET is being increasingly used as it shows significant correlation with tumor grade and patient survival. It thus can contribute to individualized patient diagnosis, treatment planning, and response evaluation in such patients.[10] This is the first reported use of 18F-FDG PET/CT in detecting leiomyosarcoma in the oral cavity.

On histopathology, leiomyosarcoma of head and neck region may easily be mistaken for other more common spindle cell lesions in this location, such as tumors of neural sheath, malignant melanoma (spindle cell type), and spindle cell squamous carcinoma. A confirmatory diagnosis can be established by the histomorphology of interlacing fascicles, and bundles of spindle cells with brisk mitotic activity along with IHC for SMA and desmin.[1,3,8] There are no specific criteria to distinguish between sporadic and RIS. However, tumor cells and surrounding tissue may show radiation induced changes such as dense fibrosis, necrosis, atrophy, and vascular damage as was seen in our case [Figure 2].[4]

As surgical excision of RIS of head and neck remains the only definitive treatment option, early diagnosis and a correspondingly better chance of complete surgical resection is essential. Previous radiation and marked fibrotic changes in the irradiated area often limit the effectiveness of any adjuvant chemoradiation. Widely variable latency periods of RIS therefore necessitate lifelong monitoring of the radiated field, even when the patient is free from the primary tumor.[1,2,4]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of intrest.

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