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CASE REPORT

Radiation-Induced Maxillary Osteosarcoma and Synchronous Oropharyngeal Squamous Cell Cancer: A Rare Case Report

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Abstract

Radiotherapy is a treatment option for nasopharyngeal cancer. However, ionizing radiation may lead to development of secondary malignancies. In this case report, we will present a case of radiation-induced osteosarcoma of the maxilla and synchronous oropharyngeal squamous cell cancer following treatment of nasopharyngeal cancer. History, latency period, physical examinations, computed tomography, magnetic resonance imaging and biopsy results are provided. Diagnosis was confirmed by excision biopsy. Radiation-induced tumors are possible long-term side effects of radiotherapy. Although rare and possible to confuse with recurrent disease, this possibility should be considered in any patient who has received radiation therapy. Diagnostic imaging plays a pivotal role in recognition of radiation induced neoplastic disease. Accurate identification and reporting of key imaging findings allows referring physicians to choose the most appropriate treatment options.

Keywords

Radiation-Induced sarcoma, Radiation-induced tumor, Squamous cell carcinoma, Head and neck cancer, Nasopharyngeal cancer, Imaging findings

Introduction

Radiation therapy in high doses is one of the initial treatment options of Nasopharyngeal cancer (NPC) and aside from the primary site the neck is also irradiated [1]. Radiation-induced tumors (RITs) are defined as tumors that develop after a postradiation latent period within the site of radiation, either in the irradiated soft tissues or bone [2]. The incidence rate of postradiation osteosarcoma in nasopharyngeal carcinoma was reported to be approximately 0.037%, according to the largest study in the English literature [3]. The crude incidence of radiation-induced squamous cell cancer in the oral cavity was 1.4% [4]. The incidence of RITs ranges from 0.037%-7% in different series in the literature [3-7]. Although rare, these tumors are often very aggressive, strongly suggesting the need for early detection in order to allow timely intervention.

To our knowledge, radiation-induced osteosarcoma of the maxilla together with synchronous oropharyngeal squamous cell cancer has not been reported earlier. We present a case of osteosarcoma of the maxilla and synchronous squamous cell carcinoma of the oropharynx along with CT and MRI findings.

Case Report

A 65-year-old man was treated in 2004 for Stage 1 nasopharyngeal cancer with radiotherapy. The tumor was in the nasopharynx with no extension to the oropharynx or nasal cavity.

External beam radiation therapy (EBRT) using Intensity-modulated radiation therapy (IMRT) technique was delivered. Cobalt source was used. Dose prescriptions in cobalt Gray equivalent for gross tumor volume of the primary tumor and lymph node stations were 70 GyE (2.0 Gy/fraction). 35 fractions were delivered. Faciocervical fields and complementary sphenoid body and maxilla were included. Doses were same for included volume Radiation doses of 70 Gy/fraction were given 5 days a week for 7 weeks in opposing facio-cervical fields Follow-up care after radiation therapy was scheduled, but the patient did not return until October 2014 when he presented with pain and swelling of the

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left cheek, left nasal obstruction and difficulty in swallowing. He had no history of smoking or alcohol abuse. Otorhinolaryngological examination was done and two masses were found: one in the left tongue base and one in the left nasal cavity. Targeted biopsies were taken from nasal cavity and tongue base.

CT and MRI show osteosarcoma with osseous matrix predominantly involving the left maxillary bone but extending to skull base, petrous wing, orbit and nasal cavity and synchronous SCC (Squamous Cell Cancer) of the floor of the mouth tongue base (Figure 1).

Histological examination of the bony mass showed proliferation of spindle cells, atypical chondrocytes and neoosteogenesis. There were also noted necrotic tissues and some fibrosis. Immunohistochemistry showed expression of pancytokeratin, CD117, p63, desmin, CD34, actine and S100. Proliferation index of K67 was about 30%. The findings were consistent with radiation induced osteosarcoma with chondroblastic differentiation.

Histological examination of oropharyngeal soft tissue mass showed lobules, thick basement membrane, cribriform small basaloid cells with peripheral palisading, cells with minimal cytoplasm and moderately pleomorphic with hyperchromatic nuclei. There was abrupt transition to squamous epithelium and mitotic activity with hyalinized stroma and cell necrosis.

Immunohistochemistry was as follows: 34betaE12 (100%), EMA (83%), AE1/AE3 or CAM 5.2 (80%), neuron specific enolase (75%, weak), CEA (53%) and S100 (39%). These findings were consistent with basaloid squamous cell carcinoma.

Discussion

Radiation-induced tumors are a well-known but rare entity. Radiation-induced tumors seen in radiation fields include both carcinomas and sarcomas. The most common area for RIT is the NPC sinonasal region following radiotherapy in the NPC sinonasal region [1,2]. According to a study by Liu, et al. [3] of 15 radiation induced osteosarcomas, 8 arose from maxilla, paranasal sinuses or nasal cavity. Following the maxillary region, the second most common regions for radiation induced tumors are the oral cavity and oropharynx. Almost all radiation induced tumors in this region were SCC, the most common site being the tongue base because of its very close location to the radiation field of NPC treatment [6,8]. The approximate incidence of squamous cell cancer in the oral cavity after radiotherapy was 1.4% [4]. Abri-

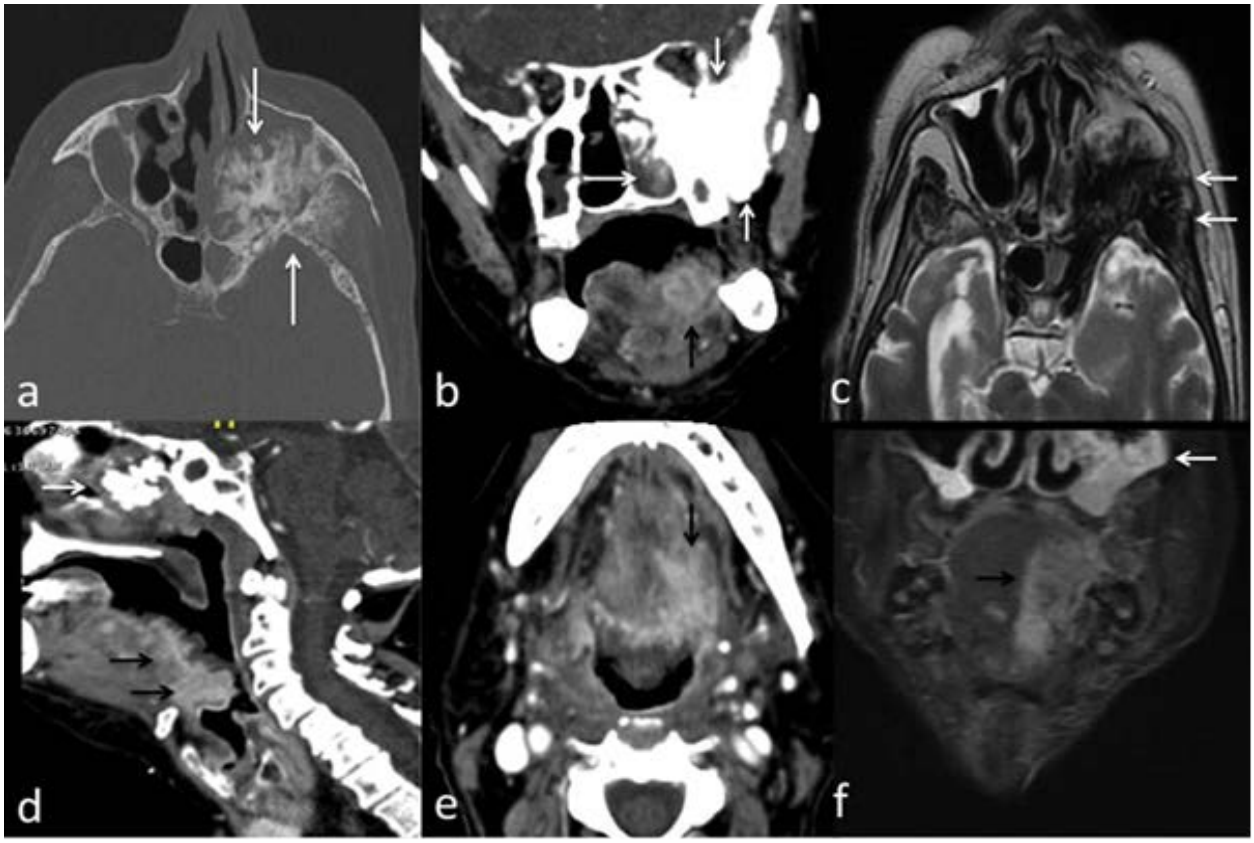

Figure 1: Left maxillary bone and sphenoid wing osteosarcoma in a 65-year-old man with synchronous squamous cell carcinoma of the floor of the mouth (tongue base) a) Bone window axial CT image shows osseous matrix (arrows); b) Soft tissue component of the mass (long arrow); c) T2-weighted axial MR image shows signal void areas of osseous matrix (arrows); d) Sagittal contrast enhanced CT image shows maxillary tumor (white arrow) and synchronous oropharyngeal mass (black arrows) in the same plane; e) Contrast enhanced axial CT; f) Coronal contrast-enhanced T1-weighted MR images show the extension of oropharyngeal mass to the floor of mouth (tongue base) (black arrow) and MRI shows maxillary mass (white arrow).

go, et al. [9] investigated 884 patients with previously treated NPC retrospectively and reviewed 21 radiation induced tumors. They found that 11 of the patients developed squamous cell carcinomas in the radiated field and 6 of the patients developed sarcomas in the radiated field. Further, they concluded that the risk of head and neck squamous cell cancer and radiation induced sarcomas increases after radiation therapy. Scelo, et al. [6] showed that patients with the NPC have an increased risk of carcinoma in the upper aerodigestive tract after radiotherapy. Our patient developed both maxillary osteosarcoma and oropharyngeal SCC synchronously. To our knowledge the development of both in same patient has not been reported earlier.

The radiation for treatment of NPC affects the skull base, maxilla, mandible, thyroid, skin and muscles. Therefore malign tumors of these regions can arise after radiation therapy as one of the late complications. The latent period following radiation therapy for nasopharyngeal carcinoma and the development of secondary tumors was 5-30 years with a mean of 12.9 years [3,9]. Our patient developed the secondary tumors 10 years after primary radiation therapy.

The minimum radiation dose needed for development of radiation-induced sarcoma is 30 Gy [6,7]. The radiation doses in reported cases varied from 25 to 110 Gy, with a median dose of 45 Gy [10]. Our patient received 70 Gy.

The tumors in our patient were determined to be Radiation-induced tumors (RITs) based on the criteria adopted by Cahan, et al. [9] for radiation-induced sarcomas: (1) Radiation had been previously delivered to the site of the new malignancies, (2) The histological type of the newly developed tumors was different from the primary lesion, (3) The latency period between the radiation exposure and the development of the new malignancies was more than the 5-year cure period. In our case it was 10 years and both newly developed tumors were proven histologically.

Liu, et al. [3] reported that postirradiation osteosarcoma was determined 33.3% in maxilla, 46.7% in mandible and 20% from a mixture of nasal cavity and paranasal sinuses. The most common pathologic subtype of the radiation induced osteosarcomas included fibroblastic osteosarcoma (53.3%), chondroblastic osteosarcoma (33.3%), and mixed type osteosarcoma (13.3%). In our patient chondroblastic osteosarcoma was diagnosed pathologically.

The CT scan of our subject shows bone destruction, soft tissue mass and osteoneogenesis while the MRI is good in defining the extension into the adjacent soft tissues in osteosarcomas. Follow-up within the radiation field by CT and MRI and a recognition of the expected latency period may help in making early diagnosis of RIT. Abrigo [9] emphasized that radiation induced sarcomas were large with extension of soft tissues at the time of MRI examination because of the aggressive characteristics of these tumors. Radiation-induced changes such as osteoradionecrosis and pathologic fracture may cause diagnostic difficulties. RITs are usually large tumors with extensive local invasiveness and bone destruction. These are the main clues helping to make the diagnosis. Pain and swelling are the most common symptoms of radiation induced osteosarcoma of the head and neck [3].

From a radiological point of view, the MRI features of radiation induced SCC are the same as non-radiation induced SCC or recurrent NPC. The distinction is made therefore by location. Recurrent nasopharyngeal carcinoma arises around the margin of the original tumor, while radiation induced SCC arises from the peripheral to the NPC. Differential diagnosis of radiation induced sarcoma from SCC may be difficult. A wide range of histologic subtypes of sarcomas cause variable signal characteristics, heterogeneity and more contrast enhancement on MRI when they are compared with the SCC or recurrent NPC [9]. In our patient the osseous matrix of the large tumor with the soft tissue component extending to the nasal cavity can easily be detected by both CT and MRI.

In order to prevent radiation-induced tumors, it is important to give attention to radiation doses in planned fields. In our case, the preferred radiation dose is lower now than in the past for the treatment of nasopharyngeal carcinoma. Moreover, the exposure of normal tissue to radiation is decreased by intensity modulation radiotherapy [10].

Long-term and careful follow-up of patients receiving radiotherapy is of great importance for early detection and timely intervention in RITs. Chemotherapy is included if the stage of the cancer is advanced, unresectable and has positive tumor margins. Five-year disease-free survival rates range from 10% to 30% [9].

Conclusion

Radiation-induced tumors are possible long-term side effects of radiotherapy. Although rare and possible to confuse with recurrent disease, this possibility should be considered in any patient who has received radiation therapy. Diagnostic imaging plays a pivotal role in recognition of radiation induced neoplastic diseases. Precise recognition and reporting of main imaging findings allows referral to the most appropriate treatment options. Radiation therapy has become more common and long term cancer survival has improved. Attention to obtain the optimal radiation dose remains the main goal in these patients.

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