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RADIATION INDUCED SARCOMA OF ORAL CAVITY: A CASE SERIES

Radiation Oncology

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ABSTRACT

Radiation-induced sarcoma of the head and neck is a rare long-term complication of treatment of head and neck cancers with radiation. However, as the population ages, radiation-induced sarcomas are becoming more common as a result increased patient survival for head and neck cancer with better treatment regimens. Diagnosis and management of this problem can be extremely challenging and the overall prognosis of radiation-induced sarcoma is worse than other types of sarcomas at a similar stage. In this article, we present two case reports of radiation induced sarcoma of oral cavity. The first patient was a 57-year-old man was radiated for squamous cell carcinoma of retromolar trigone previously and the second patient was a 37-year-old man was radiated for squamous cell carcinoma of tongue. These were presented in our hospital with various complications.

KEYWORDS

Squamous cell carcinoma, Radiation-induced sarcoma, Oral cavity

INTRODUCTION

Sarcomas are malignant tumors that arise from mesenchymal tissues from any location. Radiotherapy is the standard treatment modality for malignant tumors, and 60% of patients need radiotherapy for radical treatment and palliation [1]. Unfortunately, a second malignancy can develop years later as a result of this life-saving therapy [2]. Radiation-induced sarcoma is a rare but recognized complication of radiotherapy arising in 0.035-0.2% of all irradiated patients, and represent less than 5% of all sarcomas [3].

Radiation-induced sarcoma is a well-known long-term side effect of radiation therapy for most of the sites, but it rarely affects the head and neck, with the skin and thyroid being the most frequently affected tissues[4,5]. It was considered that part of the reason for the low incidence in the head and neck is the higher mortality rate of head and neck cancers. However, this low incidence is probably increasing and radiation-induced sarcomas are likely to be more frequent. Incidence of radiation-induced sarcomas of head and neck after radiotherapy between 1960 and 1989 is 0.06%. Between 1990 and 2010 this incidence is 0.17% compared to former times, indicating a possible increase in radiation induced sarcomas of head and neck [6]. It was summarized in a review article on radiation-induced sarcomas that out of 10 reports with a total of 14,000 patients, 0.16% of the incidence was reported [7].

The definition of radiation-induced sarcomas has never been well established. The generally accepted criteria of radiation-induced sarcoma include, treatment with therapeutic irradiation at least three years prior to development of sarcoma, a sarcoma arising within the field of previous therapeutic irradiation and differing histology between the sarcoma and the primary tumor that required radiotherapy [8,9]. Surgery is the standard treatment for radiation induced sarcoma of the head and neck. However, complete resection of the lesion is very difficult because of the proximity of vital organs and multifocality of tumors [10]. The tumor is insensitive to radiation and chemotherapy so incomplete resection of tumor results in a much worse prognosis [11]. This article discusses two cases that came to our hospital with a previous history of radiation therapy and postoperative radiation induced oral cavity sarcoma.

CASE 1

A 57-year-old patient presented in our hospital on November 2013 with complaints of ulcer over the retromolar trigone measuring 5x3 cm. He was evaluated and biopsy from the ulcer was suggestive of moderately differentiated squamous cell carcinoma, clinically staged as $cT_{4a}N_0M_0$. He received radical radiotherapy to a dose of 68Gray in 34 fractions from December 2, 2013 to January 13, 2014 without any break. He had a good clinical response after treatment.

After four months, during a routine follow-up, he developed a reddish-colored, irregular 2x2 cm exophytic growth in the left retromolar trigone region (RMT), along with areas that were ulcerated. Biopsy from the lesion was consistent with recurrent squamous cell carcinoma for which he underwent left composite resection and neck dissection. Post operative histopathology report was suggestive of 1.3x1.6 cm (r/R T1 lesion) with clear margins and all nodes were negative for malignancy. On regular follow-up, a small swelling was detected over the alveolar mucosa involving the vestibule of the lower lip in September 2016 after a disease-free period of 2 years. Swelling was insidious in onset, rapidly progressed in size, painless and bleeds on touch.

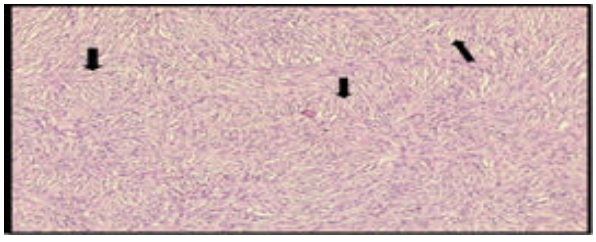

Fig 1 Spindle cell lesion

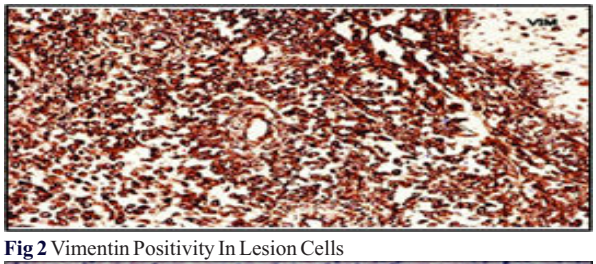

Fig 2 Vimentin Positivity In Lesion Cells

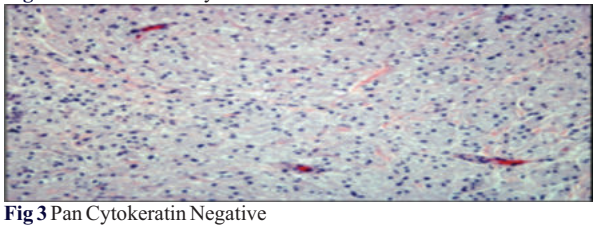

Fig 3 Pan Cytokeratin Negative

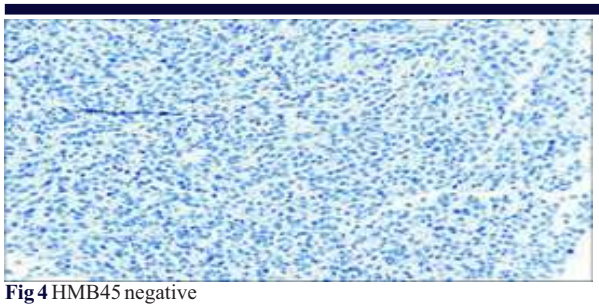

Fig 4 HMB45 negative

On clinical examination, a 6×6 cm proliferative growth was noted arising from left lower alveolus involving the vestibule and extending over lower lip without involving its mucosa. No lymph nodes were palpable. A lesion biopsy revealed an infiltrating neoplasm made of spindle cells (Fig 1) Immunohistochemistry (IHC) showed Vimentin positivity (Fig 2), whereas Pan cytokeratin (PAN CK) (Fig 3) and HMB45 (Fig 4) was negative which was suggestive of sarcoma. Treatment option of radical surgery with reconstruction was explained to the patient. He then underwent left composite resection and reconstruction by primary closure. Subsequently patient had recurrence post complete resection eventually succumbed to the illness.

CASE 2

A 37-year-old patient who had been experiencing swelling over the alveolar process towards the right side came to our hospital in November 2021. According to the patient, the lesion started 30 days ago, and it increased in size. He opened his mouth without any pain. He had no prior history of neck swellings or other relevant family history. He was in good health. Upon local examination, a large 4 x 4 cm irregular reddish mass was found proliferated (Fig 5). He was evaluated and advised for biopsy.

Fig 5 Patient with the symptoms of radiation induced Sarcoma

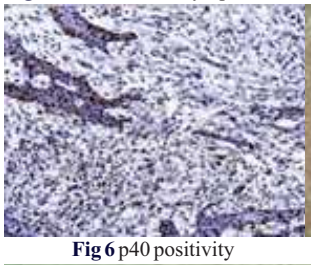

Fig 6 p40 positivity

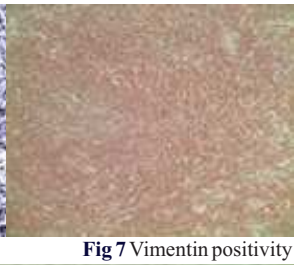

Fig 7 Vimentin positivity

Fig 8 PAN CK Negative

Sections from the biopsy submitted shows fragments of tissue showing ulceration, necrosis and granulation along with a lesion measuring 5x4.3x3.2 cm composed of atypical spindled cells arranged arranged in bundles and intersecting fasicles. These atypia cells with atypical mitosis have large pleomorpic bizzare nuclei with nuclear hyperchromasia. The lesion invaded the bone of maxilla and infiltrating the maxillary sinus mucosa. Present findings are consistent with recurrence in a diagnosed and treated case of carcinoma tongue of post-surgery and radiotherapy suggesting Sarcomatoid Carcinoma with clinical staging as $cT_2N_0M_0$. The patient underwent a course of treatment with 30 sessions of conventional external beam radiation of 60 Gray combined with surgery during October 2018 to November 2018.

Current Immuno histochemistry of these tumor cells (IHC) showed p40 positive (Fig 6) and Vimentin postivity (Fig 7) and whereas Pan cytokeratin (PAN CK) (Fig 8) was negative which was suggestive of sarcoma. Treatment option was explained to the patient and he was subjected to resection of the tumor and reconstruction by primary closure. Following a year, there was no evidence of a change or recurrence.

DISCUSSION

Since the early 1900s, radiotherapy has been shown to be a major factor in the pathogenesis of sarcomas. The association between radiotherapy and sarcomas in a patient who developed a spindle-cell sarcoma following radiation for lupus, a long-term autoimmune disorder that may affect the skin, joints, kidneys, brain, and other organs [12].

The latency period for development of RIS is typically 5-20 years Consensus does not prevail to agree the duration of latency after radiation exposure. The sarcoma team at MSKCC suggests that a latency of six months is sufficient to affirm the diagnosis of RIS [13]. Our patients had a latency period of 2 years in case 1 and 3 years in case 2 after the radiation exposure that fell within the accepted latency duration.

The risk factors for developing RIS are young age, high radiation dose and simultaneous chemotherapy with alkylating agents [14,15]. Our patients had received a total radiation dose of 68Gray and 60 Gray (Age 37 years) with concurrent weekly cisplatin chemotherapy. Although a clear dose-response relationship for radiation-associated malignancies is not established, it is generally accepted that carcinomas arise in tissues exposed to lower doses, whereas sarcomas are induced in heavily radiated tissues in or close to the radiation fields [16]. Our patients developed the tumor at the edge of the radiation field in the left and right alveolar mucosa, but well within the field of radiation. As with all soft tissue sarcoma, core needle biopsy is mandatory in confirming the diagnosis of radiation-induced sarcoma. The biopsy will distinguish between a new sarcoma, recurrence of the primary malignancy, and post-operative or post-radiotherapy changes [17]. Both of our patient's suggestive biopsies revealed the reoccurrence of cancer. The suggestive biopsies for both our patients have reported the reoccurrence of cancer The tumour cells of our patients were positive for vimentin, pan cytokeratin (PAN CK), p40 in Case2 whereas in Case 1 HMB45 negative was also observed.

It is unclear whether treatment should be modified in radiation-induced sarcoma versus traditional soft tissue sarcoma. Radical resection with negative histological margins (R0) is the treatment of choice for localized disease. Limited outcomes of radiation-induced sarcomas are due to a delay in diagnosis due to local post-radiational changes, proximity of major structures of neck limiting the surgical resection, the dangers of reirradiation of the primary area, insensitivity of tumors to chemotherapy and host immunosuppression caused by the first tumor and treatment [18].Our patients underwent complete resection but tumor recurred within one month and eventually succumbed to illness in Case1 whereas Case 2 there was no reoccurrence. Radiation-induced sarcomas of the head and neck indicate a poor outcome of 8% with 5-year disease free survival [19].

CONCLUSION

Radiation-induced sarcoma is a potentially fatal condition that should be known by clinicians, as most cancer patients undergo radiotherapy. Any abnormality should be biopsied, and surgical resection with negative margins is the preferred treatment for radiation-induced sarcomas. In carefully chosen cases, adjuvant chemotherapy and re-

irradiation may be beneficial.

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