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CASE REPORT
Reconstructive

Radiation-induced Sarcoma in the Head and Neck: Clinical, Imaging, Histopathological, and Therapeutic Characterization

Wilber Edison Bernaola-Paredes, DDS, OMS, MSc, PhD*
Eloah Pascuotte Filippetti, MD*
Monica Lucia Rodrigues, MD, MSc†
Henrique Perez Carvalho, MD†
Marcelo Carvalho Coutinho, MD†
Arthur Ferrari Arruda, MD‡
Pedro Jorge Joffily Pinto, MD*
Felipe D'Almeida Costa, MD, PhD‡
Miriã Andrade Celestino, MD§
Antonio Cassio Assis Pellizzon, MD, PhD*

Summary: Radiation-induced head and neck sarcoma (RIHNS) is a rare and serious long-term complication of radiotherapy (RT), with poor prognosis and high morbidity and mortality. Diagnosis is based on immunohistochemistry and molecular biomarker analysis, and therapy is usually surgical. Other adjuvant therapies might be considered. This case report aimed to describe the clinical, imaging, histopathological, and therapeutic characteristics of a rare case of RIHNS in the mandible after 21 years of RT. A 68-year-old male patient underwent a partial left parotidectomy in 1995, was diagnosed with pleomorphic adenoma, and after recurrence of the lesion in 2000, underwent an ipsilateral total parotidectomy with adjuvant RT. In May 2021, he complained of an ulcerated nodular lesion on the tongue that extended toward the lower gingiva, associated with oral bleeding and difficulties with swallowing. After biopsy in the gingival margin and histopathological analysis, the diagnosis of high-grade spindle-cell sarcoma was established. Complete surgical resection with microsurgical reconstruction using a fibular osteomusculocutaneous free flap was performed. RIHNS could appear after a period of almost 20 years after RT. Surgical resection with reconstructive surgery was a reliable and feasible therapeutic option that showed favorable clinical results after an appropriate follow-up. *(Plast Reconstr Surg Glob Open 2022;10:e4418; doi: 10.1097/GOX.0000000000004418; Published online 15 July 2022.)*

Radiotherapy (RT) is a well-known treatment for malignant head and neck tumors (HNC), in which ionizing radiation is used to damage or destroy malignant cells. RT is incapable of differentiating normal from malignant cells, causing adverse effects such as radio-induced head and neck sarcoma (RIHNS), which is a rare and serious long-term complication of RT.[1] These classically present as a painless palpable mass, trismus, or asymmetry in the maxillofacial region, accompanied by pain or paresthesia.[2,3]

*From the *Department of Radiation Oncology, A.C. Camargo Cancer Center, São Paulo, Brazil; †Department of Head and Neck Surgery & Otorhinolaryngology, A.C. Camargo Cancer Center, São Paulo, Brazil; ‡Department of Anatomic Pathology, A.C. Camargo Cancer Center, São Paulo, Brazil; and §Department of Stomatology, School of Dentistry, University Center "UNIFAMINAS," Muriaé, Minas Gerais, Brazil.*

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Their development is associated with or caused by the accumulation of ionizing radiation from RT, the initial age, and time of exposure to radiation, whereas some are associated with genetic disorders.[1] Radiation doses that induce lethal damage to malignant and normal cells result in disorganized mutagenic responses, inducing a carcinogenic process. The exact dosage range responsible for the induction of this tumor is still uncertain, with doses above 30, 40, and 60 Gy having been described in the literature.[2,3] Currently, an increase in its incidence has been observed due to the increasing survival of cancer patients undergoing treatment, with a high latency period between the times to exposure and radiation until the diagnosis of RIHNS is established. In the majority of patients, the prognosis is poor and might lead to local recurrence, distant metastasis, or even death.[4]

The final diagnosis is based on histopathological assessment (HA), immunohistochemistry (IHC) analysis, and detection of molecular biomarkers. Their prognosis will be established based on their grade of cell differentiation and local invasiveness. Thus, their treatment is surgical;

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however, it is not always possible to obtain free surgical margins due to limitations posed by the surrounding anatomical structures. Therefore, surgical treatment could be accompanied by other adjuvant therapies, such as chemotherapy, RT, or combined therapy.[5,6]

CASE REPORT

A 68-year-old male patient complained of paresthesia in the left lower lip and tongue, and difficulty with speech since September 2020. In April 2020, he noticed the appearance of two overlapping nodular lesions in his tongue and the lower gingiva, associated with intermittent oral bleeding and progressive difficulty with swallowing.

With reference to his medical history, there were no comorbidities, and he was a former smoker in abstinence and a social drinker, who underwent superficial left parotidectomy in 1995, of which the HA was pleomorphic adenoma. The first relapse occurred in 2000, and he was submitted to total parotidectomy with microsurgical reconstruction of the facial nerve. HA confirmed the diagnosis of pleomorphic adenoma again, and he was submitted to RT using the 3D-conformal technique with a total dose of 6040 cGy delivered in 33 sessions, from August 24, 2000 to November 7, 2000.

In May 2021, after a new biopsy of the exophytic lesion in the left alveolar gingiva of the retromolar region, HA confirmed high-grade spindle-cell sarcoma. The intraoral evaluation showed an ulcerated nodular lesion that measured 5 cm in diameter and bleeding with intense clots, in the left hemimandible toward the oropharynx. Thus, magnetic resonance imaging (MRI) was performed that showed two expansive lesions, one of them localized in the center of masticatory space, on the inner surface of the left mandibular ramus. The other one, localized on the left side of the soft palate, consisted of a single, irregular, contoured, and lobulated lesion measuring approximately 57 × 41 × 52 mm. The positron emission tomography–computed tomography imaging analysis showed a heterogeneous expansive lesion involving the left side of soft palate, associated with erosion of the ipsilateral mandibular ramus, without signs of a residual tumor (Fig. 1).

Left segmental mandibulectomy extended to the anterior arch and mandibular ramus associated with selective neck dissection of left lymph nodes from levels II and III was performed. Microsurgical reconstruction was performed using the fibular free flap. Finally, the flap was fixed to the floor of the mouth, and anastomosis was performed on the buccal mucosa and pedicle to interconnect them with the facial artery and the concomitant veins of the thyrolinguofacial trunk (Fig. 2). After HA and IHC analysis, the diagnosis of high-grade spindle-cell sarcoma was confirmed, the bone margin of which was compromised by the tumor measuring 4.5 × 3.8 cm, without vascular, lymphatic, or perineural invasion (Fig. 3).

This irradiation protocol was based on stereotactic body radiation therapy (SBRT) with a dose of 36 Gy, delivered in six sessions of 600 cGy on alternate days. Gross tumor volume (GTV) was delineated from fusion of the preoperative MRI and computed tomography images to identify the site

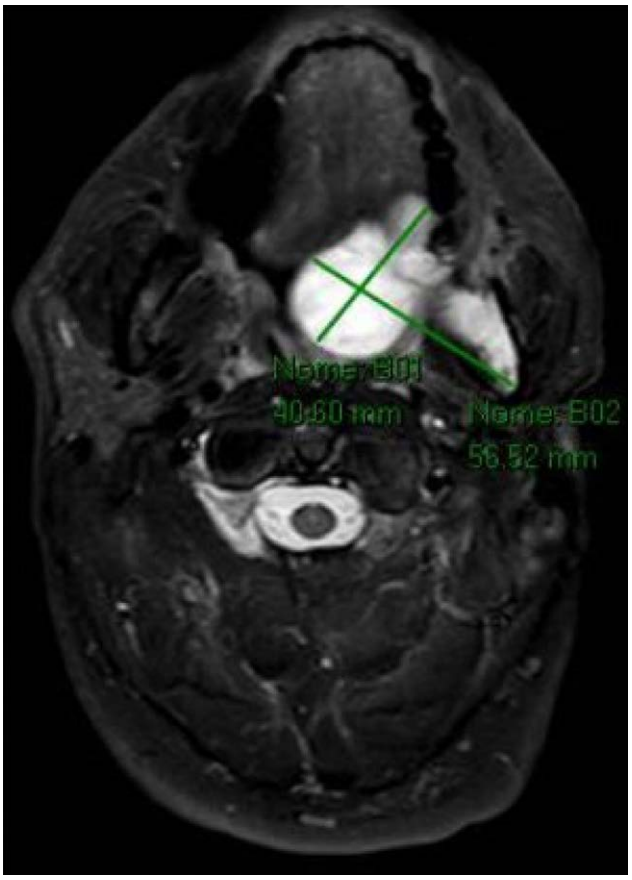

Fig. 1. Presurgical imaging analysis. MRI-axial section showed lower and higher signals on T1 and T2, respectively, with intense contrast enhancement, approximately 3.5 × 3.5 × 2.0 cm that extended laterally toward the left mandibular angle.

of compromised margin, and a 0.5-cm margin was added for the planning target volume, as seen in Figure 4. After 3 months of follow-up, intraoral and extraoral evaluation

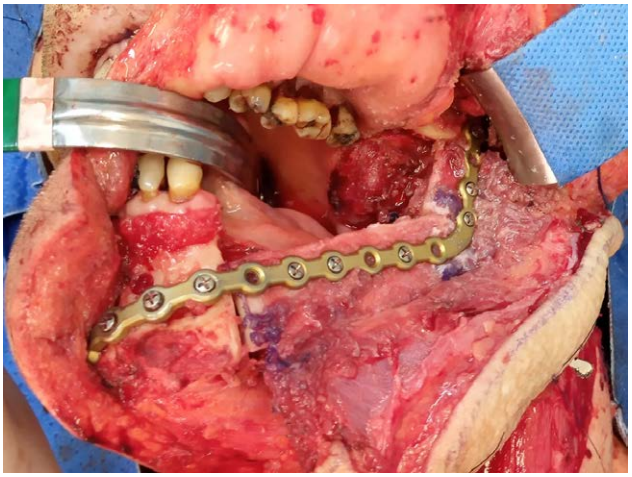

Fig. 2. Reconstructive microsurgery with fibular free flap. Reconstructive titanium plate placed and fixed in the anterior arch and remnant left hemimandible. Microsurgical reconstruction with fibular osteomusculocutaneous free flap.

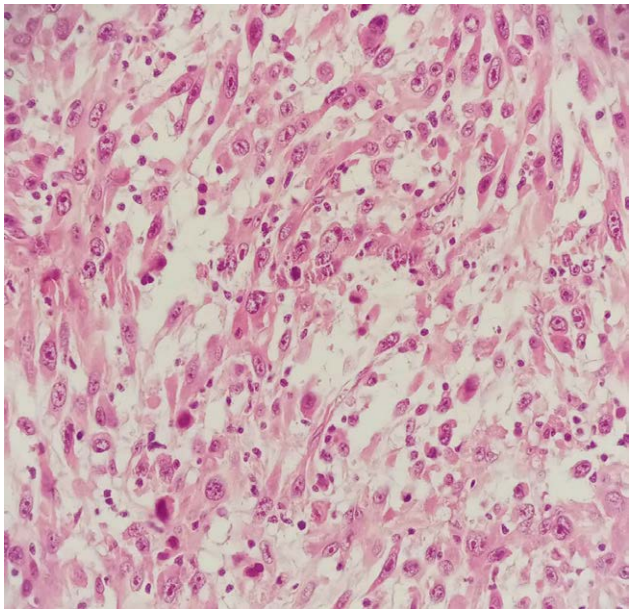

Fig. 3. Histopathological assessment and IHC analysis. After H&E, at 400× magnification, exacerbated nuclear atypia, including marked pleomorphism, heterogeneous chromatin distribution, and multiple nucleoli, was visualized.

showed complete healing in the flap area, without dehiscence, and in the remnant tumor bed, in addition to the neck region on the left, as seen in Figure 2.

DISCUSSION

RIHNS represents 12% of postirradiation adverse effects and has an incidence of less than 1% in patients undergoing RT.[7] It is a challenging task to establish the incidence of these tumors, due to their rarity and differential diagnosis. They occur in patients who have undergone RT, with a mean age ranging between 50 and 60, with a ratio of 2.4 men to one woman, and might remain in latency for a period ranging from 5 to 20 years.[2,4,8]

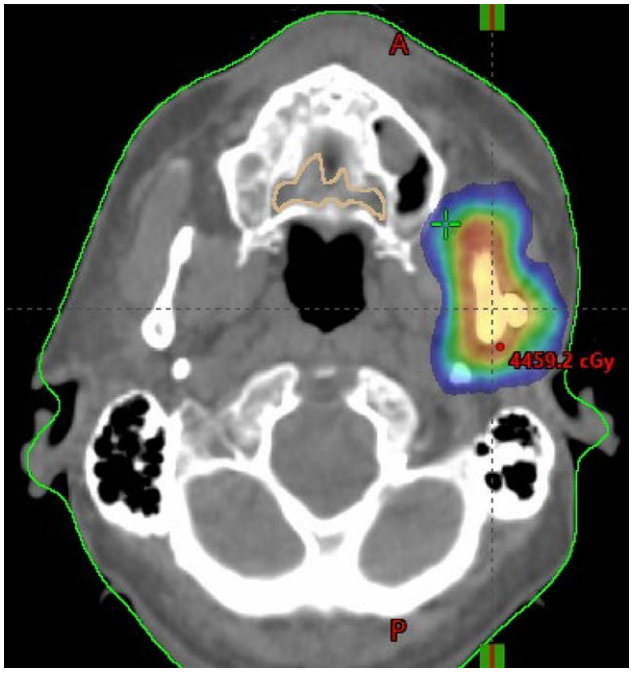

Fig. 4. Reirradiation protocol using stereotactic body radiation therapy technique after reconstructive surgery. Color wash of RT planning dose distribution in the axial.

The age of patients at the time of irradiation could affect the incidence of induced tumors, but it does not seem to change the period of latency. However, RT for pediatric patients is associated with a higher risk for developing RIHNS in a brief period. RT is indicated for tumors in the head and neck region, associated with the risk of multiple local relapses, as described primarily in this case. With reference to the primary local appearance, RIHNS has shown a relative trend toward the same distribution between the maxilla and mandible, with a minority affecting the surrounding soft tissue.[4]

It has been described that an accumulated radiation dose is related to its incidence, but there is no consensus about the possibility that a final dose higher than 30 Gy could be responsible for increasing the risk of its development.[2,8,9] Surgery is the gold standard treatment that offers better long-term survival rates. However, surgical margins are difficult to obtain due to limitations imposed by the surrounding anatomical structures; the fact that the remnant clinical condition is usually found to be at an advanced stage for radical excision, and therefore, unable to achieve the complete healing process; and the occurrence of local complications associated with radiation changes. Another challenge to the surgical approach would be the unacceptable functional and aesthetic deformity; however, microsurgical reconstruction with the use of microvascularized free flaps would be often indicated.[8]

RIHNSs have a low sensitivity to chemotherapy and tumor aggressiveness against a depressed immune system caused by the primary tumor and/or its treatment, which could contribute to poor prognosis. RT showed better locoregional control results, but its effectiveness is rarely reduced.[4,8,10] There is a risk and limitations to its use due to the dangers of radiating a field that has previously been irradiated.

Reconstructive surgery of the head and neck is a well-established field in many cancer centers; however, the training and experience for performing extensive resections that could result in full-thickness tissue defects should be considered. Extensive surgeries, including full-thickness flaps, are feasible, and reconstructive surgery becomes the best choice for restoring function and aesthetics and could be associated with higher rates of locoregional control. The fibular flap is one of the most frequently used flaps as an alternative for the reconstruction of extensive defects, because given its volume, good pedicle length, and low morbidity of the donor area, resection of the tumor can be collected simultaneously.[11]

On the other hand, reconstruction surgeries in the head and neck region have showed some challenges, such as the difference in thickness between the flap and the area to be repaired, which can lead to aesthetic defects such as the formation of a depression at the indicated site and increased risk of failure when larger flaps are needed for total thickness

defects. Potential morbidities of the donor and repaired area site, such as vessel scarcity, surgical scars, and previous irradiation with decreased tissue vascularization, are also risk factors for flap failure.[12,13] Thus, the surgical defect repair procedure requires extensive surgeon training and a thorough evaluation of the tissue to be used according to the patient's history to minimize the possibilities of reconstruction failure.

CONCLUSION

RIHNS, a rare condition resulting from higher doses of ionizing radiation, can remain in latency for up to 20 years. Nowadays, surgery has been associated with higher survival rates. The esthetic and functional defects could be restored with microsurgical reconstructions using free flaps. However, RIHNSs have a poor prognosis, due to higher rates of local and distant relapses requiring multimodal therapy, which will depend on the tumor response to these therapies.

Wilber Edison Bernaola-Paredes, DDS, OMS, MSc, PhD
Department of Radiation Oncology
A. C. Camargo Cancer Center
Sao Paulo 01509-010, Brazil
E-mail: edison.bernaola@gmail.com

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