


Management of oral late sequelae in head and neck cancer long-term survivor awaiting re-irradiation: Case report and literature review

Larissa Fernanda dos Santos
Lima Macedo¹
Juliana Mota Siqueira¹
Luara Maria Cerioni Gonçalves¹
Camila de Barros Gallo¹
Carina Domaneschi^{1*} 

Abstract:

Head and Neck Squamous Cell Carcinoma (HNSCC) constitute more than 90% of the head and neck cancer cases, often presenting as a locally advanced disease. As techniques are improving, life expectancy of HNSCC patients have risen overtime, leading to a larger number of people facing late sequelae that often culminate in a direct and significant impact on their quality of life. For those individuals, recurrence may represent a concern for curative attempts and overall survival rates. This paper reports a clinical case of a long-term HNSCC survivor who developed multiple oral sequelae from previous cancer treatment and recent second malignancies; in order to proceed for re-irradiation, she was referred for oral assessment. Due to her age and comorbidities, private professionals reportedly refused to provide oral care, causing an immense delay to her oncology treatment that led to the progression of diverse oral symptoms and cancer itself. Considering the urgency of head and neck re-RT, the outlined oral treatment plan was conservative and included scaling and root planing, oral prophylaxis, direct resin composite restorations and hygiene orientation, in a single session. She was also referred for low-level lasertherapy. Afterwards, her health had deteriorated to such a stage she did not qualify to actually proceed for re-RT, and instead was treated with end-of-life care until the time of her death, 8 months after the above-mentioned appointments. The authors believe the prolonged search for proper oral care was significant to her already poor prognosis, as it caused an immense delay to the start of the cancer treatment.

Keywords: Head and neck cancer, Radiotherapy, Survivor, Dental care, Quality of life.

¹ University of São Paulo - USP, School of Dentistry, Department of Stomatology, São Paulo, SP, Brazil.

Correspondence to:
Carina Domaneschi
E-mail: domaneschi@usp.br

Article received on August July 30, 2020
Article accepted on September 8, 2020

DOI: 10.5935/2525-5711.20200017



INTRODUCTION

Head and Neck Cancers (HNC) are a group of malignant neoplasms considered the seventh most common type of cancer worldwide, with 600,000 new cases annually, often presenting as a locally advanced disease. Head and Neck Squamous Cell Carcinoma (HNSCC) constitute more than 90% of these cases¹. The incidence is higher among men, increases with age and tobacco smoking is considered the most important etiological agent. Alcohol consumption, HPV infection and genetic abnormalities are other risk factors for HNSCC^{2,3}.

Surgery, chemo and/or radiotherapy are treatment options for HNSCC, depending on TNM stage, primary site and adjacent structures³. The usual approach for localized cancers is single modality whilst, for locally advanced HNSCC, it is multimodal⁴. Upfront surgery combined with an adjuvant therapy prevails as the standard guideline for oral cavity and oropharyngeal sites - for those patients, recurrence may represent a concern for curative attempts and overall survival rates⁵.

As techniques are improving, life expectancy of HNSCC patients have risen overtime, leading to a larger number of people facing late sequelae that often culminate on a significative impact on their quality of life (QoL)⁶. For some cases, control measures are the only achievable dental management, considering the extension and nature of the damages caused by the cancer and its treatment⁷. Oral care is recognizably intricate for oncology patients, playing a pivotal role on those individuals' survivorship⁸.

This paper reports a clinical case of a long-term HNSCC survivor who developed multiple oral sequelae from previous cancer treatment and also recent second malignancies, evidencing particularities of oral health assessment, strategies adopted under these circumstances and aspects that can be perceived in patients with such peculiar needs.

CASE REPORT

A 73-year-old female presented to the Oral Neoplasms Clinics at the University of São Paulo School of Dentistry, accompanied by her daughter, for pre-radiotherapy evaluation in June 2019, due to the diagnosis of oropharynx and colorectal carcinomas in early 2018.

Her medical history revealed previous invasive HNSCC diagnosed in late 2001, surgically treated with partial glossectomy and ipsilateral cervical lymphnodes dissection, followed by adjuvant radiotherapy. Tracheostomy was performed immediately after surgical

intervention because of a flap reconstruction and a nasogastric tube (NGT) needed to be placed for feeding purposes. Complete remission was confirmed in 2007.

The patient used to consume three packs of cigarettes per day for 45 years and reportedly quit after her first cancer diagnosis in 2001. Additionally, she informed keeping heavy drinking habits for 53 years, quitting only after the recent carcinomas were diagnosed, in 2018. She also had several controlled chronic diseases such as hypertension, hypothyroidism, diabetes, depression and anemia; recent hospitalization due to malnutrition and previous episodes of stroke were disclosed as well. Routine medications included anticoagulant, opioid analgesic, antidepressant, antihypertensive and antiepileptics. Family medical history included multiple malignancies.

By reason of her age and comorbidities, she related difficulties on having dental care provided by private professionals, resulting on a delay of almost one and a half years between diagnosis and proper oral care, circumstance that led to the progression of diverse oral symptoms and cancer itself.

Her face exhibited no asymmetry and an oval, well-delimited ulcer, measuring approximately 0,5 cm, was visible in the mental region, presenting no signs of malignancy. It was also possible to observe the tracheostomy and the nasogastric tube (Figure 1). Intra-oral examination exposed several complications linked to previous cancer treatment, including decreased tongue mobility, dysphagia, hyposalivation, trismus, orofacial pain, radiation-related caries in all remaining maxillary teeth and also edentulous mandible.



Figure 1. Extraoral examination before interventions. Tracheostomy and a nasogastric tube are displayed.

A white coating plaque was evident on the surface of her tongue dorsum and hard palate, probably related to the decreased salivary flow and lack of tongue mobility, combined with residuals from the feeding tube. Poor oral hygiene, gingival inflammation and the presence of calculus deposits were detected, in addition to deficient marginal adaptation of class IV restorations in the central incisors (Figure 2).

It was also possible to observe the malignant oral lesion characterized as a deep, painful ulcer, displaying a yellowish background as well as irregular edges that extended from the posterior region of the tongue through the palatoglossal arch reaching the soft palate. This lesion was considered unresectable by her oncologist, who reportedly referred her for re-irradiation.

Other oncological symptoms were identified such as speech disorders, breathing and swallowing difficulties, alongside the presence of cervical lymphadenopathy in the right supraclavicular nodes with referred pain elicited by palpation. It was also noted that the patient most likely suffered from cachexia, as she related asthenia and lost more than 5 kilos in the month prior to the appointment.

Considering the necessity of head and neck re-RT, the outlined oral treatment plan was conservative and included scaling and root planing, oral prophylaxis, direct resin composite restorations and hygiene orientation, in a single session (Figure 3).

Different approaches were adopted to perform dental procedures due to the patient's limitations. Dental chair was positioned at less than 45 degrees to provide comfort breathing and reduce her risks of ingesting any



Figure 2. Intraoral examination before interventions. Several unsatisfactory teeth restorations are displayed.



Figure 3. Post-procedure examination. Restorative dental procedures were performed in a single session.

liquids or even choking on saliva. Manual root scaling was performed using Gracey curette, gauze swabs and uninterrupted suctioning, preventing the patient from swallowing debris. The length of the procedures was decreased and filled with pauses by reason of reported oral pain related to trismus and dry mouth symptoms. Presuming the possibility of the white plaques being associated with oral candidosis, the patient was recommended to perform oral hygiene using gauze swabs moistened in Nystatin 100,000 IU/mL, in oral suspension, four times a day for fifteen days.

After the conclusion of dental assessment, our patient was referred to a specialized department for low-level lasertherapy protocols, in order to inhibit radiation-induced oral mucositis.

Intending to conduct follow-up, our team contacted her daughter who informed that by the time the patient was supposed to start the cancer treatment her health deteriorated, and she did not qualify to proceed for re-RT; end-of-life care was implemented by her oncology team and she died on february 2020, eight months after the reported dental appointments.

DISCUSSION

Head and Neck Cancer survival rates have improved as a result of prominent advances in oncology therapies, and consequently a higher number of patients are dealing with at least one unmet need⁹. Any modality of HNC treatment is invasive and its severity depends on parameters such as TNM stage, patient's clinical history, modality of therapy, pre-treatment approach and follow-up¹⁰. As a result, those individuals manifest diversified

and intricate necessities, both medical and psychosocial, demanding a multidisciplinary collaboration for a satisfactory recovery⁴.

HPV infection has been recognized as the etiological agent for an increasing fraction of HNSCC cases, especially those located in the oropharynx. Nonetheless, this association only became scientifically evident in the past decade¹¹. Our patient was not tested in 2001 since, by that time, studies regarding this correlation were still being conducted. Her HPV status remains unknown.

Exposure to carcinogens such as tobacco and alcohol promotes field cancerization of the upper aerodigestive tract and reportedly increases the chances of developing second primary malignancies (SPMs). Long-term HNSCC survivors beyond three years face greater risks of dying from late recurrence or head and neck SPM and also non-HN SPM - colorectal cancer is the third most common site of SPM to cause death and has been associated with tobacco smoking¹². As the patient was a heavy smoker for four and a half decades and maintained unhealthy drinking habits even after the first cancer diagnosis, it is believed that these practices contributed to the development of oropharyngeal and colorectal SPMs, consequently leading to a poor prognosis.

Oncology patients generally have to deal with numerous stressors, such as treatment side effects, late sequelae and psychosocial problems, including the fear of recurrence and death¹³. Thus, a substantial number of those individuals develop some level of emotional distress or depression, specially head and neck cancer survivors - phenomenon linked to the stigma caused by disfigurement that leads to social isolation^{13,14}. Furthermore, it is well established that lifestyle disruptions as the dependence on nasogastric tube feeding and communication disorders play an important role in this scenario¹³. Accordingly, creating a gentle environment and performing active listening was decisive to build a trustworthy relationship with our patient and to improve her compliance with the oral treatment.

HNC patients who undergo radiotherapy generally develop dysphagia, enduring serious swallowing impairments¹⁵. It is important to adapt oral hygiene orientations to the patient's morbidities, especially those with NGT feeding and lack of tongue movement, in order to inhibit conditions such as fungal infections that lead to decreased QoL.

Trismus is a common late-sequelae related to head and neck irradiation; it causes severe orofacial pain, often leading to poor oral hygiene and impacting on nutritional habits¹⁶. Other recurrent morbidity after RT for HNC is salivary gland hypofunction, clinically translated into decreased salivary secretion and xerostomy¹⁷. Our patient expressed high discomfort during long procedures that aggravated dry mouth symptoms and pain on masticatory muscles. The use of saliva substitutes is a conventional protocol for relieving the lack of moisture in the oral cavity¹⁷. Regular short pauses were stipulated for her to drink water and rest, contributing for the patient's welfare.

The loss of salivary flow due to gland hypofunction also culminates in a diminished remineralization of the enamel which, along with changes in the composition of saliva, dysbiosis and direct radiation damage to dental structures, increases the patient's risk of developing radiation caries. This condition, well-known for displaying an aggressive, rampant form, may lead to the need of dental extractions if not thoroughly treated¹⁸.

Our patient exhibited extensive radiation caries and dental calculus in most of her remaining teeth. Generally, it is recommended that tooth extractions must precede head and neck radiotherapy as a prevention strategy for osteoradionecrosis of the jaws (ORNJ). However, this measure, instead of being a protective factor, can lead to ORNJ in the dental sockets if these alveoli are not fully repaired at the time of radiation exposure, which must be of at least 21 days. Considering the previous radiotherapy and the urgency to start re-irradiation protocols, teeth extractions were discarded at this point due to the high risk of ORNJ¹⁹. Therefore, in order to improve oral health condition and remove possible infection sites without causing any trauma to her jaw bones, the outlined treatment plan was essentially conservative.

Up to 60% of patients who undergo head and neck RT develop severe swallowing dysfunction with aspiration, frequently eliciting no cough reflex²⁰. Aspiration pneumonia's risk is related to neck dissection²⁰, and is also described as the most common cause of death among individuals with nasogastric tube feeding²¹. Besides uninterrupted suctioning and regular pauses, our team decided to shift the dental chair position to 45 degrees, allowing her to breathe comfortably and to refrain from aspiring fluids and foreign objects or debris.

Low-level lasertherapy (LLL) is well-recognized for successfully preventing and treating oral mucositis,

regularly associated to head and neck RT²². After concluding the dental procedures, our patient was referred to a specialized department for preventive photobiomodulation with LLL in order to diminish the severity of such morbidity, since she was supposedly proceeding for radiotherapy.

Afterwards, the patient's health deteriorated to such a stage that re-RT was no longer suitable. She was treated with end-of-life care until february 2020, time of her death. The authors believe the prolonged search for proper oral care was significant to her already poor prognosis, as it caused an immense delay to the start of the cancer treatment.

It is notorious that many community dentists are not prepared to manage oral complications of cancer due to lack of training in dental schools; special post-graduate programs offer the opportunity to acquire knowledge and experience dealing with medically complex individuals. Dentists are involved in the integral care of oncology patients as early as diagnosing loco-regional malignancies and local manifestations of systemic cancers. Oral management must begin promptly and prepare the patient for the treatment, advance with approaches to prevent or diminish oral toxicities during the cancer therapy and guarantee follow-up appointments to detect eventual recurrences and likewise deal with late sequelae. Notwithstanding, not all cancer centers offer integrated dental treatment. Given the relevance such measures represent for those patients QoL and survivorship, it is recommended that the oncology team includes a dental care provider with the required expertise⁸.

Viral, bacterial and fungal infections, oral mucositis, radiation caries and osteoradionecrosis of the jaws may be avoided or reduced if a few strategies are implemented by the dental team before and during HNC treatments⁸. Follow-up protocols for HNC patients preconize early detection of second malignancies and should also control post-treatment morbidities, such as xerostomia, trismus, speech and swallowing disorders⁴.

As long-term HNC survivors are a *sui generis* group of patients, their appraisal demands an exceptionally meticulous expertise. Repercussion of oral late sequelae on their QoL induces the emergence of other complications, such as malnutrition and depression, therefore impacting on cancer survival rate itself; hence, oral care is a critical component of those individuals' treatments. This scenario emphasizes the importance

of dentists incorporated into the multidisciplinary oncology team, providing integral care and thus an improved QoL for cancer survivors.

ACKNOWLEDGMENT

The authors would like to thank the Journey of the Interdisciplinary Academic League of Oral Neoplasms (JOLINB) at the University of São Paulo for the award received from this event.

REFERENCES

1. Reibel J, Gale N, Hille J, Junt JL, Lingen M, Müller S, et al. Oral potentially malignant disorders and oral epithelial dysplasia. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, eds. WHO classification of tumours of the head and neck. 4th ed. Lyon, France: IARC Press; 2017.
2. Madathil S, Rousseau MC, Joseph L, Coutlée F, Schlecht NF, Franco E, et al. Latency of tobacco smoking for head and neck cancer among HPV-positive and HPV-negative individuals. *Int J Cancer*. 2020 Jul;147(1):56-64.
3. Jou A, Hess J. Epidemiology and molecular biology of head and neck cancer. *Oncol. Res Treat*. 2017;40(6):328-32.
4. Nekhlyudov L, Lacchetti C, Davis MB, Garvey TQ, Goldstein DP, Nunnink JC, et al. Head and neck cancer survivorship care guideline: American Society of Clinical Oncology clinical practice guideline endorsement of the American Cancer Society guideline. *J Clin Oncol*. 2017 May;35(14):1606-21.
5. Zenga J, Gross J, Fowler S, Chen J, Vila P, Richmon JD, et al. Salvage of recurrence after surgery and adjuvant therapy: a systematic review. *Am J Otolaryngol*. 2018 Mar/Apr;39(2):223-7.
6. Simcock R, Simo R. Follow-up and survivorship in head and neck cancer. *Clin Oncol (R Coll Radiol)*. 2016 Jul;28(7):451-8.
7. Taberna M, Moncayo FG, Jané-Salas E, Antonio M, Arribas L, Vilajosana E, et al. The multidisciplinary team (MDT) approach and quality of care. *Front Oncol*. 2020 Mar;10:85.
8. Epstein JB, Güneri P, Barasch A. Appropriate and necessary oral care for people with cancer: guidance to obtain the right oral and dental care at the right time. *Support Care Cancer*. 2014 Jul;22(7):1981-8.
9. Nguyen NTA, Ringash J. Head and neck cancer survivorship care: a review of the current guidelines and remaining unmet needs. *Curr Treat Options Oncol*. 2018 Jul;19(8):44.
10. Samim F, Epstein JB, Zumsteg ZS, Ho AS, Barasch A. Oral and dental health in head and neck cancer survivors. *Cancers Head Neck*. 2016;1:14.
11. Vokes EE, Agrawal N, Seiwert TY. HPV-associated head and neck cancer. *J Natl Cancer Inst*. 2015 Dec;107(12):djv344.
12. Baxi SS, Pinheiro LC, Patil SM, Pfister DG, Oeffinger KC, et al. Causes of death in long-term survivors of head and neck cancer. *Cancer*. 2014 May;120(10):1507-13.
13. Chen AM, Daly ME, Vasquez E, Courquin J, Luu Q, Donald PJ, et al. Depression among long-term survivors of head and neck cancer treated with radiation therapy. *JAMA Otolaryngol Head Neck Surg*. 2013 Sep;139(9):885-9.

-
14. Clarke SA, Newell R, Thompson A, Harcourt D, Lindenmeyer A. Appearance concerns and psychosocial adjustment following head and neck cancer: a cross-sectional study and nine-month follow-up. *Psychol Health Med*. 2014;19(5):505-18.
 15. Greco E, Simic T, Ringash J, Tomlinson G, Inamoto Y, Martino R. Dysphagia treatment for patients with head and neck cancer undergoing radiation therapy: a meta-analysis review. *Int J Radiat Oncol Biol Phys*. 2018 Jun;101(2):421-44.
 16. Gebre-Medhin M, Haghanegi M, Robért L, Kjellén E, Nilsson P. Dose-volume analysis of radiation-induced trismus in head and neck cancer patients. *Acta Oncol*. 2016 Nov;55(11):1313-7.
 17. Mercadante V, Al Hamad A, Lodi G, Porter S, Fedele S. Interventions for the management of radiotherapy-induced xerostomia and hyposalivation: a systematic review and meta-analysis. *Oral Oncol*. 2017 Mar;66:64-74.
 18. Moore C, McLister C, Cardwell C, O'Neill C, Donnelly M, McKenna G. Dental caries following radiotherapy for head and neck cancer: a systematic review. *Oral Oncol*. 2020 Jan;100:104484.
 19. Chronopoulos A, Zarra T, Ehrenfeld M, Otto S. Osteoradionecrosis of the jaws: definition, epidemiology, staging and clinical and radiological findings. A concise review. *Int Dent J*. 2018 Feb;68(1):22-30.
 20. Lindblom U, Nilsson P, Gärskog O, Kjellen E, Lauren G, Wahlberg P, et al. Aspiration as a late complication after accelerated versus conventional radiotherapy in patients with head and neck cancer. *Acta Otolaryngol*. 2016;136(3):304-11.
 21. Chang WK, Huang HH, Lin HH, Tsai CL. Percutaneous endoscopic gastrostomy versus nasogastric tube feeding: oropharyngeal dysphagia increases risk for pneumonia requiring hospital admission. *Nutrients*. 2019 Dec;11(12):2969.
 22. Mallick S, Benson R, Rath GK. Radiation induced oral mucositis: a review of current literature on prevention and management. *Eur Arch Otorhinolaryngol*. 2016 Sep;273(9):2285-93.