Oral medicine case book 53: Radiation-induced xerostomia

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CASE REPORT

A 76-year old male presented at the Oral Medicine Clinic, complaining of a persistent feeling of a dry mouth, subsequent to having undergone surgery, chemotherapy and radiation therapy for nasopharyngeal carcinoma, 18 months previously. Other than the cancer, he had no systemic problems of note and was otherwise in good physical health. Upon further questioning, the patient reported that the dry mouth condition was affecting his quality of life and that he was losing weight due to difficulty in eating. He further emphasised that his mouth felt dry within five minutes of rinsing his mouth with the palliative agents suggested by his dentist and oncologist. The regimen he followed to relieve his symptoms included glycerine BP oil, Candacide® (a nystatin containing product), Biotene® mouth spray and mouthrinse (these products contain lactoperoxidase, glucose oxidase, lysozyme and lactoferrin), Orbit® sugar free gum and an increased frequency of water intake.

The oral examination revealed the following signs: the oral cavity was very dry and the examining dental mirror even stuck to the oral mucosa as a result; and no saliva could be detected in the patient's mouth even after "milking" the submandibular and sublingual salivary gland ducts. The tongue appeared erythematous and lobulated and flat erythematous patches were evident on the palatal mucosa (Figures 1 and 2).

Based on the history and signs, a diagnosis of erythematous candidiasis associated with radiation-induced xerostomia, was made. As a result, the patient was treated with a broad spectrum antiseptic mouthrinse of 0.2% aqueous solution of chlorhexidine gluconate and was encouraged to use the carboxymethylcellose-based artificial saliva supplied. The maintenance of good oral hygiene and the need for frequent dental evaluation to detect and correct early caries lesions, was emphasised. Two weeks later the patient reported a significant improvement and felt that the artificial saliva produced a prolonged moisturising effect of his mouth. He also stated that he was now able to eat with minimal discomfort.

Figure 1: The patient presented with buccal mucosae appearing dull and dry

Figure 2: The tongue of the patient appeared dry with a cobble-stone appearance and with prominent papillae in the posterior third of the tongue.

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Table 1: The preventive and palliative measures for xerostomia. (RT=radiation therapy)*

Preventive measures to manage the consequences of reduction of salivary flow	Palliative measures to improve moisture retention in oral cavity
Change in dietary habits: • reduced consumption of dry/spicy/acidic food • avoid beverages containing alcohol or caffeine • low sugar diet • reduced frequency of food intake • increased frequency of fluid intake **Application of topical neutral-pH sodium fluoride agents** (for teeth remineralisation) Apply gel once/day (with fluoride tray) or rinse twice/day **Regular dental recall visits:** • first two years: every four months post- RT • after two years, every six months **Radiographs** • bitewings once/year (to detect early carious lesions) • panoramic once/year (to detect any bony pathoses) **Prophylactic antifungal therapy** • for existing oral candidasis: clotrimazole troches 10mg, one troche/day). • prophylactic treatment : chlorhexidine mouthwash	**Topical measures** Increased frequency of water intake (frequent sips of water) **Saliva substitutes containing** • carboxymethlycellulose • mucin • xanthan gum • polyglycerylmethacrylate • salivary enzymes **Mechanical stimulation of salivation** • sugar-free candy or chewing gum • acidic sweet/drinks (not ideal) **Acupuncture** • alternative medicine based on the concept of neuronal activation **Systemic saliva stimulants/cholinergic agonist (pilocarpine):** • stimulate remaining gland function • use after RT completed • use for three months and reassess

* Adapted from the publication by Shiboski, Hodgson and Schiødt, 2007[4]

DISCUSSION

Xerostomia, or dry mouth, is a subjective feeling or sensation of oral dryness and may be actual or perceived. Pathological xerostomia is defined as a salivary flow reduction or salivary hypofunction of greater than 50% and is a common complication in patients who receive radiation therapy for head and neck cancer.[1] The radiation may cause long term irreversible damage to vital tissues such as salivary glands, connective tissues, blood vessels and bone in the radiated field.[2]

Patients with head and neck cancer are often exposed to a total radiation dosage of between 50-70Gy.[2] The tolerance dose for parotid salivary gland varies,[3] but it is suggested that the serous acinar cells of the parotid gland are vulnerable to permanent damage if the radiation dose exceeds 60Gy.[4] Radiation injury causes DNA damage, affects the cell cycle and can result in cell senescence and cell death. Consequently, degenerated acinar cells of the salivary glands become dysfunctional and this leads to hypo-salivation. During the first week of radiation therapy, saliva production from the parotid and sub-mandibular glands starts to reduce and by six to eight weeks, saliva production is minimal.[4] This has long-lasting effects that may continue for several months/years, depending on the total radiation dosage received and the volume of irradiated tissue. Recovery of the major salivary glands takes between three months and one year after therapy, provided the total maximum dosage did not exceed 39Gy and where the turnover rate of acinar cells, of 60-120 days, remains unaltered.[6] On the other hand, minor salivary glands are more resistant to radiation therapy and they may play an important role in the stimulation of remaining vital glandular tissue, the mainstay of the treatment of radiation-induced xerostomia. However, minor salivary glands contribute less than 10% of total salivary production in the oral cavity and therefore cannot be expected to fully compensate for the decrease in saliva production.[1]

Clinically, patients suffering from radiation-induced xerostomia show characteristic features. The saliva may have an increased viscosity, a decreased transparency and in certain cases, may become yellow-brown in colour.[4] Extra-orally, these patients may suffer from dry and chapped lips whilst intra-orally, the common clinical features include glossy and dehydrated oral mucosae; a fissured, erythematous or depapillated tongue; and the absence of salivary pooling in the floor of the mouth. Clinicians should palpate the ducts of the major salivary glands in an attempt to express saliva, i.e. Stensen's duct of the parotid gland that empties on buccal mucosa opposite the first upper molar, Wharton's duct of the sub-mandibular gland and the duct of the sub-lingual gland, both the latter emptying in the region of sub-lingual papilla on the floor of the mouth. Xerostomia may also predispose the patient to infection of the salivary glands and a cloudy or purulent discharge from the salivary ducts may be an indication of this complication.[1]

Consequences of xerostomia include:[6,7,8]

1. radiation caries due to the shift of the oral microflora to favour cariogenic bacteria indicated by an increase in counts of *Streptococcus mutans*;
2. decreased oral clearance due to salivary flow reduction;
3. suscepibility to trauma and oral infections, especially candidiasis, due to dry and atrophic oral mucosae;
4. difficulty with managing prosthetic appliances;
5. impaired normal oral function, i.e mastication, swallowing, speech and taste;
6. burning sensation that may, on occasion, lead to insomnia;
7. halitosis;
8. malnutrition due to dysphagia-induced decrease in food intake.

Ideally, dental care should begin before radiation treatment commences and must be continued during treatment and post-treatment phases. It is estimated that about 58-97% of patients require dental care prior to radiation therapy.[2,5] In the pre-treatment phase, patients should receive a comprehensive oral assessment and management of all dental problems, e.g. dental caries, periodontal diseases, oral infections, defective restorations and ill-fitting dentures. Should extraction of teeth with a poor prognosis be needed, such should be performed two weeks prior to the commencement of radiotherapy in order to avoid post-radiation complications such as osteo-radionecrosis. For the dentate patient, a fluoride tray should be constructed for the prophylactic delivery of fluoride

during radiation therapy and, for the edentulous patient, a split denture with a reservoir for artificial saliva, may be of benefit.[8] Moreover, the patient should be made aware of the importance of maintaining good oral hygiene and of regular dental visits to manage complications as they arise.[2] Patients should be advised to use a soft toothbrush, gauze or mouth sponge to clean their mouths and the frequent use of chlorhexidine-containing mouth rinses should be encouraged to prevent the development of superficial mucosal infections. In this event, however, the patient should be warned that the rinse will affect taste and may produce tooth discolouration. Therefore, a watchful brief should be kept on tooth staining and the stains removed before they become troublesome to the patient.

The management of xerostomia may be divided into preventive and palliative measures (Table 1).[1] Products available include a range of artificial saliva products, mouth rinses, gels, sprays and toothpastes to help reduce symptoms of xerostomia. Locally available brands include Biotene® and Oral Balance® gel (contains xylitol and lysozyme).[10] Carboxymethylcellulose-based artificial saliva has proven to be effective in reducing xerostomia-related symptoms and reports suggest that carboxymethylcelluose-based products are more acceptable to patients than mucin-containing ones.[4,9] Pilocarpine, a sialogogue, is approved by the U.S. Food and Drug Administration for the treatment of radiotherapy-induced xerostomia.[1] It may be used after radiation therapy to directly stimulate the muscarinic receptors in the remaining salivary tissue.[11] Pilocarpine is prescribed at an oral dose of 5-10mg, three times daily and the efficacy of the drug should be assessed after three months of therapy. Although pilocarpine may have positive effects on salivary gland stimulation, the side effects of the drug include headaches, sweating and urinary frequency and may limit its widespread use.[6,11] The drug is contra-indicated in patients with gastric ulcers, hypertension, narrow-angle glaucoma, acute iritis, uncontrolled asthma and in patients on beta-blockers and with known hypersensitivity.[11]

In the post treatment phase, the clinician should reinforce the importance of good oral hygiene, the maintenance of a healthy dentition and of regular follow-up dental visits. The latter will allow the opportunity to reassess plaque-control and to manage early radiation caries. Extractions should be avoided - However, when mandatory, a chlorhexidine mouth rinse regimen and antibiotic prophylaxis should be employed, before any procedure is carried out. In all cases, the extraction should be performed with as little trauma as possible and it may be beneficial to place a splint over the site to prevent trauma during the post-extraction healing period.[2]

CONCLUSION

Xerostomia impairs oral function and significantly impacts on a patient's quality of life. Post-radiation salivary gland dysfunction is common and it is essential that the clinician recognises the problems and provides appropriate treatment to prevent and manage the complications associated with salivary hypo-function. Management of xerostomia involves a multi-disciplinary approach with regular dental visits and the use of palliative and preventative modalities of management, as required. Salivary stimulants and substitutes are helpful in treating the symptoms arising from xerostomia and the various products can be combined in order to suit individual needs. Patients should also be made aware of the importance of maintaining good oral hygiene and a healthy dentition, as well as the benefit of adopting a long term dental and oral health care programme.

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