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Oral mucositis inducted by chemo-radiotherapy in patients with head and neck cancer

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CONTENTS

Prevention and treatment of chemoradiotherapy-induced mucositis in a head and neck cancer patient

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Abstract
Concurrent radiation therapy (RT) with cisplatin is the standard treatment for head and neck cancer. Oral mucositis remains a common toxicity of RT for the treatment of head and neck cancer. Our patient was diagnosed with p16-positive invasive squamous cell carcinoma and was treated with chemoradiotherapy during which radiation-induced mucositis developed. Several supportive agents were administered, which alleviated her symptoms slightly. In general, further studies are needed to define the best supportive care procedures in patients with head and neck cancer.

Introduction
Head and neck cancer (HNC) accounts for 5% of cancers worldwide (1). HNCs may develop due to various factors including demographic parameters, smoking habits, alcohol consumption and viral infections (2). Almost 90% of HNCs are squamous cell carcinomas (HNSCC). Concurrent radiation therapy (RT) with cisplatin has improved locoregional control in squamous cell cancer compared to RT alone; it is now the standard therapy for HNC. The purpose of RT is to damage the tumour maximally with minimum side effects, although it can be accompanied by several short- and long-term side effects (3). Modern intensity-modulated radiation therapy (IMRT) may help to reduce the dose to different organs at risk of toxicity, but side effects cannot be avoided entirely.

Oral mucositis (OM) remains a common, debilitating toxicity of RT for HNC. Mucositis is characterized by erythema and ulceration of the mucosal lining of the oral cavity. Oral mucositis is associated with pain, difficulty eating and swallowing, and in severe cases enteral or parenteral nutrition is needed (4). Additionally, 11% of patients undergoing RT for HNC have unplanned interruptions in RT due to severe mucositis (5). Approximately 70% of HNC patients receiving RT with concurrent cisplatin experience severe OM, defined as grade 3 to 4 on the WHO scale (6-9). Severe OM is usually accompanied by pain that potentially requires analgesic therapy; adversely affects nutrition (including requiring a feeding tube), hydration, speech and swallowing (10,11); leads to radiation treatment breaks, which compromise tumour control (12-14); and increases care costs, especially due to hospitalization (15-17). In addition, chemoradiotherapy causes or exacerbates mucositis and other symptoms, such as alteration or loss of taste, xerostomia, fatigue, nausea and vomiting, with consequent worsening of malnutrition. The development pathophysiology of mucositis is not fully known, but its progression may be caused by direct or indirect mechanisms. RT can have direct effects on the mucosa. Chemotherapy causes damage to the oral mucosa by inhibiting cell regeneration and increasing early cell death. Indirect effects lead to the release of inflammatory substances, loss of protective elements of saliva. These factors may increase the likelihood of bacterial, viral and fungal infections of the damaged mucosa.
Several drugs are currently available that may reduce the duration, incidence, or severity of severe OM.

Clinical case
On 20 March 2021, a 47-year-old woman presented at the ear nose and throat (ENT) outpatient department

complaining of a periodically painful swelling. On physical examination, a 4 cm, indolent, hard, mobile cyst was found on the left side of the neck. Initially it caused no symptoms, but at the time of the first examination she sometimes felt pain on the left side of her face, with referred pain in the jaw and the ear. On 22 March 2021 a CT examination of the neck revealed a 38x42x22 mm centrally hypodense lump on the left side of the neck adjacent to the occipital muscle. On 25 March the lesion was aspirated. The cytological examination showed the morphology of apoptotic dead squamous cells and raised the suspicion of malignancy.

Patient description

On 12 April during a laryngomicroscopic examination, a suspected superficial lesion was observed in the left root of the tongue, which was removed by CO2 laser, followed by left cervical dissection.

The pathology examination confirmed a p16-positive invasive squamous cell carcinoma. The tumour was moderately differentiated (grade 2). The size of the tumour was 5x5x3 mm (pT1). There was no invasion of the surrounding tissues. The distances from the resection surfaces were the following: lateral – less than 0.5 mm, medial – 7 mm, basal – 1 mm, so the resection can be considered to be complete (R0). There was no vascular or perineural invasion, but lymphatic invasion was present. The ratio of tumour infiltrating lymphocytes was 60%. Tumour cells were detected in 1 of the 24 lymph nodes removed (pN1). The largest tumour in the lymph node measured 39 mm.

After the operation on 25 April, the tumour board (radiologist, pathologist, oncologist, radiation oncologist, ENT specialist, head and neck and maxillofacial surgeon, isotope diagnostic specialist) discussed the case and decided that the patient should receive chemoradiotherapy based on 18F-fluorodeoxyglucose (FDG)-positron emission tomography (PET/CT). A non-contrast CT examination was performed at the radiotherapy department. CT slices were acquired every 5 mm. The patient was positioned on a flat-top couch and immobilized with a five-point thermoplastic mask in the radiotherapy treatment position for all imaging modalities (CT and PET/CT). The PET/CT examination revealed no FDG-avid lesions, only the postoperative status.

Based on the CT examination performed before the operation, the clinical target volume (CTV) and also the bilateral lymphatic regions (CTV N) were delineated. The CTV-PTV (planning target volume) and the CTV N-PTV margin were 1 cm and 3 mm, respectively. The prescribed dose for the PTV was 50.4 Gy, in 1.8 Gy daily fractions from Monday to Friday. It was followed by a 6x1.8 Gy boost dose for the site of the primary tumour (Fig. 1).

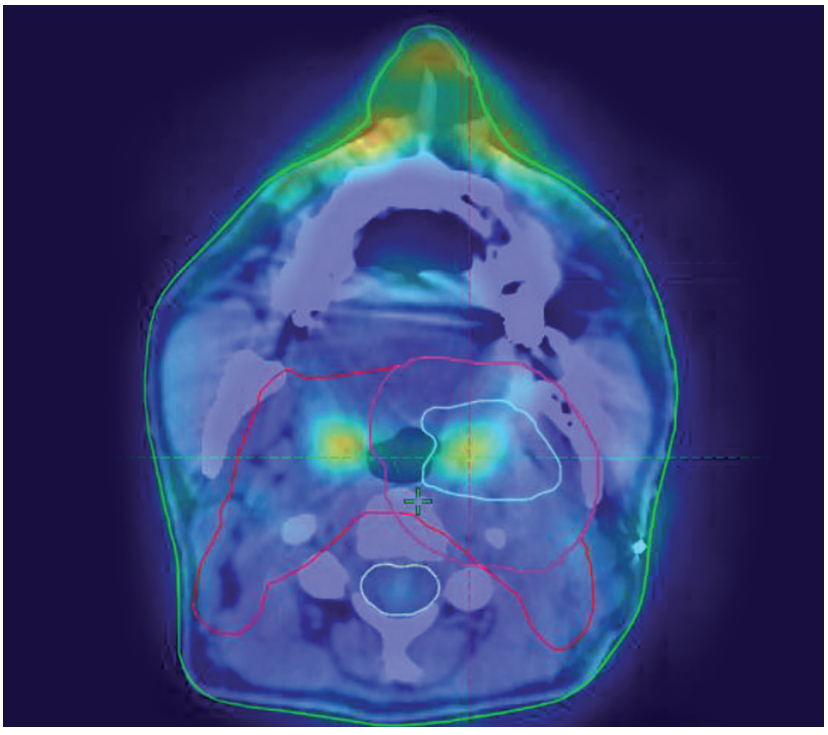

Figure 1. Different contours delineated on planning CT: clinical target volume – CTV (yellow) and planning target volume – PTV (red) and volume for boost dose (pink)

Case history

Radiotherapy was started on 7 June 2021. The patient received the first dose (47.05 mg) of cisplatin therapy on 10 June, after which she had complained of grade I nausea and vomiting for 3 days. She received the second and third dose of cisplatin therapy on 17 June and 24 June respectively. After each cycle of chemotherapy, she suffered from severe fatigue, nausea and lack of appetite. Due to her continuous complaints, especially the significant fatigue and weakness after chemotherapy, she refused to undergo any other intravenous therapy, even though we provided detailed information about its potential benefits. Radiotherapy could be administered continuously from Monday to Friday without any delay. We performed cone-beam CT daily in order to maintain set-up accuracy. Chemoradiotherapy ended on 23 July 2021.

Physical examination findings

At the beginning of the therapy the scar could be seen on the left side of the patient's neck; she complained of slight pain during palpation. As seen in Table 1, grade I radiation-induced mucositis was detected after the 2 weeks of therapy. Several small white plaques appeared in the 4th week and grade 1 radiodermatitis developed in the oral cavity in the 5th week.

Mucositis assessment and findings

Adverse events were assessed using the National Cancer Institute Common Terminology Criteria for Adverse Events, version 4.03. Assessed side effects were recorded twice a week during IMRT. The observed side effects and their severity are shown in Table 1. Adverse events were assessed twice a week with at least 48 hours between assessments during IMRT.

Table 1. Observed side effects and their severity during intensity-modulated radiation therapy (IMRT)

Side effect	1st week 1	1st week 2	2nd week 1	2nd week 2	3rd week 1	3rd week 2	4th week 1	4th week 2
Radiodermatitis (grade)	0	0	0	0	0	0	0	0
Radiation-induced mucositis (grade)	0	0	0	0	1	1	1	1
Pain grade	1	1	1	1	1	1	2	2
Difficulty swallowing (grade)	0	0	0	0	0	0	0	0
	5th week 1	5th week 2	6th week 1	6th week 2	7th week 2	7th week 2		
Radiodermatitis (grade)	1	1	1	1	2	2		
Radiation-induced mucositis (grade)	2	2	2	2	2	2		
Pain (grade)	2	2	2	2	2	2		
Difficulty swallowing (grade)	1	1	1	1	1	1		

Treatment plan

As prevention, we started administering calcium phosphate rinse 3-4 times a day. It was planned that benzydamine hydrochloride spray or chlorhexidine solution would be used in the event of pain or development of plaque in the oral cavity. If extensive white plaque was detected on the oral mucosa, antifungal therapy could be administered. In case of painful swallowing, benzocaine solution could be administered. If more severe pain developed, other pain killers could also be used.

Expected outcome of treatment plan

Other side effects can be avoided with proper use of supportive therapies, multiple medications and stronger pain killers. If the patient's complaints are limited to a tolerable level, a therapeutic interruption can be avoided.

Actual outcome

Our patient used the calcium phosphate rinse throughout the therapy. After development of radiation-induced mucositis, we tried to administer chlorhexidine therapy, but it did not decrease the patient's symptoms significantly. In the 4th week, she started using benzydamine hydrochloride spray, which alleviated her symptoms slightly. At the start of chemoradiotherapy, the patient complained moderate pain in the operated region and took 1-2 diclofenac tablets a day. As the patient's complaints increased, and it became difficult to swallowing tablets, she began to take aceclofenac powder twice daily. Stronger pain killers were not needed.

Discussion

Even at the time HNC is diagnosed, patients often present swallowing difficulties due to tumour location and size. Further oncological treatments, such as surgery and RT, may also worsen these symptoms and cause major nutritional problems.

Treatment of HNC most frequently affects mastication, salivation, swallowing or even speaking. Impairment of the sense of hearing, taste or smell, along with possible aesthetic changes can have a negative impact on patients and their relatives.

Therefore, it is crucial to prevent the development or the severity of side effects during chemoradiotherapy. Prophylactic nasogastric or percutaneous gastrostomy feeding tubes may be necessary in some cases, to prevent weight loss and hospitalizations, along with avoiding treatment breaks (17).

In 2004, the Mucositis Study Group of the Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ISOO) published evidence-based clinical practice guidelines on the prevention and treatment of OM (4). This review examined the literature from January 1966 to May 2002.

Some medications such as calcium phosphate can effectively decrease the incidence and severity of OM (18). Updated guidelines recommend benzydamine for the prevention of OM in patients with HNC receiving chemoradiotherapy (4,19). New evidence supports use of the following agents in the treatment of radiation-induced mucositis: morphine (topical), sucralfate (topical/systemic), fluconazole (systemic), miconazole (topical and systemic), mucoadhesive hydrogel (topical) and fentanyl (transdermal) (4).

As in our case described above, there are currently no agents available that can totally prevent the development of chemoradiotherapy-induced adverse events. However, several agents are recommended for this purpose, and we can choose from the most effective ones available at our Institute, based also the individual patient's preference.

Summary points

Overall, it seems that further adequate prospective, randomized studies are needed to define the best supportive care treatment in patients with HNC undergoing chemoradiotherapy.

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Benzydamine – standard treatment for mucositis in patients with head and neck cancer treated with radiochemotherapy: a case report

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Abstract
Oral mucositis is a common toxicity of cancer therapy, especially in head and neck cancer. Several products are available for the prevention and treatment of oral mucositis, but there is still no gold standard strategy for preventing and treating it. After a comprehensive systematic review of the literature, the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO) recommend basic oral care for this condition, which includes mechanical cleaning (tooth brushing, flossing), mouthwashes to reduce bacterial film, hydration and lubrication of the oral mucosa, benzydamine rinses.

Introduction
Oral mucositis (OM) is a common toxicity of cancer therapy, especially in head and neck cancer (1). All patients treated with radiation therapy alone or in combination with chemotherapy for the head and neck region develop mucositis in the oral cavity, with a negative impact on the overall treatment time and quality of life.
Mucositis typically manifests as erythema, swelling, atrophy and ulceration (2,3). Radiation-induced mucositis typically begins at cumulative doses of about 10–15 Gy and lasts for several weeks after treatment is completed. The severity of mucositis depends on many factors, including the dose per fraction, the total dose, the treatment strategy, oral hygiene during therapy, and the individual's genetic predisposition. Most patients treated for head and neck cancers develop severe OM. Severe mucositis may be a reason for prolonged hospitalization and therapy interruptions. Modern irradiation techniques help spare healthy tissue but do not significantly alleviate OM. The biological model of mucositis from cancer therapy proposed by Sonis in 2004 presents this mechanism as a cascade of pro-inflammatory cytokines TNF-, IL-1, and IL-6 activated by free radicals. This pathobiological cascade is described in five phases: initiation, up-regulation with generation of messengers, signalling and amplification, ulceration with inflammation, and finally healing (2). Understanding these molecular mechanisms of radiation-induced mucositis has opened up new possibilities for finding proper strategies for preventing and treating mucositis. Several products are available for the prevention and treatment of OM (4-6), but there is still no gold standard strategy for preventing and treating it. After a comprehensive systematic review of the literature, the Multinational Association of Supportive Care in Cancer and the International Society of Oral Oncology (MASCC/ISOO), the National Comprehensive Cancer Network (NCCN) and the European Oral Care in Cancer (EOCC) Group provide recommendations for preventing and treating OM (7-12). At the Head and Neck Department of the National Institute of Oncology in Warsaw, every patient is given the following recommendations: basic oral care, which includes mechanical cleaning (tooth brushing, flossing), mouthwashes to reduce bacterial film, hydration and lubrication of the oral mucosa, benzydamine rinses, supersaturated solution of calcium phosphate, fluconazole 100 mg, oral nutrition 800-1000 Kcal daily.

Case report

A 42-year-old woman was diagnosed with stage T2 HPV-related cancer of the right tonsil. The patient's performance status was very good at WHO 0. During a multidisciplinary meeting (surgeon, medical oncologist and radiation oncologist) she was referred to receive concurrent chemotherapy and radiation therapy. The patient underwent seven weeks of volumetric modulated arc therapy (VMAT) in 35 fractions totalling a dose of 70 Gy. The total dose of 70 Gy in fractions of 2 Gy was delivered to the macroscopic disease. A dose of 63 Gy was administered in daily fractions of 1.8 Gy in the clinical target volume (CTV) region of the microscopic disease. The dose distribution is shown in Figures 1-4 (Fig. 1: isodoses 70 Gy – 60 Gy; Fig. 2: isodoses; Figg. 3-4: isodoses 70 Gy – 26 Gy).

Two courses of cisplatin (DDP)-based chemotherapy were administered from the first day of treatment and for the 21 days of radiotherapy. The patient was told how to manage the oral complication and skin reaction. She received standard care: rinsing with benzydamine, rinsing with a supersaturated solution of calcium phosphate twice daily in the morning and evening from the first day of treatment, fluconazole 100 mg daily as antifungal prophylaxis, and oral nutrition of 800 Kcal daily. The patient saw a radiation oncologist once a week for a physical examination. The severity of acute side effects, such as mucositis, dysphagia, and xerostomia, was assessed according to the criteria of the European Organization for Research and Treatment of Cancer (EORTC) and the Radiation Therapy Oncology Group (RTOG) once a week by a radiation oncologist during therapy. During the third week of treatment, the oncologist reported the first sign of mucositis as stage I on the EORTC/RTOG scale. The patient could swallow soft food (dysphagia I) and the severity level of xerostomia was grade I. At the next examination, the mucositis was level II on the EORTC/RTOG scale. The patient required light analgesic medication 3 times a day and could only swallow soft food and oral nutrition. Complete regression of the tonsil tumour and lymph node metastases was shown by nasopharyngeal endoscopy and at the clinical examination which took place during the fourth week of treatment.

Figure 1. isodoses 70 Gy – 60

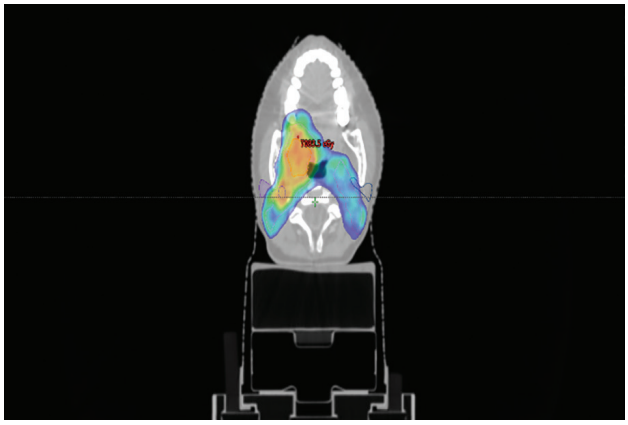


Figure 2. isodoses

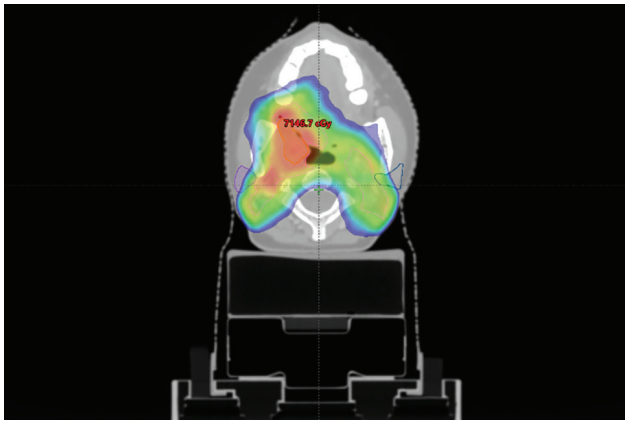


Figure 3. isodosesd 70Gy- 26 Gy

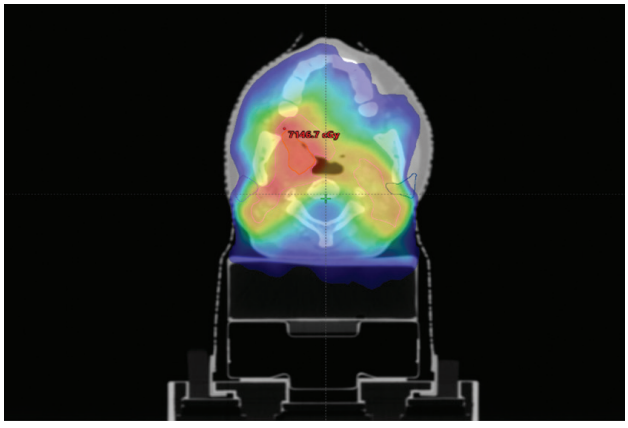
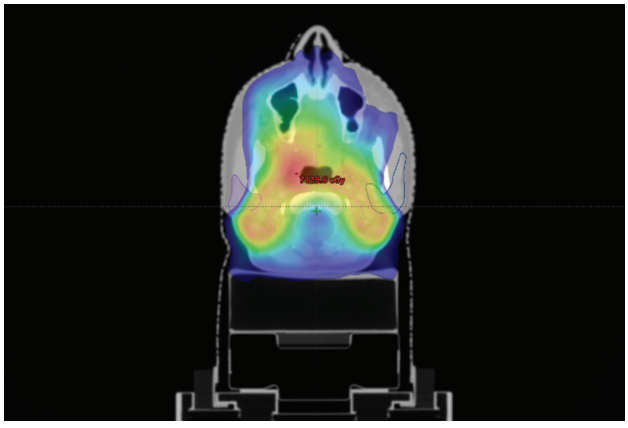


Figure 4. isodosesd 70Gy- 26 Gy



During the sixth week, the patient reported a stinging sensation from the benzydamine rinse. She was advised to stop rinsing with benzydamine and to increase rinsing with the supersaturated solution of calcium phosphate to 6 times a day. The patient completed treatment without interruption. Complete local and nodal regression was reported at the end of treatment. Grade III mucositis on the EORTC/RTOG scale was reported in the boost area (macroscopic disease receiving 2 Gy per fraction) (Fig. 5), along with grade II dysphagia according to EORTC/RTOG, grade II xerostomia according to EORTC/RTOG and dermatitis (Fig. 6).

Discussion

OM is a common side effect for patients with head and neck cancer treated with radiotherapy or radiochemotherapy. Radiation-induced OM produces oral pain, swallowing difficulties, loss of taste, nausea, vomiting, loss of appetite, fatigue, weight loss, and a decrease in quality of life. The biological model of mucositis from cancer therapy proposed by Sonis in 2004 provides insight into the pathobiology of this side effect.

This model presents the mechanism as a cascade of pro-inflammatory cytokines TNF-, IL-1, and IL-6 activated by free radicals. Management of OM is the subject of many publications every year. After a comprehensive systematic review of the literature, MASCC and ISOO reassessed the Clinical Practice Guidelines for OM in 2020 (9). The 2014 guidelines recommended benzydamine hydrochloride rinses to prevent OM in patients with head and neck cancer receiving moderate doses of radiation therapy of up to 50 Gy without concomitant chemotherapy (level I evidence) (10,11). A multicentre, randomized study comparing use of benzydamine hydrochloride to sodium bicarbonate rinse has showed that prophylaxis with benzydamine hydrochloride rinses can be more effective at reducing the severity of chemoradiotherapy-induced OM (12).

New guidelines (2020) have added benzydamine rinses as a recommendation for the prevention of OM in patients with head and neck cancer receiving radiochemotherapy (level II evidence) (9). Benzydamine hydrochloride mouthwash is a nonsteroidal anti-inflammatory agent with local analgesic and antibacterial properties (12). Use of benzydamine has been demonstrated in theory against a pro-inflammatory model activated by free radicals, and validated in practice (12). Both NCCN and EOCC recommend the use of benzydamine for the prevention and treatment of OM (12). The 42-year-old female patient who was treated at the Department of Head and Neck Cancer in Warsaw received standard supportive care during radiochemotherapy, including benzydamine mouthwash. She completed her therapy without interruption or severe side effects.

Summary points

Benzydamine helps prevent severe mucositis in patients with head and neck cancer treated with chemoradiotherapy.

Figure 5. Oral miucositis at the end of treatment

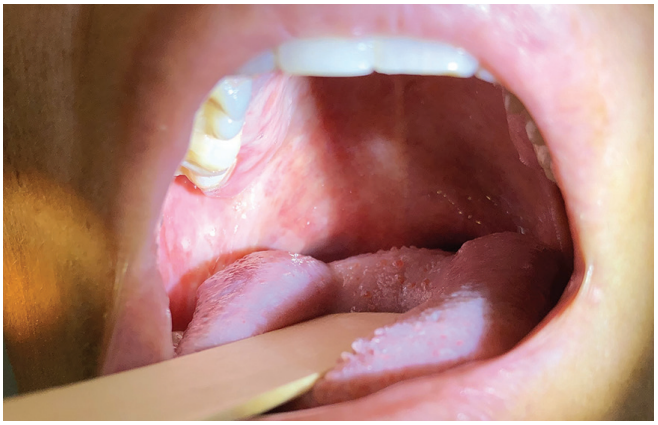
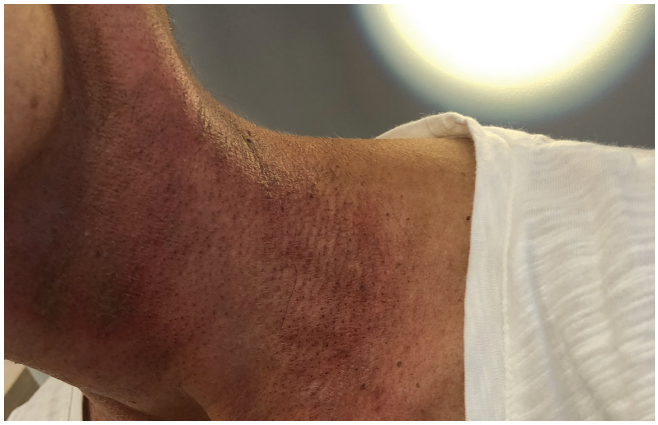


Figure 6. Dermatitis at the end of treatment



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Role of benzydamine mouthwash in the prevention of oral mucositis in a patient with tonsil cancer treated with chemoradiation therapy

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Abstract

Oral mucositis is one of the most common toxicities of cancer therapy. It occurs in almost all patients who receive radiation therapy where the treatment field includes areas of oral and oropharyngeal mucosa. Although it is rarely life-threatening, oral mucositis does interfere extensively with the treatment of cancer. Management of mucositis relies on the control of symptoms, along with measures to prevent complications, such as pain management, nutritional support, prophylaxis, and treatment of secondary infections. Oral care is a key factor in the prevention of oral injury. Other preventive measures include benzydamine mouthwash, photobiomodulation therapy, morphine mouthwash, glutamine and honey.

Here, we report the case of a healthy, middle-aged man, diagnosed and operated for tonsil cancer. He was found to have signs of microbiological colonization of the oral mucosa even before starting adjuvant chemoradiation therapy, which was indicated for his stage 4 disease. Antimicrobial treatment together with the preventive measures implemented and the patient's compliance helped prevent the worsening of his oral symptoms as he underwent cancer treatment and played an important role in his fast recovery.

Introduction

Oral mucositis (OM) has generally been a prominent toxicity of cancer therapies ever since radiation was first used to treat tumours. It occurs in almost all patients who receive radiation therapy where the treatment field includes areas of oral and oropharyngeal mucosa. Although it is rarely life-threatening, OM does interfere extensively with the treatment of cancer. Studies have shown that the risk of OM increases in step with the intensity of the therapy (1).

In its most advanced clinical form, OM presents as deep, confluent, and devastatingly painful ulcerations of the oral mucosa. However, like most diseases, mucositis is on a clinical continuum. In the beginning stages or in its mildest form, mucositis presents as mucosal erythema and is accompanied by a sensation of burning. Many patients go on to develop the more severe and classic form of mucositis, which is characterized by ulcerative lesions. Ulcer development is associated with increased pain and inability to tolerate normal foods. It is not unusual for patients with significant mucositis to refuse solid foods altogether. Any part of the movable mucosa can be involved, although the buccal mucosa, floor of the mouth, lateral borders of the tongue and soft palate are most frequently affected.

The more heavily keratinized mucosa is usually not involved in mucositis. Lesions in these areas are most commonly the consequence of a viral or fungal aetiology (2). Management of mucositis relies on the control of symptoms, along with measures to prevent complications, such as pain management, nutritional support, prophylaxis and the

treatment of secondary infections (3). Oral care is a key factor in the prevention of oral injury in patients with head and neck cancer. According to the Mucositis Guidelines of the Multinational Association of Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO), other preventive measures include benzydamine mouthwash as an anti-inflammatory agent, photobiomodulation therapy, topical morphine mouthwash for its analgesic effects, oral glutamine and honey (4).

Clinical case

This 56-year-old patient with a negative family history for cancer, and former smoker, with co-morbidities including arterial hypertension and chronic obstructive pulmonary disease (COPD), presented with a two-year history of sore throat, mostly when swallowing solids, and productive cough. After several courses of antibiotics to no effect, he was referred to ear nose and throat (ENT) specialists who, on clinical examination of the oropharynx and hypopharynx, identified the obvious tumour of the left tonsil with infiltration of the root of the tongue. The suspicious area was biopsied in January 2021, with the resulting histology analysis confirming grade 2, p16-negative squamous cell carcinoma of the left tonsil. The CT scan also confirmed the tumour of the left tonsil, with infiltration of the base of the tongue and pathological locoregional lymphadenopathy on the left side of the neck.

On the basis of these results, he underwent intraoral resection with the neck block dissection l.sin and prophylactic tracheotomy in February 2021. The outcome of final TNM staging was pT3pN3b, Stage IV disease with no spread to distant sites. A multidisciplinary meeting involving ENT specialits was held for this patient in which the decision was taken to go ahead with adjuvant chemoradiation. External beam radiation therapy was indicated using simultaneous integrated boost (SIB) RapidArcTM in three phases up to a total dose of 66 Gy, together with a regimen of weekly cisplatin in view of his co-morbidities. This treatment was administered from 21 April to 2 June 2021.

Given that most of the oropharynx was included in the irradiated field and that the radiation limits for the oral cavity are a maximum mean dose of 40 Gy, prophylactic measures had to be taken before starting radiotherapy to ensure the patient's good nutritional condition and to avoid OM for as long as possible. First, a percutaneous endoscopy gastrostomy (PEG) tube was inserted, and full enteral nutrition was prescribed. On initial physical examination by the radiation oncologist before the start treatment for the cancer, although the patient had good dental health, he was already found to have signs of microbiological colonization of the oral mucosa, mostly involving the hard palate and the dorsal surface of the tongue, with no problems of dysphagia. Microbiology swab testing confirmed colonization by several bacteria, including Pseudomonas, Klebsiella and Escherichia coli, along with candidiasis. Thus, this patient had to be placed on combined targeted antibiotic and antifungal therapy, just before the planned start of chemoradiation therapy.

Benzydamine mouthwash together with glutamine and other supportive products were advised to prevent the worsening of the oral symptoms as he underwent the cancer treatment. He was monitored carefully with routine check-ups every week before each administration of chemotherapy. After 14 days of antibiotics, preventive measures and good oral hygiene his mouth swab was negative. After 3 weeks of chemoradiation he began to have worsening dysphagia as a result of mild mucositis, which presented as a burning sensation and erythema, although he still tolerated fluids orally. On clinical examination after completion of his treatment, OM was still grade 1 according to RTOG (Radiation Therapy Oncology Group) criteria (5), with greater erythema but minimal fibrin-like coating. The patient was able to swallow fluids, however the PEG tube was used for nutritional support to maintain his physical strength and weight.

On clinical assessment, three weeks after finishing chemoradiotherapy, the patient was completely off the PEG tube and had no signs of OM, as required for tracheostomy and PEG tube removal.

Discussion

The implementation of OM prevention measures and addressing other complications through, for example, targeted antimicrobial treatment and anti-inflammatory agents, lead to better tolerability and outcomes in patients undergoing chemoradiation therapy for head and neck cancer. The MASCC/ISOO guidelines were first published in 2004. The latest edition from 2020 is updated with a new systematic review based on strong evidence. Our case

report is noteworthy as it describes a patient who, by following all the recommended preventive measures and demonstrating excellent compliance, was able to complete his cancer treatment without experiencing unpleasant side effects and achieved rapid recovery post treatment.

Summary points

In conclusion, OM is a burdensome toxicity of antineoplastic therapies for head and neck cancers and its treatment still remains a challenge.

By following the latest updated MASCC/ISOO guidelines and using the recommended anti-inflammatory prophylactic agents like benzydamine mouthwash, it is possible to achieve a good treatment response and minimal toxicity.

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Patient-related risk factors and management of oral mucositis in cancer patients undergoing palliative head and neck irradiation

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Abstract

Oral mucositis is one of the most common toxicity to radiation therapy for head and neck cancers. Risk of mucositis has been attributed to treatment-related factors and patient-related factors. Patient-related factors include oral care which, together with other preventive measures, including benzydamine mouthwash as an anti-inflammatory agent, are key factors in the prevention of oral injury. Therefore, it is essential to reduce microbial load and educate the patient regarding oral hygiene.

Here we report the case of a healthy, middle-aged man, diagnosed with and operated for tonsil cancer. We opted for palliative radiotherapy because the patient refused concomitant chemotherapy. Detailed information about proper oral hygiene and other preventive measures helped prevent early acute onset of oral mucositis symptoms at the end of week 1. Actual soreness and dysphagia had begun to build up by the end of week 3. However, poor oral health before treatment played a role in a longer recovery time.

Introduction

Oral mucositis (OM) is one of the most common toxicities to radiation therapy for head and neck cancers. It can limit the patient's ability to tolerate radiation therapy and, in addition to compromising nutritional status, it can have a dramatic effect on the patient's quality of life. The incidence and severity of OM will vary from patient to patient (1). It is also affected by radiation dose and field, and concomitant use of chemotherapy and radiation. Studies have shown that the risk of OM increases as the intensity of therapy increases (2). In general, when induced by radiotherapy, mucositis is less acute, in both its onset and resolution, than if induced by chemotherapy. Patients begin to develop mucosal soreness by the end of week 2, which then consolidates to form ulcers by the end of week 3. In a review of 33 studies involving approximately 6,000 patients, the mean incidence of OM in irradiated patients was found to be 80% (3). Not all patients are at equal risk of OM, however. Risk of mucositis has been attributed to treatment-related factors and patient-related factors. Patient-related factors include age, malnutrition, gender, pre-existing medical conditions, alterations in salivary production, poor oral health, malignancy type and mucosal trauma (4). Poor dental health has been identified as an environmental factor that can increase the severity of OM (5).

Oral care is a key factor in the prevention of oral injury. Therefore, it is essential to reduce microbial load and educate the patient regarding oral hygiene. Diet also plays a role in oral health. Therefore, patients should be advised on selecting foods that promote oral health. Since patients can experience changes in taste and appetite, along with dysphagia, food recommendations should balance the need to maintain intake with the increased risk of oral disease. Regular oral assessment during therapy is an important part of a programme to ensure maximum oral health (6). According to the Mucositis Guidelines of the Multinational Association of

Supportive Care in Cancer (MASCC) and the International Society of Oral Oncology (ISOO), other preventive measures include benzydamine mouthwash as an anti-inflammatory agent, photobiomodulation therapy, topical morphine mouthwash for its analgesic effects, oral glutamine and honey (7).

Clinical case

The case presented is that of a 57-year-old active smoker and chronic abuser of alcohol, with a negative family history of cancer. On clinical examination he was found to have a large, ulcerated tumour of the left oropharynx, with obvious infiltration of the hard and soft palate and the retromolar trigone. From the confirmatory biopsy conducted in December 2020, the histopathology findings were of grade 2, p16-negative squamous cell carcinoma of the left tonsil. A local CT scan confirmed a very advanced tumour of the tonsil with a left-sided pathological lymphadenopathy, classified clinically as cT4acN2a, stage IVA disease with no distant metastases. Surgical management was ruled out and he was referred for further oncological treatment. The original potentially curative intent of our management changed to palliative after he refused to receive concurrent chemotherapy. We opted for hypofractionated one-phase external beam radiotherapy in 18x3 Gy fractions, which he underwent from February to March 2021.

The patient's poor oral health resulting from his social condition, advanced disease and his status as an active smoker, along with the fact that the entire oropharynx would be included in the irradiated field led us to choose percutaneous endoscopic gastrostomy (PEG) as the first prophylactic measure to secure enteral nutrition, as he had already had difficulty swallowing solids before starting radiation therapy. A detailed explanation was provided to him of the importance of oral hygiene as a key factor in the prevention and mitigation of later oral injury (8). Other preventive measures, including benzydamine mouthwash and enteral use of glutamine, were also advised. He was also prescribed analgesics for painful trismus and mucosal coating agents. Clinical and mucositis assessments were held on a weekly basis, and he was still tolerating enteral supplements orally at the end of week 2 of radiation therapy. Actual soreness and mucositis without obvious ulcerations, but with build-up of a fibrin-like coating on the hard palate, had appeared by the end of week 3, without microbial colonization, according to mouth swab findings. At this point he became fully dependent on the PEG tube. On treatment completion, the patient's OM was classed as grade 2–3 according to the Radiation Therapy Oncology Group (RTOG) scale and he began to lose weight rapidly. Although his oral symptoms had resolved completely four weeks post radiation therapy, oral realimentation was only started more than three months after treatment. A post-treatment PET/CT scan did not show a complete response to radiation therapy, thus he was placed on systemic palliative treatment.

Discussion

The importance of oral care alongside other preventive measures, including benzydamine mouthwash as an anti-inflammatory agent, are key factors in the prevention of oral injury in patients undergoing head and neck irradiation.

Our case report is noteworthy as it describes a patient who, by following the preventive instructions provided, managed, despite poor oral health before treatment, to complete palliative cancer treatment without early acute onset of the symptoms of OM in the first weeks of radiotherapy.

Summary points

In conclusion, OM is one of the most common toxicities to radiation therapy for head and neck cancers.

Following the latest guidelines for prevention, including detailed education about the importance of oral hygiene and using recommended anti-inflammatory prophylactic agents including benzydamine mouthwash, it is possible to delay acute onset of the symptoms of OM.

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