



Review Article

Open Access, Volume 4

Oral Tissue Lesions Manifestation in Cancer Patients Following Chemotherapy and Head and Neck Radiation Therapy

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Abstract

Background: As is known, cancer therapy includes a complex of therapeutic measures: chemotherapy, radiotherapy and radical.

The purpose of this study was to review the literature on the main oral tissue complications arising from chemotherapy and radiation therapy in the head and neck region.

Methods: In Google Scholar, Medline, Scopus, Web of Sciences, PubMed a systematic review was conducted. Search keywords terms included: Cancer patients, oral tissue lesions, head and neck, chemotherapy, radiation therapy. Conducted a preliminary search and reviewed 134 titles and abstracts in this literary review included 58. Cancer patients in the oral cavity exhibit a variety of oral tissue lesions during and shortly after radiation therapy to the head and neck.

Results: Our search showed that cancer patients following chemotherapy and head and neck radiation therapy often experience oral manifestations. Among these lesions, increased susceptibility to dental caries, periodontal disease, oral mucositis, tissue fibrosis, salivary gland dysfunction, opportunistic infections of the mucous membranes, and neurosensory disorders are often encountered.

These manifestations represent a serious problem for patients and require special strategies from treating physicians to mitigate the harmful effects of radiation therapy on vital functions and improve the quality of life of these patients. Complications in the oral cavity, chemotherapy and head and neck radiation therapy creates many social problems and difficulties for cancer patients. Arguments for an interdisciplinary approach to the management of these patients are recommended in many studies.

Conclusion: This review will help dental practitioners manage the risks of dental interventions and prevent potential complications in patients with cancer requiring dental care. Prevention, supportive care, and symptom management by health care providers are important for patients with oral problems related to cancer treatment and can help the patient cope with cancer and its complications.

Keywords: Oral manifestation; Head and neck; Cancer; Chemotherapy; Radiation therapy.

Manuscript Information: Received: Dec 26, 2023; Accepted: Feb 07, 2024; Published: Feb 14, 2024

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Citation: Mathevosyan D, Hakobyan G. Oral Tissue Lesions Manifestation Cancer Patients Following Chemotherapy and Head and Neck Radiation Therapy. *J Oncology*. 2024; 4(1): 1127.

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Introduction

The American Cancer Society estimates that in 2023, the number of new cases and deaths of oropharyngeal cancer will be 54,540 and 11,580, respectively [1].

In patients with oropharyngeal cancers chemotherapy and head and neck radiation therapy associated with cancer treatment leads to numerous side effects, their overall survival and quality of life [2,3].

Treatment of malignant diseases can lead to inevitable lesions to the oral organs, including the mucous membrane, since the oral cavity is very sensitive to the toxic effects of chemotherapy and ionizing radiation [4].

The current times to reduce the side effects of chemotherapy and head and neck radiation therapy include the use of minimally invasive surgical techniques whenever possible (transoral robotic surgery, transoral laser microsurgery) [5]. Etiopathogenesis oral complications associated with chemotherapy and radiation therapy for cancer are multifactorial [6]. Chemotherapy and radiation therapy lead to the death of basal epithelial cells.

One of the main reasons is damage to oral tissues, disruption of normal healing, weakening of the immune system due to loss of tissue immune cells [7,8].

Chemotherapy and radiation therapy can cause changes in the salivary glands that produce saliva and the protective components of saliva [9,10]. Chemotherapy and radiation therapy slow or stop the growth of new cells. Other factors may also play a role, including proinflammatory cytokines and bacterial metabolic products. Chemotherapy disrupts the replication of basal epithelial cells. During chemotherapy, the mucous membrane of the lip, cheek, tongue, floor of the mouth and soft palate is affected to a greater extent than the hard palate and gums, covered with keratinized and adjacent tissue, which is associated with the relative rate of renewal of epithelial cells in the tissue of the oral mucosa with the submucosal layer [11]. Radiation therapy can directly damage and destroy oral tissue, salivary glands, and bones. Complications in the oral cavity during cancer chemotherapy include, dental caries, periodontitis, mucositis, fibrosis, oropharyngeal candidiasis, oral infection (viral, fungal, bacterial), salivary gland hypofunction and xerostomia, neurosensory disorders (mucosal pain and taste dysfunction) [12-14]. Some chemotherapy drugs (Methotrexate, Doxorubicin, 5-FU, Busulfan, Bleomycin, cisplatin and carboplatin, rapamycin) tend to damage the oral mucosa [15].

Oral complications of cancer chemotherapy develop during therapy and once chemotherapy is stopped, the damaged tissue usually recovers. With high-dose chemotherapy, during the first 2-3 weeks of therapy, approximately 40% of patients develop ulcerative mucositis it progresses to ulceration and becomes covered with a whitish pseudomembrane and surrounded by an erythematous zone and which requires complex medical intervention [16,17]. Ulcerative lesions are painful and can lead to significant functional impairment affecting oral function, including nutrition, which can lead to weight loss. Patients' quality of life is significantly impaired [18,20]. Other oral complications of complications of chemotherapy oropharyngeal candidia (pseudomembranous and erythematous candidiasis, angular cheilitis) [21,22].

Clinical manifestation Candidiasis can range from no symptoms to burning, a plaque sensation in the mouth, dysgeusia (often described as a metallic taste) and a yeast infection odor [23]. This lesion manifests itself with pain in the mucous membrane, changes in taste and can spread to the esophagus and lead to dysphagia [24]. This may make eating difficult and may negatively affect nutritional status and ability to take oral medications. Patients receiving chemotherapy drugs are predisposed to the risk of periodontal disease, which can cause tooth loss [25,30]. The reasons may be hyposalivation, decreased protective effect of saliva, changes in the oral microbiome with a shift towards the flora associated with periodontal disease.

Chronic asymptomatic periodontal disease focus of chronic infection and bacterial cell wall substances and inflammatory cytokines may migrate into the bloodstream thereby increasing the prevalence of pulmonary infections in patients. On the contrary, complications of radiation therapy of cancer develop both during therapy but also develop after cessation, causing irreversible tissue damage, leading to a deterioration in the patient's quality of life. Complications in the oral cavity during and after cancer radiation therapy include mucositis, infections, saliva change, fibrosis, sensory dysfunctions, dental caries, periodontal disease, and osteoradionecrosis [31,32]. In patients with head and neck cancer the incidence of radiation therapy-induced oral mucositis varies depending on the treatment regimen used and individual patient characteristics and occurs in the majority of patients [33-35]. Symptoms of radiation mucositis appear at a dose of 15Gy (about 10 days) and progress to full severity at a dose of 30Gy and persist until completion of radiotherapy. Radiation mucositis within 3 weeks after completion of treatment tends to heal, and chronic mucosal lesions have also been reported membranes of the oral cavity, lasting more than 3 months.

Patients after radiation therapy have an increased risk of dental caries. Demineralization first appears as enlarged white lesions at the gum line and cusp tips of the teeth. Subsequently untreated caries at this stage can quickly progress and the process of damage to the teeth at a deeper level will begin. With complications of caries, there is a need for tooth extraction, which, against the background of high doses of radiation therapy in this area, may increase the risk of osteoradionecrosis, which dictates timely treatment and prevention of caries. The main reason for the occurrence caries in patients, hyposalivation, changes in the composition of saliva pH. These changes can disrupt the balance of demineralization - remineralization, this leads to loss of minerals, damage to the organic phase of tooth structures. Among the late complications of various structures of the maxillofacial area exposed to irradiation, damage to blood vessels, nerves and muscles, lymphatic vessels can occur. With radiotherapy, one of the late complications is fibrosis of the lingual muscles, pharyngeal constrictor muscles, which can affect the function of the tongue and swallowing.

Radiotherapy can also lead to fibrosis of the masseter muscles (masseter, temporalis, medial and lateral pterygoid muscles) which can lead to trismus [36]. Trismus makes it difficult to chew, swallow, and speak, which can impair digestion [37,39]. Late side effects of radiation therapy may include temporomandibular disease and fibrosis, which limits the function of the lips and tongue [40-42]. Osteoradionecrosis can develop at any time af-

ter radiation therapy [43]. Radiation damage differs from changes caused by chemotherapy in that when irradiated tissues undergo irreversible damage, which puts the patient at risk of developing complications in the oral cavity [44]. With cancer radiation therapy the cause of osteoradionecrosis is ischemic bone necrosis associated with necrosis of soft tissues without the presence of a tumor [45,47].

In the pre-fibrotic phase of the histomorphometric analysis, increased activity of endothelial cells and inflammation is observed; in the subsequent phase, abnormal activity of fibroblasts is observed in the final phase of fibroatrophic remodeling and loss of osteocytes in the bone occurs. Histopathological analysis shows in the first phase hyperemia, endarteritis and thrombosis in the subsequent phase, observed with cell loss, hypovascularization, increased bone marrow fat and fibrosis [48,49].

Treatment of osteoradionecrosis includes the use of medications, ultrasound, hyperbaric oxygenation, as well as surgical resection and reconstruction in the absence of late respons [50,52]. The best approach to the treatment of osteoradionecrosis is prevention [53]. To prevent complications and achieve optimal integrated oral care for patients, ongoing chemotherapy and radiotherapy is key is an organization of oral care rooms in oncology centers to reduce the risk of this complication, it is very important to pre-treat existing diseases of the oral cavity and in this aspect, the cooperation of the dentist and oncologist as a team is very important. All of these complications of oral cancer therapy lead to secondary dehydration, dysgeusia and malnutrition and can directly affect patient survival.

Assessing oral health during cancer therapy and promptly treating oral lesions before initiating chemotherapy and radiation therapy are critical to minimizing the risk of oral lesions and associated systemic complications [54,55]. Treatment is symptomatic, for pain relief, topical analgesics may be useful.

For oral care, it is recommended to use standardized oral care protocols [56]. Despite the constant updating of protocols for the management of patients in this category, there are no universally effective protocols for preventing side effects of chemotherapy and radiation therapy for cancer [57,58]. Arguments for an interdisciplinary approach to the management of these patients are recommended in many studies. The main role of the dentist during chemotherapy and radiation therapy is to minimize undesirable effects and timely treatment of complications. Prevention, supportive care, and symptom management by health care providers are important for patients with oral problems related to cancer treatment and can help the patient cope with cancer and its complications.

Declarations

Conflicts of interest statement: All the authors declare no conflicts of interest.

Funding: No funding.

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