

# PATHOLOGICAL ASPECTS OF THE ORAL MUCOSA CAUSED BY CHEMOTHERAPY OR RADIOTHERAPY IN PATIENTS WITH CERVICAL MALIGNANT ADENOPATHIES. DRY MOUTH AND ORAL MUCOSITIS

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**Keywords:** oral mucositis, xerostomia, chemotherapy, radiotherapy, cancer

**Abstract:** Chemotherapy and radiation therapy are the modern methods for the treatment of cancer disease, which in the last decade has seen a dynamic development. Most of the times, cancer pathology requires in terms of curative surgical and therapeutic perspective adjunctive therapy namely chemotherapy or radiotherapy.

**Cuvinte cheie:** mucozită orală, xerostomie, chimioterapie, radioterapie, proces canceros

**Rezumat:** Chimioterapia și radioterapia reprezintă metode moderne de tratament a bolii canceroase, care în ultimul deceniu au cunoscut o dezvoltare vertiginoasă. De cele mai multe, ori patologia canceroasă necesită din punct de vedere al perspectivei terapeutice curative chirurgicale și terapie adjuvantă respectiv chimioterapie sau radioterapie.

Oral mucositis is a major complication of short duration postchemo or radiation therapy generated by local effects of radiant therapy of head and neck cancers on the oral mucosa, but also by systemic effects of cytotoxic agents of chemotherapy. It generally occurs 4-10 days after starting adjuvant therapy and lasts up to 7-14 days.

**Figure no. 1. Patient 1. B., 62 years have oral mucositis in the ventral face of the tongue and in the mouth angle postirradiation**



From the point of view of oral mucositis pathophysiology this is the result of a complex interaction involving factors such as local tissue damage, the buccal environment, the level of myelosuppression of the patient but also the inherent predisposition to develop all these conditions.

Pathogenesis of oral mucositis incriminates direct and indirect mechanisms. Chemotherapy and radiation therapy presents increased efficiency in destroying cancer cells, which are cells that divide rapidly, and cells with an increased rate of cellular turnover.

Unfortunately, the human body contains many normal cells showing an increased rate of cellular turnover and which may be affected also like the cancer cells by chemotherapy or radiotherapy. The oral cavity is composed of cells with a high proliferative activity (which divide rapidly) due to which it is more sensitive to the effects of adjuvant therapy which through direct mechanisms interferes with the cells turnover and generates oral mucositis.

Indirect stomatotoxic effects resulting from the release of the inflammation mediators, loss of the salivary protective constituents, and therapeutic induced neutropenia contributes to the development of oral mucositis and promotes the emergence of opportunistic infections with gram negative bacteria, and fungal species in the lining of the oral cavity.

New pathophysiological concepts describe 4 phases in the production of oral mucositis: initial inflammatory phase/vascular, epithelial, ulcerative and healing.

The release of free radicals, modified protein and of the proinflammatory cytokines (Interleukin 1 B, prostaglandins, TNF- $\alpha$ ) by the exposed cells (epithelial, endothelial cells, and connective tissue) inducing initial inflammatory phase through production of oral tissue damage.

The second phase, namely the epithelial phase is responsible for the appearance of the oral mucosa erythema and it's mediated by cytotoxic effect or proapoptosis of chemo or radiation therapy by inhibiting cell division in the oral mucosa epithelium.

Daily routine which involves mundane activities such as mastication, deglutition or speaking may encounter difficulties because these activities can represent microtraumas for oral mucosa already aggrieved, inducing ulceration.

Ulcerative phase/bacteriology (pseudomembrana) usually occurs after 7 days of chemotherapy treatment and is produced by epithelial apoptosis and by the formation of a fibrinous exudate which generates pseudomembranes and ulcerations. In this phase are promoted opportunistic infections with gram negative bacteria or fungal species through microbial

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## CLINICAL ASPECTS

colonization of the existing oral lesions.

Ulcerative oral mucositis is an important factor in the etiology of systemic infections with streptococcus in neutropenic cancer patients.

The rate of proliferation of oral epithelium, restoring the local microbial flora and the absence of the factors which interfere with the healing process are factors that influence the healing phase of oral mucositis, which takes place usually between 12-16 days.

The erythema, the edema, the burning sensation from the oral cavity mucosa as well as increased sensitivity to hot or spicy foods are the initial symptoms of oral mucositis of cancerous patient's.

The areas affected with predilection by oral mucositis are represented by the nekeringating moving mucosa of the soft palate, cheeks, lips, ventral surface of the tongue and buccal floor, while the gum, the dorsal surface of the tongue and hard palate are rarely affected due to the low rate of cellular turnover.

Oral mucositis healing is usually without the formation of scars except the case when mucositis is complicated with severe infection or xerostomia.

Another common complication of radiotherapy is xerostomia or dry mouth which has a negative impact on the quality of life such as oral mucositis and which can be acute or chronic.

As a response to the inflammatory reaction of the salivary glands from radiation therapy appears acute xerostomia, while chronic xerostomia may occur up to a year postradiotherapy being produced by the fibrozation phenomenon of the salivary glands. Usually, xerostomia is permanent.

**Figure no. 2. Schirmer modified test**



**Figure no. 3. The result of Schirmer modified test indicates hyposalivation**



The severity of the xerostomia is subject to the dose of radiation to which the patient was exposed but also the volume of the exposed salivary gland, namely if the total dose of radiation exceeds 5.200 cGy, the salivary flow is reduced, and

the saliva that crosses the salivary ducts is very little drooling or absent.

Usually during the first week of radiation the first changes in the oral cavity are occurring, namely that it causes a decrease in the salivary flow, the saliva becoming more viscous and more vitriolic. In addition to quantitative changes occurs qualitative salivary changes consisting in reduction of the buffer capacity of the saliva and salivary pH.

Both the irradiation dose applied and the amount of glandular tissue exposed represents two key factors in determining the degree of glandular hypofunction which influences the degree of destruction of the salivary glands, the severity of the xerostomia is being subjected to the initial volume of the salivary glands, especially the parotid.

Parotid glands are most sensitive to radiation, followed by the submandibular, sublingual and small salivary glands. Pathophysiology postirradiation xerostomia describes vascular damage, appearance in nerve transmission interference or destruction of glandular parenchyma.

### Conclusions:

Oral mucositis and xerostomia are common complications of chemotherapy and radiotherapy which may adversely affect the development of adjuvant therapy and the conduct of the patient's life.

Although it is a short-term complications, oral mucositis can damage the treatment of malignant cervical adenopathy, decreased quality of life by limiting the patient's nutritional status and patient tolerance to anticancer therapies therefore more attention should be paid to the prevention of this disease.

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