The Management of Oral Mucositis, Angular Cheilitis and Acute Pseudomembranous Candidiasis Induced by Radiotherapy and Chemotherapy Treatment of Nasopharyngeal Cancer Patient

Supriatno[1], Fauzi Adityawan Pritama[2], Sartari Entin Yuletnawati[3]

[1]Associated Professor at Department of Oral Medicine, Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia, [2]Student of Faculty of Dentistry, Muhammadiyah University of Surakarta, Indonesia, [3]Lecturer at Faculty of Dentistry, Muhammadiyah University of Surakarta, Indonesia

Abstract

Radio-chemotherapy of the head and neck area can cause mucositis in cases of nasopharyngeal cancer that is felt as swallowing pain, dry mouth and loss of taste. This condition is often exacerbated by the onset of candidiasis on the oral mucosa. The aim of the case report was to inform the side effects of chemotherapy and radiotherapy treatments in nasopharyngeal cancer patients that occur in the oral cavity include angular cheilitis, acute pseudomembranous candidiasis and oral mucositis type 1 and their management. Case report, a 69 year old-man, came to the dental clinic of the Sardjito hospital with complaints of pain to swallow food, and his mouth had many white spots. Complaints were felt one week after the 3rd chemotherapy and 9th radiotherapy. The patient was diagnosed with nasopharyngeal cancer (NPC) with T2N3M0 classification. Clinical examination showed the presence of a white layer on the mucosa of the tongue, cheeks, palate and lip mucosa. The entire oral mucosa was dark red, and angular cheilitis on both corners of the lips was found. Treatment of this case by eliminating the necrotic tissue and debris by 3% hydrogen peroxide solution mouth rinse and administration of drugs, including candystin droops and betadine mouth rinse for 1 week. The patient can swallow and eat a little hard without any more pain after 1 week treatment. Clinical examination found that the white spots on the tongue, palate, cheeks and lips were gone. The color of the oral mucosa appeared the same as the surrounding tissue. The oral hygiene and general conditions were good. In conclusion, oral mucositis and acute pseudomembranous candidiasis due to chemo-radiotherapy treatment in nasopharyngeal cancer patient were disappearing, and the oral condition has improved. Patients can chew and swallow food without any pain.

Keywords*: nasopharyngeal cancer, oral mucositis type 1, candidiasis, angular cheilitis, chemotherapy, radiotherapy*

Introduction

Radiotherapy and chemotherapy in the head and neck area in case of nasopharyngeal cancer involves a large portion of the oral mucosa and the parotid gland. As a result, there will be side effects on the oral mucosa in the form of radiation mucositis in acute circumstances that the patient feels as swallowing pain, dry mouth (hyposalivation) and loss of taste. This condition is often exacerbated by the emergence of candidiasis infections in the mucosa of the tongue, cheeks and palate.[1] Oral mucositis can affect a patient's quality of life, increase the risk of infection, and cause failure of cancer treatment itself. The incidence of oral mucositis is estimated at 40% in patients receiving chemotherapy, 70% -90% in patients undergoing blood transplants and bone marrow stem cells, and 80 -100% in patients undergoing radiotherapy involving the oropharynx

Corresponding Author:
Dr. Supriatno., DDS.,
M.Health., MDSc., Ph.D
Department of Oral Medicine, Faculty of Dentistry,
Universitas Gadjah Mada, Yogyakarta, 55281
Tel & Fax: +62-0274-515307
E-mail: supriatno_fkg@ugm.ac.id

region.[2] Mukositis is an ulceration and pain-causing inflammation in the mucous membrane layer caused by the effects of cancer treatment using chemotherapy and radiotherapy.[3] It was reported that 100% oral mucositis occurs in patients receiving high-dose chemotherapy and hematopoietic stem cell transplantation, while 80% occur in cancer of the head receiving radiotherapy.[4] Diagnosis of oral mucositis is based on symptoms that arise in oral tissue due to chemotherapy, spinal cord transplantation or radiotherapy. Ulceration with the appearance of red burn-like sores in the mouth is sufficient to diagnose oral mucositis.[5]

Oral candidiasis is a fungal infection that often occurs together with oral mucositis on radiotherapy treatments. Oral candidiasis is caused by Candida albicans species which can be acute or subacute, the infection is seen as a white layer on the mucosa of the cheeks, tongue, lips and palate. If the layer is lifted, the mucosa will bleed, the mouth feels dry and burning, and the taste sensitivity on the tongue decreased.[6]

In the present case, the side effects of chemotherapy and radiotherapy treatments in nasopharyngeal cancer patients that occur in the oral cavity in the form of acute pseudomembranous candidiasis (thrush), angular cheilitis and oral mucositis and their management were informed.

Case Report

A 69 year old man came to the Dental clinic in the reference from the Internal Medicine Department, Dr. Sardjito Hospital. He was complaint of pain to swallow food, and his mouth had many white spots. Complaints were felt one week ago with the mouth feeling dry and difficult to swallow food, so patients rarely consumed food. A few days later, white patches appeared on the edge of the tongue and other mouth areas (Figure 1).

Figure 1. The oral condition of the patient at the first visit

Medical history showed the patient had nasopharyngeal cancer (NPC) with T2N3M0 classification or grade 3. The patient had received the 3rd chemotherapy treatment using carboplatin 100 mg in a 500 cc 0.9% NaCl solution in 90 minutes, and the 9th radiotherapy. During the treatment at the Internal medicine department, the patient received vomceran injection 8 mg/24 hours intravenous (i.v) and dexamethasone injection 2 ampules / 24 hours i.v. Past dental history, the patient had ever extracted and filled teeth in Dr. Sardjito hospital, 4 years ago. Clinical examination found a white layer on the lateral right and left tongue, posterior dorsum of the tongue, right and left cheek mucosa, hard and soft palate, and mucosa of the upper and lower lips. Gingivitis appeared at all oral regions, oral mucosa was dark red, and cheilitis angular at both corners of the lips (Figure 2).

Figure 2. Patients with acute candidiasis pseudomembran, mucositis and angular cheilitis

Based on clinical examination and oral mucositis classification according to WHO,[5] patient was diagnosed with degree 1 radiation mucositis. Examination of vital signs showed blood pressure 130/80 mmHg, pulses 84 times/minute, respiration 20 times/minute, temperature 38.5^0C, and general condition: thin and weak.

Treatment was done by removing the necrotic tissue and debris using mouth rinse of 3% hydrogen peroxide solution for 1 minute 3 times a day. Medication consisted of candystin droops and betadine gargle for 1 week. Control patient at 1st visit, he can swallow and eat a little hard food, including meat, soft vegetables and side dishes that were not fried without any pain. Objective examination found a white layer on the tongue, palate, cheeks and lips had disappeared. Mild gingivitis at the anterior lower area still exists. Furthermore, the oral hygiene and general conditions were good. The color of the oral mucosa was the same as the surrounding tissue (Figure 3). Vital signs at 1st control revealed the blood pressure 120/60 mmHg, pulse 80 times/min,

respiration 20 times/min, and afebrile. Suggestions for patient included maintaining oral hygiene, continuing mouthwash, cleaning tartar and calculus, and finally making dental prostheses.

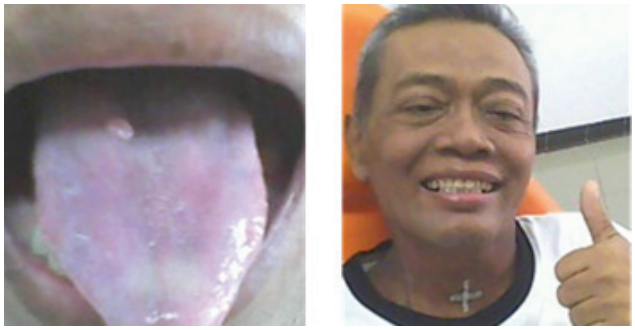

Figure 3. The oral mucositis and acute pseudomembranous candidiasis have healed, the patient did not feel pain and can swallow solid food. Finally, the patient looks happy.

Discussion

Treatment of the head and neck cancer includes nasopharyngeal cancer has a variety of problems that require careful handling by considering many factors that will affect the final outcome of treatment. Patients with smoking habits or heavy alcohol drinkers have a tendency to fail in radiation therapy followed by the lower tolerance of mucosal tissue to radiation.[7] Head and neck cancers have a type of histological anaplastic carcinoma that is sensitive to radiation. Other types such as squamous carcinoma and transitional carcinoma have lower levels of radiation sensitivity compared to anaplastic carcinoma. Nasopharyngeal cancer has the property of rapid propagation through the lymph channels to the neck lymph nodes and infiltratively to the skull base which can result in paralysis of some cranial nerves, especially the optic nerve.[8] It was reported that based on the radiation field area and radiation dose given to the neck region, the parotid gland can be ensured to have a disorder that causes hyposalivation and radiation mucositis.[7]

In this case, nasopharyngeal cancer patients had a T2N3M0 classification with complaints of pain when ingesting food. The oral mucosa was covered with fungi and angular cheilitis on both corners of the lips. Patients consumed less food so that the patient's body weight drops dramatically. This complaint was felt after receiving the 9th radiation therapy and 3rd chemotherapy. Moreover, the patient had undergone radiation mucositis with symptoms as described above,[1] namely pain due to dry mouth (xerostomia), the entire mucosa experiences erythematous, and loss of taste. According to WHO classification,[5] patient suffered from grade 1 oral mucositis, with the criteria that there was widespread erythema, and the patient cannot swallow solid food. These symptoms are compounded by the onset of candidiasis in the mucosa of the tongue, cheeks and palate. Interestingly, the patient's oral mucosa had experienced increased sensitivity due to radiation therapy in the nasopharyngeal irradiation. It was proven that radiotherapy was effective and successful because tissue sensitivity increased after chemotherapy.[1]

Oral mucositis is one of the most complications of chemotherapy and radiotherapy treatments. This result was produced from the cytotoxic effects of chemotherapy materials and the local effects of radiation on the oral mucosa. Oral mucositis is an oral mucosal inflammation with reddish-colored mucosal symptoms to severe ulceration. The mucositis symptoms are vary from pain to discomfort to the taste and mastication of food. Severe oral mucositis can cause treatment to be longer so that the secondary infection is easy to arise.[4] Patients who have the risk of developing oral mucositis need to get good and correct oral care with the aim of maintaining oral hygiene and preventing opportunistic infections through damage to the oral mucosa. Pull-out and treatment of dental caries must be done before radiation therapy, as well as education about the importance of oral hygiene and dental health.

Oral candidiasis is established based on clinical features supported by laboratory examination.[9] White patches that can be removed with the basis of erythema on the tongue, cheeks, palate and buccal mucosa show a picture of acute pseudomembranous candidiasis, while cracked lip angles describe angular cheilitis. It was reported that the most common infection in patients undergoing head and neck radiotherapy was candidiasis, and the most frequently involved candida species were Candida albican which is an opportunistic infectious agent.[10] Patients with decreased oral mucosal damage and immunity due to radiotherapy tend to occur opportunistic infection in his oral cavity. In this case, various factors that can increase susceptibility to oral candidiasis were decreased salivary production, changes in mucosal epithelium, nutritional deficiencies, and poor oral health.[11] Saliva is important in maintaining normal oral microflora. Saliva dilutes pathogenic antigens and mechanically cleanses the mucosa. Salivary antibodies (sIgA) and nonspecific antimicrobial factors are

important to reduce fungal attachment and colonization, therefore decreased salivary flow due to radiotherapy spurs candida infection in this patient. Radiation to the head-neck region can change the speed of normal epithelial replacement, causing a direct cytotoxic effect that can change the integrity of oral epithelium and promote secondary infection. Nutritional deficiencies can cause a decrease in body resistance and loss of cell integrity, which will facilitate candida invasion and infections.[2] Poor oral hygiene helps a conductive environment in increasing colonization and attachment of candida. It has been reported that oral mucositis can be aggravated by candidiasis because the infection aggravates mucosal epithelial damage.[12]

Treatment of oral mucositis, angular cheilitis and acute candidiasis as a side effect of irradiation in nasopharyngeal cancer patient was by removing necrotic tissue and debris by 3% hydrogen peroxide solution mouth rinse, and giving medication of candystin droops and betadine gargle for 1 week. Perhydrol (hydrogen peroxide) 3% solution is a strong oxidizer, used as a disinfectant, antiseptic, and includes bacterial agents that have generally recognized as safe (GRAS).[13] Nystatin is an antifungal drug that is effective and sensitive to candida infections, and safer if given orally like topical administration because of its minimal absorption through mucocutaneous membranes. The mechanism action of nystatin is by binding to ergosterol, a major component of the fungi cell membrane. Nystatin can cause membrane leakage of fungal cells which results in the release of K + ions and the death of these fungi cells.[14] Betadine gargel is a mouthwash containing 1% povidone iodine, one of the strongest antiseptics in the oral cavity. Betadine also has an antiviral and antibacterial effect that is widely used for inflammation of the oral cavity. Betadine can overcome throat and mouth problems such as itching, sore throat, phlegmon, tonsillitis, hoarseness, canker sores to bad breath.[15]

Based on the treatment that had been given it was known that patients can already swallow and eat a little hard food including meat, soft vegetables and side dishes that were not fried, without any complaints of pain. White spots on the tongue, palate, cheeks and lips were gone, angular cheilitis had disappeared, although mild gingivitis in the lower anterior area still exists. Interestingly, the general condition of the patient was good and he can eat a lot.

In conclusion, acute pseudomembranous candidiasis and oral mucositis type 1 as a result of combination of chemotherapy and radiotherapy treatments in nasopharyngeal cancer patients had disappeared and oral conditions had improved. Current clinical management of oral mucositis and acute candidiasis is largely focused on palliative measures such as pain management, nutritional support and maintenance of good oral hygiene. However, several promising therapeutic agents are in various stages of clinical development for the management of oral mucositis and acute candidiasis. In this case, the results of treatment given to patient was in accordance with the expectations of the operator.

Source of Funding: This work was supported by Grant from the Ministry of Research and Technology of Higher education, Republic of Indonesia, through BPP-UGM T.A 2018.

Conflict of Interest: The author declares no conflict of interest.

Ethical Clearance: All the clinical treatment procedure has been ethically approved by the Ethical Committee of Faculty of Dentistry, Universitas Gadjah Mada, Yogyakarta, Indonesia.

References

1. Susworo R. Nasopharyngeal cancer, epidemiology and current treatment. The world mirror med 2004; 144: 16-19.
2. Sufiawati I. Identification and control of oral mucositis risk factors during radiotherapy of nasopharyngeal cancer. Padjadjaran University Tesis, Bandung, 2008.
3. Ridge JA, Glisson BS, Lango MN: Head and Neck Tumors in Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds) Cancer Management: A Multidisciplinary Approach. 11 ed. 2008. P. 254-78.
4. Rubenstein EB: Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. Cancer 2004; 100 (9 Suppl):2026-2046.
5. Sonis ST, Eilers JP, & Epstein JB: Validation of a new scoring system for the assessment of clinical trial research of oral mucositis induced by radiation or chemotherapy. Mucositis Study Group. Cancer 1999; 85:2103-2113.

6. Patussi C, Sassi LM, Munhoz EC, Zanicotti RT, Schussel JL.Clinical assessment of oral mucositis and candidiasis compare to chemotherapic nadir in transplanted patients. Braz Oral Res. 2014; 28:1-7.
7. Djakaria M.Radiotherapy in several types of head and neck cancers. In Head and Neck Tumors, Diagnosis and therapy. FK UI press, 1993, Jakarta.
8. Marcial VA, Gelber R, Kramer S, Snow JB, Davis IW, & Vallecillo IA: Does preoperative irradiation increase the rate of surgical complications in carcinoma of the head and neck?. Cancer 1982; 49:1297-1302.
9. Rubenstein EB: Clinical practice guidelines for the prevention and treatment of cancer therapy-induced oral and gastrointestinal mucositis. Cancer 2004; 100 (9 Suppl):2026-46.
10. Cawley MM, Benson LM: Current Trends in Managing Oral Mucositis. Clin J Oncol Nurs 2005; 9(5):584-592.
11. Supriatno. Biocompatible inhibition of Alpinia galangal rhizome extract of rubra varieties on the growth of Candida albicans. Postgraduate Thesis Program, Airlangga University, Surabaya. 1998.
12. Ridge JA, Glisson BS, Lango MN: Head and Neck Tumors in Pazdur R, Wagman LD, Camphausen KA, Hoskins WJ (Eds). Cancers Management: A Multidisciplinary Approach. 11 ed. 2008. P. 254-78.
13. Jones CW & Clark JH: Applications of Hydrogen Peroxide and Derivatives. Royal Soc Chem, 1999.
14. Akaike N, Harata N: Nystatin perforated patch recording and its applications to analyses of intracellular mechanisms. Jpn J Physiol 1994; 44 (5): 433–73.
15. Mangano A, Albertin A, La Colla L: Povidone-iodine versus chlorhexidine in skin antisepsis before elective plastic surgery procedures: a randomized controlled trial. is statistical correctness always pursued ?. Plast Reconstr Surg. 2009; 124(3): 1014.