MULTIDISCIPLINARY APPROACH ON ORAL SIDE EFFECT OF CHEMOTHERAPY TREATMENT: A CASE REPORT

Mohamad Zulfikar Idris[1], Widya Apsari[2], Anandina Irmagita Soegyanto[3*]

[1]Oral Medicine Residency Program Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia
[2]Oral Medicine Division, Department of Dentistry, Dharmais Cancer Hospital, Jakarta, Indonesia.
[3]Department of Oral Medicine, Faculty of Dentistry, Universitas Indonesia, Jakarta, Indonesia

Corresponding Email: **anandina.irmagita74@ui.ac.id**

ABSTRACT

Introduction: *Chemotherapy is one of nasopharyngeal cancer treatment used to improve the patient's quality of life, but it can cause several side effects such as mucositis, salivary gland dysfunction, and pain, that might lead to secondary complications like dysgeusia and malnutrition.* ***Objectives:*** *This article will discusses a case of oral side effects of chemotherapy treated with multidisciplinary approach.* ***Case Presentation:*** *A 58-year-old male patient who underwent 4th time neoadjuvant chemotherapy for nasopharyngeal cancer was referred to oral medicine specialist of Dharmais Cancer Hospital from hemato-oncology division with mouth and throat pain and dysphagia since 3 days ago, with 5 kgs of weight loss in two weeks due to eating difficulties. Intraoral examination showed multiple ulcers surrounded by erythema on almost all oral mucosa, with white pseudomembranous on the gingiva, dorsum tongue and buccal mucosa. The working diagnosis were grade IV Oral Mucositis, pseudomembranous candidiasis, and mild malnutrition.* ***Case Management:*** *The patient was treated with multidisciplinary team of hemato-oncologist, nutrition specialist, nurse, and oral medicine specialist, while Nystatin oral suspension 100.000IU, NaCl 0.9% gargle, and methylprednisolone 4 mg were administered for oral lesions. After three days, patient's clinical condition showed improvement in oral mucositis lesion and complete healing of oral candidiasis, restoring patient's ability to talk and eat solid food.* ***Conclusion:*** *In managing oral side effects of chemotherapy, it is essential to apply multidisciplinary approach and patient compliance encouragement to follow proper instruction and perform follow-up visits.*

Keywords: *chemotherapy, candidiasis, mucositis, multidisciplinary approach.*

INTRODUCTION

Nasopharyngeal carcinoma (NPC) is an epithelial cancer that develops from the mucosal lining of the nasopharynx, and is one of the top five most frequent malignant tumors, with the head and neck region taking the top spot.[1,2] Data from GLOBOCAN 2020, NPC is the 4th ranked of head and neck cancer with the new cases of NPC is 133.354 and Asia become the 1st ranked wordwide. In indonesia the number of new cases of NPC is19.943 and become the 5th most cancer in Indonesia.[3]

Advanced NPC is typically treated with a combination of radiation and chemotherapy (CT). [4] Chemotherapeutic drugs are a diverse class of substances used to either induce apoptosis in cancer cells or stop them from the replication and targeting quickly proliferating cells to achieve their toxic effects.[5] The delivery of chemotherapy is possible in neoadjuvant, adjuvant, combination, and metastatic settings. A treatment administered prior to the main therapy is called neoadjuvant CT.[6]

Side-effects of CT observed directly or late in life, such as nephrotoxicity, hepatotoxicity, neurotoxicity, cardiotoxicity, hematological toxicity, ototoxicity and gastro-intestinal toxicity.[7] Chemotherapy also can cause a variety of oral side effects, including oral mucositis (OM), candidiasis, and other infections, xerostomia, oral bleeding, nausea, vomiting, and difficulty swallowing.[5] All of these conditions can affect a patient's ability to eat well, cause weight loss, and lower their quality of life, which can raise the cost of therapy and impact the disease's prognosis.[8] This case report will discuss about the management of oral side effect of chemotherapy requires a holistic approach, including of hemato-oncologist, nutrition specialist, nurse, and oral medicine specialist, to provide patients with a proper care.

CASE REPORT

A-58-years old male patient was referred to oral medicine specialist of Dharmais Cancer Hospital from hemato-oncology division with complaint of mouth and throat pain, difficulty in opening his mouth, dysphagia and also dry mouth since 3 days ago, with 5 kgs of weight loss in two weeks due to eating obstacles and getting diagnosed with mild malnutrition the nutrition specialist. He was a T4N2M0 nasopharyngeal cancer patient who had already receive 4th time neoadjuvant chemotherapy (NACT) with cisplastin and 5-fluorouacil (5-FU) and planned to had chemoradiation therapy, hereafter. Due to his oral complaints, the patient was fitted with a nasogastric tube (NGT) to support his nutritional intake. He went to dentist a month prior this visit for focus infection elimination and fluoridation.

Extra oral examination showed no abnormality, while intra oral examination revealed multiple extensive ulceration surrounded by erythema on almost all oral mucosa (Figure 1), with white pseudomembranous patches on the gingiva, dorsum tongue and buccal mucosa (Figure 2).

a b

The complete blood count result was within normal limits.

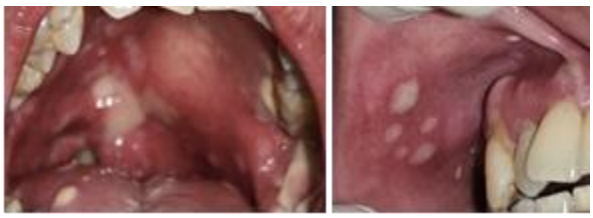

Figure 1.

a) oral mucositis on palatum and oropharynx area, b) oral mucositis on labial mucosa at 1st visit.

Figure 2.

Oral candidiasis at 1st visit.

Based on the subjective and objective examination, the working diagnosis established were Oral Mucositis grade IV, pseudomembranous candidiasis, and xerostomia.

CASE MANAGEMENT

The patient was treated by multidisciplinary team that consisted of hemato-oncologist, nutrition specialist, nurse, and oral medicine specialist. The hemato-onclogist decided to delay the chemotherapy commencement and waited for the general condition improvement and prescribed the patient with intravenous cefotaxime 3x1/gram and mycamin 2x50 mg. The nutrition specialist recommended NGT feeding of 1700 Kcal, contained of 70 grams protein, high potassium filtered porridge, filtered snacks and 2x250 ml of special diet supplement. Meanwhile, treatment from oral medicine specialist for the patient's oral conditions consisted of NaCl 0.9% solution to be gargled for 1-2 minutes 4x10ml/day and nystatin oral suspension 100.000IU 4x1ml/day to be swished and swallowed, along with methylprednisolone 3x4mg peroral for three days. The patient was refrain from eating, drinking, or rinsing 30 minutes after gargling with NaCl, and apply the nystatin drops 30 minutes hereafter. On follow-up visit, 3rd days after the first encounter, the patient admitted that his oral condition was better, his talking ability was returned and he could drink and eat solid food again. Intraoral examination showed improvement of oral mucositis lesion that decrease from grade IV to grade II, which the clinical sign showed size decrease of the ulceration and patient able to eat solid food (Figure 3), complete healing of oral candidiasis (Figure 4) and improved of his dry mouth. Based on the improved condition, the use of nystatin drops and methylprednisolone were discontinued and the patient was returned to hemato-oncologist division to continue his NPC treatment.

Figure 3.

Oral mucositis on a) palatum and oropharynx, b) labial mucosa showed improvement after 3rd days.

Figure 4.

Oral candidiasis completely healed after 3rd days.

DISCUSSION

In this case report, the diagnosis of oral mucositis grade IV was established based on subjective and objective examination of which revealed multiple ulcer of the mucosa, along with pain and disability to eat, drink, and talk, . One of the most common and irritable side effects of chemotherapy is oral mucositis (OM), which can affect the non-keratinized mucosa of the soft palate, ventral tongue/floor of mouth, and buccal and labial mucosa and characterized by the development of ulcerative erosive lesions after erythema and edema of the oral and oropharyngeal mucosa. OM starts 5–10 days after the start of chemotherapy and lasts for 7–14 days.[9,10] The scale of OM providing by WHO combines subjective and objective aspect and classifies into four grades: grade 0, normal; grade I, soreness with/without erythema; grade II, presence of ulceration and erythema; grade III, ulceration and extensive erythema, disability to eat solid food; grade IV, alimentation is not possible.[11] The functional abilities of the patient may be severely compromised by this lesion because it can be extremely uncomfortable.

The current understanding of chemotherapy-induced OM pathogenesis of is mainly described by a "stage model" which consist of 5 phase: (a) Initiation of oral mucosal damage, (b) Injured mucosa releases reactive oxygen species generation (ROS) which damage DNA, (c) damage amplification due to the host inflammation response, and (d) mucosal ulceration as a result of epithelial apoptosis and necrosis, and ultimately followed by (e) healing stage, keratinocytes, stimulated by extracellular matrix, migrate and proliferate to reconstruct epithelial layers.[12,13] Based on our patient condition, that showed multiple extensive ulcers and surrounded by erythema on almost all oral mucosa, that was in correspond with the pathogenesis of the oral mucositis, which is on the ulceration phase.

There are currently few evidence-based options for the prevention and treatment of oral mucositis, despite its prevalence, impact on patients' health, and financial consequences. The ideal goal would be one that emphasizes prevention as well as nutritional support and the prophylaxis/treatment of secondary infection.[14,15] The Multinational Association of Supportive Care in Cancer/International Society of Oral Oncology (MASCC/ ISOO) recommends interventions for the prevention or treatment of OM begins with assessment and oral hygiene measures, diet modifications,

and pain management.[15,16] One of the oral care regimens advised by clinical practice guidelines for radiation or chemotherapy-induced OM is mouth rinsing. When giving normal saline or sodium bicarbonate to the chemotherapy patient, the solutions might reduce the mild to moderate pain of mucositis and increase their comfort. Gargling with frequently enough hydrate the mouth, prevent crusting, and giving sooting effect to the mucosa.[16,17] We also prescribed patient with methylprednisolone for treat the OM because it's potent antiinflammatory effect and considering the mechanism of OM. This consist with the study from *saito et al.*, that corticosteroid agents can be used as prevention or treatment of CT induced OM.[18] The follow up after 3rd days of therapy, patient admitted that the pain is release and he can eat and swallow solid food.

In this case report, diagnosis of oral candidiasis also established based on the clinical oral mucosal examination which revealed white pseudomembranous patches that can be removed and leaving erythematous area. During the progression of chemotherapy, myelosuppression may occur and may be linked to an increase in the frequency of opportunistic infection of bacterial, viral, and fungal. The patient's immunological status is known to be further weakened by the use of radiation therapy, chemotherapy, or a combination of the two, predisposing these patients to opportunistic infections such oral candidiasis. Oral candidiasis present as white pseudomembranous, scrapable and leaving erythematous area, most commonly on the tongue and buccal mucosa. Candida albicans is predominantly involved in OM.[17,19] About 20–40% of chemotherapy patients develop oral candidiasis.[8] Treatment for cancer may impair the host's immune system and worsen the C. albicans infection. Anticancer medications inhibit neutrophil activity, cause neutrophil depletion, and increase C. albicans virulence. In addition, cytotoxic drugs used in CT cause dryness of the oral mucosa, which facilitates infections by various pathogens, including fungi and also causing OM and changes in the salivary glands that result in quantitative and qualitative changes in saliva, where thick saliva also creates a favorable environment for fungal colonization. Antibiotics and other CT-related medications may alter the oral flora, increasing the risk of Candida overgrowth.[19,20] The predisposing factor of oral candidiasis in this case including, local and systemic condition that influenced by the side effect of CT such as mild nutrition, xerostomia and mucositis. Our patient also suffer from xerostomia, that may lead to speech difficulty and loss of appetite. Xerostomia is a potential side effect of chemotherapy that characterized by subjective sesnsation of dry mouth and is typically accompanied by a decrease in salivary flow. This condition also can be one of predisposing factor of oral candidiasis.[21]

The oral cavity is particularly vulnerable to both the direct and indirect harmful effects of chemotherapy because of the rapid rate of cellular turnover, the microflora and oral tissue injury associated with routine oral function.[22]

Infection, oral mucositis, bleeding, dry mouth, periodontal disease, dysphagia, and altered senses of smell, taste, are among the most common oral adverse effects of CT.[23] Approximately 60% of chemotherapy patients experienced at least one or more oral symptoms.[24] In this case, patient was suffer from pain in the mouth and throat leading to difficult to eat and drink, dry mouth and fungi infection that consist as the oral side effect of the CT.

This case also showed that sometimes it is impossible or very difficult for patient under chemoterapeutic to eat and swallow because to the severe oral adverse effect of CT. Patients who experience nausea, vomiting, dysphagia, oral mucositis, or dry mouth may lose the desire to eat. This explains why soft and liquid diets may be necessary. Their quality of life might be drastically reduced, disrupting daily routines and social interactions, and this condition can increase their risk of malnutrition and dehydration.[9,22] Sometimes, patients who are anticipated to experience severe oral mucositis symptoms have a nasogastric tube inserted as a preventative measure.[25] This unfavorable consequence may also discourage patients from sticking with their chemotherapy program, leading to incomplete or delayed treatment and a lower chance of cancer cure.[9]

Incorporating a multidisciplinary approach has made it easier for clinicians to satisfy the expanding demands of cancer patients. The best method for identifying and treating cancer is a multidisciplinary approach, which is a developing field of oncology.[22,26] The goal of this team, which consists of all the specialist engaged in a patient's care, is to speed up professional meetings and interactions and, as a result, shorten the time it takes to diagnose and/or start treating a patient.[27] Depending on the type of cancer, the "core team" typically consists of oncologists, pathologists, radiotherapists, and other specialists.[26] In this case report, it is shown that the multidisciplinary team consisted of hemato-oncologist, nutrition specialist, nurse, and oral medicine specialist work together to treat the oral side effect of chemotherapy and its impact to patient’s systemic condition.

The majority of people with mucositis experience significant reductions in quality of life due to pain. To enhance patients' quality of life and shorten the length of time to stay in the hospital, oral mucositis must be managed properly.[25] The role of the dentist is essential in the care of patient before, during, and after the chemotherapy, because not only provide benefit terms of eradicating oral foci quickly and safely, but also positve impact on oral status and improve patien’s quality of life.[27,28]

CONCLUSION

In managing oral side effects of chemotherapy treatment, it is essential to apply multidisciplinary approach and patient compliance encouragement to follow proper instruction and perform follow up visits.

REFERENCES

1. Yang SS, Guo JG, Liu JN, Liu ZQ, Chen EN, Chen CY, et al. Effect of Induction Chemotherapy in Nasopharyngeal Carcinoma: An Updated Meta-Analysis. Front Oncol. 2021;10(January):1–9.
2. Suryoseto R. Radiotherapy with Neoadjuvant Chemotherapy on Nasopharyngeal Carcinoma (NPC) Advanced Stage. International Journal of Nasopharyngeal Carcinoma (IJNPC). 2021;03(01):20–4.
3. Global Cancer Observatory (GLOBOCAN): Cancer Today. International Agency for Research on Cancer; 2020. Accessed June 19, 2023. https://gco.iarc.fr/today/data/factsheets/cancers/4-Nasopharynx-fact-sheet.pdf
4. Chan WL, Chow JCH, Xu Z yuan, Li J, Kwong WTG, Ng WT, et al. Management of Nasopharyngeal Carcinoma in Elderly Patients. Front Oncol [Internet]. 2022;12. Available from: https://www.frontiersin.org/articles/10.3389/fonc.2022.810690
5. Harris JA, Ottaviani G, Treister NS, Hanna GJ. An Overview of Clinical Oncology and Impact on Oral Health. Frontiers in Oral Health. 2022;3(April):1–8
6. Amjad MT, Chidharla A, Kasi. A. Cancer Chemotherapy [Updated 2023 Feb 27] [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK564367/
7. van den Boogaard WMC, Komninos DSJ, Vermeij WP. Chemotherapy Side-Effects: Not All DNA Damage Is Equal. Cancers (Basel). 2022;14(3):1–27.
8. Liang L, Liu Z, Zhu H, Wang H, Wei Y, Ning X, et al. Efficacy and safety of thalidomide in preventing oral mucositis in patients with nasopharyngeal carcinoma undergoing concurrent chemoradiotherapy: A multicenter, open-label, randomized controlled trial. Cancer. 2022;128(7):1467–74.
9. Yasmin Mohamed Ali, Mohamed Sabry El–Kady, Hanan Said Ali, Dalia Abd-Allah Abdelatief, Shimaa Nabil Abdelslam. Effect of educational guidelines on reducing chemotherapy induced oral mucositis based on patients' needs assessment. International Journal of Research in Pharmaceutical Sciences. 2020;11(SPL4):2570–4.
10. Pavithran S, Sreeleksmi M V., Sreelekshmi R. Oral-health related quality of life of patients on chemotheray. Biomedical and Pharmacology Journal. 2020;13(1):107–18.
11. Jena S, Hasan S, Panigrahi R, Das P, Mishra N, Saeed S. Chemotherapy-associated oral complications in a south Indian population: a cross-sectional study. J Med Life. 2022;2022(4):470–8.
12. Poulopoulos A, Papadopoulos P, Andreadis D. Chemotherapy: oral side effects and dental interventions. A review of the literature. Stomatological Disease and Science. 2017;1(2):35–49.

13. Chaveli-López B, Bagán-Sebastián J V. Treatment of oral mucositis due to chemotherapy. J Clin Exp Dent. 2016;8(2):e201–9.
14. Shankar A, Roy S, Bhandari M, Rath GK, Biswas AS, Kanodia R, et al. Current trends in management of oral mucositis in cancer treatment. Asian Pacific Journal of Cancer Prevention. 2017;18(8):2019–26.
15. Jané-Salas E, Escobar-Álvarez Y, Álvarez-García R, García-Miragall E, Clemente-Tejada L, Beorlegui-Murillo P, et al. Consensus on Oral Care in Cancer Patients Multidisciplinary Consensus on Oral Care in Cancer Patients.
16. Huang BS, Wu SC, Lin CY, Fan KH, Chang JTC, Chen SC. The effectiveness of a saline mouth rinse regimen and education programme on radiation-induced oral mucositis and quality of life in oral cavity cancer patients: A randomised controlled trial. Eur J Cancer Care (Engl). 2018;27(2):1–10.
17. Brown TJ, Gupta A. Management of cancer therapy-associated oral mucositis. J Oncol Pract. 2020;16(3):103–9.
18. Saito Y, Takekuma Y, Takeshita T, Oshino T, Sugawara M. Impact of systemic dexamethasone administration on oral mucositis induced by anthracycline-containing regimens in breast cancer treatment. Sci Rep [Internet]. 2022;12(1):1–8. Available from: https://doi.org/10.1038/s41598-022-16935-4
19. Aslani N, Janbabaei G, Abastabar M, Meis JF, Babaeian M, Khodavaisy S, et al. Identification of uncommon oral yeasts from cancer patients by MALDI-TOF mass spectrometry. BMC Infect Dis. 2018;18(1):1–11.
20. Berardi R, Morgese F, Rinaldi S, Torniai M, Mentrasti G, Scortichini L, et al. Benefits and limitations of a multidisciplinary approach in cancer patient management. Cancer Manag Res. 2020;12:9363–74.
21. Pinto VL, Fustinoni SM, Nazário ACP, Facina G, Elias S. Prevalence of xerostomia in women during breast cancer chemotherapy. Rev Bras Enferm. 2020;73(Suppl 4):e20190785.
22. Begoña GC, Figuero E, Castelo B&, José-Luis C carretero, Cerero-Lapiedra Rocío. Prevalence of oral side effects of chemotherapy and its relationship with periodontal risk: a cross sectional study. Supportive Care in Cancer. 2019;27.
23. Arghavan T. The Prevalence of Chemotherapy Induced Oral Lesions in Cancer Patients. Oral and Maxillofacial Pathology Journal. 2020;24–6.
24. Kusiak A, Alicjajereczek-Fossa B, Cichońska D, Alterio D. Oncological-therapy related oral mucositis as an interdisciplinary problem—literature review. Int J Environ Res Public Health. 2020;17(7).
25. Scott B. Multidisciplinary Team Approach in Cancer Care: A Review of The Latest Advancements.

Multidisciplinary Team Approach in Cancer Care:A Review of The Latest Advancements. 2021;(November):1–13.

26. Taberna M, Gil Moncayo F, Jané-Salas E, Antonio M, Arribas L, Vilajosana E, et al. The Multidisciplinary Team (MDT) Approach and Quality of Care. Front Oncol. 2020;10(March):1–16.
27. Bertl K, Savvidis P, Kukla EB, Schneider S, Zauza K, Bruckmann C, et al. Including dental professionals in the multidisciplinary treatment team of head and neck cancer patients improves long-term oral health status. Clin Oral Investig [Internet]. 2022;26(3):2937–48. Available from: https://doi.org/10.1007/s00784-021-04276-x