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Case Report

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Nisin ZP Combined with Limited Chemotherapy in Oropharyngeal Squamous Cell Carcinoma: A Case Report

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Abstract

Objective: This case report describes and discusses the therapeutic potential of nisin ZP as adjunctive therapy in patients with oral squamous cell carcinoma (OSCC).

Case Report: A 43-year-old Asian male with OSCC initiated treatment with Paclitaxel and Cisplatin chemotherapy. Nisin ZP was administrated during and after the chemotherapy.

Results: The patient experienced symptom relief and significant tumor regression following administration of nisin ZP.

Conclusion: Nisin ZP shows promising potential as an adjunctive therapy for OSCC, offering symptom relief and contributing to tumor size reduction.

Keywords: Nisin ZP; Oral squamous cell carcinoma; Adjunctive therapy.

Introduction

Oral squamous cell carcinoma (OSCC) is a common oral cancer that originates from squamous cells. The complexities of OSCC present formidable treatment challenges, given its impact on essential functions like swallowing, speech, and respiration [1]. Considering the variability in outcomes and notable side effects associated with standard cancer treatments, including chemotherapy and targeted therapies, the pursuit of novel, effective treatments becomes imperative [2].

Innovative therapeutic strategies include the use of antimicrobial agents. Among these, nisin, a natural antimicrobial peptide produced by the gram positive Lactococcus lactis probiotic, has emerged as a promising candidate for cancer treatment [3]. Due to its broad spectrum activity against both Gram-positive and Gram-negative bacteria [4], [5], nisin is renowned for its role as a natural food preservative in the food industry [6], [7]. Its FDA-approved status and established safety for human consumption have spurred substantial interest in exploring its therapeutic potential beyond food preservation. Recent attention has focused on the potential of nisin, particularly its ultrapurified form, nisin ZP, as a viable option for cancer treatment [8], [9]. Studies have unveiled the selective effects of nisin against cancer cells while preserving healthy cells, positioning nisin as a promising agent for cancer therapy.

In this context, we present a unique case report where incorporating nisin ZP alongside chemotherapy reduced tumor size in a patient with OSCC. By evaluating the therapeutic role of nisin, our aim is to fortify the growing body of evidence supporting nisin as an adjunctive treatment for cancer.

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Case Report

The case involves a 43-year-old Asian male presenting with a diagnosis of OSCC involving the left buccal mucosa posterior to the maxillary premolar region and left oropharynx, with extension to the base of the tongue (cT1N1M0, Stage III). The patient's condition was characterized using computed tomography (CT) imaging, which disclosed a soft tissue mass situated within the left lateral oropharynx, with involvement of the base of the tongue (Figure 1). The measured size of this mass was approximately 11 x 9 mm, adjacent to the left mandibular angle. Bilateral maxillary sinuses exhibited mucosal thickening and calcifications indicative of maxillary sinusitis (Figure 2), accompanied by increased density changes in the maxillofacial and skull base bones, suggesting sclerosis. Notably, an enlarged lymph node was detected at the left mandibular angle, while several bilateral cervical lymph nodes showed slight enlargement. No evidence of distant metastases in other organs was observed, although certain limitations in evaluation were encountered due to pseudoshadows in CT.

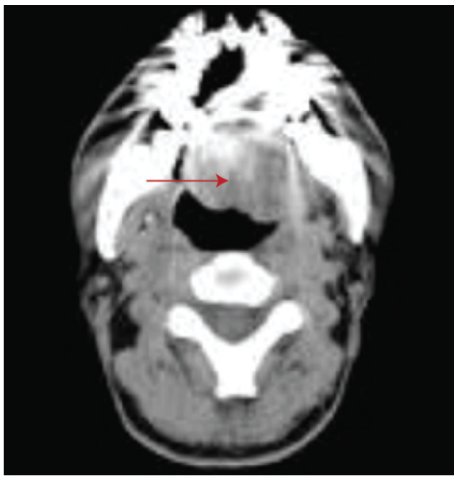


Figure 1: Soft tissue mass in the left lateral oropharynx (pointed by the arrow).

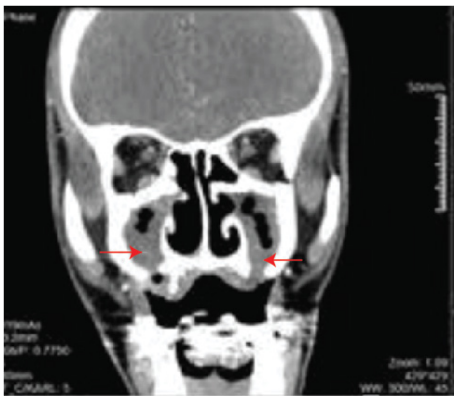
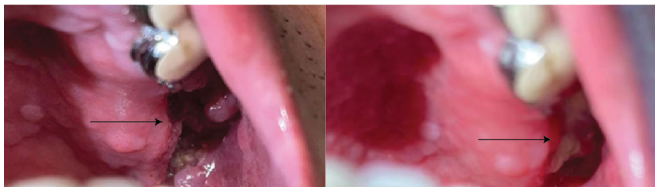


Figure 2: Sinus mucosal thickening and intrasinus calcification (pointed by the arrow).

A biopsy procedure yielded a dark gray-yellow specimen, measuring 0.5 x 0.5 x 0.3 cm, collected from the left oropharynx. The subsequent histopathological examination confirmed the presence of squamous cell carcinoma. These findings underscored the intricate nature of oral cancer, emphasizing the necessity for a comprehensive treatment approach.

The patient's treatment started on June 17, 2023, with the initiation of the first round of chemotherapy, comprised of a 270 mg Paclitaxel injection and 140 mg Cisplatin injection. During the chemotherapy session, 1g nisin ZP was administered twice daily. Subsequently, from July 1 to July 23, the patient continued with nisin ZP (Handary) treatment, receiving 0.8g nisin ZP with 160g lemon juice twice daily.

Remarkably, after 23 days of nisin administration coupled with a single round of chemotherapy, the patient experienced relief from symptoms and a significant reduction in OSCC lesion size (Figure 3). Notably, due to certain circumstances, the patient received 300 mg of Trastuzumab on July 12, a targeted therapy for HER2-positive cancer [10]; however, the expected responses were not achieved. Subsequent genetic analysis revealed a mutation in Notch1 (c.166C>T) but no mutation in Her2, potentially explaining the suboptimal Trastuzumab response. Consequently, the patient chose to continue chemotherapy while also receiving ongoing administration of nisin ZP. As of March 2024, the patient has shown alleviated symptoms with significant reduction in tumor size.



(A) (B)

Figure 3: (A) OSCC lesion at the left buccal mucosa before the first chemotherapy on June 17th. (B) Reduced lesion size after 23-day nisin administration. (pointed by arrows)

Discussion

This report discusses a case where a patient diagnosed with OSCC experienced reduced symptoms following nisin ZP administration combined with a single round of chemotherapy. This case report supports the same findings from another prior case report in a patient with tongue OSCC [11]. While the simultaneous use of nisin ZP and chemotherapy presents challenges in isolating their individual effects, the potential role of nisin ZP in enhancing the treatment and possibly reducing the required chemotherapy warrants attention. Typically, chemotherapy extends over a span of 3 to 6 months. However, the patient's substantial alleviation of symptoms following just one chemotherapy session, coupled

with a 23-day course of nisin ZP administration, underscores the potential pivotal role of nisin ZP in cancer treatment.

Investigations have demonstrated the selective toxicity of nisin and nisin ZP against diverse cancer cell types, including non-small cell lung cancer [12] (NSCLC), hepatocellular carcinoma [13], cervical cancer [8], and head and neck squamous cell carcinoma (HNSCC) [3], [14], [15]. Nisin ZP was originally shown to mediate selective apoptosis and cell cycle arrest in OSCCC cells compared to primary oral keratinocytes via specific modulation of calcium ion influxes and CHAC1 signaling [14]. Subsequently, others have shown the same effects of nisin ZP on NSCLC cells, leading to apoptosis, cell cycle arrest, and mitochondrial membrane depolarization [12]. Similar promising outcomes have been observed in hepatocellular carcinoma, where growth inhibition and apoptosis induction have been observed, alongside potential benefits in countering drug resistance mechanisms [13]. Furthermore, nisin has exhibited apoptotic activity through mitochondrial dysfunction and oxidative stress in cervical cancer cells. In the context of HNSCC, both nisin and nisin ZP exhibit anti-tumor effects, with nisin ZP displaying enhanced potency, primarily mediated via a calpain-dependent apoptosis pathway [3], [14]. Despite these significant findings and the proposed calcium ion fluxes and CHAC1 signaling that have been proposed as the mechanistic effects of nisin, the precise mechanisms of nisin's anti-cancer actions warrant further exploration. The NOTCH signaling pathway has been implicated as hyperactive in several cancers. The presence of a Notch1 mutation in the patient suggests that nisin may reduce tumor size via the inhibition of the NOTCH signaling pathway.

Nisin's safety profile and validation enhances its potential as a cancer treatment. Notably, a 90-day subchronic toxicity study in rats found no adverse effects [16]. That study observed no significant adverse effects with 225 mg nisin A/kg body weight per day. The feasibility of large-scale production and purification further strengthens its potential as an adjunct therapy for cancer patients.

Conclusion

The alleviation of cancer symptoms following nisin treatment, coupled with its demonstrated selective toxicity against cancer cells, suggests its potential application in cancer treatment. As our understanding of its role in cancer therapy continues to evolve, nisin may prove to be a valuable adjunctive treatment alongside conventional therapies, potentially improving patient outcomes. A phase I/II clinical trial is planned to further investigate the efficacy and safety of nisin as an adjunct treatment for cancer. This National Cancer Institute funded clinical trial with Nisin ZP to treat patients with oral cancer specifically with OSCC is starting to recruit patients in March, 2024 (https://clinicaltrials.gov/study/NCT06097468).

References

1. Ihara Y, Kato H, Tashimo Y, Iizumi Y, Fukunishi Y, et al. Changes in oral function, swallowing function, and quality of life in patients with head and neck cancer: a prospective cohort study. BMC Oral Health 22 (2022): 293.
2. Johnson DE, Burtness B, Leemans CR, Lui VWY, Bauman JE, et al. Head and neck squamous cell carcinoma. Nat Rev Dis Primer 6 (2020): 1-92.
3. Kamarajan P, Hayami T, Matte B, Liu Y, Danciu T, et al. Nisin ZP, a Bacteriocin and Food Preservative, Inhibits Head and Neck Cancer Tumorigenesis and Prolongs Survival. PLoS ONE 10 (2015): e0131008.
4. Zhao C, Kuraji R, Ye C, Gao L, Radaic A, et al. Nisin a probiotic bacteriocin mitigates brain microbiome dysbiosis and Alzheimer's disease-like neuroinflammation triggered by periodontal disease. J Neuroinflammation 20 (2023): 228.
5. Shin JM, Gwak JW, Kamarajan P, Fenno JC, Rickard AH, et al. Biomedical Applications of Nisin. J Appl Microbiol 120 (2016): 1449–1465.
6. Popa EE, Miteluț AC, Râpă M, Popescu PA, Drăghici MC, et al. Antimicrobial Active Packaging Containing Nisin for Preservation of Products of Animal Origin: An Overview. Foods 11 (2022): 3820.
7. Anumudu C, Hart A, Miri T, Onyeaka H. Recent Advances in the Application of the Antimicrobial Peptide Nisin in the Inactivation of Spore-Forming Bacteria in Foods. Mol 26 (2021): 5552.
8. Sadri H, Aghaei M, Akbari V. Nisin induces apoptosis in cervical cancer cells via reactive oxygen species generation and mitochondrial membrane potential changes. Biochim Biol Cell 100 (2022): 136–141.
9. Patil SM, Barji DS, Sophia Aziz S, McChesney DA, Bagde S, et al. Pulmonary delivery of spray-dried Nisin ZP antimicrobial peptide for non-small cell lung cancer (NSCLC) treatment. Int J Pharm 634 (2023): 122641.
10. Pollock NI, Grandis JR. HER2 as a Therapeutic Target in Head and Neck Squamous Cell Carcinoma. Clin. Cancer Res Off J Am Assoc Cancer Res 21 (2015): 526–533.
11. Wendy Fu, Yvonne L Kapila. Nisin, A Probiotic Bacteriocin, Combined with Limited Chemoradiation Therapy in Head and Neck Cancer. Arch Clin Med Case Rep 5 (2021): 531-536.
12. Patil SM, Kunda NK. Nisin ZP an Antimicrobial Peptide, Induces Cell Death and Inhibits Non-Small Cell Lung Cancer (NSCLC) Progression in vitro in 2D and 3D Cell Culture. Pharm Res 39 (2022): 2859–2870.

Ye Q, et al., Arch Clin Med Case Rep 2024
DOI:10.26502/acmcr.96550671

13. Balcik-Ercin P, Sever B. An investigation of bacteriocin nisin anti-cancer effects and FZD7 protein interactions in liver cancer cells. Chem Biol Interact 366 (2022): 110152.

14. Joo NE, Ritchie K, Kamarajan P, Miao D, Kapila YL. Nisin, an apoptogenic bacteriocin and food preservative, attenuates HNSCC tumorigenesis via CHAC1. Cancer Med 1 (2012): 295–305.

15. Kamarajan P, Ateia I, Shin JM, Fenno JC, Le C, et al. Periodontal pathogens promote cancer aggressivity via TLR/MyD88 triggered activation of Integrin/FAK signaling that is therapeutically reversible by a probiotic bacteriocin. PLoS Pathog 16 (2020): e1008881.

16. EFSA Panel on Food Additives and Nutrient Sources added to Food (ANS), Younes M, Aggett P, Aguilar F, Crebelli R, et al. Safety of nisin (E 234) as a food additive in the light of new toxicological data and the proposed extension of use. EFSA J Eur Food Saf Auth 15 (2017): e05063.