International Summit on Science Technology and Humanity
ISETH 2024
ISSN: 2615-1588 (online)

The Effect of Radiotherapy on Skin Reactions in Nasopharynx Cancer Patient

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Abstract

Nasopharyngeal cancer is a squamous cell carcinoma with a high frequency in East and Southeast Asia. Radiotherapy is the main treatment method often used in the management of nasopharyngeal cancer. Although effective in destroying cancer cells, radiotherapy often causes significant skin reactions, including radiation dermatitis, which can appear as erythema, desquamation, and even ulceration. These reactions can affect the sufferers' quality of life and interfere with the continuity of therapy. This study aims to explore factors that affect the intensity of radiation dermatitis, including location of radiotherapy and concurrent chemotherapy. In addition, radiation dermatitis management strategies, such as the use of moisturizers, topical steroid therapy, and sun protection, are packaged to accelerate the healing process and reduce symptoms. Assessment criteria such as CTCAE and RTOG are used to assess The intensity of dermal responses. It is expected that a thorough understanding of the causes and management of radiation dermatitis would improve the prognosis for patients with nasopharyngeal cancer and increase the effectiveness of therapy. More research is needed to develop more effective preventative and therapeutic measures for radiation-induced dermatitis.

Introduction

Over 70% of new occurrences of nasopharyngeal cancer occur in East and Southeast Asia, and the disease is a carcinoma that arises from the nasopharyngeal squamous epithelium. Its annual incidence is 1.5 per million people globally. Patients with nasopharyngeal cancer often get radiation as a component of a multimodal treatment strategy. Radiotherapy, in conjunction with surgery, cytotoxic chemotherapy, and immunotherapy, is a component of first-line cancer treatment for about 30% of patients in the United States (Fang, 2023; Wang, 2021). Regions with high NPC incidence, such as Southern China and Southeast Asia, early screening and prevention strategies are crucial. The high incidence in these areas is attributed to genetic predisposition, environmental factors, and lifestyle habits, including the consumption of preserved foods. The role of Epstein-Barr virus (EBV) infection is also significant, as EBV DNA can be used as a biomarker for monitoring disease progression and response to treatment (Fang, 2023).

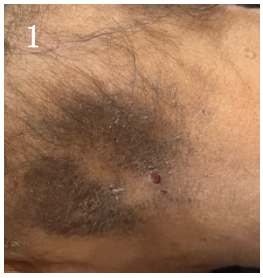
Radiotherapy is an effective treatment modality for malignancies, using ionizing radiation to eradicate cancer cells. Radiotherapy treatment in nasopharyngeal cancer patients often induces substantial responses and is a prevalent side effect of therapy, including harm to adjacent healthy tissues, such as the skin. These cutaneous responses may range from erythema to severe dermatitis and ulceration, thereby impairing the quality of life of the patient and obstructing the continuation of therapy (Pazdrowski, 2024).

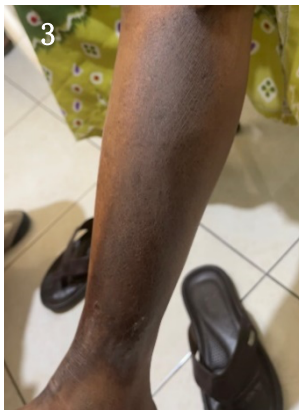
Radiodermatitis manifests in 95% of people receiving radiation. Skin atrophy, telangiectasia, and fibrosis are examples of chronic symptoms of radiation dermatitis, as well as acute erythema and desquamation. The distance between the skin and the radiation target, the energy of the radiation used, the radiation dose and treatment fractionation schedule, the amount of skin surface area exposed to radiation, and the presence or absence of concurrent chemotherapy that heightens radiosensitivity can all have an impact on skin reactions (Leventhal, 2017; Xie, 2021).

Case Description

A 60year old woman came to the Hospital on Saturday, October 19 2024 with complaints of intermittent pain in the left cheek, back of the neck and left leg. Complaints that sometimes it feels itchy. The patient said the blackness of the skin had reduced. Before blackening, the skin is red and peels slightly. The first complaints appeared when the second chemotherapy was carried out after radiotherapy on the second day. Radiotherapy was carried out for 1 month and the complaints have persisted to this day. There are other complaints such as ringing in the left ear which have been present since the start of chemotherapy.

Previous medical history was recognized as nasopharyngeal cancer. The patient was first diagnosed with cancer in 2021. The patient was then routinely checked at the oncology clinic and is currently receiving Taceral, Doxitacel and cisplatin chemotherapy. The patient denies any drug allergies and there is no family history of similar complaints.The physical examination indicated satisfactory overall health and vital sign within normal parameters. The dermatological status of the whole body is good except for the facial area, there are multiple discrete patches of hyperpigmentation, some with scaling on the left zygomatic, left lateral cruris region and posterior cervical region.





Figures 1 & 2. On the posterior cervical and left zygomatic areas, a well-defined hyperpigmentation patch with light desquamation is visible.
Figure 3. On the lateral cruris sinistra, a well-defined patch of hyperpigmentation with light desquamation is visible.

Based on the patient's clinical condition and history, the patient experienced post-inflammatory hyperpigmentation with mild dry desquamation due to ongoing cancer therapy.

The therapy given to patients is Noroid lotion applied two to three times a day, then desoximetasone 0.25% is applied once a day in the morning, topical antibiotic mupirocin 2% is applied twice a day in the afternoon and evening. Patients are advised to have a control 2 weeks later to monitor the situation.

Discussion

Radiodermatitis, or radiation dermatitis, is a skin response generated by radiation, resulting in harm to the subdermal fat. It may also result from many kinds of radiation exposure, including other interventional treatments, environmental influences, or occupational exposure, as shown in nuclear power plant employees, even when the skin is not the main target. Radiation dermatitis often manifests within several weeks after the initiation of radiation treatment (Singh, 2016; Kao, 2022).

The increased prevalence of radiodermatitis in these tumors results from the closeness proximity the skin to the targeted radiation region and the difficulty of shielding the skin from high radiation doses. Radiation dermatitis affects up to 95% of people undergoing radiation (Singh, 2016; Wei, 2018).

Intrinsic and extrinsic variables affect the patient's skin reaction to radiation treatment. Intrinsic variables include age, gender, sun exposure, a BMI beyond 25, smoking, inflammatory skin conditions, autoimmune illnesses, the anatomical position of skin folds, and radiosensitive disorders. Concurrently, the extrinsic determinants are dosage per fraction, overall dose, and radiation method. Radiotherapy, whether coupled with chemotherapy, immunotherapy, or anticancer treatment using EGFR inhibitors, may contribute to the exacerbation of radiodermatitis severity. Certain chemotherapy drugs, such as paclitaxel and docetaxel, may act as radiosensitizers. The combination of treatment with radiation, especially concurrent chemoradiotherapy may result in more severe skin responses for gynecological or head and neck cancers. Individuals referred for 5-fluorouracil induction treatment have advanced head and neck cancer prior to chemoradiotherapy may have aggravated radiodermatitis. Certain systemic medications may enhance the susceptibility of skin cells to radiation. This

treatment may be provided before to, simultaneously with, or after radiation. The mechanism of these medications closely parallels that of radiation. As a result, the negative effects are more evident. The molecular and clinical features of radiation dermatitis in patients with advanced head and neck cancer undergoing concurrent cetuximab and radiation treatment are distinct (Kiprian, 2022; Pazdrowski, 2024).

Based on the timing of development, radiation-induced dermatitis may be divided into two types: acute and chronic. While chronic radiation-induced dermatitis is skin damage that occurs months to years after radiation exposure, acute radiation-induced dermatitis may manifest within days or months after irradiation. Furthermore, 6%–9% of patients who have previously been exposed to radiation may have radiation withdrawal responses, which are localized acute inflammatory skin reactions brought on by chemotherapy or targeted treatment. After radiation treatment is over, this response might happen weeks, months, or even years later (Fan, 2023).

Research suggests that radiation may modify growth factor expression, and reduced growth factor expression might hinder wound repair and healing (Fan, 2023). In 1906, Bergonie and Tricondeau posited that any actively proliferating cell has more radiosensitivity than a non-dividing mature cell. This phenomenon occurs in both malignant cells and healthy tissue. The main targets of radiation are hair follicle stem cells and basal keratinocytes, but melanocyte function is influenced by radiation energy (Fan, 2022; Kiprian, 2022).

The basal germ layer cells are radiation-sensitive, and radiation-induced reactive oxygen species and free radicals may readily harm these basal cells. Elevated IL-1 and TNF-α levels cause metalloproteinases to be produced, which breaks down the components of the dermal matrix and disrupts the basal cell layer of the epidermis. This disrupts the normal metabolism of epidermal cells and causes radiation damage by impeding cell division, proliferation, migration to the surface, and keratinization. Dermatitis brought on by external factors (Fan, 2022; Kiprian, 2022).

The irradiated location produces histamine-like compounds during the first phases of radiation, which increases capillary permeability and causes transient irritation and erythema. Erythema results from the infiltration of leukocytes and erythrocytes into the dermis during the latter phases of radiation therapy. The basal layer cells are damaged as radiation doses increase, leading to ulceration, necrosis, dry desquamation, and wet desquamation (Kiprian, 2022).

The clinical manifestation of radiation dermatitis includes erythema, followed by dry desquamation. The subsequent phase involves moist desquamation, which may be accompanied by severe skin lesions such as ulcers. This phase of moist desquamation and ulceration is frequently associated with bacterial and fungal infections (Markiewickz, 2022). Radiation dermatitis also influenced by the dose and duration of radiation exposure. Higher doses and prolonged exposure increase the risk of severe skin reactions. Additionally, the combination of radiation therapy with other treatments, such as chemotherapy or immunotherapy, can exacerbate the severity of radiodermatitis. Certain chemotherapy drugs, like paclitaxel and docetaxel, act as radiosensitizers, enhancing the sensitivity of skin cells to radiation. Concurrent chemoradiotherapy is particularly associated with more severe skin reactions in patients with gynecological or head and neck cancers (Bontempo, 2021).

The patient in this instance acknowledged experiencing erythema and desquamation, which progressively darkened to a black hue over time. This pertains to the occurrence of post-inflammatory hyperpigmentation in patients. Erythema and desquamation indicate inflammation, which damages the basal layer of the epidermis and prompts melanocytes to release melanosomes carrying pigment into adjacent skin cells. Pigment granules may persist for an extended duration, resulting in epidermal discoloration. Post-inflammatory hyperpigmentation may affect the epidermis, since cytokines, chemokines, and ROS produced during inflammation promote melanocyte proliferation and melanin synthesis, then transferring it to adjacent keratinocytes (Markiewickz, 2022).

All skin types may develop post-inflammatory hyperpigmentation, although darker-pigmented people are more likely to experience it and notice it more. Skin types IV, V, and VI according to Fitzpatrick exhibit increased vulnerability to long-term damage and consequences after certain chemical peels or laser and radiation therapies, including erythema, hypertrophic scars, and keloids (Markiewickz, 2022). Post-inflammatory hyperpigmentation increased susceptibility is attributed to the higher melanin content in darker skin, which makes it more prone to hyperpigmentation following inflammation. The molecular mechanisms underlying PIH involve the release of cytokines, chemokines, and reactive oxygen species (ROS) during inflammation, which stimulate melanocyte proliferation and melanin synthesis. These inflammatory mediators, including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α), play a crucial role in promoting melanin transfer to adjacent keratinocytes, thereby exacerbating hyperpigmentation (Flauto, 2025).

Manifestations of post-inflammatory hyperpigmentation vary depending on the depth of melanin deposition. Epidermal PIH typically presents as tan, brown, or dark brown macules, which may resolve over time without treatment. However, dermal PIH, characterized by a blue-gray appearance, can be more persistent or even permanent due to the phagocytosis of melanin by macrophages in the dermis (Moolla, 2022).

Assessment standards including the Common Terminology Criteria for Adverse Events (CTCAE) from the National Cancer Institute (NCI) and the Radiation Therapy Oncology Group (RTOG) may be used to diagnose, assess, and evaluate radiation-induced dermatitis (Fan, 2022).

Table 1. General Evaluation Criteria for Radiation-Induced Dermatitis

Criteria	Grade 0	Grade I	Grade II	Grade III	Grade IV	Grade V
NCICTCAEV5.0 (Dermatitis radiation)	None	Faint erythema or dry desquamation	Moderate to rapid erythema; patchy moist desquamation, mostly confined to folds and depressions of the skin; moderate edema	Moist desquamation in areas other than skin creases and creases; bleeding caused by minor dermabrasion	Life-threatening; necrosis or ulceration of the entire dermis; spontaneous bleeding; indications for skin grafting	*Death*
RTOG Acute Radiation Injury	None	Follicular, faint, or dull erythema/ hair removal/ dry desquamation/ decreased sweating	Soft or bright erythema, patchy moist desquamation/moderate edema	Confluent desquamation, moist apart from skin folds, pitting edema	Ulcer, bleeding, necrotic	
RTOG Chronic Radiation Injury	None	Mild skin atrophy; pigment changes; hair loss	Patchy atrophy; moderate telangiectasia; total hair loss	Significant skin atrophy; gross telangiectasia	Ulcer	

Patient in this case, the lesion findings developed into hyperpigmentation with mild dry desquamation with a long re-epithelialization process. Re-epithelialization usually begins approximately ten days, but may be extended by exposure to radiosensitizing agents, particularly platinum-based chemotherapy (Bray, 2016). It is known that the patient is currently still undergoing chemotherapy using Taceral, Doxitacel and Cisplatin which are classified as platinum-based chemotherapy and are radiosensitizer.

The principles for managing radiation dermatitis are reducing symptoms, preventing infection and speeding up healing by protecting the skin from sun exposure using sunscreen. Ultraviolet (UV) radiation also can worsen post-inflammatory hyperpigmentation by increasing melanin production and promoting inflammation, underscoring the importance of sun protection in preventing and managing (Kashetsky, 2024 ; Mar, 2024).

Use moisturizer to maintain skin hydration, strengthen the barrier and speed up the healing process. topical corticosteroids with moderate to high potencies, such as mometasone furoate 0.1% (once daily), fluticasone 0.05% (twice daily), triamcinolone 0.1% (twice daily), betamethasone 0.1% (once or twice daily), and clobetasol 0.05% (twice daily) can be used due to their anti- inflammation by inhibiting the IL-6 pro-inflammatory cytokine cascade which is stimulated by free radicals caused by radiation (Kiprian, 2022; Sherman, 2024). Providing topical/systemic antibiotics and dressings if there is wet desquamation with skin infections such as silver sulfadiazine dressings, this is because A humid atmosphere helps expedite re-epithelialization and wound healing. Oral analgesics can be given to reduce pain, but the use of topical analgesics is not recommended due to phototoxic effects. Aesthetic medicine can use Photo-biomodulation Treatment (Pazdowski, 2024).

Radiodermatitis significantly impacts the quality of life of patients undergoing radiation therapy. The high incidence of radiodermatitis, especially in regions like the head and neck, underscores the need for standardized management protocols. Studies have shown that the incidence of radiodermatitis varies by irradiated site, with the head and neck region being the most affected (Bontempo, 2021). The development of effective treatments and preventive measures is essential to mitigate the severity and duration of radiation dermatitis, thereby improving patient outcomes and quality of life.

Conclusion

This case shows that nasopharyngeal cancer patients undergoing radiotherapy with chemotherapy initiating Docitaxel, Cisplatin and Taceral can experience significant skin reactions such as radiation dermatitis to post-inflammatory hyperpigmentation.

Docitaxel, Taceral and Cisplatin are platinum-based chemotherapy agents that have radiosensitive properties. The lesions in this case arise around the area of the radiation site. Meanwhile, if it affects other parts, it can occur because of a systemic reaction from radiation therapy, it can cause a skin reaction. This skin reaction often appears as a result of high radiation exposure, especially in areas close to the radiation target.

The therapy given, such as Noroid lotion, desoximetasone, and mupirocin, aims to reduce symptoms and prevent infection. The need of consistent monitoring and appropriate care of these skin responses is paramount, since they might impact the patient's quality of life and adherence to medication. By comprehending the determinants that affect the severity of radiation dermatitis and executing effective management techniques, it is anticipated that treatment results and patient quality of life would be enhanced during and post-therapy. Additional study is required to provide improved recommendations for the avoidance and management of radiation dermatitis, particularly in patients undergoing multimodal treatment for nasopharyngeal cancer.

Conflict of Interest

There is no conflict of interest.

Consent Form

We confirm that the patient gave verbal consent for the publication of the images and all of her medical history

Acknowledgement

We would like to express our gratitude to PKU Hospital Solo for agreeing to share the details of patient medical condition and treatment for the purpose of advancing medical knowledge.

We confirm that we have obtained verbal informed consent from the patient to publish this case report, including relevant images and medical information. Efforts have been made to maintain patient anonymity, and no personally identifiable information has been disclosed in the manuscript.

This case report complies with the ethical standards and guidelines set forth by Medical Faculty Universitas Muhammadiyah Surakarta.

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