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A RARE CASE OF PHOTO-ALLERGIC CONTACT DERMATITIS IN A PATIENT OF CARCINOMA LARYNX TREATED WITH POST-OPERATIVE RADIATION THERAPY: DECIPHERING A CLINICAL CONUNDRUM

Radiation Oncology

Dr. Mukti Nath Singh*	Senior Resident, Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow *Corresponding Author
Dr. Akanksha Manral	Junior Resident, Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
Dr. Ajeet Kr Gandhi	Associate Professor, Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
Dr. Kiran Preet Mehrotra	Professor, Department of Pathology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
Dr. Soumya Agrawal	Assistant Professor, Department of Dermatology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
Dr. Anoop Shrivastava	Professor Jr, Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow
Dr. Madhup Rastogi	Professor & Head, Department of Radiation Oncology, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow

ABSTRACT

Background: Photo-allergic contact dermatitis (PACD) is a skin disease where the precipitating factors are usually exposure of ultraviolet (UV) radiation and chemical agents. Exposure to such agents triggers the delayed type of hypersensitivity reactions resulting into flaring up of skin reactions. Herein, we describe a rare case scenario of a patient with a long history of PACD who reported for post operative radiotherapy for cancer larynx (pT4N2) where the aggravation was due to post-operative radiation therapy (Megavoltage). **Case Report:** A 63-year-old male with known case of PACD and diagnosed with carcinoma larynx primarily was treated with total laryngectomy and then was planned for post-operative radiotherapy. The patient developed cutaneous eruption within 10 fractions of start of radiation therapy. Given the concern of photo-allergic dermatitis, radiation therapy was discontinued, and supportive care was provided including topical and oral steroids administration. His cutaneous eruptions improved after the interruption of radiation therapy and was re-challenged but again due to same generalized reactions, radiation therapy was discontinued leading to suboptimal tumor control. **Conclusion:** PACD could be aggravated with megavoltage radiation therapy as was observed in our case. Despite two interruptions during Radiotherapy and repeated dermatological interventions the required treatment of radiotherapy could not be completed because of aggravation of skin lesions. Our thorough literature survey did not provide any substantive information about the referred scenario. This case report might provide an insight into gray area which has not been evaluated thus far.

KEYWORDS

PACD, carcinoma larynx, Radiation therapy, Hypersensitivity reactions

INTRODUCTION:

Allergic contact dermatitis is a cutaneous manifestation of delayed type hypersensitivity (Type IV) usually manifesting as pruritis and eczematoid change of the skin.This type of response to a photo-activated allergen applied to the skin is known as photo-allergic contact dermatitis (PACD). The PACD lesions often only affect areas that are exposed to light.[1,2] Exposure to ultraviolet (UV) radiation and chemical agents are the two main causes of PACD.

The processing and presentation of allergen to naïve T cell by dendritic cell is defined as sensitization and after repeated exposure of the same allergen, the second phase elicitation occurs. Depending on the level of sensitization and frequency of repeated elicitation some patients developed intermittent dermatitis while others develop persistent dermatitis.[4] The persistent dermatitis may expand from a localized presentation to a generalized dermatitis. Until now, X-ray or gamma radiation therapy are not recognized as established or definite causes of PACD.

Case Summary

This is the case of a 63-year-old man who was receiving therapy from a local physician for the past 10 years for intermittent dermatitis. He reported in November 2021 with the chief complaints of hoarseness of voice and difficulty in breathing. Detailed clinical examination and direct laryngoscopy showed fixed left vocal cord and left cervical lymphadenopathy. On biopsy from primary site, histopathology was reported as squamous cell carcinoma. Imaging with contrast enhanced computed tomography of face and neck was suggestive of a soft tissue lesion of size 4*3.5 cm involving left aryepiglottic fold with involvement of strap muscles and left cervical lymphadenopathy which was suggestive of a locally advanced disease and was staged as cT4a N1 (Group Stage IVa) as per AJCC 8th edition. He was referred to the surgical oncologist for further management. During this period, he was having similar episodes of dermatitis, for which he consulted dermatologist and after thorough history, a skin biopsy was done and the cutaneous lesions were reported as Photo-allergic contact dermatitis for which he was prescribed oral hydroxychloroquine, topical steroids and advised to avoid sun exposure.

In April 2022, patient underwent total laryngectomy with left hemi-thyroidectomy with modified radical neck dissection and the post operative histopathology was reported as moderately differentiated squamous cell carcinoma with clear margins, evident lympho-vascular invasion, depth of invasion-18 mm and two out of fifty-three lymph nodes without any extra nodal extension and staged as pathological T4N2.

Based on the high-risk pathological features, the patient was referred for adjuvant radiation therapy and was planned for 60 Gray in 30 fractions at 2 Gray per fraction, 5 fractions per week over 6 weeks. After first 10 fractions of radiation therapy, his symptoms of the dermatitis flared up and worsened for which the treatment was paused and he was conservatively managed. After resolution of his symptoms, a detailed multidisciplinary tumor board discussion was held, and it was decided to restart radiation treatment and assess the response of the patient. Due to recurrence of the dermatitis, it was decided to stop further treatment as patient could not tolerate radiation therapy. He could receive only 16 fractions out of 30 planned fractions of radiation therapy which is sub optimal for loco-regional tumor control in the adjuvant setting and can further lead to increase in chances of loco-

regional recurrence and distant failures. The PACD resolved after interruption of radiotherapy at the time of last follow up and the patients was loco-regionally controlled. The patient has been kept on continuous follow up to monitor for disease status and activity of PACD.

DISCUSSION

The delayed-type hypersensitivity of skin in response to light is known as photo-allergic contact dermatitis (PACD). PACD is a cell-mediated immune response in which the antigen is a photo-activated allergen [1]. It primarily affects body parts that are often exposed to sunlight.[2] The sun is the primary component of the solar system and emits a continuous spectrum of electromagnetic radiation, ranging from the most energetic cosmic, gamma rays, X-rays with shorter wavelengths (10 nm), Ultraviolet Ray (10-400 nm), visible light (400-760 nm) and infrared rays. In severe cases, the lesions may also be seen in covered areas of the body (760-1700 nm).[1] The ability of UV rays to penetrate the skin deeply depends on its wavelength and there may be a delayed type hypersensitivity (DTH) reaction to unidentified endogenous, cutaneous photo-induced antigens.[3] The absorption of radiation by photosensitizer results in oxygen-dependent photodynamic process leading to the formation of free radicals causing cytotoxic injury.[4]

The response to exogenous or endogenous substances is known as photosensitivity. Typically, these substances have unsaturated double bonds, which absorb Ultraviolet A wavelength radiation. The Fc receptor of the IgE antibody binds to the surface of the mast cell, activating the mast cell, and releasing pro-inflammatory cytokines and reactive oxygen species when ionizing radiation exposed to the body surface activates Langerhans cells, dendritic cells in the dermis, and binds to the IgE antibody. As a result, there is inflammation, oxidative damage, tissue damage, and cell death.[4]

A photo-allergic reaction may be triggered by the inflammatory cytokines and oxygen species, which also activate humoral and cell-mediated immunity. Cell-mediated immunity can change into memory cells and stay there for days, months, years, or even for the rest of one's life. The memory cells revive upon exposure to the same allergen type and repeatedly trigger cell-mediated immunity (viscous cycle).

Radiation therapy is a crucial part of cancer treatment that works to eradicate cancer cells by inflicting irreparable DNA damage, which results in cell death or cell cycle arrest. Immunogenic cell death is a procedure that induces some anti-tumor immunity.[5,6]. The electromagnetic radiation, including X and gamma rays, is indirectly ionizing; as it passes through a substance, it absorbs energy to create fast-moving charged particles that can damage DNA. Any type of radiation that is absorbed by biological material damages DNA either directly or indirectly. Direct effects include ds-DNA or ss-DNA damage, while indirect effects include the production of free radicals when it interacts with water. When radiation interacts with water molecules, both an ion and a free radical are produced.[7]

Stage-III or IV laryngeal squamous cell carcinoma is primarily treated with surgery when organ preservation is not an option. Postoperative radiotherapy (RT) with or without chemotherapy is the standard of care to minimize the risk of recurrence. Adjuvant therapy mostly benefits patients at risk of local and regional failure.[8,9] The rate of local recurrence after resection of primary head and neck cancer can be as high as 80% in those with positive / close margins and 15% to 32% in those with a negative margin.[10]

The rate of primary failure is higher in patients with a total radiation dose of ≤54Gy, compared with >57.6 Gy.[11,12] Treatment should be started as soon as possible after surgery. In patients with such locally advanced tumors, surgery is usually followed by adjuvant radiotherapy. The advantage of postoperative radiotherapy is well documented.

Once the offending agent is eliminated or avoided, photo-dermatitis is a self-limited condition that resolves on its own. In addition to avoiding UV radiation, the appropriate course of action to avoid the phototoxic or photoallergic agent that is causing the problem should be determined first. On quality of life (QoL) and psychological health, it has a very significant impact. A very significant impact on quality of life was noted by between 31% and 39% of photosensitive patients.[13] PACD may get aggravated to clinically significant and bothersome dermatitis if the inciting agent is not removed/stopped. In our case, initiation of radiation therapy led to aggravation of PACD which was diffuse and generalized in nature and did resolve on interruption of radiation therapy implicating a plausible connection between the megavoltage radiation therapy and PACD. The PACD was re-aggravated upon rechallenge with reinitiating of radiation therapy after a gap, again emphasizing a plausible clinical correlation between the two.

This aggravation of PACD with megavoltage radiation therapy has not been reported earlier in literature, the mechanism of PACD could be like that seen with UV rays. Although, the megavoltage radiation therapy has a skin sparing effect, scatter radiation may lead to deposition of radiation in epidermis and dermis leading to aggravation of PACD. This case report highlights the rare phenomenon and in patients with already established case of PACD, it would be then prudent to use non-radiation therapy measures for the management of cancer as far as possible to avoid this undesirable clinical dilemma.

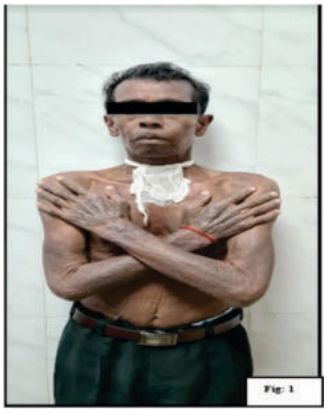

Figure 1: Whole body covered with eczematous pruritic papules.

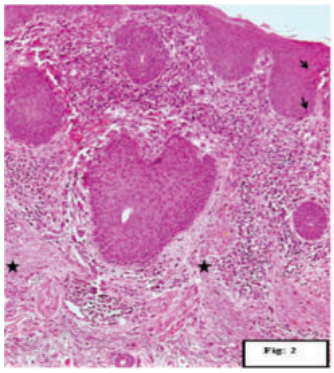

Figure 2: H & E stain: Arrow depicts Epidermal hyperplasia and asterisk denotes lymphocytic infiltration , Langerhans cells and macrophages seen in upper dermis.

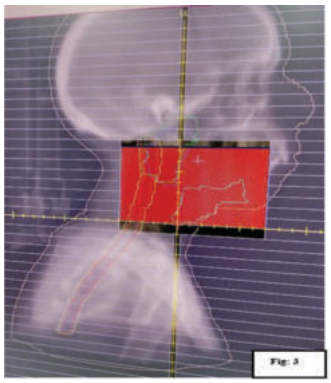

Figure 3: Conformal Radiation treatment portal

CONCLUSION:

PACD presents difficulties for both the physician and the patient. A methodical strategy is essential for the proper diagnosis and management of the PACD. PACD is primarily aggravated by ultraviolet radiation, but we noted this aggravation with gamma rays

(megavoltage radiation therapy), which has not been reported before. This case reports highlights the clinical dilemma faced in this rare scenario and we suggest to use non-radiation therapy measures in known case of PACD for the management of cancer wherever possible. In patients, where radiation therapy has to be given, patient should be counselled beforehand about the aggravation of PACD and chances of interruptions/discontinuation of radiation therapy with inferior oncological outcome.

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