



Research paper

A Clinico-Epidemiological Study of Cutaneous Manifestations in Patients on Chemotherapy and Radiotherapy at a Tertiary Care Centre

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ABSTRACT

Background: The newer and traditional targeted anticancer modalities have tremendously improved the survival rate in cancer patients, however the associated increase in the incidence of cutaneous side effects can negatively affect the quality of life. The aim of this study was to determine the incidence of cutaneous manifestations in patients undergoing chemotherapy and radiation therapy for the treatment of internal malignancies.

Material and Methods: This cross sectional observational study included all diagnosed cases of internal malignancies with cutaneous manifestations following chemotherapy and radiotherapy, referred from the oncology OPD between January 2020 to June 2021. In each patient, detailed history, cutaneous and systemic examination, as well as treatment information were recorded. Skin biopsies were performed when necessary. Patients who had undergone both chemotherapy and radiotherapy were excluded from the study.

Results: Out of 3741 patients who were referred from the oncology OPD, 80% (2992) were on chemotherapy, with 8.51% (255) experiencing cutaneous manifestations. Among the 45% (1689) patients who were on radiotherapy, 3.73% (63) developed cutaneous manifestation.

Conclusion: Early detection and management of the cutaneous manifestation following treatment with chemotherapeutic and radiotherapeutic agents can be of utmost importance in improving the quality of life, increasing the therapeutic compliance and preventing the long term sequelae.

1. Introduction

Different treatment modalities for malignancies, including surgery, chemotherapy, radiation therapy, im-

muno-therapy and hormonal therapy can lead to a range of cutaneous manifestations.

New chemotherapeutic agents have been introduced for cancer treatment, leading to an

increase in the incidence of cutaneous adverse effects and a subsequent decline in quality of life. The most common cutaneous adverse effects include anagen effluvium, hyperpigmentation, hand-foot syndrome, radiation recall, hypersensitivity, extravasation injuries and nail dystrophies. Although these conditions are rarely fatal, they can cause significant morbidity, cosmetic disfigurement and psychological distress.

2. Material and Methods

This cross-sectional observational study, approved by the institutional ethical committee (Ref: MGMCH/IEC/JPR/2020/532), included all diagnosed cases of internal malignancies receiving either chemotherapy or radiotherapy, who developed cutaneous manifestations and were referred from the oncology outpatient department (OPD) between January 2020 and June 2021. A detailed history and clinical examination were conducted for all consenting patients, and additional investigations, including histopathological examinations, were performed as necessary. Patients who underwent both chemotherapy and radiotherapy were excluded from the study.

3. Results

A total of 3741 patients were referred from the Oncology OPD. Among them, 80% (2992) were on chemotherapy, of which 8.51% (255 patients) developed cutaneous manifestations. Out of the 45% (1689) patients who were on radiotherapy, 3.73% (63 patients) experienced the cutaneous manifestations.

Table 1 Total number of patients receiving chemotherapy and radiation therapy

TOTAL PATIENTS (n=3741)	Number of cases with cutaneous manifestations	Percentage (%)
CHEMOTHERAPY (2992)	255	8.51
RADIOTHERAPY (1689)	63	3.37

Table 2 Cutaneous manifestations associated with chemotherapy

Manifestations	Number of cases (255)	Percentage (%)
Anagen effluvium	75	29.55
Drug-induced dermatitis	34	13.6
Erythroderma	23	9.09
Chronic urticaria	23	9.09
Maculopapular rashes	17	6.82
Generalized pruritus	17	6.82
Xerosis	17	6.82
Hand-foot syndrome	11	4.55
Bullous photo dermatosis	6	2.27
Acneiform eruptions	6	2.27
Facial melanosis	6	2.27
Acquired ichthyosis	6	2.27
Leukocytoclastic vasculitis	6	2.27
Sweet syndrome	6	2.27

The most common cutaneous manifestation was anagen effluvium (29.55%), followed by drug-induced dermatitis (13.6%), erythroderma (9.09%) and chronic urticaria (9.09%). Other manifestations included maculopapular rashes, generalized pruritus and xerosis (each 6.82%), with less common conditions such as hand-foot syndrome (4.55%) and acquired ichthyosis (2.27%).

Table 3 Cutaneous manifestations associated with radiotherapy

Manifestations	Number of cases (63)	Percentage (%)
Acute Radiation Dermatitis	56	88.88
Alopecia Areata	7	11.11

Acute radiation dermatitis occurred in 88.88% (56) followed by alopecia areata in 11.11% (7) of cancer patients following radiotherapy.

4. Discussion

4.1 Cutaneous manifestations associated with chemotherapy

The overall incidence of chemotherapy-related cutaneous adverse drug reactions (CADR) in our study was 8.51%, which is in concordance to the findings from previous research by Bassiouny et al. (10.32%)¹.

4.2 Anagen Effluvium

Anagen effluvium was identified as the most frequent cutaneous manifestations, affecting 29.55% (75) of patients. This condition, characterized by sudden hair loss due to inhibition of hair matrix cell division by chemotherapeutic agents, was noted predominantly in patients undergoing combination chemotherapy. The incidence observed in our study align with established literature by Biswal et al (78.6%)² and Treub et al (65%)³ emphasizing its impact on patients' psychological well-being as it is the most common side effect.



Fig. 1 Anagen effluvium in a patient with NHL following Bendamustine + Rituximab therapy

4.3 Erythroderma

Erythroderma, occurring in 9.09% (23) of cases, manifested as widespread erythema and desquamation, primarily associated with chemotherapy agents such as ATRA (All-Trans Retinoic Acid) in acute promyelocytic leukemia (APML), as well as combinations like Bendamustine + Rituximab and Filgrastim + Azacytidine. Effective management involved the immediate discontinuation of the offending drugs and modification of the treatment regimen, consistent with findings reported by Yonal et al⁴. and Aghedo et al.⁵ Notably, chemotherapy-induced erythroderma had not been previously documented in the literature.



Fig. 2 Erythroderma in a patient with small cell variant of T cell prolymphocytic leukemia on oral Fludarabine and Prednisolone therapy

4.4 Other Cutaneous Reactions

Various other CADR were identified, including maculopapular rashes in 6.82% (17) following ATRA, Paclitaxel and Docetaxel therapies.

Generalized pruritus was seen in 6.82% (17) patients receiving Nilotinib, Bendamustine+Rituximab and Carboplatin + Paclitaxel therapy. This is similar to the findings suggested by Biswal et al² (2.5%) with carboplatin and paclitaxel therapy.

In our study, Hand-Foot syndrome was noted in 4.55% (11) of patients receiving Capecitabine and Adriamycin therapy, which aligns with findings from Martin et al.⁶ However, Jindal et al.⁷ reported a much higher incidence of Hand-Foot syndrome, with it being the most frequent dermatosis linked to chemotherapy, occurring in 15.55% of cases. This is notably higher than the 4.55% observed in our study, where the most common cutaneous manifestation was anagen effluvium.

Bullous Photo-dermatosis was identified in a patient with Non Hodgkin's Lymphoma (NHL) undergoing rituximab therapy, though no prior literature has documented this association.

Acquired Ichthyosis with carboplatin was also noted by Honda et al.⁸ Sweet syndrome, facial melanosis was seen in 2.27% (6 each) patients.

Each of these reactions presented distinct clinical features and temporal correlations with specific chemotherapeutic agents, highlighting the need for tailored management strategies based on the underlying disease and the severity of symptoms.



Fig. 3 Facial melanosis with diffuse blue-grey pigmentation over B/L cheeks in case of Small Cell Ca Lung on Paclitaxel therapy

4.5 Radiotherapy-Related Cutaneous Manifestations

Manifestations

Cutaneous manifestations associated with radiotherapy were noted in 3.73% (63) of cases in our study. These reactions were primarily site-specific, localized to areas exposed to radiation therapy.

4.6 Acute Radiation Dermatitis

Acute radiation dermatitis was the most common reaction, occurring in 34.15% (56) of patients undergoing radiotherapy in our study. It typically manifested within four weeks of treatment initiation, highlighting its acute nature. The condition was characterized by erythema, desquamation, and varying degrees of discomfort, depending on the radiation dose and treatment site. Notably, all cases observed in our study were acute, with no instances of chronic radiation dermatitis developing after 90 days.

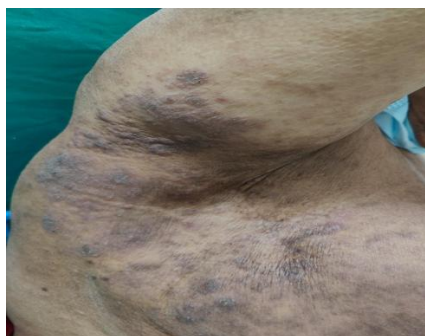


Fig. 4 Radiation dermatitis in a patient with Ca Breast occurring within 4 weeks of Post Radical Mastectomy

4.7 Alopecia Areata

Patchy Alopecia Areata was noted in 4.27% (7) of patients, predominantly affecting the scalp or beard areas following radiotherapy sessions and this was in concordance with Ali et al¹⁰ and Seol et al¹¹.

The susceptibility of anagen follicles to radiation-induced damage was evident resulting in complete reversible alopecia with 3Gy and permanent alopecia which begins with radiation over 5 Gy highlighting the need for supportive care and patient education regarding potential hair loss outcomes.



Fig. 5 Radiation induced patch of hair loss over scalp in a patient of Atypical Meningioma

5. Conclusion

Approximately 29.55% of patients experiencing anagen effluvium were primarily attributed to alkylating agents. Other prevalent dermatologic conditions linked with chemotherapy were drug-induced dermatitis (13.6%), erythroderma and chronic urticaria (9.09% each), alongside maculopapular rash, generalized pruritus, xerosis, and hand-foot-mouth syndrome (6.82% each). Acute radiation dermatitis was predominant (88.88%) following radiation therapy, with alopecia areata noted in (11.11%) of cases. Timely identification and treatment of these cutaneous manifestations post-chemotherapy and radiotherapy can be extremely helpful for ensuring treatment adherence, enhancing quality of life and averting potential long-term complications.

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