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Review Article

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Dermatological Aspects of Nursing Oncology: Meaningful Observations Ensuring Better Quality of Life

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ABSTRACT

Modern cancer management has changed over the period of time and now shifted to multidisciplinary care approach to ensure a better quality of life (QOL) of the surfing patients. Every form of cancer treatment has side effects and affects the QOL. Many of the side effects have been discussed in detail because of the need for timely interventions to prevent the consequences of the side effects. Dermatological adverse events due to cancer treatment are important but most commonly ignored in our clinical practice. Nursing staffs have a critical role in the early identification of such events and by briefing and training of the nursing staff in the identification of adverse events which can aid in the prevention of complications. As dermatologists may not be available round the clock, nursing staff are looking after the patients round the clock can prove very vital in screening cutaneous AE and adequately setting up referrals to aid early recognition and treatment of not only mild but also potentially life-threatening complications. The nursing staff, which is a cadre of health caregivers that are intimately involved in cancer care, can be trained to identify timely, skin-related adverse events. A literature search of scientific publications was done using the electronic databases PubMed, Science Direct, Cochrane Library, and Google Scholar. The search included terms 'Adverse events (AEs) post-chemotherapy,' 'AE post-radiotherapy,' 'AE post-immunotherapy,' 'AE post-hormonal therapy for cancer' and 'AE post-cancer surgery.'Data obtained from these studies and case reports were compiled and interpreted to prepare this review. This review focuses on various ways in which skin can be involved adversely as a part of cancer management and their classic and tell-tale signs to help the nurses in their better and quicker identification so that dermatologists are timely intimated and the treatment can be instituted to improve the patient's QOL.

Keywords: Quality of life, Nursing oncology, Cutaneous adverse events, Radiation recall dermatitis, PRIDE complex

INTRODUCTION

Increasing westernisation of lifestyle, unhindered consumption of tobacco and alcohol, better awareness regarding cancer symptomatology, and improved sensitivity of diagnostic procedures have led to increased incidence of malignancies worldwide. Keeping in pace with this surge, medical research has come up with various new treatment modalities for the same. However, needless to say, all these treatment options, be it surgery, chemotherapy, ionising radiation, targeted therapy, immunotherapy, or hormone therapy, are not without adverse effects (AEs) of their own. While monitoring the majority of these side effects requires invasive or expensive investigations, cutaneous AEs are easily discernable and amenable to symptomatic treatment, without the need for withholding treatment, unless life threatening. The cadre of healthcare professionals that spends maximum time in tending to the patients is the nursing staff and hence their important role in recognition of the side effects. Cutaneous AE may involve skin, hair, nails, or mucosae. While a majority of these are cosmetic and reversible on discontinuation of therapy, they invariably hamper the quality of life and can sometimes snowball into serious consequences like Steven–Johnson syndrome. Therefore, briefing and training the nursing staff in the identification of these can aid in prompt communication to the dermatologist. This review aims to highlight the commonly experienced AE in cancer care.

MATERIALS AND METHODS

A literature search of scientific publications published in English was done for this comprehensive or narrative review

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using the electronic databases PubMed, Science Direct, Cochrane Library, and Google Scholar. The search included terms 'AE post-chemotherapy,' 'AE post-radiotherapy,' 'AE post-immunotherapy,' 'AE post-hormonal therapy for cancer' and 'AE post-cancer surgery.' Fifty articles and references within the articles so obtained were reviewed to identify additional studies available. Studies and case reports which met the following criteria were included in the present review:

- 1. English language publications
- 2. Those focusing on cutaneous adverse of cancer care.

Data obtained from studies and case reports were compiled and interpreted to prepare this review.

Post-chemotherapy dermatological events

Various specific and non-specific dermatological AEs may follow the administration of different classes of chemotherapeutic agents. Most of these are because of cytotoxic effects of these drugs on the actively multiplying cells of skin and appendages or because of direct toxicity due to local drug deposition.

Cutaneous events

Toxic erythema of chemotherapy

It includes palmoplantar erythrodysesthesia (PPED), intertriginous eruption of chemotherapy (IEOC), and neutrophilic eccrine hidradenitis (NEH). Direct toxicity of chemotherapeutic agents after their excretion through eccrine sweat glands, which are maximally concentrated on palms and soles, explains predominant acral affliction. Other factors such as friction and trauma may play a role in distribution. They usually present between 2 days and 3 weeks and doxorubicin, docetaxel, cytarabine, and capecitabine are most commonly implicated.

PPED is characterised by a prodrome of burning and itching followed by the appearance of well-defined erythema and oedema. This eruption may become bullous and erode. Paclitaxel has emerged as one of the drugs responsible for this eruption^[1,2] IEOC has dusky erythema, papules, and coalescing plaques in flexures, which resolves with hyperpigmentation.^[3,4] Similar eruption over palms, face, and trunk, along with pustules, urticated plaques and purpura is seen in NEH.^[5,6]

No standardised treatment regimen is available and thus symptomatic management is to be done.

Papulopustular eruptions

It is characterised by sterile pustules and papules in the seborrheic distribution of the face, scalp, chest, and back, usually within 2 weeks of drug administration. The most common culprits include EGFR inhibitors like cetuximab, tyrosine kinase inhibitors like erlotinib, and mitogenactivated protein kinase inhibitors like selumetinib.^[7]

Multinational Association of Supportive Care in Cancer has given a severity grading scale.^[8]

Dyspigmentation

Dyspigmentation may involve hyperpigmentation and hypopigmentation and occurs within a few days to 6 months. Former may be generalised, involve nail or mucosa, localised to the injection site, or maybe in distinct patterns. Flagellate hyperpigmentation due to bleomycin and serpentine supravenous hyperpigmentation along the distribution of veins, secondary to drugs such as fluorouracil are welldescribed patterned pigmentation.^[9] Hyperpigmentation usually resolves post drug discontinuation.

Hypopigmentation due to melanocyte toxicity, induced by drugs such as doxorubicin, imatinib, and dasatinib, occurs in symmetric distribution on the trunk or acrally and persists despite treatment termination.^[10]

Photosensitivity

Abnormal light reactivity following administration of certain chemotherapeutic drugs may be of phototoxic, photoallergic, or recall reactions to UV and visible lights.^[11] The phototoxic reaction appears within 12–24 h of culprit drug administration, presenting as well demarcated, painful erythema and oedema which may progress to vesiculation and desquamation, predominantly affecting photo exposed sites. This is due direct cytotoxic effects of the locally accumulated drug, which causes cell damage after absorption of a specific wavelength of light.^[11] Drugs commonly implicated include methotrexate, fluorouracil, and dacarbazine.^[12]

Eczematous eruption appearing primarily in photo distribution, after about 2–3 days, due to T-cell-mediated response to drug metabolite acting as photoantigen, is called photoallergic reaction. It resolves within 3 weeks with pigmentation. Tegafur and flutamide are implicated.^[13]

Recall reaction

It will be discussed in AE to radiotherapy.

Others

Less commonly encountered events include xerosis secondary to cetuximab, paclitaxel; hand-foot syndrome secondary to sunitinib, docetaxel, and ichthyosis secondary to methotrexate and generalised pruritus secondary to cyclophosphamide and epirubicin.^[14-16]

Hair and nail changes

Hair changes

Chemotherapy-induced alopecia is due to hair being involved as an innocent bystander of cytostatic toxicity of hair matrix cells. Incidence is almost 65%.^[17] Taxanes, doxorubicin, and cyclophosphamide are most commonly implicated. Initial hair fall is focal, mainly confined over the vertex and above ears. By 2–3 months, a more diffuse pattern of hair loss becomes established. Resolution post discontinuation becomes evident between 3 and 6 months.^[18]

Chemotherapy-induced hypertrichosis on treatment with cetuximab, erlotinib, and gefitinib may involve face, scalp, or eyelashes (trichomegaly).^[19] Scalp hair may become a slow growing, brittle and curly. Trichomegaly causes trichiasis and facial hypertrichosis causes cosmetic concerns. These changes occur 2–6 months into chemotherapy and may resolve on stopping treatment.^[20]

Nail changes

The incidence of nail changes ranges from 0 to 44%.^[21] Nail plate, matrix, and bed may all be involved and lead to onycholysis, beau's lines, onychomadesis, subungual haemorrhages, paronychia, and pigmentation. EGFR inhibitors, taxanes, and bleomycin are primary culprits. Photo-onycholysis and Mees lines secondary to Melphalan are well documented.^[22]

Chemotherapy-induced mucositis

Both chemotherapy and radiotherapy can lead to oral mucositis. This leads to dysphagia and consequently reduced oral intake and weight loss. Upregulation of proinflammatory cytokines and generation of reactive oxygen species leads to mucosal DNA damage and inflammation.^[23] Clinically, there are mucosal erythema, aphthae, and ulceration, predominantly on buccal mucosa but any part of the oral cavity can be involved. Secondary infection of ulceration may occur.^[24] National Cancer Institute has given a severity grading system.^[25]

Post-radiotherapy dermatological events

Radiotherapy consists of high-energy ionising radiation to target and kills cancer cells. It can be administered as external beam radiotherapy or as internal radiotherapy. Skin AE can be divided into early (days to weeks) and late (months to years).

Radiation dermatitis (RD)

It generally manifests as well-demarcated cutaneous changes in the irradiated field. It can be classified into acute and chronic RD. Acute RD occurs within 90 days of irradiation as erythema and oedema followed by desquamation. Severe cases may progress to necrosis and ulceration. Chronic RD may occur anytime between 15 days and 10 years, primarily due to increased collagen deposition, damaged elastin, and follicular structure loss.^[26]

Recall reaction

Anticancer drugs such as methotrexate, docetaxel, and paclitaxel lead to 'recalling' of an eruption similar to that of an acute radiation reaction, in a previously irradiated field.^[27] Irradiation and subsequent drug administration should be at least 7 days apart, with the majority of reactions occurring

when the interval is <2 months. The shorter the intervening duration, the more severe is the reaction.^[28] Occasionally, there may be the generalisation of the eruption beyond the irradiation field.

Others

Chronic ulceration, which may have to be biopsied to rule out secondary malignancy, may develop due to necrosis. Radiation-induced cutaneous vascular neoplasms such as angiosarcomas may occur in irradiated skin in breast conserving treatment.^[29] Post-irradiation burns and morphoea, erythema nodosum, and vitiligo have been reported.^[30-32]

Post-targeted therapy dermatological events

Targeted therapy aims to minimise the cytotoxic effects of chemotherapy on rapidly multiplying cells other than the tumour cells, by targeting specific tumourigenic pathways. Most commonly used therapies target epidermal growth factor receptor (EGFR), vascular endothelial growth factor (VEGF), human epidermal growth factor receptor 2 (HER2), anaplastic lymphoma kinase, and BRAF.

Common cutaneous AE associated with EGFR inhibitors has been clubbed together in an acronym-PRIDE complex which incorporates papulopustules and/or paronychia, regulatory abnormalities of hair growth, itching, and dryness due to EGFR inhibition.^[33] Since VEGF inhibitors interfere with angiogenesis, which is an important step in wound healing, wound dehiscence has been reported with the use of VEGF inhibitors.^[34] Cutaneous AE is rare with HER2 targeting agent but morbilliform rash and flagellate erythema have been reported with trastuzumab.^[35,36]

Among the targeted therapies, BRAF inhibitors have most commonly been reported to have cutaneous AE. BRIM 2, BRIM 3, and BREAK Phase II studies have mentioned several skin events post-treatment with vemurafenib and dabrafenib, most notable being pruritus, photosensitivity, maculopapular rash, Steven–Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN).^[37,38] Rarely reported AE includes panniculitis, Darier's like eruption, vasculitis, and erythema nodosum.^[37,39]

Post-immunotherapy dermatological events

Immunotherapy for cancer treatment targets the immunological checkpoints such as cytotoxic T-lymphocyteassociated antigen 4 (CTLA4) and programmed death 1 (PD1) which otherwise negatively regulate T-cell functions and thus their negation through immunotherapy boosts T-cell numbers and functions and helps to target and fight off cancer cells. Ipilimumab (CTLA-4 inhibitor) has been known to cause mild pruritus with no rash to severe eruptions such as SJS and TEN. Others include morbilliform eruptions, lichenoid exanthems, vitiligo, and prurigo nodularis.^[40,41] Nivolumab and pembrolizumab (PD1 inhibitors) have led to similar but less severe AE with the predominance of lichenoid eruptions, eczema, and vitiligo. Rarely, actinic keratoses and seborrheic keratoses have been seen after immunotherapy with nivolumab.^[42]

Post hormone therapy dermatological events

The rationale behind endocrine therapy in breast carcinoma is the presence of oestrogen and progesterone receptors. While oestrogen is responsible for the stromal proliferation, progesterone brings about glandular proliferation. Targeting their interaction with their receptors blocks their proliferative potential in ER/PR-positive breast cancers. This can be accomplished either using selective oestrogen receptor modulators like tamoxifen or by prevention of conversion of steroidogenic precursors into oestrogen using aromatase inhibitors.

Tamoxifen has been reported in various case studies to have caused porphyria cutanea tarda, subacute cutaneous lupus erythematosus, recall reaction, vasculitis, SJS/TEN, pseudolymphoma, life-threatening angioedema in patients of hereditary angioedema and melasma.^[43-48] Literature reports various rare skin side effects of AI like anastrozole, namely, maculopapular eruptions, erythema nodosum, vasculitis, subacute cutaneous lupus erythematosus, and erythema multiforme.^[49-52]

Post-surgical dermatological events

Surgical removal of the tumourigenic focus not only reduces the tumour cell load but also relieves patient stress, providing them psychological support that the underlying malignancy has been knived out. However, despite being the most established treatment modality for rooting out cancer, post-surgical complications such as dystrophic scars, hyperpigmentation, lymphoedema, and wound dehiscence have been commonly reported.^[53,54] If surgery is combined with chemoradiation, complication rates shoot up to include infection and/or flap necrosis, surgical site infection, flap necrosis, late dehiscence after suture removal, epidermolysis, seroma, and hematoma.^[55]

CONCLUSION

The nursing staff is round the clock dedicated to patient care and thus can prove very vital in screening cutaneous AE and adequately setting up referrals to aid early recognition and treatment of not only mild but also potentially lifethreatening complications such as SJS/TEN. However, identifying the skin side effects may be difficult for the untrained eye. Therefore, mandatory dermatological postings for the nursing staff involved in cancer care should be ensured.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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