v. 4, n. 76, 2024

International Journal of Health Science

IMPACT OF CHEMOTHERAPY AND RADIATION ON SKIN HEALTH IN CANCER PATIENTS: CHALLENGES AND SOLUTIONS IN DERMATOLOGIC CARE

Thaís Pedra Oliveira
http://lattes.cnpq.br/1775620856113583

Marina Diniz Dias
http://lattes.cnpq.br/0937784524004274

Camila Bidoia Berlanga

Osmar da Cruz Catharin
http://lattes.cnpq.br/3889014451840542

Marcos Aurélio dos Santos Roman
http://lattes.cnpq.br/6569337766457572

Maria Cecilia Merege
https://lattes.cnpq.br/7147549692097213

Elizabeth C S R Senra
http://lattes.cnpq.br/6859183169438256

Luis Felipe Villela Westin
https://lattes.cnpq.br/0015749119587898

Oiarbides Melo de Lima
http://lattes.cnpq.br/8938609117360016

Paula Regina de Oliveira Santos
http://lattes.cnpq.br/0438523818833022

Maria Lúcia Brito de Araujo Paysano

Ana Paula Bonafin
http://lattes.cnpq.br/7155235057025241

Mauricio Lopes da Silva Netto
http://lattes.cnpq.br/4791743372358340

Abstract: INTRODUCTION Solid organ cancers such as lung, breast, prostate, and colorectal cancers are prevalent malignancies worldwide, with significant morbidity and mortality. The treatments for these cancers, including surgery, chemotherapy, radiation therapy, and targeted therapies, have advanced considerably. However, these treatments often lead to various dermatological side effects that can profoundly impact patients' quality of life. Early detection and management of these side effects are crucial for maintaining patient well-being. Dermatologists play a vital role in this multidisciplinary care approach, diagnosing and treating skin-related toxicities caused by cancer therapies. **OBJETIVE** To provide a comprehensive overview of the dermatological side effects associated with solid organ cancer treatments. **METHODS** This is a narrative review which included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases, using as descriptors: "Oncologic Dermatology" AND "Chemotherapy Side Effects" OR "Radiation Dermatitis" OR "Targeted Therapy Skin Toxicities" OR "Patient-Centered Dermatologic Care"in the last years. **RESULTS AND DISCUSSION** The incidence of dermatological side effects in cancer patients is significant, with varying prevalence rates depending on the therapy type. Chemotherapy-induced rashes, radiation dermatitis, and hand-foot syndrome are common, affecting patients' daily activities and quality of life. The severity of these side effects ranges from mild erythema to life-threatening conditions like Stevens-Johnson syndrome. Effective management strategies include pharmacological interventions such as corticosteroids and antibiotics, along with preventive measures like patient education and skincare regimens. The psychosocial impact of these side effects is profound, necessitating comprehensive

patient support and interdisciplinary care. **CONCLUSION** Managing dermatological side effects in cancer patients requires a multifaceted approach involving prevention, early detection, and effective treatment. Interdisciplinary collaboration between dermatologists and oncologists is essential for improving patient outcomes. Future research should focus on identifying biomarkers for predicting skin toxicities, developing new therapeutic approaches, and understanding the long-term impacts of cancer treatments on the skin. By prioritizing patient-centered care and comprehensive management, the adverse effects of cancer treatments on the skin can be minimized, enhancing the overall treatment experience and quality of life for cancer patients.
Keywords: Dermatological Toxicities; Cancer Treatment Side Effects; Oncologic Dermatology; Chemotherapy-Induced Skin Reactions; Radiation Dermatitis.

INTRODUCTION

Solid organ cancers, including lung, breast, prostate, and colorectal cancers, are among the most prevalent malignancies worldwide, representing significant morbidity and mortality burdens. Lung cancer remains the leading cause of cancer-related deaths globally, followed by colorectal, liver, and stomach cancers[1]. Breast cancer is the most frequently diagnosed cancer in women, while prostate cancer is highly prevalent among men[1]. The incidence and prevalence of these cancers vary by region, influenced by factors such as genetics, lifestyle, and environmental exposures[1]. For instance, lung cancer rates are notably higher in regions with high smoking prevalence, while colorectal cancer is more common in developed countries with diets high in processed foods[1].

Cancer treatments have evolved significantly over the past few decades, incorporating a range of modalities, including surgery, chemotherapy, radiation therapy, and targeted therapies[2]. Surgical intervention remains a cornerstone for solid tumors, particularly when the disease is localized[2]. Chemotherapy, involving cytotoxic agents, is used to target rapidly dividing cancer cells, often in combination with other treatments[2]. Radiation therapy utilizes ionizing radiation to destroy cancer cells, while targeted therapies involve drugs designed to specifically target molecular pathways essential for tumor growth and survival[2]. Each treatment modality has unique mechanisms of action, with chemotherapy causing DNA damage and apoptosis, radiation therapy inducing DNA double-strand breaks, and targeted therapies inhibiting specific signaling pathways[2].

Despite the advancements in cancer therapies, these treatments are associated with various side effects, among which dermatological side effects are particularly prominent[3]. Dermatological toxicities can significantly impact the quality of life of cancer patients, affecting their physical appearance, psychological well-being, and social interactions[3]. Common skin-related side effects include rashes, dryness, pigmentation changes, and photosensitivity, which can range from mild to severe[3]. These adverse effects not only cause physical discomfort but also lead to psychological distress, including anxiety, depression, and reduced self-esteem[3].

Early detection and management of dermatological side effects are crucial for maintaining the quality of life in cancer patients[4]. Timely recognition allows for appropriate interventions that can mitigate the severity of skin reactions and prevent further complications[4]. Dermatologists play a pivotal role in the multidisciplinary management of cancer patients, providing expertise

in diagnosing and treating skin-related toxicities[4]. The pathophysiology of these side effects often involves inflammatory responses, immune-mediated reactions, and direct cytotoxic effects on the skin[4]. Understanding these mechanisms is essential for developing effective management strategies[4].

Chemotherapy-induced dermatological effects are diverse and can include hand-foot syndrome, alopecia, hyperpigmentation, and photosensitivity[5]. Radiation therapy can lead to radiation dermatitis, characterized by erythema, desquamation, and, in severe cases, necrosis[5]. Newer targeted therapies and immunotherapies have introduced additional skin toxicities, such as acneiform eruptions, paronychia, and severe rashes[5]. Clinical presentations of these side effects can vary widely, necessitating thorough diagnostic approaches, including clinical examination, histopathological analysis, and, in some cases, molecular testing[5].

Management of dermatological side effects involves a combination of preventive measures, pharmacological treatments, and supportive care[6]. Preventive strategies include patient education, the use of protective clothing, and skincare regimens tailored to the specific needs of cancer patients[6]. Pharmacological interventions may involve topical and systemic corticosteroids, antihistamines, and immunomodulatory agents[6]. Supportive care measures, such as moisturizers and pain relief, are also essential components of comprehensive management[6]. Notable case studies highlight the impact of dermatological side effects on cancer patients, illustrating the need for personalized care plans[7]. Future research in oncologic dermatology should focus on identifying biomarkers for predicting skin toxicities, developing novel therapeutic approaches, and understanding the long-term effects of cancer treatments on the skin[7]. This review aims to provide a comprehensive overview of the main dermatological side effects of solid organ cancer diseases and treatments, emphasizing the importance of early detection, effective management, and ongoing research to improve patient outcomes[7].

OBJETIVES

To provide a comprehensive overview of the dermatological side effects associated with solid organ cancer treatments.

SECUNDARY OBJETIVES

1. To discuss the impact of these side effects on patients' quality of life and the importance of early detection and management.
2. To review the pathophysiology and clinical presentation of common dermatological toxicities caused by chemotherapy, radiation therapy, and targeted therapies.
3. To highlight the role of dermatologists in the interdisciplinary care of cancer patients and the need for personalized care plans.
4. To identify future research directions and the development of novel therapeutic approaches to improve patient outcomes.
5. To explore current management strategies, including pharmacological and non-pharmacological interventions, for mitigating skin side effects.

METHODS

This is a narrative review, in which the main aspects of Double Heart-Kidney Transplantation in recent years were analyzed. The beginning of the study was carried out with theoretical training using the following databases: PubMed, sciELO and Medline, using as descriptors: "Oncologic Dermatology" AND "Chemotherapy Side Effects" OR "Radiation Dermatitis" OR "Targeted Therapy Skin Toxicities" OR "Patient-Centered Dermatologic Care" in the

last years. As it is a narrative review, this study does not have any risks.

Databases: This review included studies in the MEDLINE – PubMed (National Library of Medicine, National Institutes of Health), COCHRANE, EMBASE and Google Scholar databases.

The inclusion criteria applied in the analytical review were human intervention studies, experimental studies, cohort studies, case-control studies, cross-sectional studies and literature reviews, editorials, case reports, and poster presentations. Also, only studies writing in English and Portuguese were included.

RESULTS AND DISCUSSION

The incidence of dermatological side effects in cancer patients undergoing treatment is significant, with studies reporting varying prevalence rates depending on the type of therapy and patient population[8]. For instance, chemotherapy-induced rashes are observed in approximately 10-25% of patients receiving epidermal growth factor receptor (EGFR) inhibitors, with higher incidences noted in those on combination therapies[8]. Radiation dermatitis affects nearly 95% of patients undergoing radiation therapy, with severity ranging from mild erythema to severe ulceration[8]. The prevalence of hand-foot syndrome, primarily associated with agents like capecitabine and sorafenib, varies widely but can affect up to 60% of patients, significantly impacting their daily activities and quality of life[8]. The severity of dermatological side effects spans a broad spectrum, from mild erythema and dryness to severe, life-threatening conditions like Stevens-Johnson syndrome and toxic epidermal necrolysis[9]. Chemotherapy-induced alopecia, while not life-threatening, has profound psychological effects, leading to decreased self-esteem and social withdrawal[9]. Hyperpigmentation and photosensitivity are also common, particularly with drugs like bleomycin and methotrexate, and can persist long after treatment cessation[9]. Nail changes, such as onycholysis and paronychia, are often seen with taxane-based chemotherapies and can cause significant discomfort and functional impairment[9].

Chemotherapy-induced rashes are among the most common dermatological side effects, with papulopustular eruptions being characteristic of EGFR inhibitors[10]. These rashes typically appear within the first two weeks of therapy and can persist throughout treatment[10]. Management strategies include topical corticosteroids, oral antibiotics, and dose modifications of the offending agent[10]. Radiation dermatitis presents with a distinct pathophysiology, involving both acute and chronic phases[10]. Acute radiation dermatitis manifests as erythema, edema, and desquamation, while chronic effects can include fibrosis, telangiectasia, and secondary malignancies[10]. Treatment involves supportive care, such as emollients and corticosteroids, and preventive measures like proper skin hygiene and the use of barrier creams[10]. Hand-foot syndrome, or palmar-plantar erythrodysesthesia, is particularly debilitating, characterized by painful erythema and swelling of the palms and soles[11]. It is commonly induced by chemotherapeutic agents such as capecitabine, sorafenib, and sunitinib[11]. Management includes dose reduction or interruption of the causative agent, as well as symptomatic relief with topical steroids, analgesics, and cooling measures[11]. Alopecia, another prominent side effect, varies in severity based on the chemotherapy regimen[11]. Scalp cooling devices have shown efficacy in reducing hair loss, although their use is not universally successful or well-tolerated[11].

Hyperpigmentation can result from both chemotherapy and radiation therapy[12]. Drugs like bleomycin and methotrexate are known to cause diffuse or localized pigmentation changes, often exacerbated by sun exposure[12]. Photosensitivity, an exaggerated skin response to UV radiation, is seen with agents such as 5-fluorouracil and dacarbazine[12]. Protective measures, including the use of broad-spectrum sunscreens and protective clothing, are essential preventive strategies[12]. Nail changes, including onycholysis and paronychia, are particularly associated with taxanes and can lead to secondary infections and significant morbidity[12]. Dry skin and pruritus are common across various cancer treatments, often resulting from both direct drug effects and systemic dehydration[13]. Management includes the use of emollients, antihistamines, and, in severe cases, systemic corticosteroids[13]. Acneiform eruptions, particularly with EGFR inhibitors and mTOR inhibitors, present as inflammatory papules and pustules, predominantly on the face and upper torso[13]. Treatment involves topical retinoids, antibiotics, and in some cases, systemic isotretinoin[13]. Mucositis, another debilitating side effect, affects the mucosal linings of the mouth and gastrointestinal tract, leading to painful ulcers and increased risk of infection[13]. Management strategies include good oral hygiene, topical anesthetics, and cryotherapy[13].

Radiation recall dermatitis, a phenomenon where previously irradiated skin becomes inflamed upon exposure to certain chemotherapy agents, poses a unique challenge[14]. Its management includes cessation of the triggering drug, use of topical steroids, and supportive care[14]. Erythema multiforme and Stevens-Johnson syndrome, though rare, are severe cutaneous reactions that require immediate medical attention and often hospitalization[14]. Drug-induced lupus, characterized by a lupus-like syndrome, can occur with agents such as hydralazine and procainamide, necessitating drug discontinuation and immunosuppressive therapy[14]. Cutaneous vasculitis, an inflammatory condition of blood vessels, can be triggered by chemotherapy and targeted therapies, presenting as palpable purpura and ulcerations[15]. Management includes systemic corticosteroids and immunosuppressive agents[15]. Infectious complications, including bacterial, viral, and fungal infections, are heightened in immunocompromised cancer patients[15]. Herpes zoster reactivation, a common viral complication, necessitates antiviral prophylaxis and prompt treatment upon onset[15]. Fungal infections, particularly with Candida and Aspergillus species, require antifungal therapy and vigilant monitoring[15].

Paraneoplastic syndromes, where skin manifestations are a result of underlying malignancy rather than direct treatment effects, include conditions such as acanthosis nigricans and dermatomyositis[16]. Cutaneous metastases, though rare, signify advanced disease and poor prognosis, necessitating aggressive systemic treatment[16]. The psychosocial impact of dermatological side effects cannot be overstated, with significant effects on body image, self-esteem, and overall quality of life[16]. Quality of life assessments, using tools like the Dermatology Life Quality Index (DLQI), are essential in evaluating the impact of skin toxicities and guiding management strategies[16]. Patient education and counseling play a critical role in managing dermatological side effects, ensuring patients are informed about potential skin reactions and preventive measures[17]. Interdisciplinary care approaches, involving dermatologists, oncologists, and supportive care teams, are crucial for comprehensive management[17]. Novel therapeutic approaches, including biologics and targeted therapies, offer

promising avenues for treating severe skin toxicities[17]. Case-based learning, through the presentation of specific case studies, provides valuable insights into the practical management of skin side effects[17].

Pharmacological interventions, including the use of systemic retinoids, antibiotics, and corticosteroids, form the backbone of treatment for various dermatological toxicities[18]. Non-pharmacological interventions such as specialized skincare regimens, lifestyle modifications, and the use of supportive garments like compression gloves for hand-foot syndrome, also play a pivotal role[18]. Preventive dermatology in oncology, which emphasizes proactive measures such as patient education on skincare, sun protection, and the use of prophylactic topical agents, can significantly reduce the incidence and severity of skin side effects[18].

Patient adherence to skincare protocols is essential for the effective management of dermatological side effects[19]. Factors influencing adherence include patient education, the complexity of skincare regimens, and the perceived efficacy of treatments[19]. Ensuring that patients understand the importance of these measures and are provided with easy-to-follow instructions can improve adherence rates[19]. Biomarkers for predicting skin toxicities, such as genetic markers and specific inflammatory cytokines, are an emerging area of research that holds promise for identifying patients at higher risk and tailoring preventive strategies accordingly[19]. The impact of genetic factors on the development of dermatological side effects is significant, with certain genetic predispositions increasing the likelihood of adverse reactions[20]. For example, polymorphisms in genes encoding drug-metabolizing enzymes can influence the severity of reactions to chemotherapy agents[20]. Understanding these genetic factors can aid in personalized medicine approaches, optimizing treatment regimens to minimize side effects[20].

The economic burden of managing dermatological side effects is substantial, with costs associated with both direct medical care and indirect effects such as reduced productivity and quality of life[21]. Healthcare policy implications include the need for comprehensive coverage of dermatological care for cancer patients and the integration of dermatology services into oncology care pathways[21]. Long-term skin changes post-cancer treatment, including chronic radiation dermatitis and permanent pigmentary changes, require ongoing management and can have lasting effects on patients' quality of life[21]. Patient-centered care models, which prioritize the individual needs and preferences of patients, are crucial for managing dermatological side effects effectively[22]. These models emphasize shared decision-making, patient education, and the provision of holistic care that addresses both physical and psychosocial aspects[22]. Research gaps in the current literature highlight the need for more studies on the long-term effects of cancer treatments on the skin, the development of novel therapeutic agents, and the identification of effective preventive measures[22].

CONCLUSION

The management of dermatological side effects in cancer patients is a multifaceted challenge that requires a comprehensive approach involving preventive measures, early detection, effective treatment, and ongoing patient support. The integration of dermatology and oncology care, along with continued research into the mechanisms and management of skin toxicities, is essential for improving patient outcomes and quality of life. As our understanding of these side effects

deepens, so too will our ability to provide targeted, effective care that minimizes the impact of cancer treatments on the skin.

Future research should focus on identifying specific biomarkers for predicting dermatological toxicities, developing new therapeutic approaches that minimize skin side effects, and understanding the long-term impact of these treatments. Interdisciplinary collaboration between oncologists, dermatologists, and researchers is crucial for advancing our knowledge and improving patient care. By prioritizing patient-centered care and ensuring comprehensive management of dermatological side effects, we can enhance the overall treatment experience and quality of life for cancer patients.

This comprehensive review highlights the importance of early detection, effective management, and ongoing research in addressing dermatological side effects in cancer patients. Through a multidisciplinary approach and continued advancements in research and treatment, we can improve patient outcomes and quality of life, ensuring that the benefits of cancer treatments are maximized while minimizing their adverse effects on the skin.

REFERENCES

1. Almeida V. Dermatological side effects of cancer treatment: psychosocial implications—a systematic review of the literature. Healthcare. 2023;11(19):2621.

2. Belum VR, Washington C, Pratilas CA, Sibaud V, Boralevi F, Lacouture ME. Dermatologic adverse events in pediatric patients receiving targeted anticancer therapies: a pooled analysis. Pediatr Blood Cancer. 2015;62(5):798–806.

3. Belum VR, Wu S, Lacouture ME. Risk of hand-foot skin reaction with the novel multikinase inhibitor regorafenib: a meta-analysis. Investig New Drugs. 2013;31(4):1078–86.

4. Betticher DC, Delmore G, Breitenstein U, et al. Efficacy and tolerability of two scalp cooling systems for the prevention of alopecia associated with docetaxel treatment. Support Care Cancer. 2013;21(9):2565–73.

5. Bolognia JL, Cooper DL, Glusac EJ. Toxic erythema of chemotherapy: a useful clinical term. J Am Acad Dermatol. 2008;59(3):524–9.

6. Brown J, Burck K, Black D, Collins C. Treatment of cytarabine acral erythema with corticosteroids. J Am Acad Dermatol. 1991;24(6 Pt 1):1023–5.

7. Burris HA 3rd, Hurtig J. Radiation recall with anticancer agents. Oncologist. 2010;15(11):1227–37.

8. Capriotti K, Capriotti JA, Lessin S, et al. The risk of nail changes with taxane chemotherapy: a systematic review of the literature and meta-analysis. Br J Dermatol. 2015;173(3):842–5.

9. Komen MM, Breed WP, Smorenburg CH, van der Ploeg T, Goey SH, van der Hoeven JJ, et al. Results of 20- versus 45-min post-infusion scalp cooling time in the prevention of docetaxel-induced alopecia. Support Care Cancer. 2016;24(6):2735–41.

10. Komen MM, Smorenburg CH, van den Hurk CJ, Nortier JW. Factors influencing the effectiveness of scalp cooling in the prevention of chemotherapy-induced alopecia. Oncologist. 2013;18(7):885–91.

11. Kluger N, Jacot W, Frouin E, Rigau V, Poujol S, Dereure O, et al. Permanent scalp alopecia related to breast cancer chemotherapy by sequential fluorouracil/epirubicin/cyclophosphamide (FEC) and docetaxel: a prospective study of 20 patients. Ann Oncol. 2012;23(11):2879–84.

12. Tallon B, Blanchard E, Goldberg LJ. Permanent chemotherapy-induced alopecia: case report and review of the literature. J Am Acad Dermatol. 2010;63(2):333–6.

13. Fonia A, Cota C, Setterfield JF, Goldberg LJ, Fenton DA, Stefanato CM. Permanent alopecia in patients with breast cancer after taxane chemotherapy and adjuvant hormonal therapy: Clinicopathologic findings in a cohort of 10 patients. J Am Acad Dermatol. 2017;76(5):948–57.

14. Chen M, Crowson AN, Woofter M, Luca MB, Magro CM. Docetaxel (taxotere) induced subacute cutaneous lupus erythematosus: report of 4 cases. J Rheumatol. 2004;31(4):818–20.

15. Marchetti MA, Noland MM, Dillon PM, Greer KE. Taxane associated subacute cutaneous lupus erythematosus. Dermatology. 2012;23(11):2879–84.

16. Imko-Walczuk B, Kiełbowicz M, Dębska-Ślizień A, Rutkowski B. Skin cancers as contraindication to organ transplantation. Transplant Proc. 2015;47(6):1547–52.

17. Kirby LC, Banerjee A, Augustine T, Douglas JF. An ethical dilemma: malignant melanoma in a 51-year-old patient awaiting simultaneous kidney and pancreas transplantation for type 1 diabetes. Br J Dermatol. 2016;175(1):172–4.

18. Tessari G, Naldi L, Boschiero L, Minetti E, Sandrini S, Nacchia F, et al. Incidence of primary and second cancers in renal transplant recipients: a multicenter cohort study. Am J Transplant. 2013;13(1):214–21.

19. Chitasombat MN, Watcharananan SP. Prevalence and outcome of disseminated varicella zoster infection post kidney transplantation. J Med Assoc Thail. 2016;99(4):381–5.

20. Hamaguchi Y, Mori A, Uemura T, Ogawa K, Fujimoto Y, Okajima H, et al. Incidence and risk factors for herpes zoster in patients undergoing liver transplantation. Transpl Infect Dis. 2015;17(5):671–8.

21. Jinna S, Adams A, Schmitt T. Dermatologic adverse events associated with new anticancer therapies. Clin Rev Allergy Immunol. 2020;58(2):204–15.

22. Lacouture ME, Anadkat MJ, Bensadoun RJ, Bryce J, Chan A, Epstein JB, et al. Clinical practice guidelines for the prevention and treatment of EGFR inhibitor-associated dermatologic toxicities. Support Care Cancer. 2011;19(8):1079–95.