Review Article

Living with the Effects of Cutaneous Toxicities Induced by Treatment

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ABSTRACT

The introduction of targeted therapies in cancer treatment was accompanied with promising results including tumor control and patients survival benefits. However, these drugs just like their predecessors were associated with systemic side effects, including frequent and various cutaneous effects. Targeted therapies such as epidermal growth factor receptor, vascular endothelial growth factor receptor, kit, platelet-derived growth factor receptor, and BCR-ABL inhibitors as well as mammalian target of rapamycin inhibitors can induce cutaneous toxicities of varying severity. There are scarce studies on the actual impact of these toxicities on the patients' lives including the physical, social, and psychological aspects and overall quality of life. Patient's perspective in living with and beyond these toxicities remains largely uncharted but essential in optimizing care provided to those receiving treatment with targeted therapies.

Key words: Cutaneous toxicities, quality of life, targeted therapies

Introduction

Targeted therapies which include monoclonal antibodies and small-molecule inhibitors interfere with a specific molecular target (typically a protein) involved in tumor growth and progression.[1] These targets include growth factor receptors, signaling molecules, cell cycle proteins, modulators of apoptosis, and molecules involved in invasion and angiogenesis, which are essential for the development and homeostasis in normal tissues.

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The transition from conventional cytotoxic agents to rationally designed, molecularly targeted drugs was mainly driven by the increase in the knowledge of the molecular drivers of cell transformation and the identification of specific signaling pathways that controlled cell survival processes. Molecular-targeted therapies are being used in daily clinical practice as a component of therapy for many common malignancies including advanced colorectal and

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lung cancer, breast and pancreatic cancer to report a few. Similarly to traditional chemotherapy, targeted therapies can induce various side effects to patients.[2]

Cutaneous Toxicities

It is now well recognized that targeted therapies are not devoid of adverse effects. Cutaneous side effects are the most frequent and can lead to dose modifications or the interruption of epidermal growth factor receptor (EGFR) inhibitor treatment.[3] Targeted therapies have therefore been associated with a number of cutaneous toxicities including acneiform rash (papulopustular eruption), xerosis, pruritus, nail and periungual toxicity, and hair changes.[4] Most of these side effects are directly related to the specific molecular target in normal tissues inhibited or modulated by the specific drug. For example, the inhibitors of the EGFR are involved in proliferation, survival, and differentiation, and in the skin, the EGFR and its ligands are important in the cycle of keratinocyte maturation.[4] Inhibiting EGFR results in a typically papulopustular eruption which can be observed in most patients treated with this family of anti-EGFR agents.[5]

The (New) Life with Cutaneous Toxicities

Preceding studies have attempted to establish the negative manifestations of treatment-induced cutaneous toxicities in cancer patients. The majority of these studies concluded that these toxicities can have a negative impact on the patient's overall quality of life (QoL).[6] Other studies have emphasized on the psychological effects of these toxicities such as depression, anxiety, and vulnerability.[7] It is worth highlighting that patients may have their psychological balance threatened by necessary changes in the course of the disease and of treatments, which includes changes in self-esteem. Leite *et al*.[8] in a descriptive analytical cross-sectional study with 156 cancer patients evaluated their self-esteem when undergoing chemotherapy. Approximately one-third of the patients (29.5%) reported average self-esteem and low self-esteem. The negatively affected emotional and psychological state of the patient can subsequently lead to experiencing low self-esteem and altered self-image. The experience of psychological problems such as changes in their self-esteem materializes once the patients' perception on body image is related to the new life condition.[9] These feelings can be exacerbated by the physical changes on the patient's body, impairing his or her social interactions, and relationships with significant others.[10] There is evidence to support the association of the long-term negative effects of chemotherapy with poorer physical, social, and sexual functioning.[11]

Although the negative impact of treatment-induced toxicities on the patient's life has been acknowledged, the available studies did not explore how these toxicities interfere with the everyday living. Consistent evidence in the literature demonstrates that specific cutaneous toxicities such as the palmar-plantar erythrodysesthesia can result in dose reduction as symptoms can sometimes progress to a degree of discomfort that interrupts activities of daily living.[12,13]

The lack of comprehensive understanding of these toxicities' impact can lead to underestimating patient's reporting of symptoms and poor management. In turn, these can lead to unnecessary suffering, underreporting of symptoms, and poor adherence to treatment. Most cutaneous toxicities disorders are generally mild or moderate in severity and can be managed by appropriate interventions or by reducing or interrupting the targeted agent dose. Therefore, appropriate and timely management becomes of paramount importance to make it possible to continue a patient's QoL and maintain compliance through preventive management (where possible) and optimization of patients' care. However, if these adverse events are not managed appropriately and become more severe, treatment cessation may be warranted compromising clinical outcome.[14]

As reported above, preceding studies emphasized on studying the impact of cutaneous toxicities on patients' QoL. For example, Charles *et al*.[15] in a longitudinal quantitative pilot study explored the QoL before and 30 days after treatment. In total, 27 patients with a metastatic lung, digestive, or cutaneous cancer participated in both evaluation times. The authors concluded that in the majority of the patients, there was a significant association between dermatological symptoms with a lower QoL. Low QoL in these patients was characterized by difficulties in performing household works and leisure activities and a social functioning impairment.[15] Similarly Ra *et al*.[16] in another longitudinal prospective study, they assessed 73 patients' QoL at the time of enrollment and 3 months following the completion of treatment. Patients showed a significant change in their QoL over the course of treatment. The low QoL levels found in this group of patients were significantly lower when compared to patients diagnosed with other diseases who present with similar cutaneous conditions but comparable to findings in cancer patients with dermatological toxicities.[17] The authors reported that the cutaneous symptoms and relevant feelings generated the greatest concern among the patients. The persistence or recurrence of the skin condition was also reported by the patients as a source of anxiety as they were unsure how these adverse effects were connected to the progression of the treatment, indicating a lack of appropriate advance knowledge.

In a recent Ricoeurian hermeneutic phenomenological study, Charalambous and Charalambous[10] explored the lived experiences of 22 colorectal, pancreatic, and nonsmall cell lung cancer patients living with cutaneous toxicities following treatment with targeted therapies. The authors aimed to reveal the multidimensional impact of the cutaneous toxicities on the patients' lives. The three main themes that were identified by the authors encapsulated the significant impact and the alterations induced in one's life by these adverse effects: "ashamed of what I have become," "surrender to cancer," and "mourning for the loss of my body." Changes in the appearance of their skin, nails, face, and hair all contributed to altered body image, creating feelings of rejection and stigmatization, and exacerbating anxiety and depression. These changes not only altered the way the patients were viewing their own body but also most significantly they experienced an alteration how their loved ones and significant others viewed them. As a result, their social relationships were challenged and their intimate relationships were impaired. They concluded that the treatment-induced cutaneous toxicities distorted patients' daily living in ways that led to negative manifestations and effects on their self-image, social engagement, and intimate relationships. The alterations on body image and their subsequent effects on intimate relations and sexuality have received increased attention in the literature, and consistent evidence provides support of the associations between these variables. For example, Harcourt and Frith[18] in a qualitative study found that women experienced altered appearance during chemotherapy. As a result, women described the experience as feeling less attractive which negatively interfered with their sense of confidence and relationships with their partners. Similarly, in a study by Biglia *et al.*,[19] breast cancer patients reported worsening sexual functioning, desire, arousal, and quality of partnered relationships following chemotherapy when compared to baseline, while in other studies, chemotherapy was also associated with unmet sexual needs.[20]

Conclusion

As an increasing number of patients continue to receive treatment with targeted therapies for various types of cancer, cutaneous toxicities have become an evident challenge for patients among this population. Comprehensively, addressing these toxicities is, in turn, becoming an apparent necessity in managing the care of patients with cancer. This necessity appears to be driven by the substantial proportion of patients that do not readily adjust to life after the cutaneous toxicities and that ongoing distress may be associated with residual concerns resulting from changes to their physical appearance and how they perceive their bodies. The challenge faced by health-care professional within the clinical context is even greater taking into consideration that these cutaneous toxicities appear to have an impact on the physical, social, and psychological dimensions of the person. Informing the patients on these toxicities and the available management approaches need to be incorporated in the plan of care even before the onset of treatment. Advance knowledge of treatment-induced toxicities and proactive management approaches has been shown to decrease anxiety, improve adherence to cancer treatment, and improve QoL and patient outcomes.[21] Studies suggest that treatment-induced side effects are less anxiety provoking when anticipated and better managed overall.[6] The secondary effects of cutaneous toxicities (i.e., low self-esteem and low sexuality) need also to be acknowledged and addressed throughout the cancer care continuum. In doing so, any barriers to communication regarding such issues involving the health-care professionals and the patient need to be addressed. Identifying and developing treatment plans that correspond to the individual needs of the patient are essential in improving the QoL in patients suffering from cutaneous toxicities and other subsequent effects.

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Conflicts of interest

There are no conflicts of interest.

References

1. Widakowich C, de Castro G Jr., de Azambuja E, Dinh P, Awada A. Review: Side effects of approved molecular targeted therapies in solid cancers. Oncologist 2007;12:1443-55.
2. Izar B, Rotow J, Gainor J, Clark J, Chabner B. Pharmacokinetics, clinical indications, and resistance mechanisms in molecular targeted therapies in cancer. Pharmacol Rev 2013;65:1351-95.
3. Heidary N, Naik H, Burgin S. Chemotherapeutic agents and the skin: An update. J Am Acad Dermatol 2008;58:545-70.
4. Lacouture ME. Mechanisms of cutaneous toxicities to EGFR inhibitors. Nat Rev Cancer 2006;6:803-12.
5. Gerber DE. Targeted therapies: A new generation of cancer treatments. Am Fam Physician 2008;77:311-9.
6. Haley AC, Calahan C, Gandhi M, West DP, Rademaker A, Lacouture ME. Skin care management in cancer patients: An evaluation of quality of life and tolerability. Support Care Cancer 2011;19:545-54.
7. Rouanne M, Massard C, Hollebecque A, Rousseau V, Varga A, Gazzah A, *et al*. Evaluation of sexuality, health-related quality-of-life and depression in advanced cancer patients:

A prospective study in a phase I clinical trial unit of predominantly targeted anticancer drugs. Eur J Cancer 2013;49:431-8.
8. Leite MA, Nogueira DA, Terra Fde S. Evaluation of self-esteem in cancer patients undergoing chemotherapy treatment. Rev Lat Am Enfermagem 2015;23:1082-9.
9. Bertan FC, Castro EK. Quality of life, anxiety and depressions indicators and sexual satisfaction in adult patients with cancer. Rev Salud Soc 2010;1:76-88.
10. Charalambous A, Charalambous M. "I lost my image, the image others know me by": Findings from a hermeneutic phenomenological study of patients living with treatment-induced cutaneous toxicities. Res Nurs Health 2016;39:187-96.
11. Ganz PA, Desmond KA, Leedham B, Rowland JH, Meyerowitz BE, Belin TR. Quality of life in long-term, disease-free survivors of breast cancer: A follow-up study. J Natl Cancer Inst 2002;94:39-49.
12. Anderson R, Jatoi A, Robert C, Wood LS, Keating KN, Lacouture ME. Search for evidence-based approaches for the prevention and palliation of hand-foot skin reaction (HFSR) caused by the multikinase inhibitors (MKIs). Oncologist 2009;14:291-302.
13. Wood L. Managing the side effects of sorafenib and sunitinib. Community Oncol 2006;3:558-62.
14. Kiyohara Y, Yamazaki N, Kishi A. Erlotinib-related skin toxicities: Treatment strategies in patients with metastatic non-small cell lung cancer. J Am Acad Dermatol 2013;69:463-72.
15. Charles C, Sultan S, Bungener C, Mateus C, Lanoy E, Dauchy S, *et al.* Impact of cutaneous toxicities associated with targeted therapies on quality of life. Results of a longitudinal exploratory study. Bull Cancer 2013;100:213-22.
16. Ra HS, Shin SJ, Kim JH, Lim H, Cho BC, Roh MR. The impact of dermatological toxicities of anti-cancer therapy on the dermatological quality of life of cancer patients. J Eur Acad Dermatol Venereol 2013;27:e53-9.
17. Andreis F, Rizzi A, Mosconi P, Braun C, Rota L, Meriggi F, *et al.* Quality of life in colon cancer patients with skin side effects: Preliminary results from a monocentric cross sectional study. Health Qual Life Outcomes 2010;8:40.
18. Harcourt D, Frith H. Women's experiences of an altered appearance during chemotherapy: An indication of cancer status. J Health Psychol 2008;13:597-606.
19. Biglia N, Moggio G, Peano E, Sgandurra P, Ponzone R, Nappi RE, *et al.* Effects of surgical and adjuvant therapies for breast cancer on sexuality, cognitive functions, and body weight. J Sex Med 2010;7:1891-900.
20. Hwang SY, Chang SJ, Park BW. Does chemotherapy really affect the quality of life of women with breast cancer? J Breast Cancer 2013;16:229-35.
21. Gandhi M, Oishi K, Zubal B, Lacouture ME. Unanticipated toxicities from anticancer therapies: Survivors' perspectives. Support Care Cancer 2010;18:1461-8.