

Cutaneous toxicities of targeted cancer therapies

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With the increasing use of epidermal growth factor receptor inhibitors, toxicities are also on the rise. But there are ways to prevent and treat the side effects, detailed in this article.

Many solid malignancies are now treated with specific inhibitors of oncogenic molecules, including single-targeted kinase inhibitors and multitargeted kinase inhibitors. A welcome improvement in oncology, these drugs specifically target aberrant proteins in cancer cells and result in fewer nonspecific and hematopoietic side effects. In spite of the benefits, these agents frequently

result in cutaneous toxicities. Most notably, epidermal growth factor receptor inhibitors (EGFRs) and multitargeted agents lead to toxicities involving the skin, hair, and nails.

The toxicities

Cutaneous reactions associated with targeted therapies include a papulopustular skin rash, paronychia and hair changes, xerosis, pruritus, and ulcers in the mouth and nasal mucosa.¹ Isolated reports of cutaneous squamous cell carcinoma have also been reported with the use of sorafenib (Nexavar).³ Papulopustular skin rash is the most common cutaneous reaction to EGFR inhibitors and is frequently associated with itching and pain, which lead to anticancer drug modification in up to nearly one-fifth of patients.

Papulopustular skin rash is also referred to as acneiform eruption, rash, acne folliculitis, acneiform follicular rash, acnelike rash, maculopapular skin rash, and monomorphic pustular lesions. The rash is characterized by pustular or papular follicular eruption and usually appears on visible areas such as the face, neck, and chest 7–10 days after initiating therapy. Xerosis, pruritus, and secondary bacterial infection may accompany papulopustu-

lar skin rash. Hair may become curly and brittle, and increased hair growth in the face with long eyelashes is contrasted by alopecia of the scalp. Paronychia, or inflammation of the nail that looks like an ingrown nail, may occur. Nails may be more likely to be brittle and slow-growing.¹

Where reported

In 2006, Lacouture et al reported the case of a 60-year-old patient with chemotherapy-resistant renal cell carcinoma who was treated with sorafenib.³ This patient developed lesions on his head following several months of sorafenib treatment. Skin biopsies of the seven lesions revealed that one showed actinic keratoses (AKs) and four showed invasive squamous cell carcinomas (SCCs). Although several possibilities exist, the mechanism by which sorafenib may cause inflammation of AK and SCC has not yet been identified.³

However, the reporting, characterization, and dissemination of information about the dermatologic side effects of targeted cancer therapies have been complicated by the fact that these toxicities have often been reported by caregivers and investigators not trained in dermatology or skin toxicities. But some cases have been report-

Fast Facts

OVER THE PAST DECADE, new cancer therapies that target the human epidermal growth factor receptor (HER1/EGFR) have been developed. This receptor is dysregulated in a variety of solid tumors, including head and neck, non-small cell lung, prostate, glioma, gastric, breast, colorectal, pancreatic, and ovarian cancers. The approved agents commonly prescribed include erlotinib (Tarceva), cetuximab (Erbix), panitumumab (Vectibix), sorafenib (Nexavar), sunitinib (Sutent), and imatinib (Gleevec). Their side effects may lead to poor adherence with therapeutic regimens, dose interruption, and/or reduced quality of life for cancer patients.^{1,2}

ed to interdisciplinary centers such as the SERIES (Skin and Eye Reactions to Inhibitors of EGFR and kinaseS) Clinic.⁴ The advantage of such clinics is that their collaborative approach facilitates communication between oncologists and dermatologists, increases patient education, and encourages early diagnosis and treatment.

Actions taken

Among single- and multitargeted anticancer agents approved by the US Food and Drug Administration, dermatologic side effects are some of the most commonly reported toxicities.¹ However, it has been difficult for oncologists to appropriately identify, describe, and manage these untoward effects, as oncologists often are not familiar with dermatologic disease, descriptive terminology, and therapeutic management. Furthermore, the current grading system National Cancer Institute–Common Toxicity Criteria (NCI–CTC v3.0) applied to dermatologic toxicity is obsolete and inadequate; it does not take into consideration factors such as the impact on quality of life or the severity of lesions within different anatomical sites. Subsequently, randomized controlled trials to investigate dermatologic side effects of these targeted anticancer agents are lacking.¹ The absence of robust clinical data on these adverse events has hindered clinicians and investigators from making optimal use

of targeted treatments.

Recommendations

There are ways to prevent EGFR toxicities. Recommend to patients that they:

- Use sunscreens with an SPF > 30 containing zinc oxide or titanium dioxide;
- Avoid sun exposure;
- Wash with gentle soaps and shampoos;
- Moisturize the skin with creams or ointments.

To mitigate side effects, and ensure early intervention and uninterrupted cancer treatment, oncologists should educate patients on the importance of early detection and immediate reporting of the side effects.

Ideally, patients presenting with serious adverse cutaneous events should be evaluated in an interdisciplinary fashion. Organized referral centers and registries are needed to increase the early and immediate identification and treatment of these events. Such efforts would also identify risk factors for developing skin toxicities as well as effective management strategies, all of which would ensure maximum benefit from these novel therapies.

General recommendations for treating and preventing these reactions vary based on presentation and causal agent:

- Papulopustular rashes can be treat-

ed briefly with topical steroids/antibiotics and oral tissue-penetrating tetracycline derivatives;

- Paronychia should be treated with oral antibiotics, cultures should be obtained, and topical steroids/antibiotics used;

- Pruritus can be managed with topical anesthetics (pramoxine, lidocaine) or oral antipruritics (pregabalin [Lyrica], antihistamines).

Oncologists should give careful consideration to other chemotherapeutic agents or dose reduction when toxicities interfere with treatment.

References

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