Severe Acneiform Eruption following Trastuzumab Therapy

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Trastuzumab is a human epidermal growth factor receptor (HER)-2/neu inhibitor approved by the US Food and Drug Administration for the treatment of HER-2–positive breast cancer. Although acneiform rash, also known as papulopustular eruption, is a common cutaneous toxicity of epidermal growth factor receptor (EGFR) inhibitors,1 it has not been shown to be associated with trastuzumab therapy. In this article, we report on a patient who developed grade 3 acneiform rash (based on grading criteria by National Cancer Institute-Common Terminology Criteria for Adverse Events) after receiving trastuzumab therapy.

Case Report

A 51-year-old woman with stage I estrogen receptor–weakly positive, progesterone receptor–negative, HER-2–positive breast cancer underwent a bilateral modified radical mastectomy, followed by a regimen of docetaxel/carboplatin/trastuzumab (TCH). At the time of treatment, she was not taking any other medications or herbal supplements. After receiving the first cycle of TCH, she presented with acneiform eruptions, predominantly on the face and scalp, which became more severe and extensive after the second cycle. Compared with the classic presentations of EGFR inhibitor–associated acneiform rash, the papules and pustules were larger in size (>0.5 to 1 cm; Figure).

She was treated with oral minocycline and topical mupirocin cream, both of which produced only a modest response. She was then given a local corticosteroid injection to the scalp lesions and showed a marked improvement. Despite the improvement of the skin lesions, however, she experienced three separate episodes of bacterial skin infections in the setting of nonneutropenia (leukocyte counts: range, 5300-7400/µL), all of which occurred at 3- to 4-week intervals (Table). The first infectious episode occurred 1.5 months after the initiation of chemotherapy at the left mastectomy site, followed by an infection at the port site, then a cellulitis of the right upper extremity.

Despite the severe cutaneous complications, the patient has successfully completed all six cycles of TCH at full weight-based dose (Table), and is currently being treated with intravenous trastuzumab (6 mg/kg every 3 weeks) as single-agent therapy. She experienced complete resolution of acneiform eruption, but with residual facial hyperpigmentations.

Discussion

Drug-induced acneiform rash and acne vulgaris share a close resemblance in appearance, but they differ pathologically and etiologically.2 Unlike acneiform rash, which is predominantly inflammatory papulopustular eruptions without the presence of comedones or any apparent infectious etiology, acne vulgaris is characterized by the presence of sebum and comedones.2,4

Like EGFR, HER-2 receptors have been shown to play a role in keratinocyte differentiations in the skin5; hence, the observed cutaneous toxicity in our patient could be associated with the deregulated process of keratinocyte differentiations, which is related to trastuzumab therapy. Although “acne” has been reported in 2% of trastuzumab-treated patients,6 clinical presentations of acne differ from the acneiform rash we observed in our patient. Likewise, although docetaxel has been associated with various types of cutaneous toxicities, this specific dermatologic toxicity—acneiform rash—has not yet been described with docetaxel therapy.7

Based on an objective causality assessment scale,8 trastuzumab is a possible cause of the cutaneous toxicity observed in our patient. The pattern of trastuzumab-induced acneiform eruption appears to resemble that of severe acneiform rash...
EGFR inhibitors in that the eruption subsided with multiple exposure.

Drug-induced pustules, in general, have been shown to be sterile. Nonetheless, the increased Staphylococcus carrier state and/or the impaired skin barriers in patients with severe papulopustular eruption have been suggested as the possible causes for developing secondary bacterial infections. In fact, a recent study showed that >50% of cases with drug-induced pustules were carriers for Staphylococcus. In our patient, bacterial cultures were not obtained at the time of acneiform eruption, thus the causal relationship could not be clearly established.

Conclusion

Current management strategies for acneiform rash include alcohol-free topical emollient, oral antihistamine, topical clindamycin gel, and a tetracycline-derivative systemic antibiotic. Our patient responded well to local corticosteroid therapy, but the use of corticosteroids in acneiform rash remains controversial.

Based on our experience, vigilant surveillance for infectious complications is warranted in patients who develop severe drug-induced acneiform rash. Furthermore, in light of documented cases of methicillin-resistant Staphylococcus aureus superinfection associated with acneiform rash, nasal sterilization has also been suggested as a preventive strategy against bacterial skin infection.

Therefore, in patients who develop severe drug-induced acneiform eruption, it may be deemed appropriate to obtain bacterial cultures and prescribe a course of nasal mupirocin, at the time of eruption, to eradicate Staphylococcus colonization and minimize the risk of developing secondary bacterial infections.

Disclosure

Drs Kim and Adelson did not report any potential financial conflicts of interest.

References