A novel approach to manage skin toxicity caused by therapeutic agents targeting epidermal growth factor receptor

Inhibition of the epidermal growth factor receptor (EGFR) represents one of the most important avenues of research and development in cancer therapy.

The cutaneous toxicity [papular–pustular eruption (PPE), seborrheic dermatitis-like erythema, diffuse xerosis, inflammatory paronychia, painful fissures on fingers, hair changes] frequently described with EGFR inhibitors (EGFRI) can result in significant physical discomfort and often lead to interruption or dose modification of EGFRI.

Therefore, appropriate management of skin toxicity is mandatory to allow adequate drug administration and to improve health-related quality of life and therapy outcomes.

Although the mechanism by which inhibition of EGFR leads to skin toxicity is still largely unknown, EGFR is primarily expressed in undifferentiated proliferating basal and suprabasal keratinocytes both in the epidermis and in the outer layers of hair follicle [1]. The activation of EGFR by its ligand EGF regulates normal keratinocytes proliferation, differentiation, migration, and survival in the skin [1].

Tan et al. [2] demonstrated that MAPK activity shows a trend in association with skin toxicity after tyrosine kinase inhibitors administration and they concluded that by giving an inhibitor of MAPK phosphorylation to patients undergoing treatment with EGFR inhibitors, clinicians could control the skin toxicity.

It has recently been demonstrated that topical application of green tea polyphenols in rats prevents the UVB-induced oxidative phosphorylation of MAPK [3] and nicotinamide also inhibits the MAPK pathways in cell cultures and in rats [4, 5].

Starting from these data, we report our experience in the management of EGFR skin toxicity using a new therapeutic approach, based on the use of a combined therapy: topical application of a moisturizer cream containing green tea polyphenols twice a day and oral administration of nicotinamide (1 g/die) for 12 weeks. The moisturizer cream containing green tea was applied on face, hands, neck, back, shoulders, arms, and legs, starting when skin toxicity occurred.

Topical application of 1% clindamycin gel and/or systemic administration of minocycline 100 mg/die were provided in case of super bacterial infection, until infection resolved completely.

Treatment was variably effective on different aspects of skin toxicity: PPE and itching rapidly improved, with a significant reduction of prevalence and clinical severity in treated patients at week 6. Seborrhedic dermatitis erythema improved more slowly after 12 weeks of therapy (Figure 1). Paronychia, xerosis, and fissures were less responsive even if they demonstrated a positive trend to the treatment.

Finally, all treated patients reported a significant improvement in life quality, which represents one of the most important goals in the control of EGFR-related skin toxicity.

To date, no controlled clinical studies investigating treatment options for EGFRI skin toxicity have been fully reported and as a result, evidence-based treatment recommendations are not yet possible.
Our experience showed that in a homogeneous and prospective setting, a simple nicotinamide/green tea polyphenols-based therapy is extremely effective in order to improve skin toxicity due to EGFRI and merits further investigation.

In addition, evaluation of patient, nursing, and physician education tools is important and may aid in the promotion of prophylactic intervention, early recognition, and best practices in skin toxicity management, thereby maximizing potential clinical benefit from the EGFRI class of agents, reducing the risk of serious infection, and improving patient quality of life.

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