"Immunopeeling" Using Imiquimod for Xeroderma Pigmentosum

Dear Editor,

Patients with xeroderma pigmentosum (XP) feature dry skin, freckles, mottled hyper- and hypopigmentation, actinic keratosis, and multiple skin cancers [basal cell carcinoma (BCC), squamous cell carcinoma, and melanoma] involving sun-exposed areas like the face, neck, and hands. In addition, the underlying DNA repair defect leads to field cancerization. Besides the disease-related morbidity and mortality, social stigma and discrimination, due to dyspigmentation, significantly impair the quality of life of these patients.

Topical imiquimod has been used for the treatment of multiple BCCs and actinic keratosis in patients with XP as well as for chemoprevention of skin cancers.[1] Similarly, cryosurgery in the form of cryopeeling has been used to treat multiple actinic keratoses as well as to improve dyspigmentation in patients with multiple solar lentigines.[2] Chemical peeling using trichloroacetic acid has also been used in patients with xeroderma pigmentosum.[3] Imiquimod cream has been used as an "immune chemical peel" to assess its antiaging properties in improving the cosmetic appearance of facial skin.[4] We propose the term "immunopeeling" for immune-mediated peeling using an immune response modifier as a peeling agent. While chemical peeling and cryopeeling use chemicals and cryogens, respectively, for controlled destruction, the proposed "immunopeeling" entails the use of an immunomodulatory agent (or immunopeel) for esthetic and therapeutic purposes, leading to longer-lasting effects on the skin. Imiquimod, a Toll-like Receptor 7 and 8 agonist and a cytokine inducer, is effective against skin pre-malignancies and malignancies, and improves dyspigmentation and skin texture [Figure 1]. Imiquimod acts as a topical irritant, causing irritant contact dermatitis. However, unlike other irritants, it induces significant exfoliation. This effect is achieved through the stimulation of keratinocyte proliferation via the activation of plasmacytoid dendritic cells, ultimately leading to the activation of IL-23/Th17 pathway.[5,6] As a result, the peeling effect is brought about by the activation of immune cells rather than the conventional mechanisms of chemical peels involving a reduction in corneocyte adhesion or protein denaturation. Imiquimod is available in single-use packets containing 250 mg of the cream, which is equivalent to 12.5 mg of imiquimod. For the immunopeeling effect, it should be applied to the entire treatment area by gentle rubbing till the cream is no longer visible, and it is to be left on the skin for 8 hours, preferably overnight, avoiding the eyes, lips, and nostrils. It is advisable to wash the treatment area with mild soap and water 10 minutes before, and 8 hours after application. Each application should use no more than one

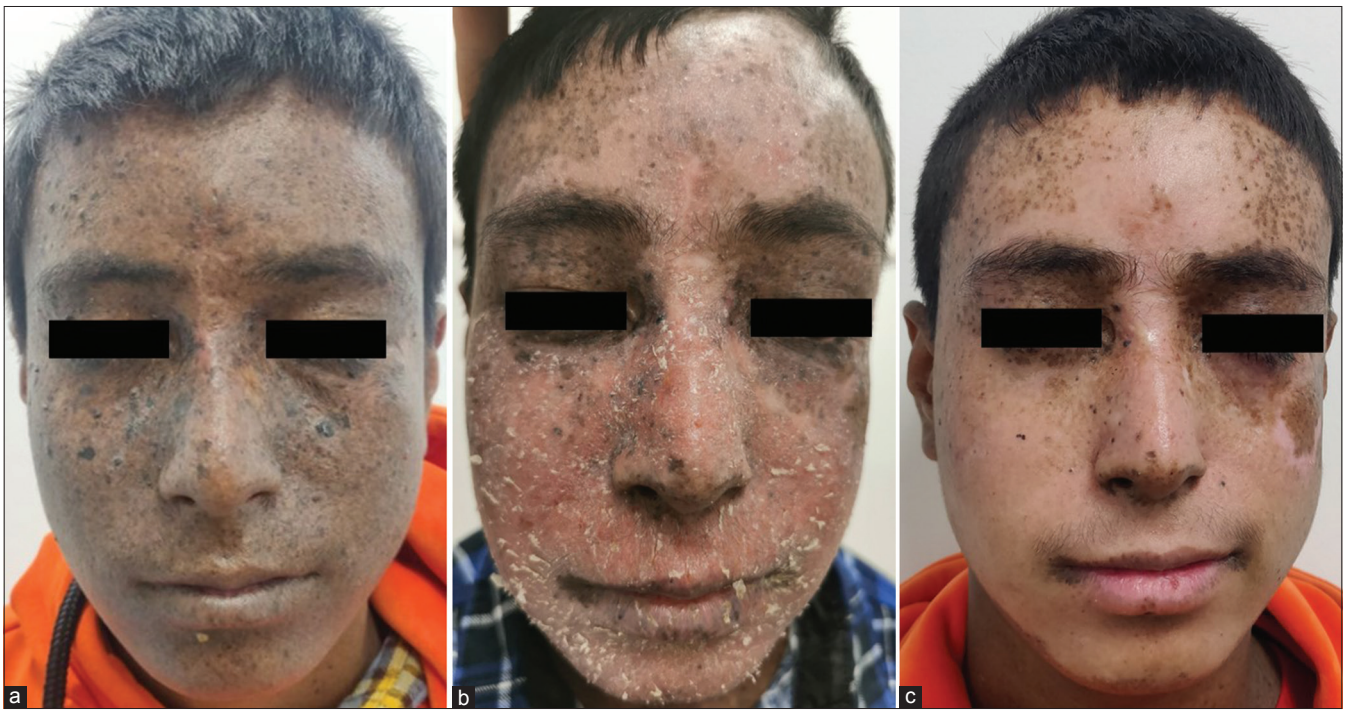

Figure 1: A 14-year-old boy with xeroderma pigmentosum: (a) at baseline, (b) after 4 weeks following imiquimod application showing exfoliation (peeling), and (c) at the end of 4 months showing marked improvement in dyspigmentation and appearance

packet for a contiguous treatment area. It should be applied every alternate day for the initial 4 months; thereafter, the frequency can be decreased to 1–2 applications every week for maintenance. If used correctly and consistently with adequate photoprotection, it results in a significant improvement in the cosmetic appearance and thereby improves the quality of life of the patients. The timeframe for clinical response varies between 4 and 16 weeks. A few patients have been followed for up to 2 years without any recurrence in the treated area, with or without prophylactic application of imiquimod.[7] However, adequate and strict photoprotection must be advised.

The most common adverse reactions are application site itching, burning, erythema, edema, erosion, ulceration, and crusting due to the stimulation of local immunity. These usually subside within 2 weeks following discontinuation. However, moisturizers and/or topical steroids may be used to hasten recovery.[8] Topical indirubin, allicin, chrysin, rhodomyrtone, astilbin, olive oil-based methotrexate-loaded nano-emulsion gel, and heat shock protein 70 (hsp70) have been used for the treatment of imiquimod-induced psoriasiform dermatitis.[9] However, flu-like systemic signs and symptoms, including malaise, fever, nausea, myalgias, and rigor, may occur due to a systemic inflammatory response warranting interruption of therapy. Long-term use frequently leads to depigmentation. Calcipotriol and 5-fluorouracil are other immunomodulatory agents that can also be used as immunopeel. These can also be tried in patients with chronic actinic damage, widespread solar lentigines, actinic keratosis, and clearance of residual pigment islands in universal vitiligo.[10]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the father has given his consent for his son's images and other clinical information to be reported in the journal. The father understands that the names and initials of his son will not be published and due efforts will be made to conceal his identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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