Dermatological toxicity

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Despite the fact that immunotherapy has entailed a paradigm shift in the treatment of cancer, the toxicity associated with these drugs can compromise overall survival as well as patient quality of life. Hence the importance of detecting and diagnosing these adverse effects early, in order to offer patients the best therapeutic approach.
Skin toxicity is one of the most commonly observed adverse effects (AEs) in patients treated with immunotherapy. Although it usually appears early in the course of treatment (generally in the initial weeks), it may develop months after starting the therapy, or even after the treatment has ended.

The majority of immunotherapy-induced cutaneous manifestations are mild and easy to manage and the treatment does not usually need to be halted. However, there have been reported cases of Stevens-Johnson syndrome, toxic epidermal necrolysis and DRESS (Drug reaction with eosinophilia and systemic symptoms) which, although rare, can be life-threatening and require the suspension of treatment (ESMO).
The incidence of AEs is higher in patients treated with ipilimumab (50%) than with anti-PD-1/PDL-1 (30-40%), and increases when these drugs are administered in combination.
Dx: for a patient treated with immunotherapy who exhibits a cutaneous AE, clinicians should be highly suspicious that this may be related to the treatment but other possible causes must also be ruled out (other drugs that the patient takes, infections, etc.)
The most common cutaneous AEs are maculopapular rash (spongiotic or lichenoid dermatitis), pruritus and vitiligo, although the latter has been reported primarily in patients treated for melanoma.
Other less common cutaneous manifestations that have been described include exacerbation of psoriasis or de novo psoriasis, lichenoid eruptions, bullous diseases, dry skin, alopecia areata, pyoderma gangrenosum, Sweet's syndrome and cutaneous sarcoidosis.

The rash may be either morbilliform or eczematous. It predominantly affects the trunk and spreads to the limbs; the face is usually spared. It tends to be accompanied by itching, although it is sometimes asymptomatic.
The rashes and itching that appear in the first weeks of treatment are predominantly grade 1-2 and can be managed symptomatically with oral antihistamines, topical corticosteroids and emollients. Class I/II corticosteroids are recommended for the body and class IV/VI for the face and folds. Treatment does not generally need to be stopped or interrupted.

Pruritus usually accompanies a maculopapular rash but may precede it or manifest with no cutaneous abnormalities (in such cases, skin dryness should be ruled out and treated). Poorly controlled pruritus can affect the patient's quality of life. As such, if it

does not respond to oral antihistamines then gabapentin, antidepressants or aprepitant can be used.

For other skin manifestations, particularly if they are grade 3-4, assessment by a dermatologist is usually necessary. This assessment should be urgent if the patient presents with bullous lesions on >1% of their body surface area, if they have a painful rash with or without blisters (excluding herpes zoster) or a rash with mucosal involvement. A non-urgent dermatological assessment is recommended when there is uncertainty in the diagnosis of the rash, if it is a grade 2 rash that is getting worse or owing to the presence of atypical lesions.

Early recognition of immunotherapy-induced skin toxicity and its proper management can achieve good control of manifestations and avoid the need to interrupt treatment. As such, collaboration between oncologists and dermatologists is crucial.