AUTOIMMUNE BULLOUS DISEASES

PRESUME DARK SIDE OF ABSCOPAL EFFECT: SEVERE NIVOLUMAB INDUCED BULLOUS PEMPHIGOID TRIGERRED BY LOCAL RADIATION IN A PATIENT WITH ADVANCED RENAL CARCINOMA.

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Introduction: Checkpoint inhibitors such as nivolumab and pembrolizumab that bind to and inhibit programmed cell death protein-1 (PD-1), have revolutionized the management of many stage IV cancers.
Immunecheckpoint inhibitors are associated with immune-related adverse events (irAEs), which can manifest as a wide range of autoimmune phenomena.
Dermatological adverse effects are generally mild (ref JEADV).
Herein, we describe a patient with metastatic renal carcinoma treated with nivolumab followed by antalgic radiotherapy which might have triggered severe cutaneous and mucous bullous pemphigoid. This immunological undesirable effect falling within the framework of a presuemd abscopal effect.

Observation: A 78-year-old man, who was being treated with 5 injections of Nivolumab for metastatic renal cell carcinoma with pulmonary and costal metastasis, was admitted for a cutaneous, oral and genital blistering exanthema. The patient was treated with local radiation of 30 Gy in 10 fractions.
Cutaneous pathologic analysis showed a separation of the epidermis from the dermis at the basement membrane zone and direct immunofluorescence revealed a strong linear staining of C3 at the dermal–epidermal junction. Immunoblottting results were positive for antibodies to bullous pemphigoid antigen 2 (BP180) consistent with BP. Nivolumab was discontinued, and
treatment for his BP was initiated with Rituximab.

Discussion: Bullous pemphigoid is a rare cutaneous side effect of programmed death 1 inhibitors such as nivolumab and pemborolizumab.
This case is, to our knowledge, the second confirmed case of BP with onset during nivolumab and triggered by radiotherapy and the first with mucous involvment.
This dermatosis occurred in conjunction with an excellent oncological response away from

the radiotherapy field. These elements make us suspect an abscopal effect. Thus, we hypothesize that radiotherapy-induced antigenic salting induced CD8 + T lymphocyte stimulation, which is responsible for anti-tumor cytotoxicity, on the one hand, but also anti-BPAG2.