Case Report

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Bullous Pemphigoid as an Adverse Reaction to PD-1 Inhibitor Avelumab: A Case Report

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Abstract

Checkpoint inhibitors targeting CTLA4 (Cytotoxic T-lymphocyte antigen-4), PD-1 (programmed death)[1] on lymphocytes and PD-L1 (programmed death ligand)[1] on tumors cells are novel and promising treatment options for different types of cancer. But these agents are double edged swords, they undoubtedly robust the anti-tumor response but also throttle up the normal immunologic homeostasis. Autoimmune adverse reactions are very common with checkpoint inhibitors. We present a case of bullous pemphigoid, as an adverse reactions to Avelumab treated urinary bladder cancer with liver metastasis.

Keywords: Bullous pemphigoid; Avelumab; Bladder carcinoma.

INTRODUCTION

Case Report

A 65 year old male with a history of high grade non-invasie urinary bladder carcinoma, for which he underwent radical cystectomy in 2014. The patient was under remission for about 3 years and then he developed metastasis to inguinal lymph nodes and liver. He was started on inj. Avelumab 10mg/kg body weight, repeated after every 14 days, under clinical trail sponsored by Pfizer. After two years of treatment cycle, he developed vesiculobulous lesions all over the body, for which he was evaluated by a dermatologist and on clinical examination we found multiple erosions with excoriation marks and numerous tense vesicles and bullae with serous fluid, few with hemorrhagic fluid, present over face, trunk, bilateral upper and lower extremities (Fig. 1). A 4mm punch biopsy was taken from the vesicle on the left side of the chest, the section showed subepidermal blister containing plasma and sparse inflammatory cells. The Upper dermal layer showed perivascular lymphocytic infiltrate with feweosinophils (Fig. 2). Direct immunofluorescence test shows a linear band along dermo-epidermal junction with IgG and C3 (Fig. 3). Tzanck smear shows scarcity of epithelial cells and an abundance of leukocytes, particularly eosinophils. Routine blood investigations showed

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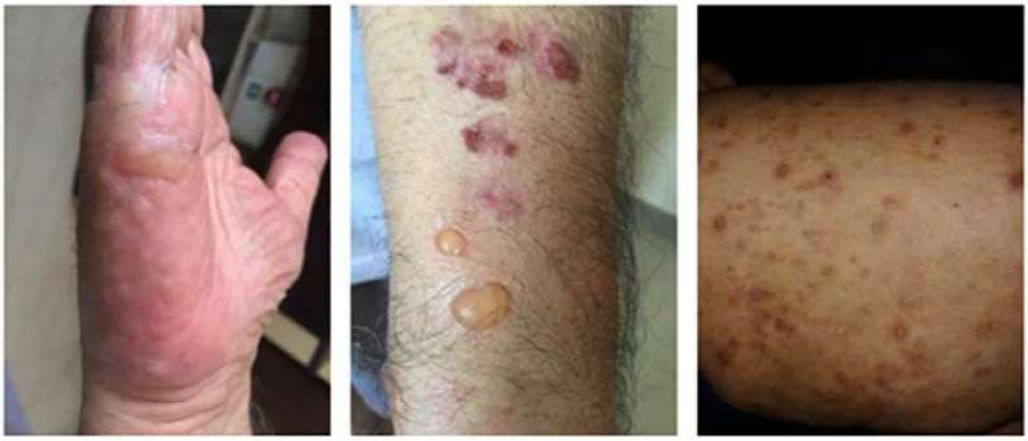

Fig. 1

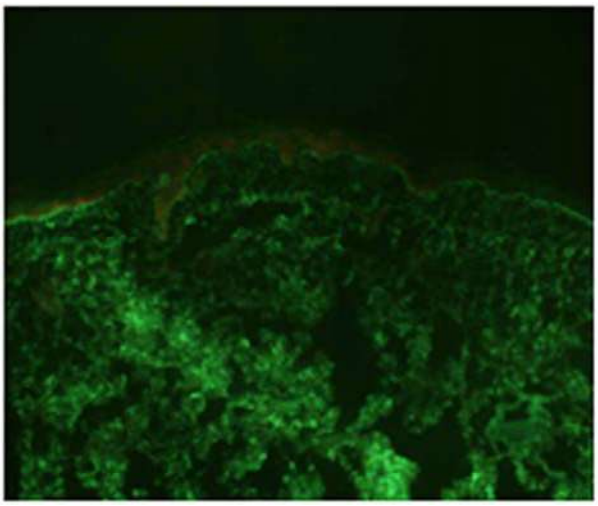

Fig. 2

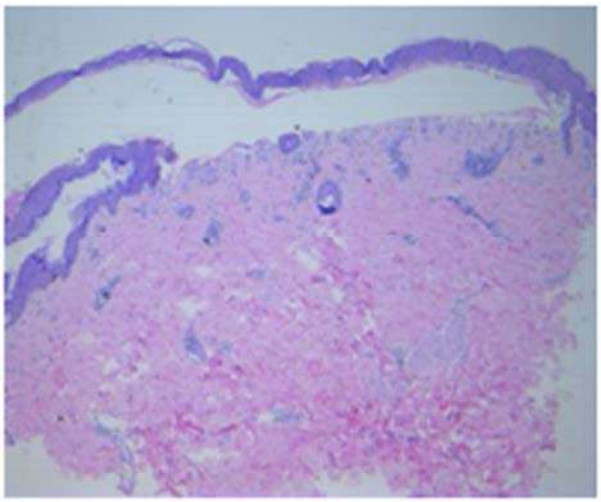

Fig. 2

increased eosinophil count.

Inj. Avelumab was continued as it was the main drug, and the patient was started on both systemic and topical corticosteroid along with them Tab Niacinamide 100mg and Tab Dapsone 100mg daily was also started. The skin lesion responded to drugs and 50% imporovement was seen. But the lesions flared up after decreasing the dose of systemic steroids. During Covid-19 pandemic, paient missed the cycle of inj. Avelumabtherapy and the skin lesions completely resolved within 20 days and again reappeared after starting the therapy. Thus, establishing the temporal correlation between the skin lesions and drugs.

DISCUSSION

Programmed cell death PD-L1, a checkpoint inhibitor which reduces the host lymphocytic and apoptotic immune response to some extent, has been found to be overexpressed in malignant tumors.[1] Accordindly, antibodies targeting PD-1 or its receptor ligand PD-L1 have been shown to unbound host antitumor processes, leading to in vivo tumor regression. Thus in the past decade, the resurgence of Checkpoint inhibitor therapy is seen in the treatment of several cancers.[2]

However, checkpoint inhibitors, on one hand show very good results in treatment of carcinoma but on the other hand, by blocking the negative regulators of immunity that are normally important for maintaining immunologic homeostasis it show some adverse skin reactions. Hence, they are associated with distinctive inflammatory adverse effects known as immune related adverse events (irAEs).[3]

Our patient had a history of developing bullous pemphigoid after starting treatment of urinary

bladder cancer with liver metastasis. Bullous pemphigoid (BP) is an autoimmune blistering disorder characterized by tense, superficial, variably pruritic bullae consisting of clear fluid that generally develops on the flexor surfaces and abdomen of elderly patients. On histopathology, acantholysi along with IgG and C3 deposits are noted under direct immunofluorescence.[4] Management of moderate to severe immunotherapy mediated bullous pemphigoid includes discontinuation of therapy and prompt initiation of systemic steroids. Treatment duration varies based on response to therapy, which can be up to 3 - 4 weeks, and is generally followed by prolonged taper. In steroid refractory cases, alternate immunosuppressive agents such as azathioprine, mycophenolatemofetil, methotrexate are recommended.[5,6]

In summary, in spite ofthe relatively lesser adverse effects attributed to PD-1 inhibitors when compared to conventional chemotherapy, it is judicious to recognize these rare adverse toxicities. Prompt initiation of systemic glucocorticoids and discontinuation of immunotherapy is pivotal in the management.

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