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Inverse psoriasis in patient treated with atezolizumab

Dear Editor,

A 76-year-old man with a history of metastatic nonsmall-cell lung cancer (NSCLC) presented with pruritic erythematous plaques involving the right and left axilla (Fig. 1a,b). The plaques appeared one week after starting atezolizumab, an anti-programmed death ligand 1 (PD-L1) antibody used in the treatment of NSCLC. He had no personal or family history of psoriasis.

On physical examination, he had symmetric, erythematous well-demarcated plaques with a minimal scale, involving only bilateral axillae and no other parts of the body, associated with extreme itching. Dermoscopically, the lesion showed an erythematous background with multiple dotted vessels arranged symmetrically (Fig. 1a,b-left frame). A punch biopsy was performed revealing (i) parakeratosis, corneal pustules, and spongiform microabscesses, and (ii) thinning of suprapapillary plate and epidermalization of papillary vessels (Fig. 1c). A diagnosis of inverse psoriasis was made.

As a result of progression of his underlying malignancy, the patient discontinued therapeutic treatment with atezolizumab with complete resolution of axillary lesions.

Inverse psoriasis, also known as intertriginous psoriasis, is an uncommon variant of psoriasis vulgaris, involving flexural or intertriginous regions.[1] Clinically, it is characterized by the presence of erythematous well demarcated plaques of shiny skin, generally associated with itching of variable magnitude. The main differential diagnosis could be made with Candidal intertrigo, which may overlap with the psoriatic plaque itself,[1] and symmetric drug-related intertriginous and flexural exantham (SDRIFE).[2]

There are many factors associated with the induction or exacerbation of psoriasis including medications such as lithium, beta-blockers, TNF-alpha inhibitors, and synthetic antimalarial drugs.[3] The necessary condition to correlate a drug with the exacerbation of psoriasis is the appearance with introduction and the disappearance on withdrawal.[4] Plaque psoriasis is the most common condition, while inverse psoriasis is reported only in a few cases.[5]

Atezolizumab is a new PD-L1 blocking antibody indicated for use in the treatment of NSCLC, urothelial carcinoma, triple-negative breast cancer (TNBC), and small cell lung cancer (SCLC).[6] Particularly in NSCLC, it is indicated in combination with bevacizumab, paclitaxel, and carboplatin, for the first-line treatment of adult patients with no EGFR or ALK genomic tumor aberrations, or in disease progression during or following platinum-containing chemotherapy.

As with other immunotherapeutic agents, side effects include fatigue, fever, abdominal pain, or diarrhea. Other reported cutaneous toxicities are bullous eruptions/bullous pemphigoid, oral lichen planus, or plaque psoriasis.

More specifically, there are only three cases of plaque psoriasis associated with atezolizumab in patients affected by metastatic tumors.[7-9]

In our case, the patient developed inverse psoriasis rash confirmed by two different punch biopsies, which appeared after 1 week of starting anti-PD-L1 therapy and disappeared with drug withdrawal. These events confirmed the association of inverse psoriasis and atezolizumab, the first description never reported before.

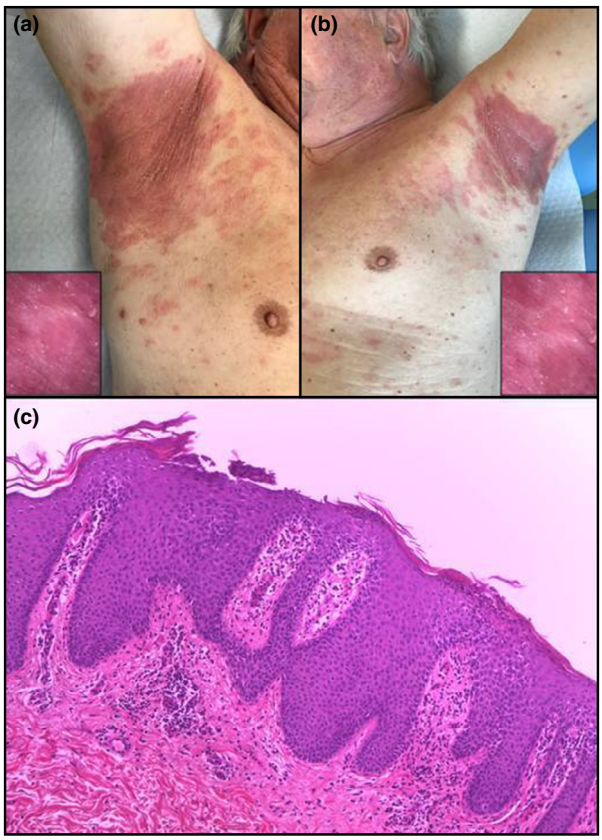

Figure 1 Plaque of inverse psoriasis in (a) right axilla and (b) left axilla; (a-b inset frames) Dermoscopy of the lesions showing reddish background with dotted vessels; (c) Histology showing parakeratosis, corneal pustules, and spongiform microabscesses and thinning of suprapapillary plaque with epidermalization of papillary vessels (Hematoxylin and eosin, ×10 magnification)

Inverse psoriasis is a rare presentation of drug-induced psoriasis, and physicians must be aware of this possible skin complication in patients treated with PD-L1 blocking antibody.

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Emergence of lymphomatoid papulosis during treatment with brentuximab vedotin

Dear Editor,

Lymphomatoid papulosis (LyP) is an uncommon CD30-positive skin disease characterized by the continuous appearance of papulonecrotic, nodular, and occasionally larger tumorous or plaque-like lesions showing histologic features suggestive of malignant lymphoma.[1] LyP can be associated with malignant lymphoproliferative disorders including Hodgkin lymphoma (HL), mycosis fungoides (MF), and anaplastic large cell lymphoma (ALCL), all of which can develop prior to or after the presentation of LyP. Brentuximab vedotin (BV) is a potent monomethyl auristatin E-conjugated anti-CD30 monoclonal antibody shown to be effective both as a single agent and in combination in the treatment of relapsed and de novo HL and relapsed/refractory systemic ALCL.[2] More recently, BV has been shown to be effective in treating severe/refractory LyP cases.[3] In contrast, there are no reports of LyP occurring during anti-CD30 treatment, and here we report a case of LyP emerging during BV treatment.

A 30-year-old man undergoing treatment for HL was referred to the dermatology service with a pruritic, erythematous eruption on his upper limbs felt to represent a drug reaction. This eruption appeared 6 days after a first infusion of BV and had been preceded by a vesicular rash on his hands consistent with pompholyx eczema that was treated with topical therapy. He had a background of stage II classical nodular sclerosing HL first treated with two cycles of adriamycin/bleomycin/vinblastine/dacarbazine (ABVD) chemotherapy to which his disease was refractory with persistent disease in left axillary lymph nodes. He was then treated with four cycles of escalated-dose BEACOPP (bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine, procarbazine, and prednisolone) chemotherapy to which he had a complete metabolic response by PET/CT imaging. Unfortunately, his disease relapsed in the left axillary lymph nodes within 3 months, and he commenced salvage treatment with BV at a dose of 1.8 mg/kg intravenously every 3 weeks. Six days after the first BV infusion, he developed a cutaneous eruption referred to above, and a skin biopsy showed features of a spongiotic dermatitis with focal lymphocytic exocytosis and vacuolar interface change. Topical steroids were prescribed, however, he then developed crops of erythematous, necrotic nodules and papules on his trunk and limbs (Fig. 1a,b), clinically consistent with LyP despite ongoing treatment with BV. Further biopsies showed a dense mixed inflammatory infiltrate present in the upper dermis composed of large, pleomorphic lymphoid cells admixed with lymphocytes, histiocytes, and rare plasma cells (Fig. 2a,b). Immunohistochemistry showed the atypical cells to be CD3 (Fig. 2c), CD45, and CD30 positive (Fig. 2d), and PCR analysis showed a clonal beta-gamma T-cell receptor gene rearrangement profile, consistent with a CD30-positive lymphoproliferative disorder. A complete metabolic response to BV was achieved, but treatment was discontinued after three cycles due to the onset of peripheral neuropathy.