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Plaque Psoriasis Flare and Peripheral Edema in a Patient Treated With Atezolizumab☆

Brote de psoriasis en placas y edema periférico en un paciente tratado con atezolizumab

To the Editor:

A 75-year-old man was referred to the dermatology clinic for evaluation of skin lesions after receiving his first dose of atezolizumab (1200 mg) for treatment of poorly differentiated stage IV urothelial carcinoma of the prostatic urethra (metastasis to the lungs, liver, bone, and lymph nodes). Twelve months previously, the patient had completed systemic treatment with chemotherapy (cisplatin 75 mg/m^2 day 1 + gemcitabine 1250 mg/m^2 on days 1 and 8 and every 21 days) in 4 cycles. No clinical or radiological response was observed, and the treatment was poorly tolerated (asthenia, vomiting, and moderate kidney failure). He had a 42-year history of mild psoriasis affecting the elbows and knees.

Twelve days after the first infusion of atezolizumab, his existing lesions began to worsen, and new lesions began to appear on the extensor aspects of both limbs and the trunk. These were intensely pruritic and compatible with a clinical diagnosis of psoriasis (Psoriasis Area Severity Index = 12, body surface area affected = 6, visual analog scale for itching = 10). These findings were accompanied by distal edema affecting both lower limbs. The patient was prescribed oral prednisone 30 mg for 7 days to be tapered by 10 mg every week, bilastine 20 mg every 12 hours, and topical treatment with clobetasol propionate 0.1% cream every 12 hours for 15 days. His lesions resolved in 3 weeks, and no residual lesions were observed. Atezolizumab was discontinued because of the skin toxicity. Given the patient's poor general status, he refused all cancer medication and is currently receiving palliative care. He was diagnosed with probable adverse reaction to atezolizumab (Naranjo algorithm, 6 points).

Programmed death 1 (PD-1) is a key immune checkpoint receptor that is expressed on T cells and functions mainly in peripheral tissue.[1] Atezolizumab is the first PD ligand 1 (PD-L1) inhibitor approved by the United States Food and Drug Administration. This human immunoglobulin G1 monoclonal antibody binds selectively to PD-L1 and prevents interaction with PD-1 and B7-1 (also known as CD80), while sparing the interaction between PD ligand 2 (PD-L2) and PD-1.[2] When PD-1 is activated, the immune system is inhibited, thus enabling tumor growth. In their various indications for different cancers, new anti–PD-1 drugs (nivolumab, pembrolizumab, pidilizumab) and anti–PD-L1 drugs (atezolizumab and durvalumab) curb this inhibition by enabling the immune system to control tumor progression.[1]

There have been various reports of adverse reactions to PD-1 and PD-L1 inhibitors in up to 50% of patients. These were mainly cutaneous (lichenoid reactions, eczema, vitiligo, and pruritus) and mild and did not require treatment to be discontinued.[3,4] However, other authors report these inflammatory reactions to be severe, requiring treatment with oral corticosteroids, and highlight an objective antitumor response.[5] One group of cutaneous reactions to this drug are those based on neutrophils, which, owing to their increased count in the skin, cause Sweet syndrome, acute generalized exanthematous pustulosis, intracorneal pustular drug eruption, and psoriasis.[6] Other, less common cutaneous adverse reactions include actinic keratosis, squamous cell carcinoma, and seborrheic keratosis.[3] Peripheral edema is an adverse reaction that affects 10% of patients receiving treatment with atezolizumab.[7]

Cases of psoriasis triggered or exacerbated by this drug family are starting to be reported, although the condition

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was due to atezolizumab in only 1 case.[8,9] In a recent series, 66% of patients had a previous history of psoriasis, which, in most cases, was controlled with topical treatment. Given the intensity of skin involvement, it was rarely necessary to suspend treatment or prescribe oral corticosteroids, as in the present case.[8,9] In most cases, psoriasis is triggered after several doses. In the only case where psoriasis was triggered by atezolizumab, onset was after the first dose, as occurred in the present case.

In terms of etiology and pathogenesis, murine models have shown that PD-1 deficiency increases the likelihood of the psoriasis-like skin disease phenotype and that PD-1 can play a regulatory role in the development of the disease.[10] Under normal conditions, the PD-1 pathway maintains normal immune homeostasis, which prevents autoimmune reactions or damage to healthy tissue. T-cell activation induced by PD-1 inhibitors—together with other factors—can contribute to development of psoriasis or exacerbations of existing psoriasis.[11]

The low number of cases of psoriasis associated with atezolizumab is probably due to the mechanism of action, which spares PD-1 and PD-L2 binding. Owing to the different nature (IgG4 isotopes or IgG1 isotope), mechanisms of action, and antitumor action of anti–PD-1 and –PD-L1 agents, it has been recommended not to consider them as a group.[9]

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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