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Trastuzumab Deruxtecan-Associated Vitiligo Treated with Topical Janus Kinase Inhibitor in Human Epidermal Growth Factor Receptor 2-Low Metastatic Breast Cancer: A Case Report

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Introduction

Trastuzumab deruxtecan (T-DXd) is an antibody–drug conjugate composed of a humanized anti–Human Epidermal Growth Factor Receptor 2 (anti-HER2) monoclonal antibody linked via a cleavable linker to a potent topoisomerase I inhibitor. It is approved for the treatment of unresectable or metastatic HER2-low breast cancer, including hormone receptor–positive disease, after progression on standard therapies. The most frequently reported adverse events include nausea, fatigue, myelosuppression, alopecia, gastrointestinal toxicity, and interstitial lung disease. Cutaneous adverse effects are usually mild and nonspecific.

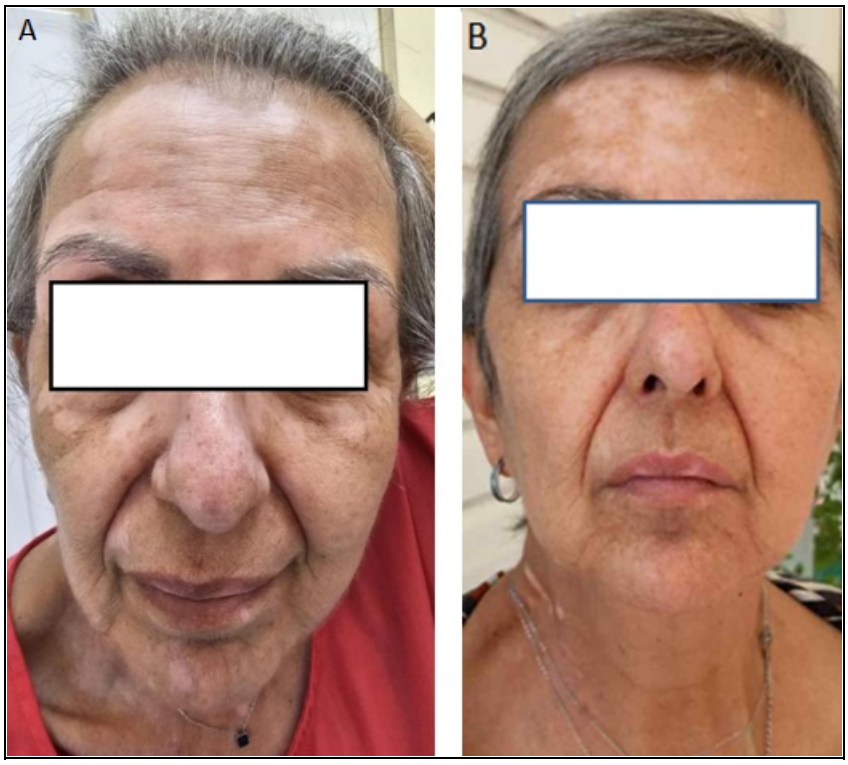
Vitiligo is an acquired depigmenting disorder caused by the loss of melanocytes, commonly related to autoimmune processes or immune-modifying treatments. To our knowledge, vitiligo has not previously been reported as an adverse effect of T-DXd. We describe a case of vitiligo occurring shortly after initiation of T-DXd in a patient with metastatic breast cancer

Materials and Methods

Clinical data were collected retrospectively from the medical records of a 60-year-old woman with metastatic HER2-low breast cancer and vitiligo treated with T-DXd. Dermatological examination, therapeutic interventions, and clinical follow-up were documented over a two-year period. The causality between drug exposure and skin manifestations was assessed based on temporal relationship, clinical evolution, and exclusion of alternative etiologies

Results

A 60-year-old woman with estrogen receptor–positive, HER2-low metastatic breast cancer with liver involvement was started on T-DXd at a dose of 5.4 mg/kg every three weeks. One week after the first treatment cycle, she developed well-defined depigmented patches on the face, suggestive of vitiligo. She had no personal or family history of vitiligo or autoimmune disease. She was initially treated with topical mometasone furoate cream, without improvement. One year after starting topical corticosteroids, vitiligo had spread to the neck, chest, upper back, and upper limbs. Topical calcineurin inhibitor therapy with ointment tacrolimus 0.03% was added twice weekly but proved ineffective. Given the progression of the disease, topical ruxolitinib cream 1.5% was subsequently initiated twice daily. Ruxolitinib is a JAK1/2 inhibitor that suppresses interferon-γ–mediated immune pathways implicated in the melanocyte destruction. After 12 weeks, perifollicular repigmentation was observed with partial repigmentation over the subsequent months. Treatment was well tolerated, and allowed the continuation of T-DXd therapy



Vitiligo-like depigmentation following trastuzumab deruxtecan therapy A) with partial repigmentation B) following ruxolitinib treatment

Conclusions

This case suggests a potential association between T-DXd and vitiligo, given its rapid onset following the initiation of T-DXd treatment and progressive course. The response to topical ruxolitinib indicates a JAK-STAT–mediated mechanism. Early dermatologic intervention may help manage this rare adverse effect and allow continuation of anticancer therapy. Further reports are needed to clarify its pathophysiology