

Successful Treatment of Immune-Related Grover's Disease with Isotretinoin

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Introduction

Grover's disease, also known as transient acantholytic dermatosis, is a rare benign condition characterized by the sudden onset of itchy papules and vesicles predominantly located on the trunk and the extremities. The exact pathogenesis remains unclear to date. Recently, Grover's disease has also been reported as rare immune-related cutaneous adverse event associated with immune checkpoint inhibitors (especially CTLA-4 blockade or anti-PD agents) in patients undergoing treatment for malignant melanoma [1-3].

While often self-limiting in idiopathic cases, its occurrence in the context of abovementioned therapies, may result in a prolonged and refractory clinical course, posing therapeutical challenges. To date [1-3], there is little known about treatment in these cases. The successful use of isotretinoin in idiopathic cases (starting with 40mg/day) is often described, however, there is no consensus on the exact duration of therapy and no report if this regime might also work in immune-related Grover's disease in melanoma patients.

Case Presentation:

A 69-year-old male patient was diagnosed with stage IV melanoma (pT1a cN0 pM1a according to the AJCC-Classification of 2017) after resection of three subcutaneous metastases on his right upper arm in August and November 2022. The patient was subsequently discussed by the interdisciplinary tumorboard. As there was no evidence of distant metastases the patient was recommended an adjuvant treatment with the programmed-death inhibitor nivolumab. The patient was scheduled to receive nivolumab at a fixed dose of 480mg intravenously every 4 weeks over a 12-month period. After the eighth infusion he developed multiple, intensively itchy papules and vesicles on the trunk and the extremities (Figure 1A-C). On dermoscopy, the lesions revealed a central whitish-yellow polygonal, star-like shaped area surrounded by a whitish-red halo (Figure 2). Based on these findings the diagnosis of Grover's disease was made and confirmed by histology. Since the exanthema was classified as grade 2 according to CTCAE 5.0, treatment with nivolumab was initially continued and therapy with a topical steroid was

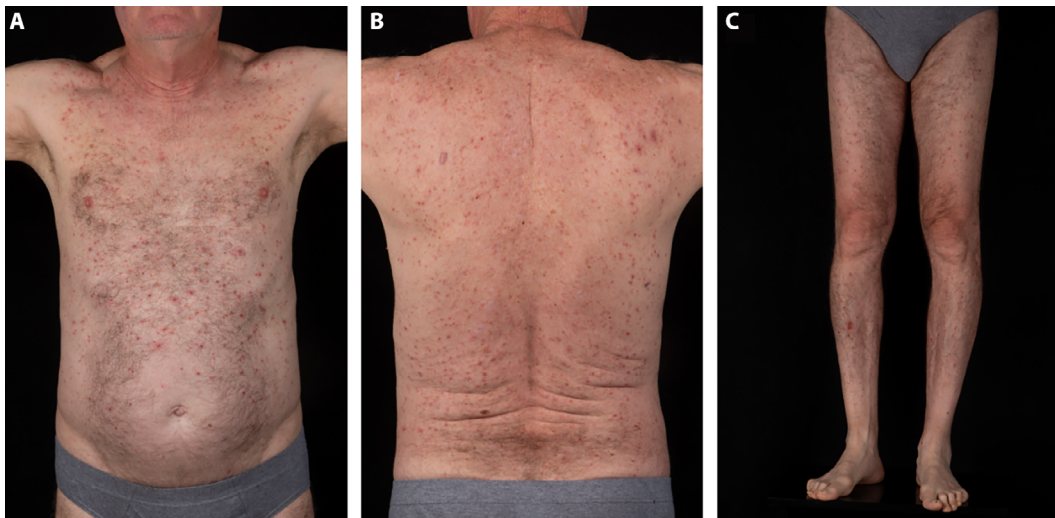


Figure 1. Multiple reddish, partially excoriated, papules and vesicles on the trunk (A+B) and the extremities (C).



Figure 2. Dermoscopic image of a lesion exhibiting a central whitish-yellow polygonal, star-like shaped area surrounded by a whitish-red halo.

initiated. However, nivolumab had to be discontinued another eight weeks later, because the rash significantly worsened. Since the precise immune polarization and cytokine drivers of Grover's disease is still unclear, we decided to initiate therapy with isotretinoin at a starting dose of 20mg/day. The itching improved significantly within a few weeks; however, the rash responded very slowly, meaning that the patient still received 10mg of isotretinoin per day after one year of therapy. To date, after about 1,5 years of therapy, a maintenance dose of 10mg every other day could be achieved, under which the rash has almost completely disappeared.

Conclusion

Given the rising use of immune checkpoint inhibitors, immune related cutaneous adverse events (irAEs) also increased. Therefore, dermatologists play a crucial role in their diagnosis and treatment. Due to the lack of standardized guidelines for many of those irAEs, especially in severe and refractory cases, treatment often relies on single case reports (as in our patient). We herein report the first case of immune-related Grover's disease successfully treated with isotretinoin. If this therapy had not been effective, Dupilumab would have been another option [1-4].

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