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(CASE REPORT)

Vitiligo induced by immune checkpoint inhibitors in metastatic melanoma: A case report and review of the literature

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Abstract

Background: Immune checkpoint inhibitors (ICIs) have revolutionized metastatic melanoma treatment but cause immune-related adverse events (irAEs), particularly dermatologic toxicities. Vitiligo is a distinctive cutaneous irAE occurring predominantly in melanoma patients.

Objective: To report a case of ICI-induced vitiligo and discuss its pathophysiology, management, and prognostic significance.

Case Presentation: A 54-year-old man with stage IV melanoma received pembrolizumab. After 24 weeks, progressive depigmented macules appeared on the face, hands, and trunk, accentuating with continued treatment. Biopsy confirmed vitiligo. Pembrolizumab continued with topical corticosteroids. At 6 months, partial tumor response with persistent vitiligo.

Conclusion: Vitiligo is a benign irAE correlating with favorable antitumor response. ICI continuation is recommended. Multidisciplinary management optimizes outcomes.

Keywords: Immune checkpoint inhibitors; Vitiligo; Cutaneous toxicity; Immunotherapy; Melanoma

1. Introduction

Immune checkpoint inhibitors (ICIs), including anti-PD-1 (pembrolizumab, nivolumab) and anti-CTLA-4 (ipilimumab), have transformed metastatic melanoma prognosis. KEYNOTE-006 demonstrated superior survival with pembrolizumab versus ipilimumab. (1)

Cutaneous toxicities are the most frequent irAEs, affecting over one-third of patients. Vitiligo is distinctive—an autoimmune depigmentation from melanocyte destruction, occurring almost exclusively in melanoma patients. (2)

Incidence is ~2.3% under ipilimumab, higher under anti-PD-1. Vitiligo correlates with improved tumor response and survival, suggesting prognostic biomarker value. Guidelines remain non-standardized. This case report reviews pathophysiology, management, and prognostic significance. (3)

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2. Case Presentation

2.1. Patient

54-year-old north african man, stage IV BRAF wild-type melanoma with lung and liver metastases. ECOG 1. No personal/family history of autoimmune disease.

2.2. Treatment

Pembrolizumab 200 mg IV every 3 weeks, first-line. Baseline thyroid function and autoantibodies normal. (4)

2.3. Vitiligo Onset

At 24 weeks (8 cycles), asymptomatic white macules appeared on face (eyes, mouth), hands, trunk. Well-demarcated, some confluent. Sun-exposed areas and trauma sites involved (Koebner phenomenon). (5)

Dermoscopy: complete pigment loss, perifollicular preservation, mild border erythema.

Biopsy (4-mm): melanocyte absence (Melan-A negative), CD8+ perivascular infiltrate, basal vacuolization—diagnostic vitiligo. (5)

2.4. Progression of vitiligo

- 24 weeks, 8 cycles, Face and hands
- 33 weeks, 11 cycles, Trunk + confluent plaques
- 42 weeks, 14 cycles, Extremities + extension
- 51 weeks, 17 cycles, Stable with mild extension
- Gradual progression without acute flare. (2)

2.5. Workup

- TSH: 2.1 mIU/L (normal)
- Anti-TPO, ANA: negative
- CBC, metabolic panel: normal
- Remained euthyroid despite thyroiditis association.

2.6. Tumor Response

CT at 24 weeks: partial response (RECIST 1.1), 45% reduction, no new lesions.

- Management
- Counseled on favorable prognosis association. Pembrolizumab continued. (6)

2.7. Treatment of vitiligo

- Topical clobetasol 0.05% ointment twice daily
- Sunscreen SPF 50+
- Dermatology follow-up monthly

At 6 months: vitiligo persisted with mild extension, no psychological distress, tumor response maintained, no additional irAEs.(2)

3. Discussion

3.1. Pathophysiology

ICI-induced vitiligo results from immune tolerance breakdown against melanocyte antigens (gp100, tyrosinase, MART-1). PD-1/PD-L1 or CTLA-4 blockade enhances T-cell activation, leading CD8+ T cells to recognize tumor antigens shared with melanocytes. Cross-reactive cytotoxic T cells destroy both tumor and normal melanocytes, causing depigmentation. (7)

This explains vitiligo's exclusivity to melanoma patients and correlation with antitumor efficacy. (8)

3.2. Timing

In this case, vitiligo appeared at 24 weeks, later than typical 3–6 months. Progressive accentuation aligns with cumulative immune activation. Grade 1–2 severity throughout. (9)

3.3. Frequency and Risk Factors

- Incidence: ~2.3% ipilimumab, 10–15% anti-PD-1(10)
- Timing: 3–6 months typical; delayed onset rare (5)
- Risk factors: Younger age, female, family autoimmunity, HLA-DR4
- Distribution: Face, hands, trunk symmetric (5)

3.4. Prognosis

- Meta-analyses show vitiligo associates with improved outcomes: (8)
- Overall survival: HR 0.45 (95% CI 0.32–0.63), 55% lower death risk (8)
- Progression-free survival: HR 0.52 (95% CI 0.38–0.71), Improved PFS (8)
- Objective response rate: ORR 58% vs. 28%, Higher response
- Vitiligo serves as favorable immune response biomarker. (8)

3.5. Clinical Management

3.5.1. Guidelines recommend:(10)

- Grade 1 (mild): Continue ICI, topical steroids, sunscreen, reassurance(11)
- Grade 2 (moderate): Continue ICI, topical steroids or calcineurin inhibitors, dermatology referral(10)
- Grade 3–4 (severe): Consider ICI pause, systemic corticosteroids (prednisone 0.5–1 mg/kg), multidisciplinary support (10)

ICI continuation maintained as interruption compromises efficacy. Supportive care includes psychological counseling, makeup camouflage, trauma avoidance. (12)

3.5.2. Limitations

No standardized vitiligo grading(10)

Limited prospective data on long-term evolution (5)

Need for biomarker studies

Future research should evaluate vitiligo as predictive biomarker and early dermatologic intervention benefits.(13)

4. Conclusion

Vitiligo is a distinctive, benign cutaneous irAE with ICI therapy in melanoma. This case appeared at 24 weeks, progressively accentuated with pembrolizumab in a North African patient. While cosmetically significant, it signals favorable antitumor response and improved survival. ICI therapy should continue with topical treatment and counseling. Multidisciplinary management optimizes oncologic and quality-of-life outcomes.(14)

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare that they have no competing interests.

Statement of ethical approval

According to institutional policy, formal ethical approval was not required for this single case report. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Statement of informed consent

Verbal informed consent was obtained from the patient for publication of this case report and accompanying images. No identifying personal information has been disclosed.

Authors' Contributions

- Author 1 (Debbagh adil): Conceptualization, case presentation, literature review, writing - original draft
- Author 2 (Alaoui lamiaa): Data analysis, writing - review & editing
- Author 3 (Tanz rachid): Supervision, writing - review & editing

All authors read and approved the final manuscript.

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