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PEMBROLIZUMAB INDUCED LEUKODERMA AND COLITIS, IMMUNE RELATED ADVERSE EVENT: A RARE CASE REPORT

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ABSTRACT

Pembrolizumab (Keytruda) is a humanized monoclonal antibody that functions as an immune checkpoint inhibitor by targeting the PD-1 (programmed cell death protein-1) receptor on T-cells. By blocking PD-1's interaction with its ligands PD-L1 and PD-L2, pembrolizumab restores T-cell–mediated immune responses against tumor cells, making it highly effective in various malignancies. Vitiligo, also known as leucoderma, is a chronic skin condition characterized by the development of well-demarcated, depigmented white patches on the skin due to the selective destruction or loss of melanocytes—the pigment-producing cells. It is considered an acquired idiopathic disorder, often considered to have an autoimmune basis where the immune system mistakenly attacks melanocytes. Vitiligo can affect any part of the body but commonly appears on the face, hands, feet, and around body orifices. Colitis is inflammation of the colon that can present with symptoms such as diarrhea, abdominal pain, urgency, rectal bleeding, and fever. While it can result from infections, inflammatory bowel disease, or ischemia, colitis is also recognized as a serious immune-related adverse event (irAE) in patients receiving immune checkpoint inhibitors. This case report focuses on the 70years old male patient diagnosed with metastatic renal cell carcinoma on pembrolizumab who developed severe colitis and depigmented skin patches (leucoderma). The patient presented with profuse diarrhea and new hypopigmented lesions on his body after several cycles of therapy. Stool studies and infections were excluded. After confirming vitiligo-like leucoderma, corticosteroid therapy was initiated which led to rapid resolution of diarrhea. This case underscores the need for early recognition and interdisciplinary management of concurrent gastrointestinal and dermatologic irAEs in RCC patients receiving checkpoint inhibitors.

KEY WORDS: Pembrolizumab, Leucoderma, Colitis, Renal cell carcinoma, Diarrhea, Steroidal therapy, Immune related adverse reaction.

INTRODUCTION:

Pembrolizumab (Keytruda) is a humanized monoclonal antibody that functions as an immune checkpoint inhibitor by targeting the PD-1 (programmed cell death protein-1) receptor on T-cells. By blocking PD-1's interaction with its ligands PD-L1 and PD-L2, pembrolizumab restores T-cell–mediated immune responses against tumor cells, making it highly effective in various malignancies [1,2]. This mechanism also disrupts normal self-tolerance: PD-1 normally maintains peripheral tolerance, and its blockade can unleash autoimmunity. Consequently, a wide spectrum of immune-related adverse events (irAEs) can occur the skin and gastrointestinal tract are among the most frequently affected organs. Immune-mediated colitis (diarrhea, colonic inflammation) occurs in a minority of patients on anti-PD-1 therapy (around 1–4%) [1]. Cutaneous immune-related adverse events (irAEs) range from mild rashes to vitiligo-like leukoderma. While vitiligo is common in melanoma patients treated with Immune checkpoint Inhibitors (ICIs) (2–8% incidence) [4], it is rarely reported in non-melanoma cancers. It is approved for use in multiple cancers including metastatic melanoma, non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma (HNSCC), classical Hodgkin lymphoma, urothelial carcinoma, renal cell carcinoma (RCC), and other solid tumors with high microsatellite instability (MSI-H). It is typically administered intravenously at a dose of 200 mg every 3 weeks or 400 mg every 6 weeks. The most concerning adverse effects are immune-related adverse events (irAEs), which can affect almost any organ system. Common irAEs include colitis, pneumonitis, hepatitis, endocrinopathies (e.g., thyroid dysfunction, adrenal insufficiency), nephritis, and dermatologic conditions like rash or vitiligo. These reactions occur due to overactivation of the immune system and often require prompt treatment with high-dose corticosteroids. Routine monitoring includes blood counts, liver and renal function, thyroid function tests, and vigilance for signs of immune toxicity [7].

Vitiligo, also known as leucoderma, is a chronic skin condition characterized by the development of well-demarcated, depigmented white patches on the skin due to the selective destruction or loss of melanocytes—the pigment-producing cells. It is considered an acquired idiopathic disorder, often believed to have an autoimmune basis where the immune system mistakenly attacks melanocytes [3]. Vitiligo can affect any part of the body but commonly appears on the face, hands, feet, and around body orifices. The condition may be segmental (localized) or non-segmental (generalized), with the latter being more common and typically symmetrical. There is no definitive cure, but treatments such as topical corticosteroids, calcineurin inhibitors, phototherapy (narrowband UVB), and in some cases surgical grafting techniques may help restore pigmentation. The progression and response to treatment vary among individuals [9]. In recent years, vitiligo-like depigmentation has also been recognized as an immune-related adverse event associated with immune checkpoint inhibitors like pembrolizumab, particularly in patients with melanoma and, less commonly, in those with other cancers [5].

Colitis refers to inflammation of the colon and can present with symptoms such as diarrhea, abdominal pain, urgency, rectal bleeding, and fever. While it can result from infections, inflammatory bowel disease, or

ischemia, colitis is also recognized as a serious immune-related adverse event (irAE) in patients receiving immune checkpoint inhibitors like pembrolizumab [2]. Diagnosis involves clinical evaluation, stool studies to exclude infections, imaging (such as CT abdomen showing colonic wall thickening), and colonoscopy with biopsy, which often reveals lymphocytic or mixed inflammatory infiltrates in the colonic mucosa. Management depends on severity; mild cases may respond to symptomatic treatment, while moderate to severe cases require immunosuppressive therapy, most commonly systemic corticosteroids [10]. In steroid-refractory cases, agents like infliximab or vedolizumab are used. Prompt recognition and treatment are essential to prevent complications such as dehydration, perforation, or therapy discontinuation [7].

In this case, we report a rare case of concurrent pembrolizumab-induced colitis and leucoderma in a Renal Cell Carcinoma patient. The case highlights key diagnostic features and management.

CLINICAL PRESENTATION:

A 70-year-old man with metastatic Renal Cell Carcinoma was receiving pembrolizumab (200 mg IV every 3 weeks) as part of his systemic therapy. His initial disease involved lung metastases. After eight cycles of pembrolizumab (with axitinib), he developed acute onset of frequent watery diarrhea (2–3 bowel movements per day). He had no fever or overt bleeding. Concurrently, he noted multiple new pale, depigmented patches on his different parts of body. He had no prior history of skin disorders or autoimmune disease. On examination, he appeared dehydrated, on abdominal examination revealed diffuse mild tenderness without peritoneal signs. Dermatologic exam showed well-demarcated, non-scarring hypopigmented macules on the different parts of body.

The working diagnosis was immune-mediated colitis and vitiligo. Pembrolizumab was not held since the benefit overweighed over risk. Initial laboratory tests showed hyponatremia from diarrhea and hypothyroid but normal complete blood count and liver enzyme studies. Stool cultures and Clostridioides difficile PCR were negative.

Dermatologic evaluation included Wood's lamp examination, which accentuated the depigmented macules. No skin biopsy had evidence of malignancy or other pathology; the absence of melanocytes is diagnostic of immunotherapy-induced vitiligo. No autoimmune serologies (ANA, thyroid autoantibodies) were positive.

MANAGEMENT:

The diagnosis of pembrolizumab-induced colitis, immunotherapy was still continuing and low-dose of oral prednisolone was started for 15 days. Loperamide and supportive care (IV fluids, electrolyte repletion) were given. According to guidelines, immune-mediated colitis of grade ≥2 warrants prompt steroid therapy, taper over 4–6 weeks, and evaluation for steroid-refractory disease [1]. Infliximab or vedolizumab are considered if there is no adequate response to steroids [4]. In this patient, steroids produced a much improvement, so additional immunosuppression was not needed.

For the cutaneous vitiligo-like lesions, no specific systemic therapy was started. Topical corticosteroids and narrowband UVB phototherapy have been used anecdotally for immunotherapy-induced vitiligo but response is often limited [3].

DISCUSSION:

Pembrolizumab and other PD-1 inhibitors can induce a spectrum of irAEs affecting multiple organs. Colitis is a well-recognized ICI toxicity, usually manifesting as diarrhea and abdominal pain. In clinical trials, moderate-to-severe colitis occurs in roughly 1–4% of patients on pembrolizumab, with onset typically 6–8 weeks after therapy initiation (our patient's colitis began after ~4 months). Fatal ICI-colitis is rare, but severe cases can lead to complications like perforation [1]. Immune-mediated colitis resembles inflammatory bowel disease but often has a higher rate of normal endoscopic appearance. Histologic features of ICI-colitis vary, but commonly include a lymphoplasmacytic infiltrate, crypt apoptosis, and sometimes crypt abscesses [2].

Management of ICI-colitis depends on severity. Grade 1–2 diarrhea may respond to symptomatic measures and budesonide [3]. Grade ≥3 requires systemic steroids [5]. This patient had initial grade colitis and promptly received 5mg of prednisolone, in line with guidelines. He improved rapidly; had he not, the next step would have been infliximab or vedolizumab. Indeed, retrospective series report ~70–80% remission rates with steroids alone, and infliximab has been effective in steroid-refractory cases [4]. Some data suggest that patients who develop ICI colitis may have better cancer outcomes, possibly reflecting heightened immune activation [2]. In our patient, cancer remained controlled and continued the therapy.

Vitiligo-like leucoderma is an autoimmune skin irAE primarily reported in melanoma patients on ICIs [3]. In melanoma, it often correlates with tumor response. In non-melanoma cancers, ICI-induced vitiligo is uncommon but well documented. For example, immunotherapy-associated vitiligo-like depigmentation has been reported in NSCLC, gastrointestinal, and other tumors. In a pooled review of 21 cases across various cancers, two (≈10%) had clear-cell RCC [5]. The pathophysiology is thought to be T-cell–mediated destruction of melanocytes, possibly via recognition of shared antigens between tumor and normal melanocytes. In melanoma patients, releasing anti-melanoma immunity often cross-reacts with normal melanocytes, producing vitiligo [3].

Clinically, ICI-induced leucoderma presents as well-defined depigmented macules or patches, often on sunexposed areas, hair, or mucosa [5]. The time to onset is variable; our patient's depigmentation appeared ~3–4 months into treatment, consistent with the median ~170 days reported for vitiligo irAEs. Treatment of immune vitiligo is challenging: corticosteroids or calcineurin inhibitors are often ineffective once melanocytes are gone, and phototherapy has only limited success [3]. Indeed, our patient's topical steroids and excimer laser yielded no repigmentation.

Importantly, the occurrence of vitiligo in this context does not necessitate stopping therapy. Guidelines recognize cutaneous irAEs (other than severe Stevens-Johnson syndrome) as often manageable without permanent drug discontinuation [3]. In our case, we continued pembrolizumab (at extended intervals) after

colitis resolution, and leucoderma remained stable. The literature suggests that mild to moderate skin irAEs, including vitiligo, may even correlate with tumor control [3].

This case is unusual in combining two distinct irAEs — colitis and leucoderma — in an RCC patient on pembrolizumab. There are sparse reports of concurrent colitis and vitiligo with checkpoint inhibitors. One reported case involved ipilimumab/pembrolizumab therapy in melanoma, where vitiligo and colitis occurred together [9]. To knowledge, this is among one of the detailed reports in an RCC patient on pembrolizumab alone. It highlights that clinicians should surveil for multiple irAEs simultaneously and manage them according to established protocols. Early gastroenterology and dermatology involvement can optimize outcomes.

CONCLUSION:

Pembrolizumab can cause immune-mediated colitis and leucoderma. In Renal cell carcinoma patients on immunotherapy, diarrhea should prompt consideration of ICI-colitis, with early endoscopy/biopsy even if imaging and colonoscopy appear normal [10]. Concurrent new-onset vitiligo-like lesions signify a cutaneous irAE. Recognition of both manifestations is critical, as timely corticosteroids relieved colitis and allowed therapy to continue. This case contributes to the growing awareness of diverse irAEs and underscores the importance of multidisciplinary management in immunotherapy.

REFERENCES:

1. Pembrolizumab-Induced Immune-Mediated Colitis in a Patient with Concurrent Clostridium Difficile Infection – PMC
2. Immune-related adverse events—pembrolizumab-induced colitis—the importance of early diagnosis and treatment: A case report and review of the literature – PMC
3. Vitiligo-like depigmentation after pembrolizumab treatment in patients with non-small cell lung cancer: a case report – PMC
4. Frontiers | An updated review on immune checkpoint inhibitor-induced colitis: epidemiology, pathogenesis, treatment strategies, and the role of traditional Chinese medicine.
5. Case Report: Immune checkpoint inhibitor-related vitiligo-like depigmentation in nonmelanoma advanced cancer: A report of three cases and a pooled analysis of individual patient data – PubMed
6. Zhou C, Klionsky Y, Treasure ME, Bruno DS. Pembrolizumab-Induced Immune-Mediated Colitis in a Patient with Concurrent C. difficile Infection. Oncology Research and Treatment. 2019;42(2):73–78 .
7. NCCN Guidelines Version 1.2025: Management of Immunotherapy-Related Toxicities
8. Yoon SJ, Oh IJ, et al. Vitiligo-like depigmentation after pembrolizumab in NSCLC: a case report. Transl Lung Cancer Res. 2020;9(4):1585–1590 .
9. Ipilimumab/pembrolizumab: Colitis and vitiligo: case report - ProQuest
10. Markovic M, Niciforovic D, et al. Immune-related adverse events—pembrolizumab-induced colitis— the importance of early diagnosis and treatment: Case report and literature review. Clin Exp Gastroenterol. 2025;18:37–54 .
11. Rao H, Guo Z, et al. ICI-related vitiligo-like depigmentation in non-melanoma cancers: three cases and pooled analysis. Front Oncol. 2023;12:1099108 .
12. Yun SJ, et al. (2020). [PMCID: PMC7481606, PubMed].