



Investigating the Dermatological Challenges of Pembrolizumab-Induced Immune Stimulation in Cancer Treatments

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ABOUT THE STUDY

Immune Checkpoint Inhibitors (ICIs) have revolutionized cancer treatment by enhancing the body's immune response against tumors. Pembrolizumab, a monoclonal antibody targeting the Programmed Cell Death Protein 1 (PD-1), is one of the prominent ICIs used across various malignancies. While ICIs have shown remarkable efficacy, their broad immunomodulatory effects can result in a range of Immune-Related Adverse Events (irAEs), including dermatological manifestations. One such dermatological irAE is lichenoid eruption, a condition characterized by inflammatory skin lesions. In this study, we will examine into the phenomenon of immune checkpoint inhibitor lichenoid eruption due to pembrolizumab, exploring its clinical significance, underlying mechanisms, and management strategies.

Clinical presentation

Immune checkpoint inhibitor lichenoid eruption typically manifests as pruritic, erythematous papules or plaques on the skin and mucous membranes. These lesions can resemble lichen planus, a chronic inflammatory disorder of the skin and mucous membranes. Although lichenoid eruptions can affect any part of the body, they often occur on the trunk and extremities. Mucosal involvement, such as oral or genital lichenoid lesions, is less common but can significantly impact the patient's quality of life.

Incidence and risk factors

The incidence of lichenoid eruptions associated with pembrolizumab and other ICIs varies among clinical trials and real-world studies. The precise mechanisms underlying the development of these eruptions are not entirely clear, but several risk factors have been proposed. Patients with a history of lichenoid eruptions, autoimmune diseases, or previous irAEs may be at higher risk. Furthermore, the onset of lichenoid eruptions often occurs within the first few months of ICI

therapy, suggesting a relationship between treatment duration and risk.

Pathophysiology

The pathophysiology of immune checkpoint inhibitor lichenoid eruption involves the complex interplay between the immune system and the skin. Pembrolizumab and other PD-1 inhibitors block the PD-1/PD-L1 pathway, thereby enhancing the activation of T cells against tumor cells. However, this heightened immune response can also lead to T-cell dysregulation, resulting in autoimmune-like reactions. In lichenoid eruptions, activated T cells infiltrate the epidermis and dermis, causing inflammation and keratinocyte damage.

Differential diagnosis

Distinguishing lichenoid eruptions from other dermatological conditions is crucial for appropriate management. Conditions such as lichen planus, drug eruptions, and graft-versus-host disease can mimic the clinical and histopathological features of lichenoid eruptions. Histopathology, including the presence of lymphocytic infiltrates and basal cell damage, can aid in the differential diagnosis. Collaboration between oncologists and dermatologists is essential to accurately diagnose and manage these eruptions.

Clinical management

The management of immune checkpoint inhibitor lichenoid eruptions involves a multifaceted approach, considering the severity of symptoms, impact on the patient's quality of life, and oncological treatment goals. In mild cases with limited skin involvement, topical corticosteroids or calcineurin inhibitors may be sufficient. However, more severe or widespread eruptions often require systemic corticosteroids, which can lead to the temporary interruption of ICI therapy. In refractory cases, other immunosuppressive agents, such as methotrexate or mycophenolate mofetil, may be considered.

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Oncological considerations

Balancing the management of irAEs with the continuation of cancer treatment is a critical aspect of care. The decision to interrupt or discontinue ICIs depends on the severity of the lichenoid eruption and the underlying malignancy. In some cases, oncologists may opt for a temporary interruption of pembrolizumab to manage the dermatological side effect while closely monitoring tumor response. Reintroduction of ICIs after resolution of the eruption may be possible, but the risk of recurrence should be considered.

Prognosis

The prognosis of immune checkpoint inhibitor lichenoid eruption is generally favorable, especially with early recognition and appropriate management. Most patients experience resolution of their skin lesions, although it may take several weeks to months. Long-term follow-up is essential to monitor for recurrence and assess the impact of lichenoid eruptions on the overall oncological outcome. In some instances, the development of irAEs, including dermatological ones, has been associated with a better response to ICI therapy, known as the "abscopal effect."

Patient education and support

Patient education is vital in managing immune checkpoint inhibitor lichenoid eruptions. Oncologists and dermatologists should provide clear information about the potential side effects of pembrolizumab and the importance of promptly reporting any skin changes or symptoms. Patients should also be educated on the importance of sun protection and skincare practices to minimize the risk of exacerbating skin irritation.

CONCLUSION

Immune checkpoint inhibitor lichenoid eruption due to pembrolizumab represents a notable dermatological side effect of immunotherapy. While it can be distressing for patients, timely recognition and appropriate management can mitigate its impact. A multidisciplinary approach involving oncologists and dermatologists is critical for both addressing the lichenoid eruption and optimizing cancer treatment. As the use of ICIs continues to expand in oncology, further research is needed to better understand the pathogenesis and optimal management of this and other immune-related adverse events.