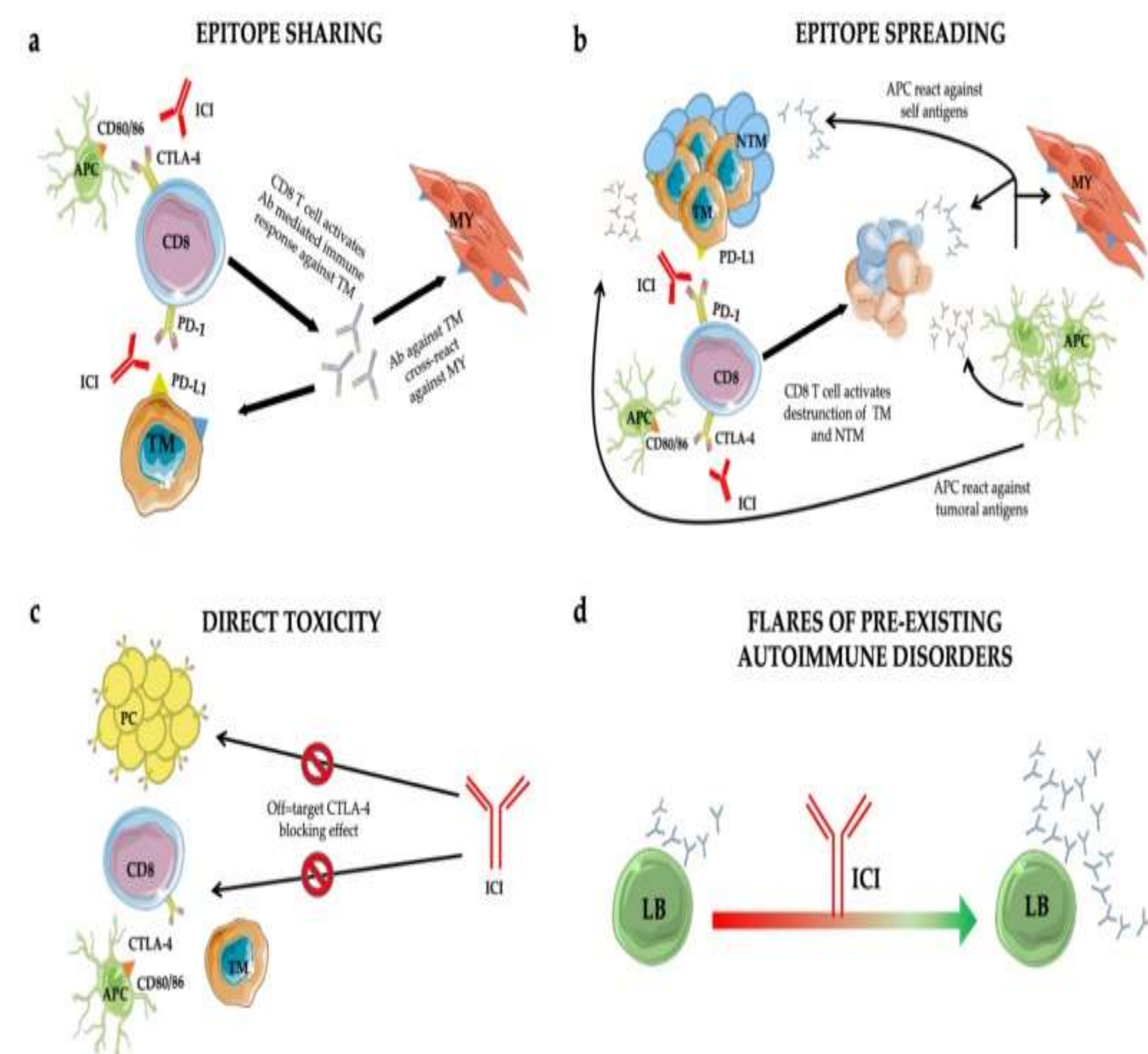


Learning Point

- ∅ Myositis associated with ICIs typically manifests as muscle weakness, pain, and elevated creatine kinase (CK) levels, necessitating early recognition for timely intervention.
- ∅ Myositis associated with ICIs typically manifests as muscle weakness, pain, and elevated creatine kinase (CK) levels, necessitating early recognition for timely intervention.
- ∅ Diagnosing ICI-induced myositis presents challenges due to similarities with other muscle disorders, requiring careful differentiation.

Background

Possible mechanisms of irAEs



Clinical Case

We present a case of a 79-year-old male with past medical history of deafness, HTN, hyperlipidemia, epilepsy maintained on Keppra, CKD stage 3 and metastatic melanoma to the brain status post craniotomy in January 2023 presented to the emergency department after an unwitnessed fall. Patient denies any loss of consciousness after fall. In the ED, labs were insignificant except Cr-1.47, trop-0.12, CK of 5277 and mildly elevated LFTs. CTA head and neck revealed post-operative changes from the left frontal craniotomy. EEG showed on active epileptiform activity. IVF was started. Patient denied any muscle aches or weakness during presentation. Denied any active medication for melanoma. RUQ USG showed no acute abnormalities. During the hospital stay CK plateau at 3000s and patient started complaining of weakness and aches in the proximal arms and thighs. No rash was observed. Rheumatology was consulted for possible concerns of inflammatory myositis and various tests were ordered like ANA by IFA, myocyte panel 11 antibodies, HMGCR antibody, and MRI of thighs to find spot for muscle biopsy. During further work-up it and history from charts, it was found that patient was taking immune-therapy (ipilimumab, nivolumab). Last dose of the medication was given 30 days prior to the admission. The patient's history of ICI treatment raised concerns about immune therapy-related myositis, prompting the initiation of prednisone therapy. When the patient started taking prednisone, their CK levels started to go down, and their muscle-related symptoms also got better. This supported the idea that they might have had immune-related myositis. The patient's experience showed how difficult it can be to diagnose and treat immune-related side effects caused by immune checkpoint inhibitor therapy.

Discussion

Our case underscores the intricate nature of diagnosing and managing immune therapy related myositis, particularly when overt rhabdomyolysis is absent. Maintaining suspicion for immune-related adverse events post ICI treatment is vital, encompassing these possibilities in the diagnostic approach for unexplained elevated CK and myopathic symptoms. Cancer treatment has been transformed by immune checkpoint inhibitors (ICI). Immune checkpoint inhibitors (ICIs) encompass inhibitors programmed cell death protein 1 (PD-1) inhibitors (nivolumab) and cytotoxic T-lymphocyte associated protein 4 (CTLA-4) inhibitors (ipilimumab) can trigger immune-related adverse events (irAEs) like myositis, myocarditis, myasthenia gravis, hepatotoxicity, hypothyroidism, and Miller-Fisher syndrome [1]. Myositis, characterized by elevated CK and muscle weakness, is a rare but significant adverse events of these ICI therapy. ICI therapy has demonstrated efficacy in treating various cancers, including metastatic melanoma. However, it's linked to diverse irAEs, some being infrequent. Proximal muscle weakness/myalgias can stem from various causes, necessitating comprehensive clinical history and lab assessments. Biomarker identification and personalized treatment aimed at minimizing toxicity while maintaining therapeutic efficacy remain unmet medical needs and thus merit further research and clinical efforts.

References

- 1) Mahdieh Fazel and Patrick M. Jedlowski. Severe Myositis, Myocarditis, and Myasthenia Gravis with Elevated Anti-Striated Muscle Antibody following Single Dose of Ipilimumab-Nivolumab Therapy in a Patient with Metastatic Melanoma. doi: 10.1155/2019/2539493. PMID: 31183226.
- 2) Solimando AG, Crudele L, Leone P, Argentiero A, Guarascio M, Silvestris N, Vacca A, Racanelli V. Immune Checkpoint Inhibitor-Related Myositis: From Biology to Bedside. *International Journal of Molecular Sciences*. 2020; 21(9):3054. <https://doi.org/10.3390/ijms21093054>