A UNIQUE CASE OF IMMUNOTHERAPY RELATED AUTOIMMUNE COMPLICATIONS

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Abstract:

• Pembrolizumab, a monoclonal antibody that inhibits programmed cell death protein-1 (PD-1), is an important treatment for various malignancies.
• Unfortunately, it is also associated with a wide array of immune-related adverse events (irAEs).

Introduction:

• Targeted immunotherapies (e.g., pembrolizumab) have become efficacious in the management and treatment of malignancies, including but not limited to renal cell carcinoma (RCC).
• Oftentimes, they can be associated with irAEs related to increased immune activity.
• Most irAEs are effectively treated with temporary discontinuation of the offending agent or by inducing immunosuppression with agents such as corticosteroids.
• Here, we highlight a case of a patient who developed multiple irAEs after a single dose of pembrolizumab, including dermatitis, hepatitis, myositis, myocarditis, and myasthenia gravis.

Purpose:

• To highlight the different adverse events associated with pembrolizumab as seen in our patient and to promote increased awareness so that they can be identified promptly and started on appropriate therapy.

Case Description:

• A 58-year-old male with a history of right nephrectomy due to metastatic RCC presented for evaluation of progressively worsening left-sided ptosis for 4 days in addition to diffuse myalgias and generalized weakness.
• He received one dose of pembrolizumab approximately 3-4 weeks prior.
• On arrival, vital signs were unremarkable. His labs were notable for troponin peak 2404 ng/L without chest pain or ischemic changes on EKG.
• His AST and ALT peaked at 740 U/L and 681 U/L, respectively (baseline <100 U/L) and CPK peaked at 11,205 U/L.
• Myositis extended panel, voltage gated calcium channel, acetylcholine binding and blocking antibody (Ab), and muscle-specific kinase Ab and IgG were unremarkable.
• Transthoracic echocardiogram was unremarkable.
• He was started on high dose steroids, IVIG and pyridostigmine with improvement in symptoms and liver enzymes, and ultimately discharged on oral prednisone.
• Within 5 weeks, he developed worsening thrombocytopenia with trough level 12K/mL by week 6-7.

Discussion:

• Our case highlights a rare example involving multiple toxicities being encountered after a single dose of immune-checkpoint inhibitor (ICI) therapy.
• Immune mediated adverse events typically occur within the first 3 months but can also occur as early as one day or as late as several years after initiation.
• In our patient, because workup for alternative etiologies causing his abnormal labs was unrevealing, it was believed that his symptoms and abnormal labs were due to pembrolizumab-induced immune-mediated response.
• Therefore, awareness of autoimmune-related complications with ICIs is advised, especially in the early phase of the treatment.

Figure 1

Haptoglobin, PT/PTT, and fibrinogen were normal.
Due to concern for checkpoint inhibitor-induced immune thrombocytopenia refractory to high dose steroids, he completed a 5-day course of IVIG with gradual improvement in cell counts.
He was seen by dermatology for diffuse body rash which was attributed to immunotherapy.
Electromyography revealed mild active myopathy of the upper extremities.
Over time his troponin, CPK and liver enzymes normalized over the span of 1 month.