PD-1 Inhibitor Induced Autoimmune Type 1 Diabetes Can Present As Potentially Fatal DKA

Smit Shah, DO; Christopher Reggio, DO; Biraj Shrestha, MD; Ronald Herb, DO
Department of Internal Medicine, Reading Hospital – Tower Health, West Reading, PA

Introduction

- Humanized antibodies against programmed cell death 1 immune check point (PD-1), such as pembrolizumab, have demonstrated anti-tumor activity across numerous malignancies.
- Now FDA-approved for treatment of metastatic malignant melanoma and lung cancer.
- However, in the process of disinhibition of the immune system, many important autoimmune side effects have been reported.

Case Description

- 91-year-old male with a past medical history of recently diagnosed stage IIIC malignant melanoma without prior diabetes, presented to his primary care physician (PCP) with a complaint of polyuria, worsening fatigue, and dehydration for 1 week. He was then sent to the hospital due to a concern for diabetic ketoacidosis.
- Had initiated pembrolizumab 3 weeks prior, with the last dose being one week before his presentation to the PCP.
- Upon admission, the patient was afebrile and hemodynamically stable. He was visibly fatigued and dehydrated with dry mucous membranes and dry axilla bilaterally. No focal deficits on thorough neurological examination. Additionally, pulmonary, abdominal, and skin examinations were unrevealing.

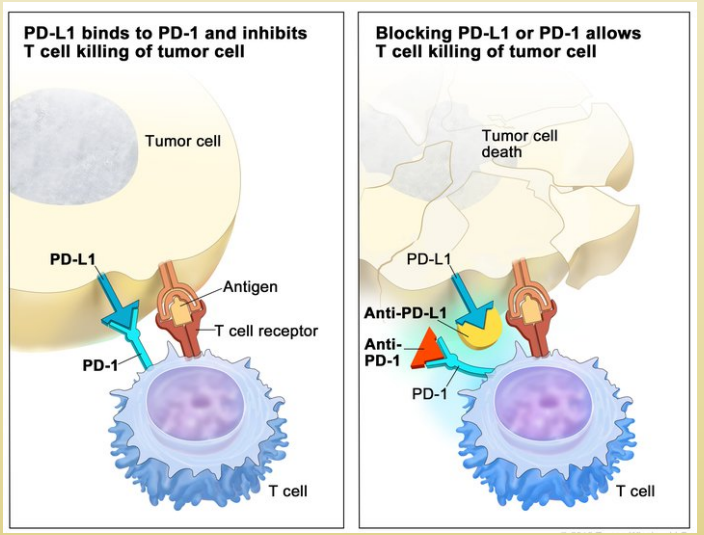

Figure 1 - Immune checkpoint inhibitor. Checkpoint proteins, such as PD-L1 on tumor cells and PD-1 on T cells, bind to regulate immune response. The binding of PD-L1 and PD-1 prevents T cells from killing tumor cells in the body (left panel). Blocking this interaction with an immune checkpoint inhibitor (anti-PD-L1 or anti-PD-1) allows the T cells to kill tumor cells (right panel).

Case Description

- Pertinent laboratory tests:
  - Blood glucose 939 mg/dL, potassium 5.9 mmol/L, bicarbonate 8.1 mmol/L, anion gap 34 mmol/L, beta hydroxybutyrate 13.4 mmol/L, and non-fasting insulin level of 1.8 uIU/mL, C-peptide <0.1 ng/ml.
  - Arterial blood gas: pH of 7.09, pCO2 16.7 mmHg, and bicarbonate of 5.0 mmol/L.
- Acute coronary syndrome and stroke were ruled out.
- Patient was stabilized with intravenous fluids and intravenous insulin, with a transition to subcutaneous basal-bolus insulin glargine and short acting insulin lispro with carbohydrate-controlled meals on day two of admission.
- Further laboratory testing revealed Glutamic Acid Decarboxylase (GAD) antibody level of >250.0 IU/mL with Islet Cell Antibody undetectable.

Discussion

- PD-1 antibodies are an emerging form of cancer immunotherapy. Accordingly, it is increasingly important to recognize their side-effect profiles, which include autoimmune endocrine abnormalities. Our case, with absent insulin and c-peptide levels and elevated GAD antibodies, demonstrates that PD-1 inhibitors can induce autoimmune Type 1 diabetes mellitus that may present with severe diabetic ketoacidosis.