5-2022

Immune Checkpoint Inhibitor Induced Type 1 Diabetes Mellitus: A Pembrolizumab Case Study

Michael R. Dirks Jr.

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Michael R. Dirks Jr, DO
Providence Oregon Family Medicine Residency

INTRODUCTION

Background:
Immunotherapy, in conjunction with chemotherapy and radiation, represents an essential modality in the strive towards individualized cancer therapy such as treatment with pembrolizumab. However, it does not come without its side effects.

Pembrolizumab (Keytruda):

Mechanism of Action:
Highly selective anti-PD-1 humanized monoclonal antibody which inhibits programmed cell death-1 (PD-1) activity by binding to PD-1 receptor on T-cells to block PD-1 ligands (PD0-L1 and PD-L2) from binding. Blocking the PD-1 pathway inhibits the negative immune regulation caused by PD-1 receptor signaling. Anti-PD-1 antibodies (including pembrolizumab) reverse T-cell suppression and induce antitumor responses.[2]

Indications:
Melanoma, breast cancer, endometrial carcinoma, metastatic non-small cell lung cancer, esophageal and gastric cancer, urothelial carcinoma

Adverse Reactions:
Arrhythmias, peripheral edema, pruritus, rash, abdominal pain, fatigue, headache, hypothyroidism, colitis, hepatitis

CASE DESCRIPTION

Chief Complaint:
fatigue, indigestion and weight loss

History of Present Illness:
70 yof with pmhx of tobacco use disorder and metastatic pulmonary adenocarcinoma s/p chemotherapy with pemetrexed (d/c'd d/t repeated afib and renal dysfxn), palliative radiation and currently undergoing immunotherapy w/ pembrolizumab q3wks that presents to outpatient infusion center w/ fatigue, poor appetite and weight loss found to have a random repeat CBG of 686.

Management:
New onset T1DM w/ hyperglycemia
- Likely d/t rare autoimmune side effect from immunotherapy
- No e/o DKA (no AG)
- IV fluids for initial volume resuscitation
- Start weight-based insulin regimen with close follow up
- Nutritionist
- Screening for other autoimmune conditions; TSH, ACTH stim test

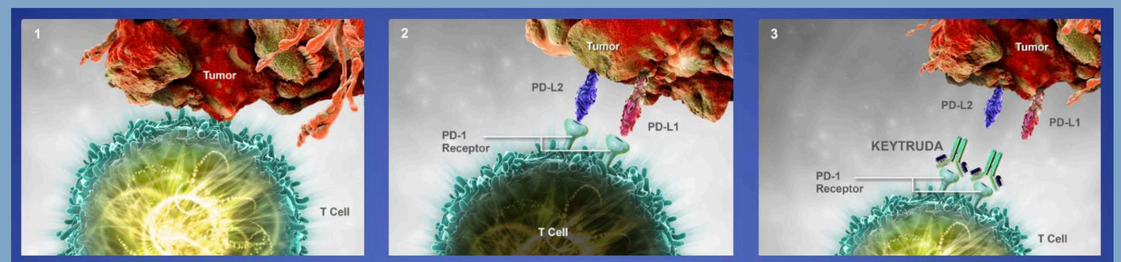

Figure 1: (1) Normal Immune response: T cell activated and attack tumor cells
(2) Tumor Evasion and T-Cell Deactivation: PD-L1 and L2 ligands on tumor can bind receptors on T cells to inactivate them
(3) T-Cell Reactivation with Pembrolizumab (Keytruda)[1]

Disclosure Statement

Authors of this presentation have the following to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation:

DISCUSSION

Immunotherapy with Pembrolizumab:
- anti-PD-1 therapy not specific towards cancer cells
- Normal, non-cancerous cells, if affected cannot inhibit T-cells from immune response and subsequent cell death
- Unknown mechanisms but likely through destruction of beta islet cells
- Previous literature review in 2018 showing six reported cases of autoimmune diabetes associated with pembrolizumab w/o sexual predilection and avg age onset 58 years old.[3]
- 4 of those cases initially presented with diabetic ketoacidosis
- No association between number of treatments and onset.
- Variation from normal to elevated A1c seen
- Of cases reviewed, 5 out of 6 had to continue insulin therapy, likely irreversible
- Use of steroid for treatment has not been established (has been used for other immune toxicities associated with pembrolizumab)

KEY LEARNING POINTS

- Pembrolizumab can induce autoimmune conditions; including Type 1 Diabetes
- While receiving pembrolizumab therapy, periodic CBG checks can prevent DKA and associated morbidity and mortality
- Treatment includes insulin therapy (steroids not yet indicated)
- Pembrolizumab induced diabetes not likely reversible
- Screen patient for other autoimmune conditions; TSH and ACTH

References

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