Durvalumab-Induced New-Onset Diabetes Mellitus in a Patient With Non–Small Cell Lung Cancer: A Case Report

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Abstract

- **Introduction**: Immune checkpoint inhibitors (ICIs) like durvalumab have revolutionized cancer therapy but may induce rare endocrinopathies, including diabetes mellitus.
- **Case Presentation**: 69-year-old man with stage III non-small cell lung cancer who developed new-onset hyperglycemia with low C-peptide levels after two doses of durvalumab infusion.
- **Conclusion**: Clinicians should remain vigilant for metabolic adverse events in patients receiving ICIs, as early detection and management are crucial.

Endocrinopathies associated with immune checkpoint inhibitors like durvalumab are a rare but noted adverse effect. Durvalumab is a programmed cell death ligand 1 (PD 1) inhibitor, which ultimately inhibits T-cell response and prevents overstimulation of immune response in peripheral tissues.[1] It has been FDA approved as part of the treatment for Stage III non-small cell lung carcinoma, advanced or metastatic biliary tract cancer, and unresectable hepatocellular carcinoma.[2] Immune checkpoint inhibitors can lead to autoimmune destruction of pancreatic beta cells, mimicking Type 1 diabetes mellitus, even in patients without a prior history of endocrine dysfunction.

Case Report

A 69-year-old man diagnosed with poorly differentiated non small cell lung cancer who had received two doses of durvalumab after completing chemoradiation initially presented to the emergency department with peeling at the base of his fingernails followed by small nonerythematous papules on his palms and soles. Dermatological findings were initially consistent with drug related eruption, oncology was consulted and recommended initiating steroids.

Incidentally during the work-up, he was found to be hyperglycemic with a glucose level greater than 900 mg/dL in mild metabolic acidosis with positive serum acetone with no anion gap elevation. His A1c was 5.8% and his C peptide levels were low at 0.11 ng/mL (reference range:0.8-3.85 ng/mL) with no prior history of diabetes, which demonstrates the acute onset of diabetes. Initial management included an insulin drip for suspected DKA, which was later transitioned to insulin glargine and sliding scale insulin during his stay. Given the timing of durvalumab initiation, no prior hyperglycemia, a low C-peptide, and new insulin dependence the diagnosis of immune check point inhibitor induced diabetes mellitus was favored. Due to the negative side effects the patient was experiencing, his immunotherapy was discontinued. His lab values are summarized in Table 1 below.

Lab	Patient's Value	Normal range
Glucose	>900 mg/dL	70-99 mg/dL (fasting)
HbA1c	5.8%	<5.7%
C-peptide	0.11 ng/mL	0.8-3.85 ng/mL
Serum acetone	Positive	Negative
Anion gap	Normal	8-12 mEq/L

His symptoms in regards to the pruritus as well as the appearance of his rash improved significantly and relatively quickly after steroid administration. Steroids were continued with counseling that hyperglycemia may persist through the taper. The patient remained medically stable and was discharged home the next day on insulin starting at 15 units daily as a good starting point and a glucometer.

Discussion

Immune checkpoint inhibitors like durvalumab have transformed the treatment for various malignancies. While they are normally well tolerated, these drugs can cause immune related adverse effects due to enhanced T cell activity against self antigens. This perpetuates the development of endocrinopathies that can affect several organ systems. ICI-associated diabetes mellitus is rare but is clinically significant due to its abrupt onset and life-threatening hyperglycemia. Our patient developed profound hyperglycemia within weeks of initiating durvalumab after receiving only two infusions of the drug. These findings are consistent with autoimmune beta cell destruction similar to the mechanisms of Type 1 diabetes. This patient's acute presentation without ketoacidosis was atypical but likely due to early detection during monitoring. Additionally in our case, the patient had a concurrent dermatologic reaction further supporting the diagnosis of ICI-induced autoimmunity. Our study emphasizes that recognizing this condition is crucial. Early intervention with insulin can prevent DKA and serve as life saving management.

There have been other reported cases of the development of endocrinopathies like diabetes and hypothyroidism;[3] therefore, further reporting of cases like this are important to monitor adverse effects of this medication. This case underscores the importance of recognizing rare but serious immune-related adverse effects like diabetes mellitus during durvalumab therapy. Early identification and routine glucose monitoring in patients receiving ICIs, even in the absence of prior metabolic dysfunction, can be crucial to prevent life-threatening complications and to guide decisions regarding continuation of immunotherapy. Also, this case emphasizes the need for interdisciplinary care between all involved providers to ensure proper long- term management of these patients.

1.Zou W, Chen L. Inhibitory B7-family molecules in the tumor microenvironment. *Nat Rev Immunol*.2008;8(6):467-477. doi:10.1038/nri2326.
2.Imfinzi (durvalumab) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022.
3.Akturk HK, Kahramangil D, Sarwal A, et al. Immune checkpoint inhibitor–induced type 1 diabetes: a systematic review and meta-analysis. *Diabetes Care*. 2019;42(4):e64-e67. doi:10.2337/dc18-1949.