concentration is generally >550 mg/dL (30.6 mmol/L), HbA1c is 7.6%–8%, about 75% have DKA, and C-peptide is reduced in >85% (1, 2). The frequency of type 1 diabetes secondary to checkpoint inhibitors will increase as use of these agents expands.

Nonstandard Abbreviations: GAD, glutamic acid decarboxylase; DKA, diabetic ketoacidosis.

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Commentary on a Case of Unexpected Hyperglycemia

Nicholas Borcherding and Ann M. Gronowski*

Fatica and colleagues describe a patient with a history of undifferentiated pleomorphic sarcoma presenting with new onset symptoms concerning for hyperglycemia. Initial investigation revealed both an increased blood glucose concentration and ketone production, key findings in the diagnosis of diabetic ketoacidosis. However, this case was complicated by bicarbonate and pH within reference limits, and an unusually low pO_2. Furthermore, although the patient had complaints of polydipsia, polyuria, and weight loss over several days, there were no signs or symptoms of acidosis or the respiratory changes that would be associated with compensation.

Anti-PD-1 therapies and other immune checkpoint inhibitors generally function to dampen the suppression of antitumor response by blocking the natural immune system brakes. For instance, PD-1 is expressed during lymphocyte activation and functions as a negative feedback for further lymphocytic activity. As agents that activate the immune system against cancer, these immunotherapies can lead to "immune activation gone astray," and target normal cells. Side effects, including colitis, hepatitis, pancreatitis, nephritis, and skin pathologies are seen in up to a third of patients on anti-PD-1 therapies (1). Retrospective cohorts have also reported autoimmune endocrinopathies including: diabetes mellitus, both hyper- and hypothyroidism, adrenal insufficiency, and hypophysitis in 6%–10% of patients receiving anti-PD-1 therapy (1, 2). As endocrinopathies can present with nonspecific symptoms, such as the case presented, these incidences are likely underestimated.

With immune checkpoint blockers now a mainstay of clinical management for many malignancies, more iatrogenic endocrinopathies can be expected. These complications do not have clear timelines and, as in the case presented, patients receive these therapies over the course of years. Thus, possible new-onset endocrinopathy is an important differential when working up a patient on immune checkpoint blockade.

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