A 44-year-old woman with ER+/Her2(-)/PI3K positive metastatic breast cancer was started on alpelisib. Previously, HbA1C was 5.4%. Hyperglycemia developed and HbA1c rose to 9.0% within 6 months of alpelisib 300mg daily. She started metformin and empagliflozin, which she was unable to tolerate due to nausea and vomiting. Her self-monitored blood glucoses were 300-400mg/dL within hours after her morning alpelisib dose. We discontinued empagliflozin when she developed metabolic acidosis with an increased anion gap. However, prior to any dose reduction, oncology discontinued alpelisib due to evidence of cancer progression. A week later, her glucoses normalized.
Second case is of a 64-year-old woman with stage IV ER+/Her2(-)/PI3K mutated breast cancer with bony metastases, who was started on alpelisib 250mg. Her prior HbA1C was 5.5%. Ten days after initiation of alpelisib, she developed grade 3 hyperglycemia (blood glucoses 200-500mg/dL). She was started on metformin 2000mg with alpelisib dosed at noon. However, she noted a marked rise in blood glucose in the afternoon, few hours following alpelisib dose. Thus, moving the alpelisib to bedtime allowed better control of glycemia by using overnight basal insulin.
Similarly, a 37-year-old woman with a history of ER+/HER2(-) stage IV metastatic breast cancer to the liver, with PI3K mutation was found to have acute, severe hyperglycemia with blood glucose of 300mg/dL, despite HbA1C being only 4.7%. This was attributed to initiation of alpelisib 2 days prior to admission. Given the severity of her insulin resistance (requiring > 100 units of insulin daily), alpelisib dose was reduced from 300mg to 150mg/day. On discharge, she was placed on metformin, dulaglutide, and basal and prandial insulins. Her HbA1C rose to 9.4% within 3 months of alpelisib initiation.
This case series demonstrate the unique challenges in managing alpelisib induced reversible hyperglycemia.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

An Atypical Case of Latent Autoimmune Diabetes of Adults

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Introduction: Latent autoimmune diabetes of adults (LADA) is an adult-onset, slowly progressing subtype of autoimmune type 1 diabetes mellitus (T1DM), that is often misdiagnosed as T2DM. We present an atypical case of LADA that was presented in an uncommonly late age with high titres of anti-glutamic acid decarboxylase antibodies(GADA). **Clinical Case:** A 78 year old male presented with alcohol intoxication and hyperglycemia. His serum glucose was 441mg/dL with negative urine ketones. Arterial blood gas showed pH 7.36, HCO3-20mmol/L, pCO2 37.1mmHg. Anion gap was 11. HbA1c level was 16%. His body weight was 43.2kg with a BMI of 16.6. He was having polyuria and polydipsia, and was recently diagnosed with T2DM. His low BMI and symptoms raised suspicion for LADA. GADA titres revealed to be greater than 250IU/mL. A diagnosis of LADA was made. He was discharged on insulin. **Conclusion:** LADA shares the same genetic and autoimmune profiles with T1DM, but its insidious presentation overlaps with that of T2DM, often delaying diagnosis and adequate treatment. Our case of confirmed LADA at a late age of 78 is atypical, but warrants that adults newly diagnosed with diabetes should be screened for LADA if there are atypical findings. Among the anti-islet antibodies, GADAs are the most sensitive self antigen-antibody markers of autoimmune diabetes. The GADA titre is often used to stratify the risk of progression to insulin dependence in LADA, as a higher titre suggests severe β-cell loss in the pancreas. High GADA titres at the time of diagnosis at an elderly age is also an uncommon finding for LADA. Autoimmune diseases with aggressive autoimmune responses present early, while indolent progressions lead to late onset of symptoms and diagnosis. Thus it is unusual for our patient to have significantly high GADA levels. As pathophysiology of LADA is yet to be understood, further research may reveal the autoimmune process of GADA and the role of titres in disease activity and progression. There are no current therapeutic guidelines for LADA. Our patient was eventually discharged on insulin given his high HbA1c with high titres of GADA, but there were questions regarding the use of oral glycemic control agents due to his history of noncompliance. The use of oral agents for LADA remains an area of ongoing research. The general understanding is that due to its autoimmune etiology, insulin is eventually required. Early insulin therapy preserves residual β-cell function, improves glycemic control, and reduces the risk of long-term complications. As treatment goals of LADA would be to improve glycemic control with preserving residual β-cell function, further research may establish treatment guidelines for LADA. Monitoring anti-islet antibodies and c-peptide titres may play a role in establishing the timing to introduce oral agents and/or insulin for optimal treatment of LADA.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

An Atypical Presentation of Hyperosmolar Hyperglycemic State Induced by SARS CoV 2

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Hyperglycemic emergencies such as Diabetic Ketoacidosis (DKA) or Hyperosmolar Hyperglycemic State (HHS) are commonly precipitated by infectious processes. Severe Acute Respiratory Syndrome-Coronavirus 2 (SARS-CoV-2) is a novel infectious process prompting hyperglycemic crisis. SARS-CoV-2 at the level of the lungs affects ACE2 functioning which in turns decrease the B cells proliferation at the pancreas and hinders insulin secretion. Advanced age and comorbidities such as hypertension, cardiovascular disease and diabetes mellitus are considered to