Marina Torres Torres, MD[1], Kimberly Padilla Rodriguez, MD[1], Norma Vergne-Santiago, MD[2], Andrea del Toro Diez, MD[1], Alex N. Gonzalez Bossolo, MD, ECNU[3], Michelle Marie Mangual Garcia, MD[4], Gabriela Torres Torres, MD[1].
[1]San Juan City Hospital, San Juan, PR, USA, [2]San Juan City Hospital of Puerto Rico, San Juan, PR, USA, [3]San Juan City Hospital Endocrine Fellowship Program, San Juan, PR, USA, [4]Hospital Muni de San Juan, SAN JUAN, PR, USA.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection primarily affects the respiratory tract, but gastrointestinal (GI) symptoms may obscure a secondary diagnosis. GI symptoms similar to the ones presented in acute pancreatitis (AP) have been reported. SARS-CoV-2 binds to angiotensin-converting enzyme 2 receptors, which have been identified in the lungs and pancreas. It has been discussed that systemic response to the infection prompts dysregulation in the affected organs. Hyperglycemia is an independent risk factor for increased mortality and thus a detailed assessment must be performed.
A 47 year-old man with dyslipidemia arrived at the ER due to a severe constant epigastric pain of 1 day of evolution with back radiation associated with nauseas, emesis, and hyporexia. Upon examination he was tachycardic and in distress due to pain. Laboratories revealed normocytosis, normal hemoglobin, mild thrombocytopenia, hyperglycemia (150 mg/dL), corrected hyponatremia (130 mmol/L), and corrected hypocalcemia (7.4 mg/dL). Amylase (2,332 U/L) and lipase (2,990 U/L) were elevated. Triglycerides were 6,256 mg/dL and glycated hemoglobin was 6.1%. Abdominal CT scan revealed pancreatitis. He was admitted to the ICU due to severe AP due to hypertriglyceridemia with IV hydration and IV insulin infusion. During the first day of admission, he developed respiratory distress requiring intubation, marked abdominal distension, hemodynamic instability, and oliguria. Intra-abdominal pressure yielded 24 mmHg leading to the diagnosis of abdominal compartment syndrome. He underwent emergent abdominal decompressive laparotomy with Bogota Bag placement. COVID-19 PCR test was performed and reported positive. 72 hours later, triglycerides improved and IV insulin was discontinued, but hyperglycemic state prompted subcutaneous basal and correction boluses. Insulin requirement progressively decreased and was discontinued after 14 days. He continued to show clinical improvement and by day 40, the patient was successfully extubated and discharged after physical rehabilitation.
SARS-CoV-2 infection has shown a complex multisystem involvement leading to variable presentations which can be fatal if not identified and addressed properly. Albeit, AP is a rare manifestation of COVID-19, clinicians should be aware and pay attention to the related complications. Proposed mechanisms for hyperglycemia and AP include β-cell damage. The pathogenetic role of COVID-19 in hypertriglyceridemia is unclear. Little attention has been paid to the extent of pancreatic injury caused by this virus. To our knowledge this is the second case presenting with hyperglycemia, hypertriglyceridemia, and AP in COVID-19 infection. As the global pandemic is still growing, elucidation of key pathways and mechanisms underlying these associations would aid in the treatment of patients with COVID-19 worldwide.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Immune Checkpoint Inhibitor Associated Type 1 Diabetes

Jose Andres Duenas, MD[1], Maria Daniela Rendon, MD[1], Syeda Sumbul Zahra Zaidi, MD[2], Jassimran Singh, MBBS[3], Lubna Mirza, MBBS[4].
[1]Universidad Catolica de Santiago de Guayaquil, Guayaquil, Ecuador, [2]Nishtar Medical College, Multan, Pakistan, [3]Institute of Medical Sciences, BHU, Jammu, India, [4]Norman Endocrinology Associates, Norman, OK, USA.

Background: Immune-checkpoint inhibitors are increasingly being used in cancer therapy. Nivolumab is a monoclonal antibody that has been used in a variety of conditions such as metastatic melanoma. Treatment with immune checkpoint inhibitors enhances immune response but is also known to diminish immune tolerance and increase autoimmune toxicity. Nivolumab works by binding and inhibiting the programmed death cell 1 receptor (PDC1). This is a negative regulator of the activity of the T lymphocytes. Normally the biding of PDC1 with PDL1 and PDL2 ligand will leads to inhibition of protein kinase signaling pathways that would lead to inhibition of T cells proliferation and production of cytokines.
So Nivolumab will increase the response of T cells by blocking PDC1 increasing selectivity with tumoral cells.
On the other hand, the use of nivolumab inhibiting the PD1 pathway could result in the loss of self-tolerance that can be related to an increase of autoimmune events. Such as autoimmune DM1. Case description: A 67-year-old woman was referred to the Endocrinology service for hypothyroidism in 2016. She had been diagnosed 5 years earlier with malignant melanoma on left forearm that was surgically removed, along with her lymph nodes. No chemo or radiation was required. There was no personal or family history of DM. Blood glucose levels were normal. About one month later, she found out her melanoma came back on her face, (edge of her mouth) and got treated with Nivolumab. A couple of months later she reported to the consult with fatigue, dry mouth, polydipsia, and polyuria. Symptoms were progressive and was hospitalized at initial dx of DM w/glucose >800. She got diagnosed with New onset diabetes. The Diagnosis confirmed with + GAD antibodies and low C-Peptide. Her hemoglobin A1C today (4 years later) is 6% with a fingerstick blood sugar of 147 mg/dl. Average glucose is 131 mg/dl with a standard deviation of 38.87. 87.1% of her blood sugars are staying in target range, low blood sugars less than 70 are 4.3%, high blood sugars are 8.6%. **Conclusion:** The diagnosis of insulin dependent DM is confirmed because of the clinical presentation, persistent hyperglycemia, and low C-peptide. The normal pre-nivolumab fasting blood glucose levels suggest the absence of diabetes prior to nivolumab. 4 years later, the patient has not shown any signs of remission, so, if develops, DM1 should be considered as a permanent complication of using Nivolumab.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Immunotherapy-Related Autoimmune Diabetes Mellitus and Exogenous Insulin Antibody Syndrome in a Patient With Metastatic Oral Squamous Cell Carcinoma

Maimoona Bahlol, MD, Yufei Dai, MD.
UNIVERSITY OF CINCINNATI - MSB R005B, Cincinati, OH, USA.

Introduction: Exogenous insulin antibody syndrome (EIAS) is a rare condition characterized by wide glycemic excursions and recurrent hypoglycemia in the presence of high insulin antibody titers. It has been described in diabetic patients treated with exogenous insulin. Programmed death ligand 1 (PD-L1) inhibitors are known to cause autoimmune diabetes mellitus, but PD-L1-related EIAS has not yet been reported to our best knowledge. **Case Description:** A 63 years old Caucasian man with history of recurrent oral squamous cell cancer presented to emergency room with polyuria, polydipsia, nausea, and vomiting 3 months after initiation of immunotherapy (Durvalumab and cetuximab). He had no prior history of diabetes mellitus or hypoglycemia. He was admitted to hospital for management of diabetic ketoacidosis (Anion gap of 24 mEq/L, venous blood glucose of 805 mg/dL, Venous PH of 7.12, large urine ketone, A1C of 8.9%). After a brief hospital stay, the patient was discharged home on insulin glargine and metformin. His immunotherapy was resumed after hospital discharge. When the patient was seen by Endocrinologist in the clinic, metformin was discontinued and prandial insulin lispro was added. This basal-bolus insulin regimen improved his glycemic control initially. However, without significant changes in his lifestyle or medical condition, he developed worsening postprandial hyperglycemia and recurrent fasting hypoglycemia. Up-titration of his mealtime insulin did not lower postprandial hyperglycemia but possibly worsened fasting hypoglycemia. EIAS was suspected after reviewing his continuous glucose monitoring data. Further work up at this point revealed mildly elevated glutamic acid decarboxylase antibodies (5.9 units/mL, normal range 0.5 - 5.0) and markedly elevated insulin antibody level (77.0 μU/mL, normal range <5). His blood C-peptide was undetectable when his venous blood glucose was 252 mg/dl. In addition, his total insulin level (198 uU/mL) was much higher than his free insulin level (38 uU/mL) following an insulin lispro injection. The patient was diagnosed with EIAS. Switching insulin lispro to insulin aspart while he was on a different immunotherapy medication (Pembrolizumab) immediately reduced his average blood glucose and reduced his total daily insulin dosage by more than 50%. This improvement in glycemic control with insulin aspart only lasted for about 1 week. Unfortunately, the patient's squamous cancer progressed on immunotherapy. He was referred to hospice care and passed away. **Conclusion:** Evaluation for EIAS would be reasonable in insulin-treated diabetic patients who develop wide glucose excursions and unexplained fasting hypoglycemia while on immunotherapy.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Intravenous Insulin Resistance in a Critically Ill Patient Secondary to Decreased Peripheral Perfusion

Deviani Umadat, DO[1], Dharscika Arudkumaran, MD[2], Deirdre Cocks Eschler, MD[3].
[1]STONY BROOK MEDICINE, Mineola, NY, USA, [2]Stonybrook Medicine, Farmingdale, NY, USA, [3]Stonybrook Medicine, Northport, NY, USA.

Introduction: Intravenous (IV) insulin infusion is the preferred treatment modality for hyperglycemia in the intensive care unit (ICU) due to its short duration of action and easy titratability. However, administration of IV insulin has challenges. These include frequent monitoring, site infiltration, and high insulin dose requirements with other ICU medications such as epinephrine. There are, however, limited reports demonstrating an elevated insulin requirement due to poor peripheral perfusion. Below illustrates such a case, necessitating a change from peripheral to central IV insulin administration.
Case Presentation: A 50 year old male with well controlled type 2 diabetes and previous aortic valve replacement presented to our facility for prosthetic valve endocarditis complicated by aortic root abscess. He was admitted to the ICU, treated with IV antibiotics, abscess washout and aortic valve replacement. Preoperatively, he was started on IV regular insulin via continuous infusion through a central line. During the pre and intraoperative periods, his hourly IV insulin requirement ranged from 2.4 to 5 units/ hour (hr). His blood glucose (BG) ranged from 107-251mg/dL (n 70-99mg/dL). The patient became hypotensive intraoperatively requiring vasopressor support. Dobutamine and norepinephrine infusions were started via central access and were continued postoperatively at steady rates. Vasopressin was added through central access as the patient failed to meet hemodynamic targets. Postoperatively, the propofol infusion was discontinued and the IV regular insulin infusion was moved to the peripheral line where the propofol had previously been administered. BG increased steadily to a maximum of 402 mg/dL despite an increase in the peripheral IV insulin rate to 152.4 units/ hr. The site of the IV insulin drip was changed to another solitary peripheral access without success in decreasing the IV insulin infusion rate. The elevated requirements were deemed secondary to the patient's lack of peripheral perfusion and should decrease with transition to a central line. A preemptive decrease in insulin drip rate to 10% of the peripheral dose was used to avoid hypoglycemia. The insulin drip was changed to a central access with a rate of 15units/ hr. BG values declined to a range of 140 -180 mg/dL. The patient remained on the multiple vasopressors for hemodynamic support, however, the insulin drip was able to be decreased and ultimately, discontinued.
Conclusion: This case illustrates a unique challenge in the treatment of hyperglycemia with multifactorial shock and our approach to management. Elevated IV insulin requirements persisted despite stability in vasopressor dose, change to a solitary peripheral IV site, and lack of interfering medications in the treatment regimen. This is the first case to demonstrate a relationship between high IV insulin requirements and poor peripheral perfusion.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Is Hypoglycemia Caused by G6PD Deficiency?