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Atypical Diabetes Mellitus Associated With Kabuki Syndrome: A Model of Epigenetic Disturbance in Insulin Resistance?

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with LADA and treated with basal insulin 1x36 unit and prandial insulin 3x20unit. **Discussion:** C-peptide is mostly undetectable in classical T1DM and normal or high in patients with newlydiagnosed T2DM, whereas individuals with LADA tend to have low but still detectable C-peptide values at the timeof diagnosis. Thus, islet autoantibodies screening, especially GADA, should be required as a second step for patientswith adult-onset diabetes showing low serum C-peptide. To date, evidence shows that patients with LADA shouldbe treated with insulin at an earlier stage. **Conclusion:** Routine GADA screening should be considered. However, since testing for islet-cell autoantibodiesmay not always be indicated because of high costs, C-peptide measurement may be a useful tool to rule outdiagnosis of LADA in case of low clinical suspicion.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Atypical Diabetes Mellitus Associated With Kabuki Syndrome: A Model of Epigenetic Disturbance in Insulin Resistance?

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Background: Kabuki syndrome (KS) is a genetically heterogeneous disorder characterized by striking facial features similar to make-up of actors in Japanese Kabuki performance together with multi-organ defects. The first identified and most frequently involved gene is *KMT2D* which encodes a histone H3K4 methyltransferase. Even though KS is a rare syndrome and associated diabetes has been rarely reported, both type 1 DM and type 2 DM had been previously reported. Understanding the function of the genes that lead to KS opens up the possibility of targeted therapies for diabetes.

Clinical Case: A 27-year-old male with unconfirmed diagnosis of Fragile X syndrome since childhood came to attend our diabetes clinic due to uncontrolled hyperglycemia (A1C 8.5%). He was a preterm baby born at 7 months and had been clinically diagnosed with Fragile X syndrome due to delayed development and moderate mental retardation from another hospital. At the age of 11 months, he underwent right nephrectomy from severe hydronephrosis. He later developed hypertension due to coarctation of aorta at the age of 14. At the age of 19, he presented with polyuria and lost 10 kilograms within 6 months (baseline BMI at 26.3 kg/m^2). Laboratory data showed A1C 14.7%, plasma glucose 432 mg/dL, no ketonemia. At that time, youth-onset type 2 DM had been diagnosed and insulin treatment had been given for a few months before switching to oral medications. He presented at our hospital at the age of 27. Based on his facial features and multi-organ involvements, KS was clinically suspected and then was confirmed to have heterozygous frameshift deletion mutation (c.7524 deletion) of the *KMT2D* gene. Evaluation of beta-cell function revealed preserved beta-cell with stimulated C-peptide at 8.7 ng/mL. HOMA-IR score suggested severe insulin resistance (HOMA-IR 5.5). Pancreatic auto-antibodies revealed negative results. Currently, his diabetes has been fairly controlled (A1C varied from 6.8–8.5%).

Conclusions: Our case highlights the importance of clinical recognizable phenotype in patients with diabetes. To study and decipher mechanistic studies of the role of epigenetic regulations in this syndrome toward insulin signaling pathways would provide an opportunity for novel insights into pathogenesis of epigenetic defects in Kabuki syndrome.

Diabetes Mellitus and Glucose Metabolism

DIABETES CASE REPORTS

Autoimmune Diabetes After Initiation of Nivolumab in a Patient With Hepatocellular Carcinoma

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Background: Immune checkpoint inhibitors have become an integral part of oncologic treatment, and their role is rapidly evolving. Nivolumab is an immune checkpoint inhibitor to anti-programmed cell death protein-1 (PD-1), which blocks PD-L1 from binding to PD-1, allowing the T cell to activate. While nivolumab has been shown to improve outcomes in certain malignancies, anti-PD-1 therapy can cause multiple endocrinopathies, including autoimmune diabetes (AD). **Case:** Here we present a 60-year-old male with a past medical history of end-stage liver disease secondary to hepatitis C and hepatocellular carcinoma (HCC). After undergoing transarterial chemoembolization for HCC, nivolumab was initiated. The patient initially tolerated the immunotherapy well. However, after three cycles, the patient acutely developed nausea, vomiting, lethargy and confusion. On presentation, he was afebrile, blood pressure of 85/46 mmHg, and a heart rate of 92 bpm. Exam was significant for abnormal mentation, and diffuse guarding of the abdomen. Laboratory workup showed hyperglycemia (1,178 mg/dL), positive serum ketones (beta-hydroxybutyrate 11.4 mmol/L), anion gap metabolic acidosis (AG 31, CO2 7 mmol/L), anemia, thrombocytopenia, acute kidney injury, leukocytosis, and elevated lipase. He was admitted to the intensive care unit, and further workup for acute pancreatitis was unrevealing. C-peptide was low (0.8 ng/mL) with corresponding hyperglycemia (1,055 mg/dL). GAD-65, islet cell, and insulin antibodies were undetectable. Hemoglobin A1c was 8.0%. Blood sugars from the previous one and a half years were in normal range. The patient was ultimately diagnosed with DKA and AD secondary to anti-PD-1 therapy. **Discussion:** This case is representative of AD secondary to nivolumab. While there have been many cases of AD reported after nivolumab, this is the fifth case that has been reported in a patient being treated for HCC. Our patient presented acutely in DKA with no prior diagnosis of diabetes. His antibody testing was undetectable, C-peptide was low in the context of hyperglycemia, and he continued to require insulin therapy until his passing. Prior case reports have demonstrated