A 26-year-old African American male previously diagnosed with Type 1 (Insulin Dependent) Diabetes Mellitus presented with difficulty controlling blood glucose, nausea, abdominal and flank pain. He was diagnosed at the initial visit with Type 1 Diabetes Mellitus. Since this initial visit he has been on regular and long-acting insulin, but his blood glucose has not been properly controlled, given a hemoglobin A1C consistently above 10. Patient has PMH significant for questionable neuropathy, hypertension and anemia. His family history is significant for Type 2 Diabetes in both his grandparents. Upon review of recent literature, we speculated that the patient’s diabetes classification may overlap with features of Latent Autoimmune Diabetes of Adults (LADA). The main lab value used to make the diagnosis of LADA is serum levels of the autoantibody Glutamic Acid Decarboxylase [GAD65]. In the normal population, this lab value ranges from 0 to 1.5, and this value is elevated in patients with LADA. This patient of interest had a serum GAD65 level of 5.4; Further, his later age of onset and low BMI coupled with various acute onset presentations (DKA, HHS) leads us to believe that he has overlap of Diabetes categories.

ABBREVIATIONS

LADA: Latent Autoimmune Diabetes of Adults; GAD: Glutamic Acid Decarboxylase; ICA: Islet Cell Auto-antibody; IAA: Insulin Auto Antibody

INTRODUCTION

Diabetes Mellitus is caused by hyperglycemia due to insulin secretion defect in beta cells of pancreas and or insulin resistance at target tissues. Diabetes Mellitus Type 1 occurs in the very young and is characterized due to lack of insulin as the beta cells of the islet cells of pancreas are destroyed. Patients are dependent on insulin and are more prone to ketoacidosis. Diabetes type 2 occurs in the middle age and the elderly basically due to relative insulin deficiency and or insulin resistance. Insulin is still produced by the beta cells and so Type 2 DM is not completely dependent on insulin administration except in the extreme cases. Hyperosmolar hyperglycemic Syndrome (HHS) is more prevalent in patients with Type 2 DM.

There is a definitive sub set of diabetic patients particularly from young adult to middle age population who do not fit exclusively to either Type 1 DM or Type 2 DM, but share some features from both the groups. This subset of a small fraction of diabetic population can be classified into the Latent Autoimmune Diabetes of Adults group (LADA). LADA patients are said to be lean with a BMI of <25kg/m² and have unique metabolic, immunological, genetic characteristics which are still under review by groups like ACTION LADA.

Reports by Fourlanos, S [2], suggests the presence of at least two distinguishing clinical features for diagnosing LADA such as - Age <50, acute osmotic symptoms, BMI <25 and personal or family history of auto-immune disease. These findings if present can detect up to two-thirds of adults with LADA and has sensitivity of 90%.

It is clear from the above description that LADA follows a slowly progressive autoimmune process leading to slow destruction of beta cells over months leading to an initial pre-diabetic state and slow onset of antibody production. The primary defect due to auto immunity is loss of insulin secretion, common to both Type 1 DM and LADA. It is reported that the loss of insulin secretion and level of hyperglycemia in LADA is comparatively less than in Type 1 DM. The C-peptides in LADA remain closer to normal, but over time decline faster than in Type 2 DM but slower than in Type 1 DM.
CASE PRESENTATION

A 26-year-old African American male previously diagnosed with Type 1 (Insulin Dependent) Diabetes Mellitus presented with polyuria, fatigue, lethargy and persistent difficulty of glucose control for 2 weeks. His glucose reportedly never dropped below 500. We learned that this was his third presentation to the Emergency Department in the past 9 months for similar symptoms and medical records showed admissions and treatment for acute presentations with diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome.

His past medical history included Pancreatitis, migraine, essential hypertension, chronic shoulder pain, gastroenteritis, Type 1 DM, anemia, peripheral neuropathy and poly substance abuse - smokes marijuana and uses cocaine. Family History was positive for Type 2 DM in grand parents. Current medications included: Insulin aspart, insulin detemir, gabapentin, trazadone, alprazolam and lisinopril.

Physical Exam: Vitals: Temp 97.7; BP = 130/94mmHg; Pulse 87; RR 20; Sats 95% on room air; BMI 25. The patient presented in mild distress. Lungs were clear. Cardiovascular exam with regular, rate and rhythm, skin was dry with decreased turgor. Extremities revealed decreased sensation with monofilaments with no other focal neurological deficits.

Labs: Sodium 133; Potassium 4.8; Chloride 95; Bicarb 23; BUN 18; Creatinine 1.5; Glucose 754; Phosphate 5.6; Magnesium 2.5; Total Protein 8.8; Albumin 4.5; AST 16; ALT 99; Alk. Phos =150; Total Bilirubin 0.8; lipase 82; HCT 44. Review of previous labs: Glutamic acid Decarboxylase Antibody – 5.40 (high) on 10/13/12 and Islet cell antibody were inconclusive.

The patient fits some of the criteria set forth by the Immunology of Diabetes society (Presence of at least one antibody – GAD65 in this case and a state of pre-diabetes). Pt’s beta cells got affected slowly over time from 2008 - Oct 2012 leading to insulin deficiency which finally precipitated DKA in Oct 2012. Pt was started on Insulin management since then. Pt had been admitted repeatedly with a picture of DKA or HHS. There seems to be a possibility of a component of insulin resistance and auto-immune Pancreatitis (positive family history of DM in grand parents) which might have triggered his symptoms, complicated by his cocaine abuse and possibly non-adherence to his medication regimen.

LADA MANAGEMENT AND RECENT ADVANCES

It is said that LADA is under diagnosed and under reported. More studies are being conducted like the ACTION LADA 8 which aims to study the LADA subset to rationalize the diagnosing criteria; patho-physiology; genetic variations etc. So far there are no different treatment guidelines for LADA due to their unclear patho-physiology. Educational awareness, early identification of these patients can reduce the slow ongoing destruction of beta cells.

Sulfonylurea medications like glibenclamide are said to accelerate the progressive beta-cell failure and so should not be used as first-line therapy in patients with LADA. A pilot randomized control study demonstrates that Rosiglitazone combined with insulin may preserve islet beta-cell function in LADA patients even if Rosiglitazone plus insulin did not improve metabolic control significantly more than insulin alone [16,17].

Diapep 277 is a recently evolving therapy to target the immune modulators in DM type 1 and LADA. Diapep277 is a modified form of HSP277 peptide which is found to be the dominant epitope of the ubiquitous protein HSP 60 [15]

REFERENCES

6. Mackay IR, Leskovsek NV, Rose NR. Cell damage and autoimmunity: a

Table 1: Glucose Readings.

<table>
<thead>
<tr>
<th>Month</th>
<th>Value</th>
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<tbody>
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<tr>
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