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Internal Medicine

A CASE OF 'FLAT BUSH' DIABETES IN INDIAN 'SUGAR-SWEETENED BEVERAGE' CONSUMER: A CASE REPORT

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ABSTRACT A34-year-oldpatientwithnoknowncomorbiditiespresentedwithahistoryofweightloss, polyuria, polyphagia, and polydipsia of 3 months duration. The patient's Blood Sugars levels were high with the presence of Ketone bodies in urine. He had no family history of Diabetes Mellitus and was not obese. Auto-antibodies were negative and c-Peptide levels were below the normal range. He was started on Insulin along with oral hypoglycemic agents. However, during the next 1 month, he was off antidiabetics and was maintaining normal blood sugar levels with dietary modification and exercise. The patient also gave a history of excessive consumption of sugar-sweetened beverages before the development of these symptoms. We discuss the course and outcome of a case of Ketosis Prone Diabetes likely 'Flat Bush'diabetes.

KEYWORDS : Diabetes Mellitus, Flat Bush Diabetes, Ketosis Prone Diabetes

INTRODUCTION

Ketosis Prone diabetes (KPD) was recognized since the early 1980s when it was noticed that some patients with Type 2 adult-onset diabetes presented with unprovoked ketosis.[1,2] Various subtypes of KPD were recognized and Flat Bush diabetes was defined as a syndrome that initially presented with unprovoked ketosis along with the absence of GAD-65 and Islet cell antibodies.[3] These patients had a phenotype resembling Type 2 Diabetes (T2DM) however after initial insulin therapy, many patients become insulin- independent and can be well controlled on diet alone or diet plus oral medications. [3] Initially recognized in the African-American community residing in the 'Flat Bush' neighborhood of Brooklyn, New York, [3,4] this entity has been increasingly being documented in other parts of the world [1,5]. There have been isolated case reports ofthis disease entity in India. [6]Here we describe an interesting case of KPD likely 'Flat Bush' diabetes, in an Indian Sailor with a history of significant intake of 'sugar-sweetened beverage' and was found to follow the classical clinical course of thissyndrome.

CASE REPORT

A 34-year-old male, sailor by profession, without any known comorbidities, presented to aclinicin Mumbai with a history of unintentional weight loss of 15Kgs (89Kg74Kg) in the last 3 months. He also gave a history of osmotic symptoms in form of polyphagia, polydipsia, and polyuria. He had no family history of diabetes mellitus and a BMI of 24.4 Kg/m^2. The patient also gave a history of not consuming any solid food for 6-10 daysand drinking 2-3 liters of sugar-sweetened beverages on daily basis, while on his last sailing before the onset of his symptoms. On evaluation, he was found to have deranged blood sugar levels (Fasting/ Post-Prandial- 352/370 mg/dl), Ketone bodies in his urine and HbA 1 Cof12 . 4%. Glutamicacid Decarboxy lase-65(GAD-65) and is letcellantibodies (ICA) were negative. C-Peptide levels were below normal range 0.56ng/ml (0.81-3.85ng/ml). He was diagnosed as having' Flat Bush' diabetes based on hisclinicalprofileandantibody results.

HewasstartedonBasalBolusinsulin(InjectionGlar gine12USCHSandL ispro8-8-8SC) along with oral antidiabetic drug (Metformin-SR 1gm BD). His medications were optimized according to his blood sugar levels. Over the next 2-months, he has shifted to Metformin 500mg BDandsubsequentlywasabletomaintaineuglycemiawithdietaryand lifestyle modification. His workup for target organ damage was negative. Abdominal imaging revealed homogenously enhancing bulky lobulated pancreas along with multiple mesenteric and peripancreatic lymphadenopathy with the possibility of autoimmune pan creatitiso r diffuse primary pancreaticly mphoma. Hisimmunog lobul inlevels werenormal and his anti-nuclear antigen was negative. Tumor markers were within normal limits. He was planned for a whole-body PET-CT to rule out malignancy however repeat abdominal imaging after 2-months suggested partial agenesis of the tail of the pancreas with the rest of the pancreas homogenously enhancing and bulky with no significant lymphadenopathy. A differential of the normal variant was considered more likely than autoimmunepancreatitisorlymphoma.HehadanormalThyroidProfilea ndfastingserum cortisol levels. At 6-months of follow-up, the patient was still euglycemic without medications, with an HbA1C of6.7%.

DISCUSSION

The traditional classification of diabetes was challenged when it was realized that some patients with ketosis at the time of diagnosis later tend to follow a clinical course more like that of T2DM as compared to Type 1 diabetes (T1DM).[5]This led to the formation of many terms like “Atypical Diabetes,” “Type 1.5 Diabetes Mellitus,” “Idiopathic T1DM,” “Diabetes Mellitus Type 1B,” “Temporary Diabetes,” “KPD,” “Ketosis Prone T2DM”.[5]With more and more cases emerging of such presentation, a consensus on 'Ketosis' was reached. The most widely accepted classification of KPD was based presence or absence ofAntibodies(A)andβ-cellfunction(b).[7]FlatBushDiabetesisasub-setofKPDwhichwas recognized initially in the African-American individuals living in the Flat Bush Neighborhood of Brooklyn, New York.[3] These patients were classified as A- b+ variant of KPD. Flat Bush usually presents with severe hyperglycemia following a period of polyuria/polydipsia/weightlosswithabloodglucoseof>500mg/dlanda meanHbA1c >10%; often accompanied by “unprovoked” diabetic ketoacidosis (DKA), new or pre- existing diabetes diagnosis with DKA (pH<7.30-β-hydroxybutyrate:>3mmol/l).[8]There is a lack of HLA genetic association, absence of auto-antibodies, and measurable pancreatic insulin reserve.[8]

There has been a lot of discussion about the pathogenesis of this entity, despite multiple case reports of KPD, the etiology for the decompensation of β-cell function and ensuing recovery is unknown, and the tendency for ketosis is inadequately understood. [5] Recent follow-up research disputes several theories proposed in earlier decades such as an autoimmune etiology, a viral etiology, or genetic predisposition for the same. [8] Studies have demonstrated that T2DM presenting with severe hyperglycemia with or without ketosis is due to the inability of the β-cells to respond to glucose. [9] However, it was observed that there was insulin secretion in response to non-glycemic pharmacologic agents such as glucagon and arginine. [10,11]There was a difference in the baseline insulin and C peptide levels in T2DM with or without ketosis, both during the active phase and after attaining euglycemia.However,thiswasnotsignificant,andhenceconcreteeviden ceregarding the pathophysiology of KPD differentiating, it from T2DM is still unknown. [1] Another interesting concept is the mechanism of the generation of ketone bodies in KPD. Some studiessuggestingthatascomparedtoconventionalketosisinT2DMwhic hwasdue to in crease ketogenesis, the ketosisin KPD was because of decrease dk etolysis.[12] Despite many studies in favor of this distinct entity the American Diabetes Association (ADA) still does not

recognize KPD as a different entity.[13,14]

Sugar-sweetened beverages have long been suspected of causing obesity and related disorders., however, only recently studies have been able to prove their association with long-term weight gain, diabetes mellitus, and cardiovascular risk. These beverages have highaddedsugarcontent,lowsatietyeffect,andrapidlyabsorbablecarbohydrates.These factors have led to sugar-sweetened beverages being implicated in the rise of lifestyle diseases.

This case highlights the syndrome of KPD especially the flat bush subtype. Our patient had normal c-peptide levels. The clinical course of his illness was also characteristic of 'flat bush'. Thehistoryofsugar-sweetenedbeveragesingestionishighlysuspiciousofbeingcausative in this individual. The normal variant of pancreatic tail agenesis observed in this patient also merits a mention though no literature has been found of such cases manifesting clinically.Hence, we recommend clinicians to have a high index of suspicion for flat bush diabetes when evaluating a fresh case of diabetes with history of significant sweet beverage consumption especially in young individuals.

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