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Case Report

Type-1.5 Diabetes Mellitus with Autoimmune Hypothyroidism: A Rare Combination

Abstract

Autoimmune hypothyroidism may associate with type-1 Diabetes mellitus (DM) is a well-known entity as polyglandular autoimmune syndrome type-3. Type-1.5 DM is also known as late onset autoimmune mediated diabetes mellitus of adulthood (LADA) describing as- patients with type-2 diabetic phenotype based on age, not etiology combined with islet-cell antibodies and progressive *β*-cell failure, requiring life-time insulin therapy. Authors report a misdiagnosed type-2 diabetic since 3-years, of 35-years-male with known case of hypothyroidism had uncontrolled hyperglycemia, 12.7% glycosylated hemoglobin (HbA1C), 1.09ng/ml serum C-peptide and 26IU/ml glutamic acid decarboxylase (GAD) antibody, with anti-microsomal antibody titre of 827IU/ml and anti-thyroglobulin antibody titre of 130IU/ml, on 3 oral hypoglycemic agents. He was diagnosed as type-1.5 DM with autoimmune hypothyroidism. During 11-months of follow-up, after initiating insulin therapy patient had 6.7% HbA1C and normal thyroid function with oral thyroxin medication. So all young diabetic adults should evaluate for type-1.5 DM with autoimmune hypothyroidism.

Abbreviations

DM: Diabetes Mellitus; FBS: Fasting Blood Sugar; GAD: Glutamic Acid Decarboxylase; HbA1c: Glycosylated Hemoglobin; LADA: Late Onset Autoimmune Mediated Diabetes Mellitus Of Adulthood, Latent Autoimmune Diabetes Of Adults; OHA: Oral Hypoglycemic Agents; PPBS: Postprandial Blood Sugar

Introduction

Approximately 20% of all persons diagnosed with type-2 diabetes mellitus (DM) might actually have type-1.5 DM also known as late onset autoimmune mediated diabetes mellitus of adulthood (LADA). This number accounts for an estimated 5-10 % of total diabetes population in the United States or as many as 3.5 million persons with type-1.5 DM [1]. The term type-1.5 DM frequently called latent autoimmune diabetes of adults (LADA), is a concept introduced in 1993 to describe slow-onset type-1 autoimmune diabetes in adults [2]. The Expert Committee on The Diagnosis and Classification of DM doesn't recognize type-1.5 DM; rather, it includes in the definition of type-1 DM [3]. Type 1.5 DM with phenotypic type-2 diabetes, is a genetically-linked, hereditary autoimmune disorder with presence of anti-islet-cell antibody, that results in the body mistaking the pancreas as foreign and responding by attacking and destroying the insulin producing β islet-cells of the pancreas. Autoimmune hypothyoidism is associated with type-1 DM in polyglandular autoimmune syndrome type-3 [4]. We report a misdiagnosed case of type-1.5 DM in 36-years-male as type-2 DM with autoimmune hypothyroidism responded to better blood sugar control with exogenous insulin administration in treatment modality.

Case Report

A 35-years-male with known case of hypothyroidism since 2009 and with type-2 diabetes mellitus since 1-year, presented in 2014, with weakness, feeling of restless after work, fatigue, weight loss and uncontrolled blood-sugar since 6 months. He was on 3-different oral hypoglycemic agents (OHA) (Tablet Glimepride 1mg twice a day, Tablet Acarbose 50mg once a day, Tablet Pioglitazone 30mg once a day) with cholesterol lowering medicine (Tablet Rosuvastatin 5mg once a day) and oral thyroxine 100 µg/day.

He had normal vital examination with unremarkable clinical examination with 71 kg of body weight, 175 cm height and body surface area, 1.86 m [2]. He had a serum T3 of 0.7ng/

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ml (normal range: 0.52-1.85ng/ ml), a serum (s.) T4 of 5.60 µg/dl (normal range: 4.8-11.6 µg/dl) and a s. TSH 63 µU/ml (normal range: 0.28 to 6.82 µU/ml) at time of diagnosis of hypothyroidism in 2012. He was with normal thyroid function at this time. He had positive anti thyroid antibodies by enzyme-linked immunosorbent assay (ELISA), including an anti-microsomal antibody titre of 827 IU/ml (>40 IU/ml, positive) and an anti-thyroglobulin antibody titre of 130 IU/ml (>125 IU/ml, positive). His fasting blood sugar (FBS) and postprandial blood sugar (PPBS) were 268 and 349 mg/dL, 12.7% of glycosylated hemoglobin (HbA1C) and 200 mg/dL of serum cholesterol, on admission. Other hematological and biochemical investigation were within normal limit. Urine routine examination revealed +4, sugar with trace, albumin without evidence of urinary tract infection and hematuria. He had normal electrocardiogram and fundus examination. During further evaluation, he had 1.09 (normal range: 0.7-1.2) ng/ml of serum C-peptide and glutamic acid decarboxylase (GAD) antibody was 26 (normal range: <10) IU/ml. Anti-islet-cell antibody was absent by immunofluorescent assay and insulin antibody was 8.87 (normal range: <12) U/ml. Then we started biphasic isophane insulin injection subcutaneously in two divided doses. Then gradually patient became asymptomatic with energetic in follow-up. During 8-months of follow-up, patient had better control of FBS and PPBS of 114mg/dL and 163mg/dL with 6.7% of HbA1C with tablet Pioglitazone 30mg and 65 IU exogenous insulin requirement per day with normal thyroid function.

Discussion

Type-1.5 DM is nomenclature as LADA, late-onset autoimmune diabetes of adulthood, latent autoimmune diabetes of aging, slow onset type-1 diabetes and latent autoimmune diabetes. Among patients with phenotypic type-2 DM, type-1.5 DM occurs in 10% of individuals older than 35 years and in 25% below that age till 25 years. From a patho-physiological perspective, it is more closely related to type-1, but based on etiology frequently diabetic adults are initially misdiagnosed and treated as having type-2 DM [5]. Human leukocyte antigen genes associated with type-1 DM are seen in type-1.5 DM, but not in type-2 DM [6]. 80% of type-1.5 diabetics initially diagnosed with type-2, but test positive for GAD progress to insulin dependency within 6 years (some study suggested between 3-12 years after diagnosis [7]. Testing for anti-GAD in adult-onset diabetic patient helps to detect latent insulin dependency at the earliest possible stage, since this assay can assist in the correct classification of diabetes and more appropriate therapy [8]. Islet-cell, insulin and GAD antibodies are used for differential diagnosis between type-1, type-1.5 and type-2 DM (Table 1). Type-1.5 diabetics typically have low/moderate, levels of C-peptide as the disease progress. Patients with insulin resistant or type-2 DM are more likely to, but will not always have high C-peptide due to an overproduction of insulin [9]. Type-1.5 DM can have long-term devastating complications same as those for type-1, 2 DM. OHA seemed to provide poorer glycemic control than insulin alone and caused earlier insulin dependence. Insulin treatment in this group of patients associated with better outcome in terms of metabolic control, insulin secretion, autoimmune responses against pancreatic β-cells and better long-term outcome by preserving remained β-cells and endogenous C-peptide secretion. Patient should be educated for diet, exercise, medication, and blood-sugar checking and stress management. Prognosis is similar as in pre-diabetic relatives of 'type-1 diabetic' patients the risk for β-cells failure in "type-2 diabetic' patients increases with the number of antibodies positive [10]. Polyglandular type lll autoimmune syndrome (PGAS type III) is a rare condition with unknown prevalence typically observed in middle-aged women but can occur in persons of any age without any racial or ethnic difference. Type III involves one of the following: (a) Thyroid autoimmune disease and type 1 diabetes mellitus /Insulin dependent diabetes mellitus (IDDM), (b) Thyroid autoimmune disease and pernicious anemia, (c) Thyroid autoimmune disease as well as one or more of vitiligo, alopecia and organ-specific autoimmune disease not in categories (a) and (b) are found [4].

In our knowledge, this was the first patient reported of 35 years male with positive for anti-thyroid antibody of thyroid gland producing hypothyroidism with type 1.5 DM till now.

Conclusion

All young adult diabetics should be checked for C-peptide and GAD/ islet cell antibody level, which makes early diagnosis of type 1.5 DM in young adults should managed with early initiation of insulin therapy for better glycemic control, to prevent early diabetic complication and may benefi t to remaining β islet-cells Thyroid function should be checked to rule-out the hypothyroidism with anti-thyroid antibody level in all diabetics.

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Table 1: Comparison of clinical features between type-1 diabetes, type-1.5 diabetes and type-2 Diabetes Mellitus.

Feature	Type-1 DM	Type-2 DM	Type-1.5 DM
Nature of onset & age of diagnosis	Usually rapid onset, Occurs in usually childhood age	Onset is months or years. Occur mainly in older adults	Onset is slow. Occurs in aged 35-40 years/ earliest at 25 years.
Genes, triggers factors	Autoimmune, idiopathic, gentic	Hereditary, sedentary lifestyle and obesity etc.	Autoimmune
ICA (islet cell antibodies) IAA (insulin autoantibodies) IA2 (islet antigen 2) GAD (GAD65-AAGAD) HLA C-peptide	ICA - Found in 80% IAA - often detected IA2 - 50-70% GAD - positive HLA - yes always low	ICA - no IAA – no IA2 - no GAD - negative HLA - no normal/high	ICA - positive IAA - yes, often IA2 - often GAD - positive HLA - yes, often Initially normal then low
Treatment	Insulin	Oral hypoglycemic agents ± Insulin	Insulin ± Sulfonylureas
Prognosis & Complications	No complete cure.	No complete cure.	No complete cure.

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Consent of Patient

Written informed consent was obtained from the patient for publication of this Case report.

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