Case Report

When it is not Type 1 or Type 2 Diabetes mellitus: A case of Slowly Evolving Immune-mediated Diabetes of Adult

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Abstract

Background: Slowly Evolving Immune-mediated Diabetes of Adult (SEIDA) previously termed Latent Autoimmune Diabetes of Adult (LADA) is a heterogenous disorder characterized by the presence of serum islet autoantibodies at diagnosis with slow progression of islet failure. These patients often require insulin therapy within six months of diagnosis. Most of the presenting clinical symptoms can mimic either type 1 or type 2 diabetes mellitus.

Methods: We report a clinical case of a 37-year-old woman who was newly diagnosed with Type 2 diabetes mellitus.

Finding: She presented with history of polyuria, polydipsia, and weight loss of six months duration with a family history of type 2 diabetes mellitus in her father. She presented with worsening glycemic control despite her adherence to her medications. A clinical suspicion of SEIDA was made in view of her age and worsening glycemic control. This was confirmed with a positive result of serum Glutamic Acid Decarboxylase -65 (GAD-65) and low serum c-peptide levels.

Conclusion: This is to alert physicians that not all diabetes mellitus is type 1 or type 2 hence SEIDA should be suspected in any young adults presenting with features of uncontrolled diabetes mellitus in spite of optimal doses of oral hypoglycemic agents.

Keywords: C-peptide, diabetes mellitus, islet cell autoantibodies, latent autoimmune diabetes of adult.

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Introduction

The World Health Organization (WHO) in 2019 reclassified Diabetes Mellitus (DM) with inclusion of Hybrid forms of DM such as slowly evolving immune mediated diabetes of adult and ketosis prone type 2 diabetes mellitus.[1] Slowly Evolving Immune mediated Diabetes of Adult (SEIDA) previously termed Latent Autoimmune Diabetes of Adult (LADA).[1,2] Slowly Evolving Immune mediated Diabetes of Adult is a clinical disorder defined by the presence of islet autoantibodies accompanied with autoimmune destruction of beta islet cell.[1,3]The prevalence of SEIDA in Nigeria ranges between 10.5% to 14%.[4-6] However, about 10% of patient wrongly diagnosed with type 2 DM have SEIDA.[2,3]It occurs in young adults usually between the ages of 25 years to 40 years but it can present at any age group.[3]The autoantibodies often seen in SEIDA are Glutamic Acid Decarboxylase (GAD), Islet Cell Autoantibodies (ICA), tyrosine phosphatase Islet Antigen (IA-2) among others.[7,8] The most common autoantibodies are GAD and ICA.[7,8]

Majority of the patients present with clinical features of both type 1 and type 2 diabetes mellitus.[8]The clinical features of type 1 diabetes mellitus are presence of islet autoantibodies and lower body mass index. The main features of type 2 DM are older age at presentation and presence of insulin resistance or deficiency.[2-4] According to the Immunology of Diabetes Society (IDS) criteria for SEIDA.[9] The patient age ≥30 years, presence of at least one autoantibodies and patient not requiring insulin therapy until more 6 months of diagnosis.

There is slow progressive decline in pancreatic beta cell function in SEIDA. It presents like a slow form of type 1 DM.[2,3] Most patient usually respond to Oral Hypoglycemic Agents (OHA) initially but as beta cell function decline they will eventually need insulin.[2,3] When they are misdiagnosed as type 2 DM and treated with OHAs, overtime glycemic control become difficult.[2,3,5-6] This delays effective treatment. The resultant outcome is poor glycemic control with development of complications of diabetes mellitus.

Case Presentation

Mrs OB was a 37-year-old woman who presented with six months history of passage of large volume of urine, polydipsia and generalized body weakness. She had a history of weight loss evidence by loosening of previously well fitted clothings. She was diagnosed with Type 2 DM about 8 months ago with good medication adherence. She has positive family history of Type 2 DM in the father now 80 years old. Her presenting random blood glucose was 430mg/dl on tabs metformin 1g twice daily, Sitagliptin 100mg daily and Tabs Glimepiride 4mg twice daily. She had a diagnosis of gestational diabetes mellitus 18 months ago during her last confinement with normoglycemia six weeks after delivery. There was a positive history of peppery sensation on both feet. She also complained of occasional blurring of her vision and frothiness of urine.

There was no history of dysuria, urgency, early morning facial swelling or bilateral leg swelling. She had no history suggestive of peripheral arterial disease, stroke or ischemic heart disease.

Physical examination revealed a young lady with body mass index of 20.6kg/m2, waist circumference 72.5cm, hip circumference 90.0cm with waist hip ratio of 0.81. Her glycated hemoglobin was 11.4%. Her peripheral pulses were palpable and 10g monofilament testing for both feet were 6/10 and 7/10 respectively. The reflexes, joint position sense and vibration sense were normal. Her fundoscopy done was normal. An initial assessment of poor glycaemic control in a recently diagnosed type 2 diabetes mellitus complicated by microvascular complication (peripheral neuropathy) to keep in view Slowly Evolving Immune-mediated Diabetes of Adult (SEIDA) was made. She was admitted and commenced on fluid therapy, potassium correction, intravenous regular insulin and later changed to basal bolus insulin therapy. Other medications were subcutaneous enoxaparin and Tabs pregabalin 75mg nocte, while oral hypoglycemic agents (metformin, sitagliptin and glimepiride) were discontinued.

Investigation results showed anti Glutamic Acid Decarboxylase (GAD) greater than 280 IU/mL (less than 17 IU/mL) and Islet cell antibody was negative.

Fasting C peptide was 40pmol/L (260-1728), fasting lipid profile showed dyslipidemia with elevated total cholesterol of 5.8mmol/L, low density lipoprotein of 3.6mmol/L, triglycerides of 1.9mmol/l while her complete blood count was normal. Her serum electrolytes, urea and creatinine (serum sodium 141mmol/L, serum potassium 4.3mmol/L, serum bicarbonate 22mmol/L, urea 6mmol/L, serum creatinine 99umol/L) were within normal. Urinalysis showed +1 of ketones and 3+ of glucose, other parameters were negative. Urine creatinine albumin ratio was also normal. Arterial doppler ultrasound scan of both lower limbs was normal.

The Dietitian reviewed her for medical nutritional therapy. She was subsequently discharged home six days after admission on premix insulin and oral Atorvastatin 20mg daily. Her next clinic visit was in two weeks with results of self-monitoring of blood glucose. She was also

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referred to ophthalmology clinic for subsequent follow up.

At presentation two weeks later, her Self-Monitoring of Blood Glucose Chart (SMBG) was reviewed and the fasting and 2hours post-prandial readings were within good glycemic control. Her next clinic visit is scheduled for 3 months with repeat glycated hemoglobin test.

Discussion

The patient had at least one islet autoantibodies (GAD-65) positivity. Studies have shown that the most implicated islet autoantibodies are GAD-65 and ICA.[7,8] The patient also met the age category as she was 37 years at the time of diagnosis.[10,11] The disease course initially resembled type 2 DM as she was initially diagnosed with GDM and later had abnormal glycemia and treated with oral medications. She later presented with suboptimal glycemic control despite adherence to medications hence, necessitating the need to screen for SEIDA. Patients being managed for SEIDA needs to be switched to insulin therapy to achieve a good glycemic control.[1,3] Also, she needed insulin therapy at 8 months of diagnosis of diabetes mellitus, hence meeting the diagnostic criteria for SEIDA.[2,4,9]

The diagnosis of SEIDA can be made by requesting for serum fasting c peptide and serum islet autoantibodies especially GAD 65 and ICA in these patients.[1,3,9] The IDS criterion makes it easy to diagnose a patient with clinical suspicion of SEIDA as not all patients with diabetes mellitus have type 1 or type 2. Treating patient to target helps to prevent the immediate and long-term complications of diabetes mellitus.[3,4-6]

She was discontinued on tabs Glimepiride which belong to the third generation sulphonylureas. Sulphonylureas enhance endogenous insulin secretion through its mechanism of action thereby not effective in the setting of beta cell exhaustion.[12]

Conclusion

This illustrates a rare case of slowly evolving immune mediated diabetes of adult despite a strong family history of diabetes mellitus. It is imperative for physicians to recognize and diagnose SEIDA early to avoid long term complications due to poor glycemic control. Patients should also be screened for other autoimmune diseases such as autoimmune thyroid disease and celiac disease.[13] High index of clinical suspicion is required to avoid a misdiagnosis of SEIDA.

Declarations

Ethical consideration: Informed consent was obtained from the patient.

Authors' contribution: All authors satisfied the criteria for authorship through their contribution to the work. The manuscript has been read and approved by all authors.

Conflict of interest: The authors declare that there is no conflict of interest

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