CASE REPORT

An Unusual Presentation of Latent Autoimmune Diabetes in Adults

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SUMMARY

Latent Autoimmune Diabetes in Adults (LADA) is an autoimmune form of type 1 diabetes mellitus presenting in adulthood. It is often confused with other types of diabetes and therefore the management is frequently inadequate. Acute hyperglycemic crisis in the form of diabetic ketoacidosis (DKA) or hyperglycemic hyperosmolar state (HHS) are unusual findings. We report a clinical case of a 66-year-old female who presented for the first time with DKA and was subsequently diagnosed as a case of LADA. Presumptive diagnosis of LADA was confirmed with the presence of autoantibody to glutamic acid decarboxylase 65 (Anti-GAD65 antibody).

KEY WORDS:

latent autoimmune diabetes in adults, diabetic ketoacidosis, anti-GAD65 antibody

INTRODUCTION

Latent Autoimmune Diabetes in Adults (LADA) is an autoimmune endocrine disorder in which despite the presence of antipancreatic islets antibodies in the moment of diagnostics, the progression to β -cell secretory insufficiency is slow [1]. It is often confused with other types of diabetes and therefore faces both mistaken diagnosis and inappropriate therapeutic management. LADA is also known as "type 1.5 diabetes" as it shares symptoms of both types 1 and 2 diabetes. Autoantibody to glutamic acid decarboxylase (anti GAD65 antibody) is the most sensitive and specific marker for this subgroup of diabetes and in cases of positivity patients generally progress to insulin-dependency within 3 years, though some do not [2].

Individuals with LADA usually present before 50 yrs of age and they are mostly non-obese with BMI <25 kg/m^2. They usually present with low magnitude hyperglycemia and normal or close to normal C-peptide values. Acute hyperglycemic crisis in the form of DKA or HHS is unusual. However, in our case both the age of presentation and the mode of presentation, as DKA, are different in this regard which is quite rare.

CASE REPORT

A 66-year-old non-hypertensive female, identified as having impaired glucose tolerance (IGT) on routine health checkup in 2005, presented to us in a disoriented and confused state. On enquiry from family members a history suggestive of urinary tract infection (UTI) was revealed. There was no history of vomiting, diarrhoea, abdominal pain, convulsion, loss of consciousness or relevant drug use. No significant disease in the past was found. There was no family history of diabetes. Her vitals were as follows: respiratory frequency-30/min; heart rate- 120/min; blood pressure- 110/60 mm Hg and temperature- 102^0 F. Her random blood glucose noted in the emergency department was found to be 609 mg/dl. Urinary ketone test by Ketostix was strongly positive. Emergency arterial blood gas analysis (ABG) showed high anion gap metabolic acidosis. Clinical diagnosis of diabetic ketoacidosis was made and she was put on treatment accordingly. Routine urine examination and culture supported the clinical suspicion of UTI. ECG was within normal limit. After stabilization of her glycemic status and control of urinary infection, her general condition improved steadily. Further examinations revealed her height was 162 cm and weight was 50.0 kg with a BMI of 19.05 kg/m^2. Subsequent investigations showed a glycosylated haemoglobin (HbA1c) of 9.5% and fasting serum C-peptide level of 0.19 ng/mL (N 1.1-4.4 ng/mL). Presumptive diagnosis of LADA was confirmed by measuring autoantibodies. The patient's GAD65 antibody was 159.18 IU/mL (cut off <10 IU/mL). IA2 antibody, thyroglobulin antibody, and thyroid peroxidase antibody were all negative. Thyroid function test was normal. She was screened for nephropathy and retinopathy and found to be negative.

She was discharged with an advice to take low saturated fat diet, limited intake of simple sugars, and high-fiber diet along with subcutaneous insulin injections in the form of premixed human insulin 30/70, 20 units in the morning and 16 units at night before meal. GAD65 antibody titre remained elevated during her follow-up visits. Her insulin requirement gradually increased over time but no further acute hyperglycemic crisis occurred till now. We have made the judgment that the she had progressed to the stage of diabetes during the five-year period since the diagnosis of IGT, a stage of pre-diabetes and presented to us for the first time with acute hyperglycemic crisis in the form of DKA.

DISCUSSION

Latent autoimmune diabetes in adults (LADA) accounts for 2%-12% of all cases of diabetes and the term 'Latent autoimmune diabetes of adults' (LADA) was given by Zimmet *et al*. This subset of adult patients who were initially

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Table I: Features and treatment of Type 1 DM, LADA and Type 2 DM

Features	Type 1 DM	LADA	Type 2 DM
Metabolic syndrome components	Less frequent	Usually absent	Frequently present
Ketoacidosis	Frequently	Usually absent at diagnosis, but could be present	Less common
Cardiovascular complications	Increased	Same as in Type 2 DM	Increased
Microvascular complications	Increased	Same as in Type 2 DM	Increased
Pancreatic autoantibodies	Positive	Positive	Absent
Treatment	Insulin at diagnosis	Requires insulin in a much earlier phase than Type 2 DM	Might need insulin, but at the end stage of disease

categorised as type 2 diabetes mellitus phenotype but were found to be positive for islet cell autoantibodies, a hallmark of β cell destruction [2,3]. The slower progression has been attributed to a more restricted antigen spreading in LADA than in type1 diabetes mellitus leading to a more aggressive disease in the latter. Due to the latent nature of the disease and its less discernible signs and symptoms, LADA patients are often misdiagnosed as cases of type 2 diabetes mellitus and started on oral hypoglycemic agents particularly.

LADA is associated with increased frequencies of genetic markers (HLA DR3, DR4 and DR3/4) but HLA DR4 DQ8 antigen that is commonly associated with rapid beta cell destruction in type 1 diabetics are less common in LADA; there lies the explanation why patients with LADA do not require insulin as readily as type 1 diabetics.

Clinical characteristics of patients with LADA are similar to those with type 1 and type 2 diabetes mellitus (Table 1). The frequency of obesity, hypertension, dyslipidemia and CHD are found to be lower in LADA than in type 2 diabetes mellitus though microvascular complications are comparable. Regarding clinical parameters or laboratory criteria for LADA screening, no current consensus is available till now. The Immunology of Diabetes Society has led three criteria to discriminate LADA from type 1 and/or type 2 diabetes mellitus: (1) Adult age of onset (> 30 years of age); (2) Presence of at least one circulating autoantibody (GAD 65/ICA/ IAA/IA-2); and (3) Insulin dependency no sooner than 6 months after diagnosis [4]. Evidences show advantages of the early initiation of insulin therapy in patients with LADA. In patients with LADA insulin therapy improves C-peptide secretion (due to better β-cell function with a higher natural insulin production), reduces HbA1c level and islet cell autoantibodies' concentration[5].

This case highlights that in the presence of clinical criteria for LADA, autoantibody measurements must be done in every patient of adult onset diabetes to diagnose it even if the age is more than 50 yrs and once diagnosed patients with LADA should receive insulin therapy as early as possible. If not properly treated, such insulinopenic patients may develop DKA like our patient.

In conclusion, LADA should be approached as a clinical entity different from type 1 and type 2 diabetes mellitus although it shows overlapping features of both types. Early initiation of insulin therapy is a must in LADA to delay the rapid islet cell failure. The adequate selection of high risk patients and early diagnosis of LADA, better provided by high GAD antibody titers, when the insulin-secretory capacity is still good permit the identification of patients that can be subjected to early insulinization for a better tomorrow.

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