Diabetic Ketoacidosis Unusual Presentation of Latent Autoimmune Diabetes of Adult (LADA)

Manish Gutch,1* Annesh Bhattacharya,2 Sukriti Kumar,3 Syed Mohd Razi4

ABSTRACT
Latent Autoimmune Diabetes of Adult (LADA) is an autoimmune form of diabetes mellitus characterised by onset in adulthood and slow progression of beta cell failure. It is commonly misdiagnosed as type 2 diabetes mellitus and treated with oral hypoglycaemic agents, ultimately resulting in delay of insulin initiation. Acute hyperglycaemic crisis in the form of diabetic ketoacidosis is a rare initial presentation of LADA with very few cases reported so far. We present the case of a 40 year old housewife with no past or family history of diabetes that presented with diabetic ketoacidosis and was subsequently discovered to be affected with LADA.

Keywords: Latent Autoimmune Diabetes of Adult (LADA); Diabetic Ketoacidosis, Autoimmune disorder, Type 1 diabetes mellitus, Type 2 diabetes mellitus.

Key Message: Latent Autoimmune Diabetes of Adult (LADA) is a variant of adult onset diabetes which is commonly misdiagnosed as type 2 diabetes mellitus (T2DM) and must be ruled out early in the disease course since the treatment strategy differs from that of type 2 diabetes mellitus.

INTRODUCTION
Latent Autoimmune Diabetes of Adult (LADA) is an autoimmune disorder characterised by autoantibodies against the pancreatic islet cells; however, unlike type 1 diabetes mellitus, the progression of LADA is slow and the affected individual usually comes to medical attention during adulthood. It is also known as type 1.5 diabetes mellitus since it shares features of both type 1 and type 2 Diabetes Mellitus. Affected patients are generally non-obese, with low magnitude hyperglycaemia and low or near normal c-peptide values. The diagnosis of LADA is made if there is evidence of adult onset of disease with positive circulating antibodies directed against pancreatic islets and the patient does not require insulin treatment for several months after diagnosis. An acute hyperglycaemic complication in the form of diabetic ketoacidosis is an unusual first presenting manifestation of this disease, with very few cases recorded in medical literature. We hereby describe the unusual case of a 40-year-old housewife who was subsequently diagnosed to be suffering from LADA and presented with diabetic ketoacidosis as the initial presentation of LADA.

CASE SUMMARY
A 40-year-old housewife was admitted with the complaints of recent onset pain abdomen, associated with on and off nausea and vomiting for the last 2 days. It was described as a diffuse pain, mild to moderate in intensity and did not relieve following vomiting or passage of stool/flatus. Her husband had also noticed drowsiness since morning, following which he had rushed her to the emergency department. Past history was non-contributory except for a history of hypothyroidism for which she was on levothyroxine replacement therapy. There was no family history of diabetes or any other chronic illness.

On examination, she was drowsy (GCS = 13/15) with a pulse rate was 90/min and acidotic Kussmaul's pattern of respiration; her respiratory rate was 26/min and blood pressure was 130/80 mm Hg. She was afebrile while her body mass index (BMI) was calculated to be 28 kg/m². Abdominal examination did not reveal any organomegaly or a palpable lump. The remaining general and systemic examination was within normal limits. There were no signs of acanthosis nigricans.

Her laboratory investigations including an arterial blood gas analysis revealed the following: Random blood glucose = 540 mg/dl, haemoglobin = 11.3 g/dl, total leucocyte count = 12,300/mm³ (N = 70%, L = 25%), sodium = 130 mmol/l, potassium = 3.8 mmol/l, chloride = 96 mmol/l, bicarbonate = 12 mmol/l, creatinine = 1mg/dl, urea = 30 mg/dl, calcium (total) = 8.9 mg/dl, pH = 7.23, pCO₂ = 24, SpO₂ = 96%, PO₂ = 86 (on O₂ mask), lactate = 1mmol/l, amylase = 30 U/L, lipase = 20 U/L. Her urine sample was positive for glucose and 3+ for ketones, while her HbA1C was 10.3%.

With the above investigations, we diagnosed her to have diabetic ketoacidosis. She was treated with intravenous fluids, insulin and prophylactic antibiotics according to standard protocols while her vitals were monitored rigorously. Over the next 36 h, her...
Patients with LADA generally do not present with acute hyperglycaemic complications and they exhibit elevated glucagon levels and insulin resistance similar to patients with type 2 diabetes mellitus. The clinical features of LADA resemble those of type 1 and type 2 diabetes mellitus. Hypertension, CAD, dyslipidaemia and obesity are less prevalent in LADA compared to type 2 diabetes mellitus. Insulin resistance has been reported to occur less commonly in LADA, comparable with type 1 diabetes mellitus. Though LADA is associated with HLA phenotypes, it is less marked compared to type 1 diabetes mellitus which might explain the slow progression of beta cell destruction and late onset of the disease. LADA is diagnosed according to the following clinical criteria recommended by the Immunology of diabetes society:

- Adult age at onset of diabetes.
- Lack of insulin requirement for at least 6 months after diagnosis.
- The presence of at least 1 circulating autoantibody [autoantibodies to glutamic acid decarboxylase 65 (GAD - 65)/islet cell cytoplasm (ICA)/tyrosine phosphatase-like protein (IA-2A)/insulin (IAA)].

There are no recommendations as regards the treatment of LADA. It mostly focusses on attaining normoglycaemia, preventing complications and beta cell protection. Most patients are misdiagnosed and treated as patients of type 2 diabetes mellitus, mainly with lifestyle modification and oral hypoglycaemic agents. Once they stop responding to these drugs, patients are switched over to insulin therapy. Immunomodulatory agents may be beneficial, but clinical trials are yet to demonstrate this fact.

Patients with LADA generally do not present with acute hyperglycaemic complications like diabetic ketoacidosis at presentation owing to slow progression of beta cell failure. There have been very few case reports highlighting such a rare presentation of LADA. Overall LADA must be approached as a separate entity from type 1 diabetes mellitus and type 2 diabetes mellitus. Early initiation of insulin delays the progression of beta cell failure and helps in preventing the emergence of complications like diabetic ketoacidosis. Hence the clinician must carefully rule out LADA in adult onset diabetic patients since the management strategy for LADA differs from that of type 2 diabetes mellitus.

**DISCUSSION**

Latent Autoimmune Diabetes of Adult (LADA) is a variant of diabetes mellitus in which beta cell failure is slow to develop despite the presence of antibodies against pancreatic islet cells. Also known as type 1.5 diabetes mellitus since it shares characteristics of both type 1 and type 2 diabetes mellitus, the onset of LADA is in adult life and initially may not be insulin-requiring, hence leading the patient to be misdiagnosed as type 2 diabetes mellitus. Such patients have islet autoantibodies, most commonly glutamic acid decarboxylase (GAD) antibody, low or near normal c-peptide secretion and gradual progression to Insulin dependency, resembling type 1 diabetes mellitus. However, they might also exhibit elevated glucagon levels and insulin resistance similar to patients with type 2 diabetes mellitus. The lack of insulin requirement for at least 6 months after diagnosis.

**CONCLUSION**

Overall LADA must be approached as a separate entity from type 1 diabetes mellitus and type 2 diabetes mellitus. Early initiation of insulin delays the progression of beta cell failure and helps in preventing the emergence of complications like diabetic ketoacidosis. Hence the clinician must carefully rule out LADA in adult onset diabetic patients since the management strategy for LADA differs from that of type 2 diabetes mellitus.

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**CONFLICT OF INTEREST**

Nil

**ABBREVIATIONS USED**

(LADA): Latent Autoimmune Diabetes of Adult; DKA: Diabetic Ketoacidosis; T1DM: Type 1 diabetes mellitus; T2DM: Type 2 diabetes mellitus.

**REFERENCES**