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Case Report

Diagnostic camouflage: A case report on Latent autoimmune diabetics of adulthood

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ABSTRACT

Introduction and importance: Latent autoimmune diabetes of adulthood is an autoimmune disease sharing similarities of type 1 and type 2 diabetics. It is also known as type 1.5 diabetes in adults. It occurs mostly at the age of 30–35 years. It is usually associated with other autoimmune diseases and patients usually have normal BMI. Patients are positive for glutamic acid dehydrogenase and islets cell autoantibodies with onset in adulthood.
Case: We present a case of a 42 year old female from the capital city of Nepal who presented with chief complaints of excessive thirst and increased frequency of micturition. . She also reported feeling hungry most of the time. She added having symptoms of dry mouth, fatigue and occasional dizziness.
Clinical findings and investigations: Fasting and post prandial blood glucose, Hba1c, blood pH and bicarbonate, Islet cell antibodies, Glutamic Acid Decarboxylase (GAD) and urine ketones were sent for diagnosis.
Intervention and outcome: The patient was started on basal bolus glargine, 14 units and rapid acting insulin, lispro 6unit each with breakfast, lunch, and dinner. Beside insulin, the patient was started on statin (10mg, rosuvastatin) and aspirin (75mg, PO). In subsequent follow-up, her HbA1c level dropped in a few months.
Conclusion: There are no studies found in LADA in Nepal. Our case report tends to highlight the importance of clinical recognition of LADA and raise awareness and importance of diagnostic methods to differentiate between Type 1, Type 2 DM and LADA.

1. Introduction

Background and rationale:

LADA is an autoimmune disease that shares some genetic, immunological, and clinical features with both type 1 and type 2 diabetes, it is also known as type 1.5 diabetes in adults. It is more heterogeneous than young-onset type 1 Diabetes mellitus [1–3]. It was first described in the year 1983 and the name LADA was given in the year 1993 by Tuomi et al. who introduced the term LADA and described this subgroup of patients who tend to share phenotypic features with type 2 and immunological features with type 1 diabetes [2,3]. LADA accounts for 3–12% of all adult diabetes [2] and It accounts for 1.5%–14.2% of type 2 diabetes [3] Its incidence is shown more in Europe than in comparison to the other parts of the world like Asia and North America [2]. In a multi centric study which was carried out in Europe, Asia, and North America showed that 4%–14% of patients who were diagnosed with type 2 DM were positive for T1DM-related autoantibodies, which lead to the diagnosis of LADA [4]. In one multi centric study done in Europe which evaluated 6000 adult-onset diabetes, it showed that 9.7% of the subject had islet cell autoantibody and they had T2DM. The rate was 4%and 10% respectively in patients who were from North and South Europe. This study also found out that Non Insulin Requiring Autoimmune Diabetes had a positive association with glutamic acid decarboxylase and/or protein tyrosine phosphatase IA-2 in Italian patients who were diagnosed with T2DM, in China the frequency was 5.9%, Korea showed the prevalence ranged between 4.4% and 5.3%. However, studies that were done on African American, Hispanic and Arab populations showed a lower prevalence of adult-onset autoimmune diabetes. The difference

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in inclusion criteria and study design along with different lifestyles, and ethnicity could be the reason for the difference in the prevalence of LADA in different countries and populations [4]. Though there are no definitive diagnostic criteria for LADA, however, the diagnosis is made on three criteria: a) onset in adults aged 30–35years b) islet autoantibodies c) insulin independence [1].(2)Presence of Glutamic acid decarboxylase antibody GADA, N- terminally truncated GAD65 autoantibody and IA-2A presence determine the future need for insulin therapy [3].

LADA is underdiagnosed in many countries including Nepal. There were no studies found on LADA in Nepal. So the main aim of this report is to present a case of a patient who was diagnosed with LADA which might help other physicians to come to the diagnosis.

Guidelines: SCARE 2020 paper [5].

This case has been reported in line with the SCARE criteria [5].

2. Case report

2.1. 1Patient information

2.1.1. Demographics and presentation

A 42 year old female from the capital city of Nepal presented with chief complaints of excessive thirst and increased frequency of micturition. She drinks almost 2–3L of water every day and has to wake 3–4 times every night to pass urine. She also reported feeling hungry most of the time and eating 4–5 meals a day. In addition, she had symptoms of dry mouth, fatigue and dizziness.

2.1.2. Past history

She has a history of Grave's disease diagnosed 9 month back. Her past surgical history include appendectomy 21 years back.

2.1.3. Family history

She had no family history of diabetes mellitus.

2.1.4. Drug and allergy history

She is under 10mg of methimazole daily. No history of any allergies.

2.2. 2Clinical findings

Her BMI during the time of presentation is 22.1kg/m2. Her vitals parameters were within normal range. Her systemic examinations were also unremarkable.

2.3. Diagnostic assessment and interpretation

Her laboratory examination revealed:

Variable	Value	Normal range
Blood glucose, fasting	320	≤100 mg/dl
Blood glucose, post prandial	400	≤140 mg/dl
HbA1c	8.2%	≤6.5%
Urine ketones	positive	
Bicarbonate	22	22-28mEq/L
pH	7.36	7.35–7.45
Islet cell antibodies	0.09	≤0.02 nmol/L
Glutamic Acid Decarboxylase (GAD)	3.1	≤0.02 nmol/L

Other basic metabolic panel were unremarkable. Patient with hyperglycemia, glucosuria, and ketonuria with ketoacidosis was diagnosed to have Latent autoimmune diabetic of adulthood (LADA).

2.4. Intervention

The patient was then started on basal bolus insulin with regular glucose monitoring due to risk of diabetic ketoacidosis. Patient glucose level was well maintained within target range of (80–130mg/dl) with basal glargine of 14 units and rapid acting insulin, lispro 6unit each with breakfast, lunch, and dinner.

2.5. Outcome and followup

In subsequent follow-up, her HbA1c level dropped in a few months. Beside insulin, the patient was started on statin (10mg, rosuvastatin) and aspirin (75mg, PO). Currently, she is in regular follow up with her physician in diabetic clinics.

3. Discussion

LADA aka Latent autoimmune diabetes of adulthood first introduced by Tuomi et al., in 1993 was initially thought to be a variant of Type 2 Diabetes Mellitus but with identification of autoantibodies, it has emerged as a separate entity. It shares features of both Type 1 and Type 2 DM [6,7]. Autoantibodies are present in LADA patients which indicates an autoimmune etiology. However, the autoimmune process appears to be milder and the progression of beta cell failure is slower as compared to Type 1 DM, as evidenced by higher levels of C-peptide and the fact that these patients are not insulin-dependent for a period of time following diagnosis. According to the findings, LADA has a stimulated insulin secretion capacity that is halfway between types 1 and 2 diabetes [8,9]. Diagnosis of LADA can be often masked due to its similarities in between Type 1 DM and Type 2 DM. Immunologic markers for LADA, particularly GAD antibody and islet cell antibody, hint to autoimmune involvement and is also a key factor for diagnosis [10].

Patients with LADA had insulin resistance and high glucagon levels, but their insulin secretion was considerably worse. GAD antibody positive patients' insulin secretion deteriorates over time, and they're more likely to need insulin therapy than GAD antibody negative patients. According to studies, despite the fact that they resemble type 1 diabetes patients in this regard, it was found that LADA patients have greater C peptide levels than individuals with adult-onset type 1 diabetes even after 10 years of diabetes. These patients also required insulin therapy earlier as compared to that of Type 2 diabetes patients ([8,9,11,12]).

In our case, the patient had all of the typical diabetes signs and symptoms. Graves' disease was also identified in the patient. When she was tested, her C-peptide level was not measured. However, she was positive for both islet cell and glutamic acid decarboxylase antibodies. Our patients meet the requirements for diagnosis; onset age >30 years old, presence of islet cell antibodies, presence of GAD and need of insulin therapy [13]. In presence of an autoimmune disease like Graves Disease the physician should also closely keep suspicion for other autoimmune disease. Patients with LADA usually have family history of autoimmune disease like Graves, Hashimoto thyroiditis, pernicious anemia, vitiligo, celiac disease, Addison's disease, premature gonadal failure, and others, but frequently lack a family history of diabetes [14,15].

Anti-GAD is the most sensitive antibody marker in LADA patients, with a sensitivity of about 85%. However, even in the absence of anti-GAD antibodies, some patients may test positive for other islet cell auto-antibodies [16]. As a result, while anti-GAD is negative but the suspicion of LADA remains high, measuring other pancreatic islet auto-antibodies (i.e., anti-ICA or anti-IA2) may help confirm the diagnosis [17].

The table below shows the major key points and comparison between Type 1, Type 2 DM, LADA and our case [12,18].

Key points	Type 1 DM	Type 2 DM	LADA	Case report
Age	Usually young	Usually adulthood	>30 years	42 years
Metabolic syndrome	Uncommon	Usually present	Uncommon	Not present
ketoacidosis	Frequent	Less common	Usually absent at diagnosis	Present

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Key points	Type 1 DM	Type 2 DM	LADA	Case report
			but could be present	
Pancreatic autoantibodies	Positive	Negative	Positive	Positive
Insulin Requirement	At the time of diagnosis	Usually years after the diagnosis	Usually >6 months after diagnosis	Required
Family history of Diabetes	Present or absent	Usually absent	Present or absent	absent
Personal or family history of autoimmunity	Usually present	Usually absent	Usually present	History of Graves Disease
Body habitus	Non- obese	Obese	Non-obese	Non-obese

4. Take away lesson

There is no specific protocol for the management of LADA. The main aim of treatment in these patients is to preserve the residual pancreatic beta cell function and to decrease long term risk complications. Insulin therapy is safe and effective in these patients as it preserves beta cell function [19]. Our patient was started on insulin therapy and was scheduled for follow up in the diabetes clinic. There are no studies found in LADA in Nepal. Our case report tends to highlight the importance of clinical recognition of LADA and raise awareness and importance of diagnostic methods to differentiate between Type 1, Type 2 DM and LADA. Furthermore, diagnostic accuracy can help cater the specific management the patients with this condition requires, improve better glycemic range, decrease long term complications and overall quality of life.

Ethical approval

Non applicable.

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Author contribution

1. Sandhya kiran Neupane, Department of Medicine, Shadhak Polyclinic, Kathmandu, Nepal. First Author: she has Presented the case
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Registration of research studies

In accordance with the Declaration of Helsinki 2013, all research involving human participants has to be registered in a publicly accessible database. Please enter the name of the registry and the unique identifying number (UIN) of your study.

You can register any type of research at http://www.researchregistry.com to obtain your UIN if you have not already registered. This is mandatory for human studies only. Trials and certain observational research can also be registered elsewhere such as: ClinicalTrials.gov or ISRCTN or numerous other registries.

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to your specific registration (must be publicly accessible and will be checked):

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Consent

Studies on patients or volunteers require ethics committee approval and fully informed written consent which should be documented in the paper.

Authors must obtain written and signed consent to publish a case report from the patient (or, where applicable, the patient's guardian or next of kin) prior to submission. We ask Authors to confirm as part of the submission process that such consent has been obtained, and the manuscript must include a statement to this effect in a consent section at the end of the manuscript, as follows: "Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request".

Patients have a right to privacy. Patients' and volunteers' names, initials, or hospital numbers should not be used. Images of patients or volunteers should not be used unless the information is essential for scientific purposes and explicit permission has been given as part of the consent. If such consent is made subject to any conditions, the Editor in Chiefmust be made aware of all such conditions.

Even where consent has been given, identifying details should be omitted if they are not essential. If identifying characteristics are altered to protect anonymity, such as in genetic pedigrees, authors should provide assurance that alterations do not distort scientific meaning and editors should so note.

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Informed consent

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Provenance and peer review

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Declaration of competing interest

There is no any conflicts of interest with this article.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.104699.

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