CASE REPORT

Association of latent autoimmune diabetes of adults with type 3 polyglandular autoimmune syndrome—a diagnostic challenge

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Abstract

Autoimmune polyendocrine syndromes (APS) encompass multiple endocrine gland insufficiencies associated with autoimmune disease. This case report underscores the importance of recognising the association between latent autoimmune diabetes of adults (LADA) and type 3 polyglandular syndrome. A 42-year-old man belonging to Rawalpindi, Pakistan, presented to the outpatient department (OPD) of Ali Medical Centre, Islamabad, in January 2023 with the complaints of extreme thirst and frequent urination. The patient reported consistently raised appetite and eating four to five meals a day along with abrupt weight loss, dry mouth, fatigue occasional dizziness, and dyspnoea. He was diagnosed with type 3 polyglandular syndrome with association of LADA. Daily administration of 10 units of glargine insulin, along with six units of rapid-acting insulin, was prescribed. The patient's HbA1c level reduced in a few months after successive follow-up. Patients who exhibit uncontrolled diabetes despite dietary and oral hypoglycaemic management should be further investigated for multiple autoimmune endocrine disorders.

Keywords: Hashimoto's thyroiditis, Type 3 polyglandular syndrome, Diabetes mellitus, Latent autoimmune diabetes, Autoantibodies, Case report.

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Introduction

Autoimmune polyglandular syndromes (APS) involve multiple endocrine gland insufficiencies associated with autoimmune diseases. The clinical classification of APS-3 proposed by Neufeld and Blizzard in 1980; is characterised by thyroid autoimmune disorders and type 1 diabetes (excluding Addison's disease and/or hypoparathyroidism).[1] LADA, or type 1.5 diabetes in adults, is a category distinct from type 1 and type 2 diabetes. It presents diverse clinical features and shares similarities with both the types. LADA can be challenging to diagnose and may lead to difficulties in controlling blood glucose levels.[2-4] It was initially discovered in 1983 and Tuomi et al termed it LADA in 1993. Tuomi et al described this category of patients as likely to have expression patterns consistent with T2DM and immunological characteristics consistent with T1DM.[3,4] About 1.5%-14.2% cases of diabetes type 2 and 3%-12% of all adult diabetes are attributed to LADA.[3,4] The diagnosis of LADA follows three criteria: onset in 30-35-year-old adults, presence of islet autoantibodies, and reliance on insulin. Glutamic acid decarboxylase antibody (GADA), islet tyrosine phosphatase 2 antibodies and N-terminally truncated GAD65 autoantibody help evaluate the need for insulin therapy in LADA patients.[4] Often underdiagnosed in Pakistan, there is a lack of comprehensive studies on the association of LADA with APS-3, its diagnostic parameters and management. The main objective to present a diagnosed case of LADA with APS-3 is to assist medical practitioners in Pakistan in improving the diagnosis and understanding of the condition.

Case Report

A 42-year-old Asian male from Rawalpindi city presented in the outpatient department (OPD) of Ali Medical Centre, Islamabad, in January 2023, with symptoms of extreme thirst, frequent urination, increased appetite, vertigo, weariness, dry mouth, breathlessness, unintentional weight loss, and poor glycaemic control despite oral medications for type 2 diabetes. He had a history of moderate hearing loss and no family history of diabetes. On initial examination, his BMI was 17.6 kg/m^2, blood pressure was 90/50 mmHg, and pulse rate was 120 per minute. No signs of adenopathy or hepatosplenomegaly were observed. No major elements that could have affected the patient's condition were noted in his psychosocial history. He continues to follow his treatment plan and has a solid social network. During his follow-up visits, these topics were covered, and the patient revealed that his strong support network within his family and social circle played a role in his treatment success. The patient was referred to an endocrinologist for further evaluation.

In January 2023, LADA with APS-3 was taken into consideration as suspected diagnosis on the basis of

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laboratory work (Table 1). As a result, oral hypoglycaemics were stopped as they were not effective for LADA. Therapeutic intervention was required because it is an autoimmune condition that involves beta cell destruction, and requires exogenous insulin. Oral medications target mainly insulin resistance, which is not the primary issue in this patient. The patient's prognosis for managing the condition was promising, but long-term outcomes may be influenced by autoimmune factors and lifestyle choices. Daily administration of 10 units of Lantus (glargine) insulin, along with six units of rapid-acting insulin, was prescribed. The patient's HbA1c level reduced in a few months after successive follow-up. Currently, he comes for routine check-ups with his doctor at diabetic clinics. Clinician-assessed outcomes included monitoring the patient's HbA1c levels. In March 2023, a reduction in the patient's HbA1c levels was noted, indicating improved glycaemic control, which is a positive outcome. Additionally, the patient's weight trended toward normalisation during the follow-up period. Patient-assessed outcomes involved the management of his symptom and overall well-being. The initial symptoms were resolved, suggesting an improvement in his overall health and well-being. This was a positive patient-assessed outcome. The patient remained adherent to the prescribed intervention and was observed to be tolerating the therapy. There were no reported adverse effects or complications.

Table-1: Diagnostic Assessment and Interpretation.

Variable	Values	Normal Range
Blood glucose, fasting	350	< 100 mg/dl
Blood glucose, post prandial	500	< 140 mg/dl
HbA1c	15.8%	5.7 % to 6.4 %
Serum ketones	8.0	Up to 0.6 mmol/l
Bicarbonates	10	22-28 mmol/l
pH	6.9	7.35 - 7.45
Anti-Insulin IgG	1.8	0 – 5 mg/L
GADA	86	<10 IU/mL
ALT	44	29-33 IU/L
FT4	0.97	0.93-1.71ng/dL
FT3	2.73	2.0-4.4 ng/dL
TSH	6.97	0.28-4.3 mIU/L
Serum Urea	88	10-52 mg/dl
AST	35	8-33 IU/L
Anti TPO	890.5	< 50 IU/ml
Anti TG	468.5	< 100 IU/ml
IgG tTG	13.8	< 12 U/ml

HbA1c: haemoglobin A1C; GADA: glutamic acid decarboxylase antibody; ALT: alanine transaminase; FT4: free thyroxine; FT3: free triiodothyronine; AST: aspartate transferase; Anti TPO: anti thyroid peroxidase antibody; Anti TG: anti thyroglobulin antibody; IgG tTG: tissue transglutaminase antibody.

Discussion

APS is a group of autoimmune disorders affecting multiple endocrine glands. APS type 3 is characterised by the coexistence of thyroid autoimmune disorders and type 1 diabetes, excluding Addison's disease and hypoparathyroidism. LADA individuals lack a family history of diabetes but often have a familial background of autoimmune diseases such as autoimmune thyroiditis, Graves' disease (GD), Biemer's anaemia, leukoderma, coeliac sprue, primary adrenal insufficiency, and others.[1-5] According to a polycentric study carried out in Europe, Asia, and North America, roughly 4% to 14% of patients with type 2 diabetes who also tested positive for T1DM-related autoantibodies were later diagnosed with LADA.[6]

Tuomi et al first described latent autoimmune diabetes of adulthood in 1993. It has since come to be recognised as a distinct disease after the discovery of autoantibodies. It possesses the characteristics of both Type 1 and Type 2 DM[7] and the presence of autoantibodies in LADA patients suggests an autoimmune origin. Because of its similarities to both categories of diabetes, the diagnosis of LADA can frequently be concealed. GAD antibody and islet cell antibody are two immunologic indicators for LADA that are particularly suggestive of autoimmune involvement and crucial for diagnosis.[8] In the current scenario, the patient showed every classic recognisable indication of diabetes. His C-peptide level was not assessed when he was tested. However, he tested positive for antibodies to glutamic acid decarboxylase and islet cells. In roughly 85% of LADA cases, the most consistent antibody indicator is GAD antibody. Nonetheless, some patients may test positive for various pancreatic cell antibodies even in the absence of anti-GAD antibodies.[5] The core characteristics of T1DM, T2DM, LADA, and the described case are presented in (Table 2).

Table-2: Comparative analysis of LADA, type 1, and type 2 diabetes in a clinical case report.[10]

Traits	T1DM	T2DM	LADA	Case Report
Onset age (years)	Usually childhood/adolescence	Adulthood (rarely before)	More than 30	42
Islet-cell antibodies	Present	Absent	Present	Present
Connecting peptide levels	Null or low	Standard to high	Less to standard	Not available
Insulin need	At the time of detection	Null or long time after detection	> 6 months after detection	>8 months when diagnosed
Metabolic syndrome	Rare	Commonly present	Rare	Negative
Familial diabetic history	Absent or present	Commonly present	Absent or present	Negative
Autoimmune disease background	Common	Null	Common	Present

LADA: latent autoimmune diabetes of adults; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus

For the management of type 2 diabetes, LADA patients may benefit from lifestyle changes such as personalised diet and activity plans. However, more research is required to fully understand the impact of lifestyle on LADA's susceptibility.[9] The patient's perspective played a crucial role in the management of his condition. He reported that his strong support network within his family and social circle played a significant role in his treatment success, which highlights the significance of taking the patient's experience and support network into account during the healthcare process. The patient gave informed consent for the prescribed treatment and interventions. Informed consent is a fundamental ethical requirement in healthcare, ensuring that patients have the necessary information to make decisions about their treatment and healthcare. The patient's consent indicates that he was actively involved in the decision-making process regarding his medical care.

Conclusions

The presented case of a 42-year-old Asian male underscores the importance of recognizing atypical diabetic presentations. His initial symptoms and ineffectiveness of oral hypoglycaemics led to the consideration of LADA with APS-3. The tailored approach, involving cessation of oral medications and initiation of insulin therapy, proved effective, showcasing the necessity for personalized interventions. The patient's robust social network played a pivotal role in treatment success, highlighting the significance of patient engagement and support systems. Long-term considerations emphasize ongoing monitoring and routine follow-up to ensure sustained management and early identification of potential complications.

Consent: Consent for publishing the case was provided by the patient.

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Conflict of Interest: None.

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Author Contribution:
ULR: Analysis, patient examination, diagnosis and management, provide raw data related to disease (LADA).
HMH: Drafting the introduction and revision, Gathering related information about LADA from different sources of medical literature.
MMM: Lab investigations, diagnosis and radiological investigations, final approval, Drafting patients' case representation.
AAA: Drafting discussion and conclusion, patient follow-up, accountable for all aspects of the work.