

Emotional exhaustion-induced latent autoimmune diabetes in adults in a young lady

A CARE-compliant case report

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Abstract

Rationale: Latent autoimmune diabetes in adults (LADA) refers to an autoimmune disorder characterized with detectable islets antibodies in the early diagnosis and increased autoimmune beta-cell failure progression. Notably, this kind of diabetes seems to be confused with other phenotypic diabetes.

Patient concerns: A young woman suffered an emotional exhaustion-induced LADA, showing asthenia, polydipsia, polyuria, and visible weight loss. The patient emotionally ended a 14-year romantic relationship, leading to the emotional flooding.

Diagnoses: The data from physical examination and laboratory tests exhibited as follows: glutamic acid decarboxylase antibody (GADA)=63.83 IU/mL, the fasting blood glucose (FBG)=13.3 mmol/L, and glycated haemoglobin (HbA_{1c})=10.9%. According to levels of GADA, the patient was diagnosed as LADA.

Interventions: The patient was clinically treated with insulin for 3-month. Then, running, diet-control, and emotional treatment were combined, such as the patient started a new relationship.

Outcomes: An emotional recovery initiated from a new romantic relationship and a baby, showing normal levels of GAD65 (27.007 IU/mL) and FBG (5.46) mmol/L.

Lessons: The emotional exhaustion might play a significant role in induction of LADA. It is important that individuals should maintain optimism, cheer, and a positive attitude.

Abbreviations: APPs = amyloid precursor proteins, APR = acute phase response, FBG = fasting blood glucose, FMD = frequent mental distress, GAD = glutamic acid decarboxylase, GADA = glutamic acid decarboxylase antibody, HbA_{1c} = hemoglobin A_{1c}, ICA = islet cell autoantibodies, LADA = latent autoimmune diabetes in adults, PE = physical examination, UGLU = urine glucose.

Keywords: emotional exhaustion, GADA, latent autoimmune diabetes in adults

1. Introduction

Latent autoimmune diabetes in adults (LADA) is a progressive form of autoimmune diabetes, characterized with clinical

Editor: Samantha Martin.

YC and YQ contributed equally to this study.

Patient Perspective: The patient agreed to share her perspective or experience.

Informed consent: Informed consent was obtained from the patient included in the study.

Funding: This study was funded by National Science Foundation of China (grant number 81270934).

The authors have no conflicts of interest to disclose.

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Medicine (2017) 96:20(e6915)

Received: 12 October 2016 / Received in final form: 21 April 2017 / Accepted: 25 April 2017

<http://dx.doi.org/10.1097/MD.0000000000006915>

symptoms of both type 1 and 2 diabetes mellitus,^[1] and thus it can be considered as type 1.5 diabetes mellitus. The major hallmarks of LADA are the expression of diabetes below 50 years old: body mass index (BMI) <25 kg/m², acute symptoms, positive family history, and positive personal history of autoimmune disease.^[2] To date, the etiology of LADA remains completely unclear and whether its onset is similar to/or different from that in type 1 diabetes needs to be further investigated.^[3] Recent researches have indicated that common genetic characteristics of LADA existed in type 1 and type 2 diabetes mellitus.^[4,5] In addition, some studies have illuminated that metabolic diseases such as obesity, family history of diabetes, and hypertension are linked to a rising incidence of LADA.^[6,7]

Here, we report an emotional exhaustion induced by LADA in a young woman. In general, patients diagnosed with LADA are over 35-year old and often have high body-mass index (BMI, ≥ 25 kg/m²).^[3,8] However, this study reports a 27-year old Chinese young woman with a BMI of 17.58 kg/m² and diagnosed as LADA in connection of emotional exhaustion. In physiology, emotions are a state of feeling that can lead to physical and psychological changes influenced the behavior.^[9]

2. Narrative of the episode of care

This study was approved by the Ethics Committee of Guilin Medical University. A 27-year old female accountant diagnosed with LADA in 2012 was used insulin for treatment, accompanied with polydipsia, polyuria, and weight loss (5 kg). Psychiatrists

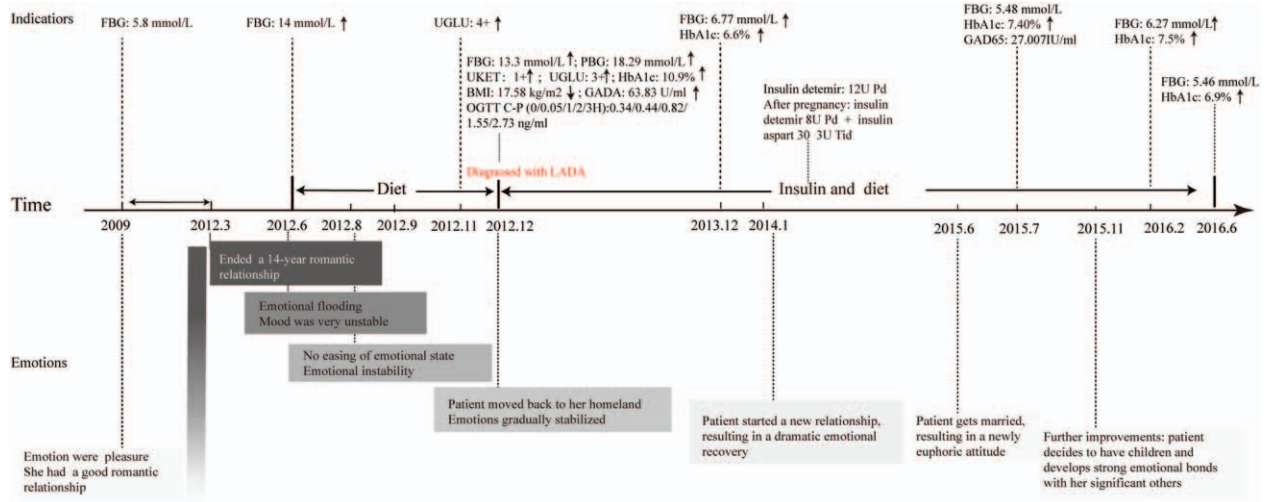


Figure 1. Trend of clinical symptom and laboratory indexes of LADA associated with emotional fluctuation. “↑” displays above the normal range; “↓” indicates below the normal range. The “black-gray-white” color gradient is to illustrate the emotional fluctuation from ghostliness to shine. BMI = body mass index, FBG = fasting blood glucose, GADA = glutamic acid decarboxylase antibodies, HbA_{1c} = hemoglobin A_{1c}, LADA = latent autoimmune diabetes in adults, OGTT C-P = oral glucose tolerance test C-peptide, PBG = postprandial blood glucose, Pd = per day, Tid = three times a day, UGLU = urine glucose, UKET = urine ketone.

had evaluated the patient’s psychopathic condition to exclude mental illness and diabetic family history.

According to the results of a specific validated questionnaire, a figure was made to show the emotional fluctuation, clinical symptom, laboratory indexes, drug treatment, and diet change of the patient during 2009–2016 (Fig. 1). During the observation and follow-up, laboratory tests such as fasting blood glucose (FBG), glutamic acid decarboxylase autoantibodies (GADA), hemoglobin A_{1c} (HbA_{1c}), and urine glucose (UGLU) were determined in 2 different teaching hospitals. The patient’s psychological diagnosis about emotional exhaustion was accessed with a subscale of the Maslach Burnout Inventory-General Survey and the subscale consisted 5 items with response options on a 7-point scale from “never” to “always, every day.”^[10] The score is from 1 to 6 and emotional exhaustion is considered as ≥3.80. In this study, the score of the young patient is 5.5 in the year 2012 and significantly displayed emotional exhaustion.

Generally, the criterion about the diagnosis of LADA is according to the presence of 4 major circulating islet autoanti-

bodies, GADA, insulinoma-associated antigen-2 (IA-2A), insulin autoantibodies (IAA), and islet cell autoantibodies (ICA), which also exist in classic type 1 diabetes mellitus (T1DM).^[11] And GADA is considered to be the most sensitive and specific biomarker of LADA.^[12] The positivity of ICA and GADA in 10% to 30% of people with type 2 diabetes reflects the fact that type 1 diabetes in older patients show type 2 diabetes-like phenotype that is known as LADA.^[7] The specific identifications of potential diagnosis among T1DM, T2DM, and LADA in this case showed in Table 1.

As shown in Fig. 1, in the year 2009, the FBG was 5.8 mmol/L. Exercise and diet-control were major methods to keep healthy for the patient. A 14-year romantic relationship was ended in 2012, which led to her emotional flooding such as anxiety, irritability, depression, and unhappiness. Then, the physical examination (PE) displayed that the FBG was 14 mmol/L. Furthermore, the level of GADA was 63.83 U/mL and HbA_{1c} was 10.9%, which significantly exceeded normal levels. According to a strongly positive GADA titer, the patient was diagnosed as LADA rather than other disease. Then, the patient, treated with insulin, moved

Table 1
The potential clinical diagnosis of this case and their characteristics.^[31]

| Characteristics | T1AD ^a | T1BD ^a | LADA | T2DM |
|----------------------------|--|---|--|---|
| Autoimmunity | Present (ICA, ZnT8A, GADA, IAA, IA-2) | Usually absent GADA can be detectable in some cases | Present (GADA, IAA and IA-2) | Absent, some reports show IgG antibodies linked to auto antibodies against pancreatic islet antigens and insulin resistance |
| Genetics | Polygenic | ? | Polygenic? | Polygenic |
| clinical presentation | Most often acute | Severely acute | A variable: from slow, mild to severe | A variable: from slow, mild to severe |
| Family history of diabetes | Maybe (2–4%) | ? | Yes | Yes (80%) |
| Age at onset | Mostly 6 months to youth, but can present at any age | Any age | Adults | Mostly adults, but can present age |
| Insulin requirement | Yes | Yes | Usually not during several months post diagnosis | Maybe |

GADA = glutamic acid decarboxylase autoantibodies, IA-2 = insulinoma-associated antigen-2, IAA = insulin autoantibodies, ICA = islet cell autoantibodies, LADA = latent autoimmune diseases in adults, T1AD = type 1A diabetes, T1BD = type 1B diabetes, T2DM = type 2 diabetes mellitus, ZnT8A = zinc transporter autoantibodies.

^aT1AD and T1BD are subtypes of type 1 diabetes mellitus;

back to her homeland and started a new relationship, which led to a new GADA level of 27.007 IU/mL and the FBG level of 5.46 mmol/L in July 7, 2015.

In this case report, type of intervention were pharmacologic and self-care. Insulin aspart 30 and insulin detemir were used for treatment. Initially, the dosage of insulin detemir was 12U per day (Pd). After pregnancy, the dosage of insulin detemir was changed as 8U Pd and insulin aspart 30 was changed as 3U three times a day (Tid). Especially, running, diet-control, and emotion treatment were combined. The medicine treatment could keep level of glucose stable^[13] and running and diet may make emotion recovery.^[14]

The clinician assessed the outcomes of PE that the patient with LADA was gradually improved especially based on glutamic acid decarboxylase (GAD) indicator. A 4-year follow-up observation was used to comprehensively evaluate the effect of emotion. The patient's parents and husband supervised the intervention adherence and tolerability. The execution of the patient was assessed according to their feedback. The 4-year duration was associated with insulin treatment, without any adverse effects.

3. Discussion

Here, we report a novel LADA case involved emotional exhaustion, with a BMI of 17.58 kg/m², ending a 14-year romantic relationship. It is interesting to note, however, that an emotional recovery based on a new romantic relationship and a baby leading to the GAD65 and FBG level within normal range.

Modern psychology has revealed that emotions have a significant effect on the onset of disease.^[15-17] Any systemic stress, psychological trauma, or emotional conflicts, induces a similar syndrome from most individuals, such as diabetes.^[18] Mirsky,^[19] who made important contributions for us to understand meaning of stress, suggested that a failure of psychological and physiological adaptation to stress indicated the development of diabetes. Furthermore, experience with stressful events usually produces depression and anxiety, which often co-exist with insufficient sleep and many chronic diseases.^[20,21] A highly significant relationship is demonstrated between insufficient sleep and frequent mental distress (FMD), also between FMD and chronic disease.^[22,23] In addition, considerable data proposed that chronic mental distress can lead to changes in appetite-regulating hormones and insulin resistance. The former conditions can further develop into chronic metabolic impairments like diabetes.^[24] It is worth noting, however, that the research has demonstrated that emotional stresses were majorly related to the occurrence of LADA.^[3] Relative mechanisms potentially underlying the influences that we have found are further elucidated subsequently.

Several suggestions of mechanisms may account for this influence. First, the stress alone can evoke the acute phase response (APR),^[25,26] which may take the form of the sickness response, and the abduction in the liver of amyloid precursor proteins (APPs) such as C-reactive protein. Cytokines, interleukin-6, are the primary inductors of the APR. To a variable extent, catecholamines and corticosteroids, the main stress inducers, reinforce this induction. Corticoids may directly stimulate the presentation of most APPs. Furthermore, together with cytokines, glucocorticoids induce an enhancement of most APPs.^[26] Therefore, chronic stress could elicit chronic APR, which may mediate the metabolism events such as diabetes.^[26] Second, the increasing evidence indicated that the stress emerged it functions was via parasympathetic stimulation or by the hypothalamic-pituitary-adrenal axis, which could significantly affect the immune systems of the

body.^[27,28] A third explanation was that the chronic stressful situations could evoke an increase in the sensitivity of α -adrenergic stimulation which would reduce insulin secretion and disturb glucose metabolism.^[29,30] LADA may be considered therefore as a problem of a regulated homeostasis in which the autonomic nervous system and emotional stress interact.

We conducted this case report through personally interview and a continuous 4-year follow-up observation to express adjusting emotion is of crucial significance for the development of disease prevention. However, this study also had some limitations. First, a 2-year window period, due to she left homeland. Second, the patient had taken Chinese medicine to decrease glucose before diagnosing as LADA.

Taken together, we present this case to highlight emotional fluctuations as a psychological factor that might play a significant role in the induction of LADA. Therefore, individuals at risk for LADA are advised to maintain optimism, cheer, and a positive attitude. This suggestion is also significant for clinical practice. Learning to develop strong relationships with significant others can really do wonders for his or her health.

Acknowledgments

The authors gratefully acknowledge all the participants for their support in this research work. They would like to thank Mr. Rong Li and Mr. Nelson for their English proofing.

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