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CASE REPORT
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# SGLT2 Inhibitor Significantly Improved Plasma Glucose Levels in a Patient with Latent Autoimmune Diabetes of Adults: A Case Report

Latent autoimmune diabetes of adults (LADA) is a type of diabetes mellitus (DM) with characteristics of both type 1 diabetes (T1D) and type 2 diabetes (T2D). LADA is a disease of adults and the Immunology for Diabetes Society (IDS) has specified three criteria for its diagnosis: 1) onset of DM after age 35, 2) positivity for either of the known anti-islet autoantibodies, 3) insulin treatment required for more than 6 months after the diagnosis of DM [1].

To date, the use of sodium-glucose cotransporter 2 inhibitors (SGLT2is) in LADA has not been well evaluated [2]. However, this single LADA case indicated that SGLT2i was significantly effective in maintaining satisfactory plasma glucose levels for over 9 years even after the complete depletion of insulin secretion.

In 2008, a 56-year-old male patient (body height: 163.0 cm, body weight: 50.3 kg, and body mass index: 18.9 kg/m$^2$) was transferred to our clinic for the continuous treatment for DM. He had no significant previous medical history. Initially, he was diagnosed with T2D at the age of 45 years and was treated with oral hypoglycemic agents alone.

The patient's routine peripheral blood laboratory test and urine examination findings in 2008 were within normal range. Chest X-ray examination and electrocardiogram were normal. He had light numbness in the bilateral lower limbs due to diabetic neuropathy and mild diabetic retinopathy. Because his anti-glutamic acid decarboxylase (GAD) antibody level was 27.9 U/mL (normal range, <5.0), according to the diagnosis criteria for LADA, we re-diagnosed his DM as LADA. The detailed treatment course is summarized in Figure 1.

SGLT2is contribute to achieve treatment goal in patients with T1D [1, 3]. By contrast, to date, the application of SGLT2is among patients with LADA have not been comprehensively assessed [1]. In our case, as shown in Figure 1, to date, mean HbA1c levels have been maintained at < 7.0 % for over 9 years without hospitalization and adverse effects including diabetes ketoacidosis (DKA) after ipragliflozin treatment was started.

In general, in patients with T1D, the risk of SGLT2i treatment must be weighed against that of DKA [4]. Therefore, the increase in absolute risk of DKA, even in closely supervised patients participating in clinical trials, raises a serious concern that DKA will be even more common if SGLTis are used in routine clinical practice by practitioners who do not have the expertise

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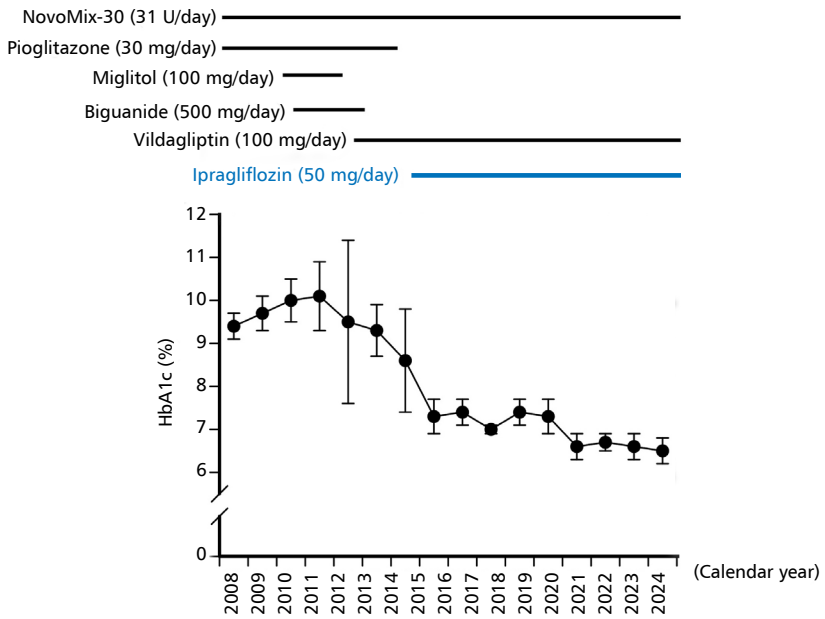


**Figure 1.** Changes in HbA1c Levels with Time between 2008 and 2021
Initially, the patient's glycated hemoglobin ( HbA1c) level was maintained at < 7.0 % with oral hypoglycemic agents. However, he received NovoMix 30 (30% insulin aspart and 70% insulin aspart protamine) at a dose of 12 U/day at the age of 52 years (which was 7 years after the initial diabetes diagnosis). Thereafter, in addition to pioglitazone (30 mg/day), he continually used NovoMix 30, and the dosage was increased to 26 U/day. Upon transfer to our clinic, his C-peptide level based on the routine blood sample test was undetectable, and his glycated hemoglobin (HbA1c) level was 9.1 %. In addition to NovoMix 30 (31 U/day) and pioglitazone (30 mg/day), miglitol (100 mg/day), biguanide (500 mg/day), and vildagliptin (100 mg/day) were added in sequence. Nevertheless, his plasma glucose level was not controlled. In order to improve his plasma glucose control, after we obtained informed consent, we acquired patient's consent besides approval of SGLT2i use for LADA from the Institutional Review Board of our hospital. Therefore, SGLT2i (ipragliflozin; 50 mg/day) was combined with NovoMix 30 (31 U/day), and vildagliptin (100 mg/day) in July 2014. The specific changes in HbA1c values as the one-year mean and standard deviation of HbA1c values in each year are summarized.
Ipragliflozin was started in 2014.
Changes in HbA1c levels are presented between 2008 and 2023. HbA1c levels are expressed as mean ± standard deviation. The Y-axis indicates the HbA1c levels, and the X-axis represents the calendar year; HbA1c — glycated hemoglobin

and resources of the clinical trialists to implement the complex recommendations necessary to mitigate risk for DKA [5]. It would be prudent to limit adjunctive use of SGLTis in T1D to specialists well versed in the risks associated with such therapy and who have the requisite resources to educate, train, and support carefully selected patients [5]. However, regarding ketosis, it has been reported that LADA is ketosis-resistant [2], which might be advantage to use SGLT2i in patients with LADA compared to other type of autoimmune diabetes.

This single case study indicated that SGLT2i had a significant contribution in producing and maintaining extremely good plasma glucose levels in patients with LADA.

## Article information

### Ethics statement

The ethics committees at Ono Naika Clinic approved this case report, which conformed to the Declaration of Helsinki (as 2024-01).

### Author contribution

Shuichi Okada and Kumeo Ono are responsible for the patients' clinical care. Shuichi Okada, Kazuya Okada, Junichi Okada, and Eijiro Yamada contributed

to the analysis of data and writing of the case report. All authors read and approved the final manuscript.

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## Conflict of interest

The authors declare no conflict of interest.

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