RHEUMATOLOGY ADVANCES IN PRACTICE

Letter to the Editor (Case report)

Rheumatology Advances in Practice 2021;0:1–3
doi: 10.1093/rap/rkab045
Advance Access Publication 7 July 2021

Rapid weight loss in a patient with anti-synthetase syndrome treated with sodium–glucose cotransporter 2 inhibitors and corticosteroids

Key message

- Interaction between SGLT2 inhibitors and CSs may induce rapid weight loss in anti-synthetase syndrome.

Dear Editor, Sodium–glucose cotransporter 2 (SGLT2) inhibitors, which block glucose reabsorption in the proximal tubules, have been used to treat type 2 diabetes mellitus (T2DM) [1]. Recently, the usefulness of SGLT2 inhibitors in patients with heart failure has also been reported [2]. Thus, SGLT2 inhibitors have become new therapeutic options for T2DM and heart failure. Body weight loss is a side effect of SGLT2 inhibitors [3]. Although body weight is not a serious problem in clinical practice, it can be problematic in specific patients.

A 71-year-old Japanese woman was admitted to our hospital because of dyspnoea. One year before admission, she was diagnosed with idiopathic pulmonary fibrosis in another hospital, where her pulmonary function remained relatively steady. Her family did not want her to undergo detailed examination; therefore, she was diagnosed with low-activity interstitial lung disease (ILD) and did not receive medication. Four months before admission, her dyspnoea worsened. On further evaluation, she tested positive for serum anti-aminoacyl-transfer RNA synthetase (anti-ARS) antibodies, suggesting CTD-associated ILD (CTD-ILD). Therefore, she was admitted to our hospital for possible CTD-ILD. She had a medical history of hypertension, T2DM and atrial fibrillation. She received empagliflozin (10 mg/day), telmisartan, amlodipine and warfarin.

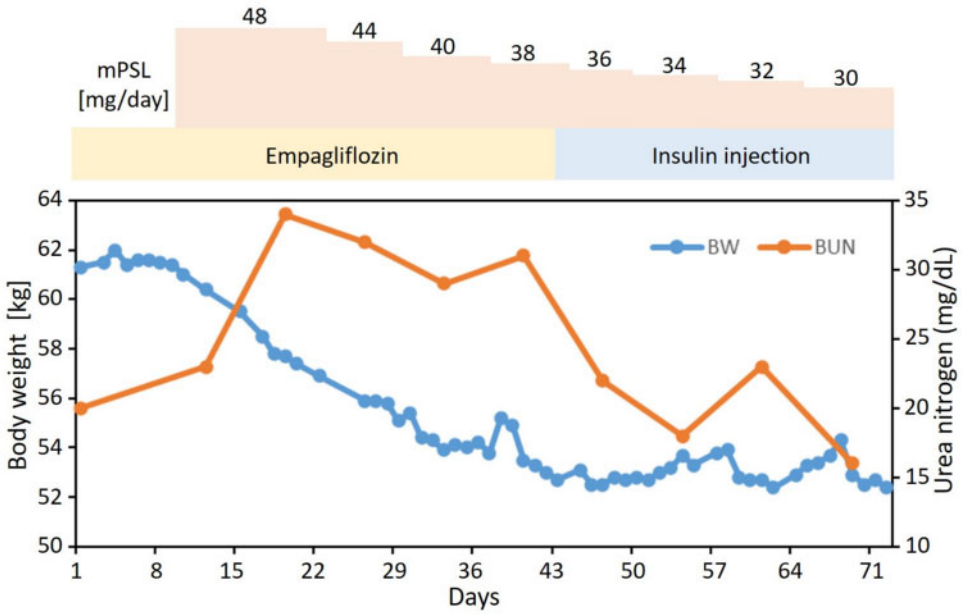
On admission, her vital signs were as follows: body temperature, 35.5°C; blood pressure, 96/64 mmHg; pulse, 96 beats/min; respiratory rate, 16 breaths/min; and peripheral oxygen saturation, 96% in ambient air. Her body weight and BMI were 61.3 kg and 23.1 kg/m^2, respectively. Physical examination revealed Gottron's papules and mechanic's hands. Bilateral digital arthralgia was also observed. On auscultation, fine crackles were heard in the left and right lower lung fields. Neurological examination revealed mild muscle weakness of the neck flexors (grade 5−) and pectoralis major (grade 4+/4+), without weakness of other proximal muscles. Laboratory investigations showed elevated levels of serum CRP (0.89 mg/dl). Serum levels of Krebs von den Lungen and surfactant protein D were significantly elevated (3363 U/ml and 259 ng/ml, respectively). Serum levels of muscle deviation enzymes (creatine kinase, myoglobin and aldolase) were within the normal limits. The ANA titre was 1:40 with a speckled pattern and 1:80 with a cytoplasmic pattern. The ELISA was positive for anti-ARS antibodies; however, the specific type of anti-synthetase syndrome antibody was not detected owing to the unavailability of immunoprecipitation in our institution. Urinalysis revealed glucosuria (4+), but the blood glucose concentration and haemoglobin A_{1c} were 124 mg/dl and 6.2%, respectively. Based on these, her T2DM was well controlled by empagliflozin. Chest CT revealed non-specific interstitial pneumonia. Skin biopsy showed liquefaction, degeneration, lymphocyte infiltration around small vessels and mucin deposition, consistent with DM.

She was diagnosed with anti-synthetase syndrome-associated ILD. She then received a CS treatment (initial dose: methylprednisolone, 48 mg/day) and tacrolimus. Her blood glucose concentration increased to ∼250 mg/dl because the CS exacerbated her T2DM. Her body weight decreased rapidly after the initiation of CS therapy, whereas her serum urea nitrogen levels increased. Orthostatic hypotension was also observed. Her rapid body weight loss was probably a side effect of the SGLT2 inhibitor (empagliflozin), accumulated by the CS. Empagliflozin was replaced with an insulin injection. She stopped losing weight, and the serum levels of urea nitrogen decreased after empagliflozin discontinuation (Fig. 1).

Patients treated with SGLT2 inhibitors lose ∼1–3 kg of body weight [4]. This is often recognized as a beneficial side effect of SGLT2 inhibitors [4]. It has been assumed that the weight loss is caused by body water loss owing to osmotic diuresis, fat reduction owing to energy loss through urinary glucose excretion, and hypercatabolism secondary to metabolic adaptations. Accordingly, it was reported that early weight loss until 4 weeks in patients treated with ipragliflozin might be largely related to fluid loss owing to osmotic diuresis, whereas ongoing weight loss until 12 weeks might represent reduction in body fat related to calorie loss [5]. The skeletal muscle mass index reportedly decreased after administration of luseogliflozin [6].

In our case, the serum levels of urea nitrogen were elevated as the patient lost weight, indicating accelerated catabolism. CSs induce hyperglycaemia and hypercatabolism [7]. Thus, we hypothesized that the CS-induced hyperglycaemia increased osmotic diuresis

Fig. 1 Clinical course and fluctuations of body weight and blood urea nitrogen



A rapid decrease of body weight and increase of blood urea nitrogen were shown after administration of CS, which persisted until discontinuation of empagliflozin. BUN: blood urea nitrogen; BW: body weight; mPSL: methylprednisolone

and that hypercatabolism was also activated by the interaction between SGLT2 inhibitors and CSs, causing rapid weight loss.

The number of patients treated with SGLT2 inhibitors is expected to increase. However, there is little evidence on the safety of CSs and SGLT2 inhibitors [8]. This case emphasizes the interaction of these drugs, particularly in patients treated with high-dose CSs; therefore, clinicians should be aware of this potential for interaction, and therefore weight loss, which may require monitoring.

Ethical approval: Our institution does not require ethical approval for reporting individual cases or case series.

Consent: Written informed consent was obtained from the patient for anonymized information to be published in this article.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: The authors have declared no conflicts of interest.

Data availability statement

Data are available upon reasonable request by any qualified researchers who engage in rigorous, independent scientific research, and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). All data relevant to the study are included in the article.

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Accepted 21 June 2021

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