



Dapagliflozin Related Severe Weight Loss in a Patient with Lung Cancer

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Abstract

Cancer cachexia with severe weight loss is recognized as an adverse effect of cancer. Here we present a case of severe weight loss related by dapagliflozin, an antihyperglycemic medication through a mechanism of increasing urinary glucose excretion, in a patient with advanced lung cancer. An unusual feature in our case was that the patient continued to experience severe weight loss while the cancer was quite stable. Increased oral intake was unable to compensate the urinary glucose excretion, but the dose reduction worked, suggesting dapagliflozin as the main reason for weight loss. Our case highlights the usefulness of a full assessment of possible contributors to weight loss, even in patients with cachexia. Identification of reversible causes can have a major effect on the severity of weight loss and overall quality of life for cancer patients.

Keywords: Cancer cachexia; Dapagliflozin; Non-small cell lung cancer

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Received Date: 07 Nov 2022

Accepted Date: 19 Nov 2022

Published Date: 22 Nov 2022

Citation:

Wang J, Ran F, Li X, Jin X, Bruera E, Qian Y. Dapagliflozin Related Severe Weight Loss in a Patient with Lung Cancer. *Ann Clin Case Rep.* 2022; 7: 2349.

ISSN: 2474-1655.

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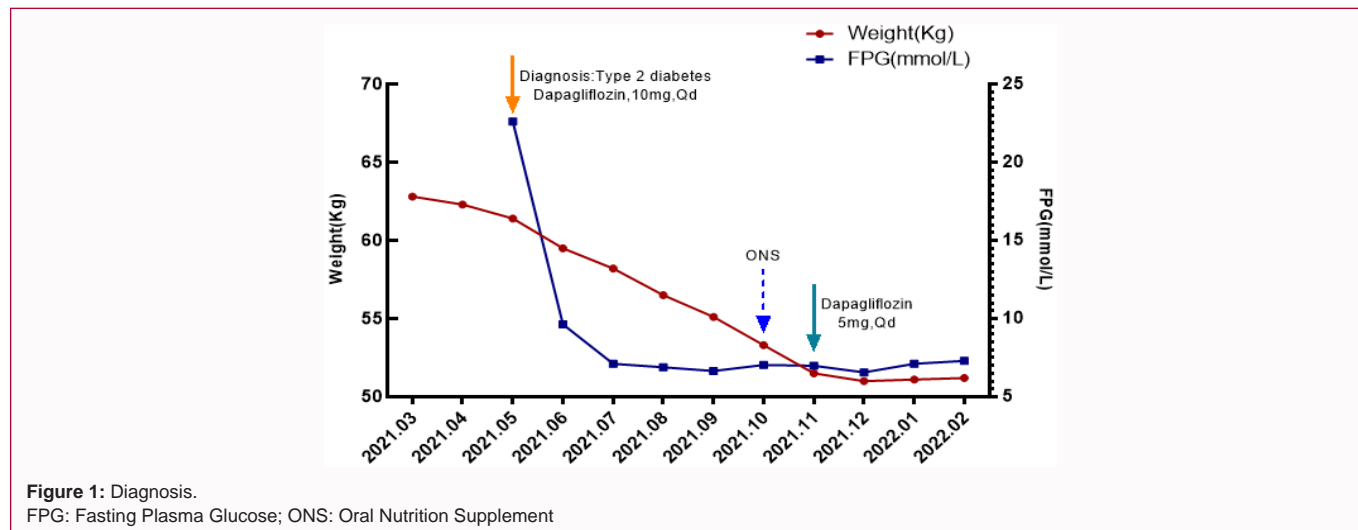
Introduction

Patients with cancer cachexia frequently experience decreased quality of life, reduced chemotherapy tolerance, reduced physical functioning, and shortened survival [1]. Between 50% and 80% of patients with advanced cancer develop cachexia, with highest incidence reported in patients with lung and gastrointestinal cancer [2]. Diabetes Mellitus (DM) is commonly found in cancer patients [3]. The relationship between DM and cancer appears to be bidirectional: DM has been associated with an increased risk of developing several types of cancer while also cancer treatments, through the induction of metabolic derangements, can facilitate the onset of DM, or worsen glucose control [4]. DM can negatively affect the clinical outcomes of these subjects, being associated with worse survival [5]. However, there is the lack of specific guidelines for DM in cancer patients, a management of DM in cancer patients refer to the general guideline for DM. Dapagliflozin was the first drug in a class of therapies that took a new approach to glycemic control in adults with Type 2 Diabetes (T2D). It can also be used for patients with cancer and T2D. Both patients with cancer and those with diabetes might experience weight loss, or cachexia. We present a case of severe weight loss, which was not caused by cancer or T2D, but caused by dapagliflozin, the antihyperglycemic medication.

Case Presentation

The patient is a 59-year-old male, 170 cm tall and weighing 53 kg with advanced non-small cell lung cancer. He was presented to Hubei Cancer Hospital, China, with an 8-kg, 13% weight loss over the past 6 months in October 2021.

He had been diagnosed with advanced adenocarcinoma 41 months before, and received first line chemotherapy of pemetrexed and cisplatin, followed by albumin-bound paclitaxel combined with pembrolizumab as second line therapy. He then continued pembrolizumab as maintenance therapy. Six months before he experienced weight loss and was diagnosed as diabetes with Fasting Plasma Glucose (FPG) at 22.6 mmol (406 mg/dL). He was diagnosed as T2D for he was negative for



glutamic acid decarboxylase antibody, islet cell antibody, and insulin autoantibody. He was first treated by metformin. Due to a severe side effect as diarrhea, he was then prescribed with dapagliflozin, an antihyperglycemic-Sodium Glucose cotransporter-2 (SGLT-2) inhibitors, 10 mg orally. His serum glucose levels became stable at approximately 7.3 mmol/L (130 mg/dl), but continued to experience severe weight loss.

On examination, his cancer was stable with the maintenance of pembrolizumab. His eating and exercise habits did not change throughout the treatment and he was not depressed. After a dietary survey, his daily dietary energy intake was appropriately 1,500 kcal, which was the same as usual. Oral Nutrition Supplement (ONS) with 500 kcal was added to his daily dietary. However, he lost 2 more kilograms within one month with additional ONS (Figure 1).

Since additional ONS did not eliminate his weight loss, we assumed that his weight loss was caused by increased glucose excretion caused by dapagliflozin. His urine glucose was positive. Therefore, the dose of dapagliflozin was reduced to 5 mg and his weight stopped losing and became stable around 51 kg without any other contributors.

Discussion

Weight loss in patients with cancer cachexia is due to a variable combination of decreased food intake and metabolic changes, leading to negative protein and energy balance [1]. Cancer cachexia can be seen in patients with normal food intake. Metabolic changes were the main mechanism in our patient rather than decreased food intake or increased energy expenditure. Weight loss without trying is one of the most common symptoms for T2D [6]. The diagnosis of diabetes was clear for this case due to hyperglycemia. However, this patient suffered weight loss related to dapagliflozin, rather than his diseases of diabetes or cancer. Special cautions of weight loss should be placed for those patients with cancer and diabetes, especially for those who undergo dapagliflozin.

Although the patient had a severe weight loss, he did not have any fatigue, anorexia, or sarcopenia. Taking together that his lab values such as serum C-reactive protein and albumin were at normal range during the treatment, he cannot be diagnosis with cachexia but only weight loss.

Dapagliflozin, an SGLT-2 inhibitors, is the latest glucose-lowering agents to become available. These drugs increase urinary

glucose excretion by inhibiting SGLT-2 in the renal proximal tubule [7]. Through a mechanism of glycosuria and urinary calorie loss of up to 320 kcal per day, substantial weight reduction was achieved when dapagliflozin was used [8]. For this patient, we might assume that his urinary calorie loss is much more than 320 kcal especially when his weight loss continued with addition of ONS with 500 kcal, but it was impossible to confirm it due to the limitation of our hospital, although his urine glucose was positive. His weight was rather stable when dapagliflozin was reduced to 5 mg without any concurrent medication.

Diabetes is one of the endocrine-related adverse events associated with immunotherapy [9]. Due to the potential mechanism that pancreatic beta cells destroyed by immunotherapy, immunotherapy related diabetes is similar to classic type 1 diabetes generally [10]. However, our case is negative for all the antibodies and is independent with insulin, which is more like T2D. Further researches, such as gene sequencing could be done in order to support the diagnosis [11]. We focused on the weight loss and will not go further on this area.

Weight loss might be necessary for diabetes patients, but is not a good sign for advanced cancer patients. It could be confused with cancer cachexia, which is related to tumor mass and progressive disease. Normally cancer patients gain weight in association with tumor response to the anti-cancer treatment. An unusual feature was that in our case the patient continued to experience severe weight loss while the cancer was quite stable. Increased oral intake was not sufficient enough to compensate the urinary glucose excretion, but the dose reduction likely worked by reducing glucose excretion.

Conclusion

Our case highlights the usefulness of a full assessment of possible contributors to weight loss, even in patients with cachexia. Special cautions should be paid for such a severe weight loss when advanced cancer patients with diabetes undergo dapagliflozin. A smaller dose, rather than the standard dose of dapagliflozin might be more suitable for them. Identification of reversible causes can have a major effect on the severity of weight loss and overall quality of life for cancer patients.

Acknowledgment

The patient involved in this case report gave his informed consent authorizing use and disclosure of his health information.

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