

Empagliflozin Improves Muscle Weakness in a Patient with Suspected Glycogen Storage Myopathy: A Case Report

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Case Report

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Abstract

Objective

To describe the clinical course of a patient with chronic progressive muscle weakness and intramyocellular glycogen deposition who received empagliflozin.

Methods

We present a case of a young male patient with chronic progressive proximal limb weakness, exercise intolerance, and supine dyspnea. Muscle biopsy revealed massive glycogen deposition in skeletal myocytes. Genetic testing for glycogen storage diseases identified no pathogenic variants. After conventional therapies failed, the patient received empagliflozin 10 mg once daily for 3 months. Clinical symptoms, laboratory parameters, and safety outcomes were assessed.

Results

Before treatment, the patient had proximal muscle strength of grade 3/5 on manual muscle testing, elevated creatine kinase (856 U/L), and abnormal liver function tests. After 3 months of empagliflozin treatment, muscle strength normalized to grade 5/5, creatine kinase decreased to 142 U/L, liver function tests returned to the normal range, and exercise intolerance resolved. Fasting blood glucose remained stable at 4.2–5.6 mmol/L, with no hypoglycemia or adverse events reported.

Conclusion

In this patient, empagliflozin was temporally associated with improved muscle weakness and metabolic parameters. However, because this is a single case report, these findings are hypothesis-generating and cannot establish causality. Further studies with

Introduction

Glycogen storage diseases (GSDs) are inherited metabolic disorders caused by defects in enzymes involved in glycogen synthesis or degradation, leading to abnormal glycogen accumulation in skeletal muscle, liver, and other tissues. Skeletal muscle involvement, termed glycogen storage myopathy (GSM), presents with progressive muscle weakness and exercise intolerance; severe cases may develop respiratory muscle dysfunction, significantly impairing quality of life. Because of overlapping phenotypes among GSD subtypes and limitations of genetic testing, some patients are diagnosed only with suspected GSD based on pathological glycogen deposition without a confirmed etiology. Current treatments are largely supportive, such as L-carnitine and coenzyme Q10, and do not target the core pathological process of glycogen accumulation, resulting in limited efficacy.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors lower blood glucose by inhibiting renal glucose reabsorption and have pleiotropic effects, including modulation of energy metabolism. However, their application in GSM has rarely been reported, and the potential mechanisms remain unclear. Herein, we describe a young male patient with muscle weakness associated with intramyocellular glycogen deposition who showed a remarkable clinical response after empagliflozin treatment. We discuss the diagnostic challenges, possible mechanisms of action, and implications for future research and clinical practice.

Case Report

Clinical Findings and Diagnosis

A young man presented with a 6-month history of chronic proximal limb weakness, exertional dyspnea, and progressive exercise intolerance. Symptoms exhibited diurnal variation, being milder in the morning and worse in the evening, with prominent supine dyspnea, difficulty climbing stairs, frequent falls, and inability to lift heavy objects. Physical examination revealed proximal muscle strength of grade 3/5 in both upper and lower limbs, distal strength of grade 4/5, normal muscle tone, and no muscle tenderness or atrophy. Deep tendon reflexes were normal, and pathological reflexes were absent.

Extensive laboratory and imaging investigations, including complete blood count, comprehensive metabolic panel, cardiac enzymes, coagulation profile, chest imaging, echocardiography, vascular ultrasound, autoantibody screening including myasthenia gravis antibodies, and brain and cervical spine MRI, were unremarkable. A neostigmine test was negative, ruling out myasthenia gravis.

Muscle biopsy of the left tibialis anterior muscle showed normal routine light microscopic morphology. Transmission electron microscopy revealed massive glycogen deposition within myocytes, mild myofibrillar atrophy, subsarcolemmal mitochondrial condensation, scattered intermyofibrillar hemorrhagic foci, and thickening of the interstitial vascular basement membrane. Genetic testing for GSD-related genes using next-generation sequencing detected only variants of uncertain significance, with no pathogenic variants identified. Based on these findings, the diagnosis was intramyocellular glycogen deposition of undetermined etiology, suspected GSD.

Treatment and Follow-up

Before presentation, the patient had received nutritional support with L-carnitine, coenzyme Q10, and B vitamins, as well as symptomatic treatments including cholinesterase inhibitors and anxiolytics, without improvement. Given the core pathological finding of glycogen deposition, targeted metabolic therapy with empagliflozin 10 mg once daily was initiated, along with mecobalamin and folic acid as background nutritional supplements; these supplements had previously been ineffective when used alone. During treatment, fasting blood glucose was monitored regularly and remained stable between 4.2 and 5.6

mmol/L, with no episodes of hypoglycemia. The patient tolerated the medication well, with no adverse effects such as diarrhea or genitourinary infections.

After 3 months of empagliflozin treatment, the patient reported marked improvement. Supine dyspnea resolved completely, and proximal muscle strength recovered to grade 5/5, enabling normal daily activities including lifting heavy objects and climbing stairs. Exercise intolerance and diurnal symptom fluctuations disappeared. Laboratory parameters normalized, including creatine kinase, alanine aminotransferase, and total bilirubin (Table 1). Follow-up neuroelectrophysiology showed attenuation of myogenic changes, with motor unit action potentials approaching normal morphology and a mixed interference pattern on maximal contraction.

Table 1
Clinical and laboratory parameters before and after empagliflozin treatment

Parameter	Before treatment	After 3 months	Reference range
Creatine kinase (U/L)	856	142	50–310
Alanine aminotransferase (U/L)	78	32	10–40
Total bilirubin (μmol/L)	28.5	15.2	3.4–20.5
Fasting glucose (mmol/L)	5.1	4.8	3.9–6.1
Proximal muscle strength (MMT grade)	3/5	5/5	5/5 (normal)
Fatigue Severity Scale (FSS) score	5.2	2.1	< 4.0*
Electromyography	Pathological myogenic changes†	Attenuated myogenic changes‡	Normal

*FSS > 4 indicates clinically significant fatigue; MMT = Manual Muscle Test (0–5 grading, grade 5 = normal muscle strength).

Shortened motor unit action potential duration, reduced amplitude, pathological interference pattern on maximal contraction.

Motor unit action potential duration and amplitude approaching normal, mixed interference pattern.

Discussion

We report a case of clinical improvement in muscle weakness associated with intramyocellular glycogen deposition following treatment with the SGLT2 inhibitor empagliflozin. To our knowledge, this is the first documented use of an SGLT2 inhibitor for this indication. The patient had failed multiple conventional

therapies, and the rapid, robust response after empagliflozin may suggest a possible therapeutic effect. However, because this is a single, open-label case report, causality cannot be established.

Diagnostic Challenges

The diagnosis of glycogen deposition myopathy remains challenging. As illustrated in this case, the clinical phenotype, including diurnal fluctuation, may mimic myasthenia gravis, and genetic testing often yields variants of uncertain significance. Muscle biopsy with electron microscopy is essential to identify glycogen accumulation and exclude other structural abnormalities. In this patient, the absence of a definitive genetic diagnosis does not preclude a primary GSD, as many rare subtypes may not be captured by standard panels. In addition, given the presence of supine dyspnea and glycogen deposition, late-onset Pompe disease should be specifically considered and excluded through GAA enzyme activity testing and GAA variant analysis, including deletion/duplication analysis, when feasible.

Possible Mechanisms of Empagliflozin

The mechanisms underlying the observed benefit remain speculative and may involve several interrelated pathways. First, by inhibiting renal SGLT2, empagliflozin reduces glucose reabsorption, leading to mild glycosuria and a modest decrease in plasma glucose. Lower ambient glucose levels could reduce glucose influx into myocytes via glucose transporters, thereby decreasing substrate availability for glycogen synthesis. This may alleviate the mechanical disruption caused by glycogen accumulation and help restore contractile function. However, SGLT2 is not primarily expressed in skeletal muscle, so this proposed mechanism remains indirect and unproven. Second, a mild hypoglycemic stimulus might activate gluconeogenesis and promote glycogenolysis, facilitating utilization of stored glycogen. Third, the observed improvement in mitochondrial morphology, including reduced condensation, may be secondary to decreased glycogen compression, although functional studies are needed to confirm this. Additionally, the systemic metabolic effects of empagliflozin, including reduced lipotoxicity and anti-inflammatory actions, may contribute to an optimized microenvironment for muscle recovery. These hypotheses require experimental validation.

Clinical Implications

If confirmed, this observation could have important implications. Empagliflozin is orally administered, generally well tolerated, and widely available. For non-diabetic patients, low-dose empagliflozin, 10 mg daily, may be considered with careful glucose and metabolic monitoring. However, SGLT2 inhibitors are associated with risks including euglycemic diabetic ketoacidosis, dehydration, genitourinary infections, and renal effects, even in non-diabetic patients. These risks should be discussed with patients, and ketone, renal function, and volume status should be monitored when clinically indicated. Early intervention might prevent irreversible muscle damage from chronic glycogen accumulation. However,

given the heterogeneity of GSDs, responses may vary by subtype, and patient selection should be guided by muscle biopsy evidence of glycogen deposition.

Limitations

This study has several limitations. It is a single case report, and the findings cannot be generalized. We lacked post-treatment muscle biopsy to directly confirm reduction of intramyocellular glycogen deposition, relying instead on clinical and indirect laboratory markers. The use of concomitant mecobalamin and folic acid, although previously ineffective, may have contributed to the outcome. The assessment of muscle function relied on subjective and semi-quantitative measures, and no specific glycogen metabolism biomarkers, such as lactate response to exercise, were measured. In addition, there was no control group, and spontaneous fluctuation, regression to the mean, and placebo effects cannot be excluded. Long-term follow-up is needed to assess durability of response and potential late adverse effects. Finally, the proposed mechanisms are theoretical and require experimental validation.

Conclusion

This case provides preliminary evidence that empagliflozin may be temporally associated with improved muscle weakness in a patient with intramyocellular glycogen deposition myopathy. The treatment was well tolerated and was accompanied by normalization of metabolic parameters. While these findings are hypothesis-generating, they suggest that SGLT2 inhibitors could represent a potential novel metabolic-targeted therapy for this condition. Prospective studies with larger cohorts, including post-treatment tissue analysis and long-term follow-up, are needed to confirm these observations and elucidate the underlying mechanisms.

Abbreviations

ALT: alanine aminotransferase

AST: aspartate aminotransferase

CK: creatine kinase

DKA: diabetic ketoacidosis

EMG: electromyography

FSS: Fatigue Severity Scale

GAA: acid alpha-glucosidase

GSD: glycogen storage disease

GSM: glycogen storage myopathy

LDH: lactate dehydrogenase

MMT: Manual Muscle Test

MRI: magnetic resonance imaging

MRS: magnetic resonance spectroscopy

MUAP: motor unit action potential

PAS: periodic acid-Schiff

SGLT2: sodium-glucose cotransporter 2

VUS: variant of uncertain significance

Declarations

Ethics approval and consent to participate

This case report was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Capital Medical University Yanjing College. Written informed consent was obtained from the patient.

Consent for publication

Written informed consent for publication of this case report and any accompanying images was obtained from the patient. A copy of the consent form is available for review by the Editor of this journal.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The author declares that they have no competing interests.

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Authors' contributions

Xinyan Tian was involved in patient care and data collection, drafted the manuscript, reviewed the literature, and revised the manuscript. The author read and approved the final manuscript.

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Authors' information

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Use of large language models

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