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CASE REPORT

A Case Report on Therapeutic Optimization and Cardiometabolic Benefits of Semaglutide Therapy in Type 2 Diabetes Mellitus

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Abstract: Metabolic management in Type 2 Diabetes Mellitus (T2DM) is being shifted from a glucose-centric approach to a multi-organ protective strategy, particularly for patients presenting with comorbid obesity and hypertension. A 48-year-old female with a decade-long history of T2DM, characterized by a baseline HbA1c of 10.2%, a BMI of 36 kg/m², and poorly controlled hypertension, underwent a structured intervention with subcutaneous semaglutide. Over a 20-week period, a stepwise titration method was followed alongside Mediterranean-style dietary adjustments and aerobic exercise. Clinical outcomes revealed a 3.1% reduction in glycated hemoglobin, bringing the final HbA1c to 7.1%. Along with glycemic improvement, the patient showed a 9% reduction in total body weight (8.5 kg), resulting in a BMI decrease to 32.8 kg/m². Most importantly, the significant weight loss facilitated a stabilization of blood pressure, reducing the dependency on high-dose antihypertensive monotherapy. Improvements in the lipid profile, specifically a reduction in triglycerides and low-density lipoprotein cholesterol, further reduced the patient's cardiovascular risk. Minor gastrointestinal side effects were transient and managed through gradual dose escalation. These results show that semaglutide provides multiple benefits of glycemic control, significant weight loss, and secondary cardiometabolic stabilization, emphasizing its utility as a high-priority agent in the management of obesity-associated diabetes.

Keywords: Semaglutide; Type 2 Diabetes Mellitus; Incretin Therapy; Cardiometabolic Risk; Glucagon-like peptide-1 receptor agonist.

1. Introduction

Type 2 Diabetes Mellitus (T2DM) is characterized by insulin resistance, progressive beta-cell failure, and systemic inflammation, often exacerbated by excess adiposity. The clinical management of T2DM is no longer confined to achieving euglycemia but extends to the prevention of macrovascular and microvascular complications, which remain the primary drivers of mortality in this population [1]. Despite the availability of traditional oral antidiabetic agents, a significant portion of patients fail to maintain glycemic targets, often due to the weight-promoting effects of certain therapies or the inability of conventional drugs to address the underlying metabolic syndrome [2].

The incretin effect, mediated primarily by Glucagon-Like Peptide-1 (GLP-1), is significantly blunted in individuals with T2DM. GLP-1 is an intestinal hormone that stimulates glucose-dependent insulin secretion while simultaneously inhibiting glucagon release from alpha cells [3]. Beyond its pancreatic actions, GLP-1 slows gastric emptying and acts on the hypothalamus to enhance satiety and reduce caloric intake [4]. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) were developed to exploit these pathways while resisting degradation by the dipeptidyl peptidase-4 (DPP-4) enzyme. These agents offer a low risk of hypoglycemia with a profound weight-loss potential [5].

Semaglutide is a potent, long-acting GLP-1 RA with a structural modification that allows for weekly administration. Large-scale clinical trials, such as the SUSTAIN and SELECT programs, have established its superiority over other GLP-1 RAs and traditional agents in reducing HbA1c and body weight [6, 7]. Semaglutide has showed significant cardiovascular benefits, including a reduction in the rate of major adverse cardiovascular events (MACE) such as myocardial infarction and stroke [8]. This is particularly relevant for patients with a long duration of diabetes, where the risk of atherosclerotic cardiovascular disease (ASCVD) is high.

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The relationship between obesity and T2DM is bidirectional; weight gain worsens insulin resistance, while poor glycemic control often leads to further metabolic dysfunction. Clinical guidelines now focus on weight management as a primary treatment goal for obese patients with T2DM [9]. Using GLP-1 RAs early in the treatment algorithm addresses this "diabesity" epidemic by targeting the hormonal dysregulation that prevents successful weight loss through lifestyle changes alone [10]. This case report provides one such observation of the metabolic and cardiometabolic improvements associated with semaglutide in a diabetic patient.

2. Case Presentation

2.1. Clinical History and Symptomatology

A 48-year-old female presented to the outpatient clinic with a decade-long history of Type 2 Diabetes Mellitus (T2DM). Despite previous therapeutic efforts, the patient reported a progressive worsening of metabolic control over the preceding twelve months. Primary complaints included persistent polyuria, polydipsia, and a marked degree of fatigue that interfered with daily activities. Significant weight gain was also noted, which the patient attributed to a sedentary lifestyle and a lack of structured nutritional guidance. The patient's medical history was significant for Stage 1 hypertension and Grade II obesity. Her existing pharmacological regimen consisted of Metformin (1000 mg twice daily) and Amlodipine (5 mg once daily). Prior attempts to manage blood glucose with secondary oral agents had been discontinued due to poor adherence or inadequate efficacy.

Table 1. Patient History and Clinical Parameters

Parameter	Value	Clinical Significance
Age	48 Years	Mid-life metabolic transition
Duration of T2DM	10 Years	Established insulin resistance/beta-cell decline
Weight	92 kg	Grade II Obesity
BMI	36 kg/m²	High metabolic risk
Blood Pressure	138/90 mmHg	Stage 1 Hypertension
Baseline Medications	Metformin 1000mg BID; Amlodipine 5mg OD	Standard dual-pathway therapy
Comorbidities	Obesity, Hypertension	High cardiovascular risk profile

2.2. Baseline Clinical and Laboratory Assessment

At the time of clinical enrollment, the patient's weight was 92 kg with a Body Mass Index (BMI) of 36 kg/m². Blood pressure was recorded at 138/90 mmHg, indicating suboptimal control on monotherapy. Laboratory investigations revealed a severely elevated glycated hemoglobin (HbA1c) of 10.2%, with fasting plasma glucose (FPG) and postprandial glucose (PPG) levels at 180 mg/dL and 310 mg/dL, respectively. Given the long duration of T2DM, a renal function panel was prioritized to assess the safety of the current Metformin dose and establish a baseline for the introduction of a GLP-1 receptor agonist. The serum creatinine was 0.85 mg/dL, with an estimated Glomerular Filtration Rate (eGFR) of 82 mL/min/1.73 m², indicating stable renal function (Stage 2 Chronic Kidney Disease). The lipid profile showed significant dyslipidemia, characterized by Low-Density Lipoprotein (LDL) at 145 mg/dL and Triglycerides at 220 mg/dL.

3. Therapeutic Intervention

3.1. Stepwise Pharmacological Titration of Semaglutide

To minimize the risk of gastrointestinal adverse effects a common barrier to GLP-1 RA adherence a cautious, stepwise titration protocol was initiated. In accordance with clinical best practices and manufacturer guidelines, the patient began subcutaneous semaglutide at a dose of 0.25 mg once weekly. This initial phase continued for four weeks to allow for gastrointestinal desensitization.

Table 2. Stepwise Semaglutide Titration

Phase	Dosage	Duration	Clinical Objective
Initiation	0.25 mg weekly	Weeks 1 – 4	Gastrointestinal tolerability and desensitization
Escalation	0.5 mg weekly	Weeks 5 – 8	Intermediate glycemic and appetite control
Maintenance	1.0 mg weekly	Weeks 9 – 20	Sustained therapeutic weight loss and HbA1c reduction

Following the successful completion of the initiation phase, the dose was escalated to 0.5 mg once weekly for an additional four weeks. Upon verifying that the patient tolerated the intermediate dose without significant nausea or dyspepsia, a maintenance dose

of 1 mg once weekly was established starting at week nine. This 8-week titration pathway ensured that the 1 mg therapeutic dose was reached safely, prioritizing long-term patient persistence over rapid escalation.

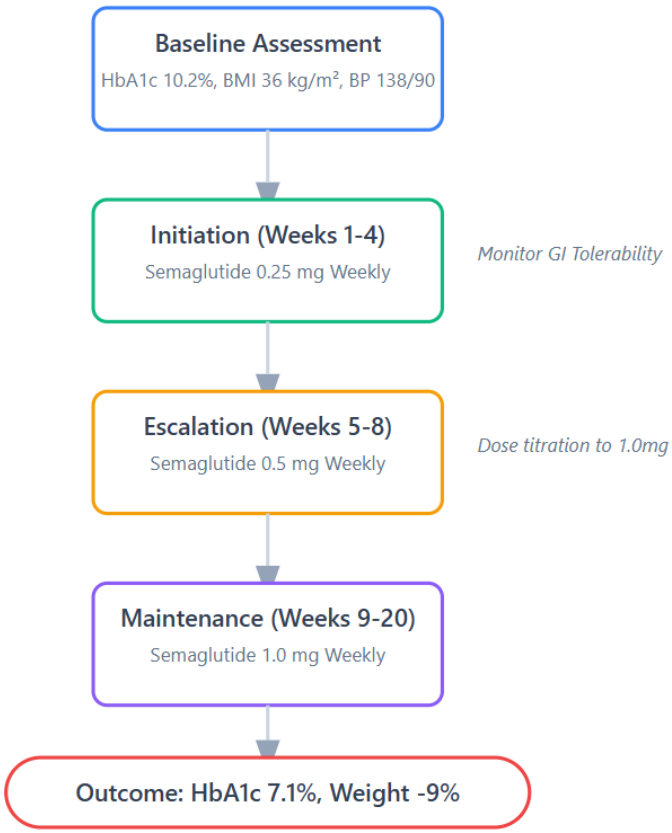

Figure 1. Clinical Management of the Patient with Semaglutide

3.2. Lifestyle and Nutritional Interventions

The pharmacological intervention was supported by a structured lifestyle modification program. The patient was shifted to a Mediterranean-style dietary pattern, involving the intake of monounsaturated fats, lean proteins, and complex carbohydrates with a low glycemic index. Total caloric intake was restricted to approximately 1,500 kcal per day. A physical activity regimen was instituted, targeting 150 minutes of moderate-intensity aerobic exercise per week, complemented by light resistance training to preserve lean muscle mass during weight loss.

4. Clinical Outcomes

4.1. Glycemic Response and Weight Reduction

Significant metabolic improvements were observed at the 12-week and 20-week follow-up intervals. By week 12, the patient's HbA1c had decreased from 10.2% to 8.0%. At the final 20-week assessment, the HbA1c reached 7.1%, representing a total reduction of 3.1% from baseline.

Table 3. Longitudinal Metabolic and Anthropometric Outcomes

Clinical Marker	Baseline	Week 12	Week 20	Net Change (Δ)
HbA1c (%)	10.2	8.0	7.1	-3.1%
Fasting Glucose (mg/dL)	180	120	110	-70 mg/dL
Postprandial Glucose (mg/dL)	310	165	145	-165 mg/dL
Body Weight (kg)	92	87.5	83.5	-8.5 kg (-9.2%)
Body Mass Index (BMI)	36	33.8	32.8	-3.2 kg/m²

Fasting plasma glucose stabilized at 110 mg/dL. The weight loss trajectory was consistent with the glycemic improvement. The patient's weight decreased from 92 kg to 83.5 kg over the 20-week period, achieving a 9% reduction in total body weight. This resulted in a BMI reduction from 36 kg/m² to 32.8 kg/m². The patient reported a substantial increase in energy levels and a marked reduction in polyuria and polydipsia.

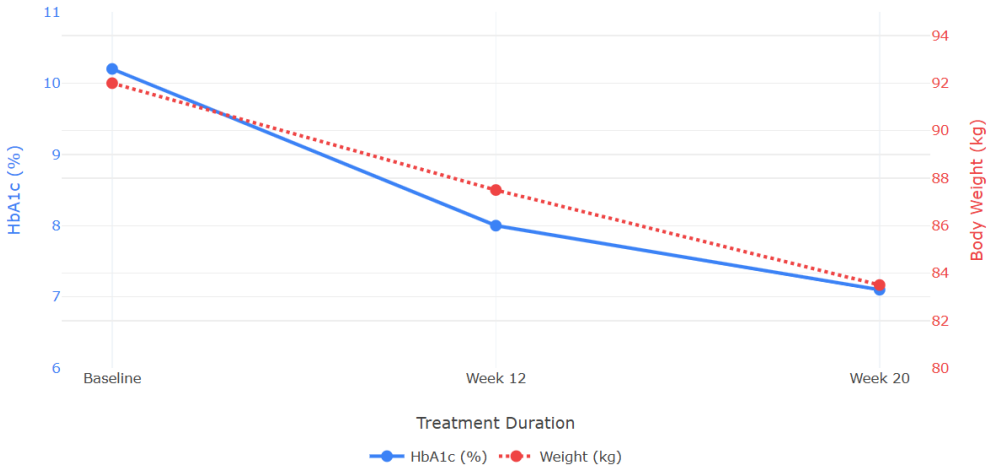

Figure 2. 20-week monitoring of HbA1c (%) and Total Body Weight (kg)

4.2. Cardiometabolic and Renal Outcomes

The reduction in adiposity had a secondary beneficial effect on hemodynamic stability. Blood pressure decreased from 138/90 mmHg to 128/82 mmHg. Given this improvement and the patient's consistent weight loss, the clinical team initiated a de-escalation of the antihypertensive regimen, ultimately maintaining stable pressure with the original 5 mg Amlodipine dose despite the patient's history of rising pressures. The lipid profile also showed favorable transitions, with LDL cholesterol dropping to 120 mg/dL and triglycerides reducing to 180 mg/dL. Renal monitoring at week 20 confirmed that the eGFR remained stable at 84 mL/min/1.73 m², indicating no adverse impact on kidney function and suggesting potential long-term renoprotective stability often associated with GLP-1 RA therapy.

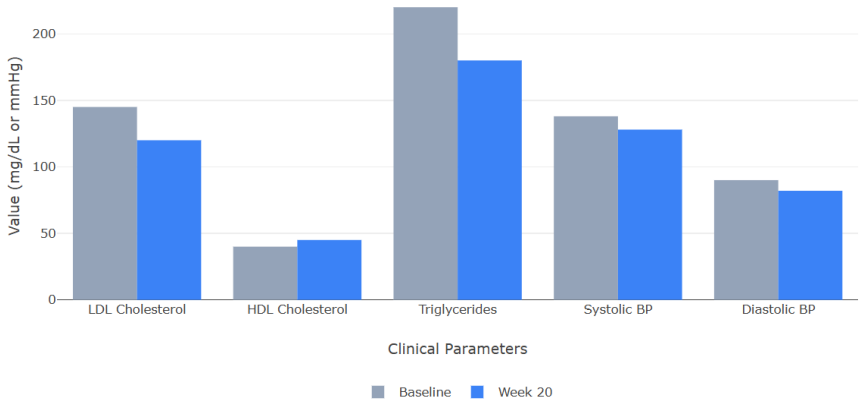

Figure 3. Secondary Cardiometabolic Improvements at 20 Weeks

Table 4. Secondary Cardiometabolic and Renal Parameters

Parameter	Baseline	Week 20	Clinical Interpretation
Blood Pressure (mmHg)	138/90	128/82	Hemodynamic stabilization
LDL Cholesterol (mg/dL)	145	120	Reduced atherosclerotic risk
HDL Cholesterol (mg/dL)	40	45	Improved lipid transport
Triglycerides (mg/dL)	220	180	Reduced insulin resistance marker
eGFR (mL/min/1.73 m²)	82	84	Renal function stability

5. Discussion

The clinical response observed in this patient, characterized by a 3.1% reduction in HbA1c over 20 weeks, exceeds the primary outcomes reported in several landmark trials. In the SUSTAIN-2 and SUSTAIN-3 programs, semaglutide consistently demonstrated HbA1c reductions ranging from 1.5% to 1.8% [11]. The heightened response in this case is likely a result of the high baseline HbA1c of 10.2%, as the magnitude of glycemic reduction with GLP-1 receptor agonists is often proportional to the initial degree of hyperglycemia. The combination between pharmacological therapy and rigorous adherence to a Mediterranean-style diet likely increased the glucose-lowering effects, showing the importance of an all round care model.

Table 5. Adverse Events and Tolerability

Symptom	Severity	Duration	Management / Outcome
Nausea	Mild	Transient (Weeks 1, 5)	Resolved without antiemetics
Dyspepsia	Mild	Occasional (Post-titration)	Managed with dietary counseling
Diarrhea	None	N/A	High tolerability achieved
Hypoglycemia	None	N/A	No events reported; Metformin continued
Treatment Adherence	Excellent	20 Weeks	Patient remained persistent on therapy

The 9% reduction in total body weight reflects the unique multi-organ mechanism of semaglutide. Unlike traditional oral antidiabetics like sulfonylureas or insulin, which are often weight-neutral or weight-promoting, semaglutide modulates the central nervous system to enhance satiety and reduce food cravings [12]. By delaying gastric emptying, the agent ensures a more gradual postprandial glucose rise while maintaining a prolonged feeling of fullness. The transition from a BMI of 36 kg/m² to 32.8 kg/m² is clinically significant, as even a 5% weight loss is associated with improved insulin sensitivity and a reduction in the pro-inflammatory markers secreted by visceral adipose tissue.

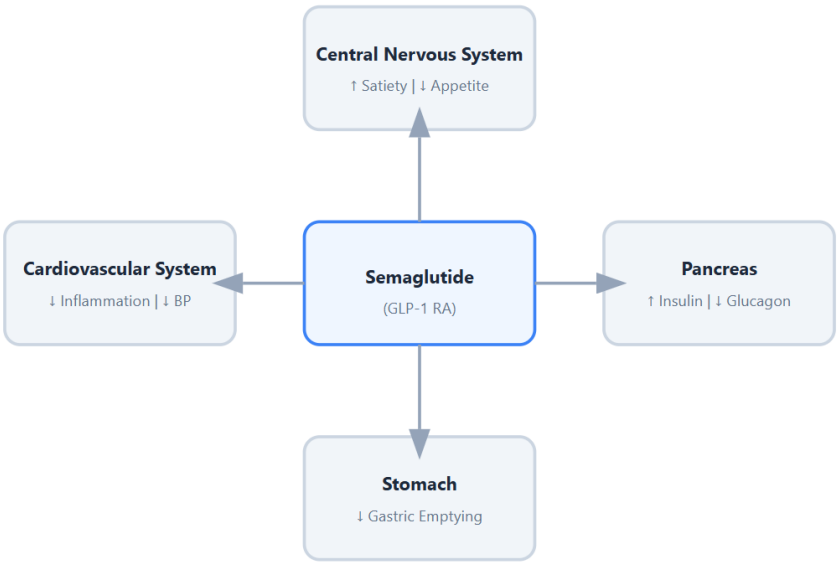

Figure 4. Therapeutic Mechanism of Semaglutide on Various Organ Systems

One of the most noteworthy outcomes in this case was the improvement in blood pressure and lipid profiles. The reduction of blood pressure to 128/82 mmHg allowed for a stabilization of the patient's cardiovascular risk profile without the need to escalate Amlodipine dosages. This hemodynamic benefit is a known secondary effect of weight loss and the potential direct effects of GLP-1 RAs on vascular endothelium [13]. Improvements in triglycerides and LDL cholesterol further suggest a systemic metabolic shift. Given the patient's 10-year history of diabetes, these cardiometabolic gains are vital for preventing long-term atherosclerotic complications, as highlighted by the cardiovascular outcomes trials (CVOTs) for this drug class [6]. A critical factor in the success of this intervention was the adherence to a standard 8-week titration schedule. Clinical experience suggests that rapid escalation of semaglutide can lead to significant nausea and vomiting, often resulting in premature treatment discontinuation. The severe gastrointestinal distress was avoided by maintaining the 0.25 mg and 0.5 mg doses for four weeks each.

The stability of the patient's renal function (eGFR) throughout the study period is reassuring. While GLP-1 RAs are not primarily cleared by the kidneys, monitoring renal function is essential in long-standing T2DM patients to ensure the safety of concomitant Metformin and to track potential renoprotective benefits [14]. The stability of the eGFR in this case suggests that semaglutide is a safe and effective option even as patients age or present with mild renal impairment.

6. Conclusion

The management of this 48-year-old patient discussed in the case report shows that semaglutide can act as a valuable drug for treating both Type 2 Diabetes and obesity. A profound reduction in glycated hemoglobin and weight, alongside improvements in blood pressure and lipid metabolism through 20-week intervention. These findings support the early adoption to GLP-1 receptor agonists in patients who fail to meet glycemic targets with metformin alone, particularly when obesity and cardiovascular risks are present. The successful stabilization of metabolic parameters in this case shows the necessity of combining advanced pharmacotherapy with lifestyle interventions to achieve desired long-term outcomes.

Compliance with ethical standards

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Conflict of interest statement

All the authors of this manuscript disclose that they have no possible conflicts of interest or competing interests with the publication of the manuscript or any institution or product that is mentioned in the manuscript. There is no financial or personal relationship with people or organizations that could inappropriately influence or bias the outcome of the study presented.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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