

Semaglutide Treatment in a Patient with Extreme Obesity and Massive Lymphedema: A Case Report

Joanne Thanh-Tâm Nguyen^a Marie-Amélie Barbet-Massin^a Emilie Pupier^a
Alice Larroumet^a Laurène Bosc^a Marie Michelet^a
Maud Monsaingeon-Henry^a Blandine Gatta-Cherifi^{a, b, c}

^aService d'endocrinologie, diabétologie et maladies métaboliques, CRM Pradort, CHU de Bordeaux, Bordeaux, France; ^bEquipe «Physiopathologie de la balance énergétique et obésité» Neurocentre Magendie. INSERM U1215. Université de Bordeaux, Bordeaux, France; ^cUniversité de Bordeaux, UFR des sciences médicales, Bordeaux, France

Keywords

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Abstract

Introduction: Extreme obesity (BMI ≥ 50 kg/m²) is a complex pathology to treat. One of the complications of extreme obesity is massive localized lymphedema (MLL), due to compromised lymphatic drainage. There is a lack of literature guiding the medical management of these conditions. **Case Presentation:** We present a 43-year-old male who was admitted to our specialized obesity center for weight management. His initial weight was 255 kg and BMI was 93.7 kg/m². He suffered from massive multifocal lymphedema of his left leg. He was bedridden due to his condition and malnourished, as shown by multiple vitamin deficiencies. The patient received care from our multidisciplinary team including nurses, dieticians, physical therapists, and psychologists. Treatment with semaglutide was started in hospital and continued at home. The maximal dose used was 1 mg/week but decreased during follow-up to 0.25 mg/week to avoid malnutrition. Protein and nutritional supplements were

added. At 28 weeks of therapy, the patient had lost 40 kg or 15.7% of his total body weight. His lymphedema decreased; he had lost at least 16 cm of his left thigh circumference. He was able to walk again and regain autonomy of his daily activities of living. **Conclusion:** Semaglutide can be effective in patients with extreme obesity, with the support of a multidisciplinary team in a specialized obesity center. It can also help decrease MLL. More data are needed to guide medical treatment of patients with extreme obesity and MLL.

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Introduction

Patients with extreme obesity (BMI ≥ 50 kg/m²) are a challenging population to treat. Indeed, they often have multiple comorbidities [1], significantly impaired functional status, and a morphology that limits the ability to perform medical investigations and treatments. Extreme obesity is likely to be encountered more often with the ongoing rise of obesity [2]. Unfortunately, there is a

paucity of literature regarding the management of this complex condition.

One complication associated with extreme obesity is massive localized lymphedema (MLL). MLL is swelling caused by compromised lymphatic drainage in the setting of obesity. Obesity causes lymphedema by various mechanisms, such as the accumulation of inflammatory cells around lymphatic vessels, increased permeability of these vessels, and augmented volume of interstitial fluid. MLL can cause discomfort, pain, and impaired mobility in affected patients and often requires excisional surgery [3].

The recent arrival of glucagon-like peptide-1 receptor agonists (GLP1-RAs) has changed the paradigm of obesity management, due to their effectiveness in producing weight loss. Of these, semaglutide has shown the most impressive results [4]. However, there is little description of their use in patients with extreme obesity. Here, we present a case report of a patient with extreme obesity complicated by multifocal localized lymphedema, who had a remarkable response to semaglutide treatment.

Case Presentation

A 43-year-old male was admitted to our specialized obesity center for the management of his extreme obesity and lymphedema. He received evaluation and care by our multidisciplinary team including nurses, dietitians, physical therapists, and psychologists.

This patient lived in his trailer with his mother and nine brothers and sisters. He was illiterate and unemployed. There was obesity among other members in his family, known for consanguinity. The patient had not had medical follow-up in years; he was thus known solely for his obesity, which arose during childhood.

Burdened by his weight, the patient had not left the trailer in over a year. He walked a few steps with the help of his brothers to use the bathroom; he was otherwise bedridden. He could only perform the hygiene of his upper body and needed assistance to get dressed. He was short of breath on effort and experienced pain in his legs, more importantly the left one, when standing. Upon dietary history, he used to eat all day, mostly lipid-rich or processed foods, and ate two to three servings per meal. He eventually only ate during mealtimes. Over the past few weeks, however, he was only able to eat fruits due to mouth ulcers.

On physical exam at admission, his vital signs were blood pressure 189/89 mm Hg, pulse 92 beats per minute,

and oxygen saturation 91% on room air. His weight was 255 kg and height was 165 cm, resulting in a BMI of 93.7 kg/m² (shown in Table 1). The most prominent feature on exam was the massive multifocal lymphedema of his left leg (shown in Fig. 1). The skin of his left leg was thickened, hyperpigmented, and showed multiple purulent or crusted wounds. His right leg had mild lymphedema.

Multiple investigations were performed to assess obesity-related comorbidities. Blood work showed pre-diabetes, mildly elevated liver enzymes, and elevated C-reactive protein (shown in Table 1). Furthermore, he had macrocytic anemia, low albumin and prealbumin concentrations, and multiple nutritional deficiencies: vitamin A, B9, D, selenium, and zinc. Pulmonary evaluation revealed severe obstructive sleep apnea (OSA) with obesity hypoventilation syndrome. An indirect calorimetry test showed a resting energy expenditure of 2,903 kcal/day; the estimated expenditure calculated via the Harris-Benedict equation for this patient was 4,108 kcal/day. Our panel genetic test did not reveal any variants in 18 genes linked to monogenic obesity. A subsequent comparative genomic hybridization array did not show any deletions or duplications within his genome.

Treatment with semaglutide was started at 0.25 mg weekly during hospitalization. During his stay, the patient ate the balanced hospital meals. He and his family received teaching and documentation on a healthy diet by our dietitians. For the wounds on his leg due to the lymphedema, the nurses performed gentle skin washing and covered them with multilayered bandages. The large size of his leg precluded compression bandaging. In addition, the patient received antihypertensive medication, vitamin supplementation, a continuous positive airway pressure machine and oxygen therapy for his blood pressure, vitamin deficiencies, OSA, and obesity hypoventilation syndrome, respectively.

The patient was hospitalized for 17 days. Upon discharge, home visits were organized with nursing to perform his weekly semaglutide injections (0.25 mg weekly for 4 weeks, then increased to 0.5 mg weekly) and wound care.

Patient Evolution

Over the following months, the patient had three short hospital stays (3–4 days) at weeks 6, 13, and 28 of semaglutide treatment, for reevaluation of his obesity and lymphedema. He continued to receive coaching and support from the multidisciplinary

Table 1. Clinical and biological parameters before and at 28 weeks of semaglutide treatment

	At baseline	At week 28 of semaglutide treatment
Clinical parameters		
Body weight, kg	255	215
BMI, kg/m ²	93.7	79.0
Weight loss, kg (%)	–	40 (15.7)
Systolic blood pressure, mm Hg	189	135 ^a
Diastolic blood pressure, mm Hg	90	72 ^a
Right-hand grip, kg	55.2	61.7
Biological parameters		
HbA1c, %	6.3	5.9
Triglycerides, <i>N</i> 0.4–1.7 g/L	1.49	1
HDL cholesterol, <i>N</i> >0.4 g/L	0.33	0.31
LDL cholesterol, g/L	1.06	1.4
Non-HDL cholesterol, g/L	1.36	1.6
AST, <i>N</i> 5–34 UI/L	54	18
ALT, <i>N</i> 6–55 UI/L	66	15
GGT, <i>N</i> 12–64 UI/L	27	12
Alkaline phosphatase, <i>N</i> 40–150 UI/L	62	48
CRP, <i>N</i> <5 mg/mL	30.7	17.1

N, normal. ^aAt the last follow-up, he was also on dual hypertensive therapy.

**Fig. 1.** A picture of the patient lying on his left side, taken from behind. The most prominent feature is the massive multifocal lymphedema of his left leg.

team during admission. With regard to his semaglutide treatment, the dose was increased to 1 mg weekly at week 6, at which weight loss had already begun. The patient and his family had difficulty understanding the dietary recommendations and tended to restrict the patient's food intake to favor weight loss. The dose was thus decreased to 0.25 mg weekly at week 13 to avoid further malnutrition. Protein powder prescribed 4 times a day was started at this time. Due to continued weight loss, semaglutide dose was maintained at 0.25 mg weekly at week 28, the time of his last in-hospital follow-up.

By 28 weeks of semaglutide therapy, the patient had lost 40 kg (–15.7% of his total body weight [TBW]), lowering his weight to 215 kg and BMI to 79 kg/m² (shown in Table 1). The massive lymphedema of his left leg improved significantly: between weeks 6 and 13, the circumference of the base of his left thigh decreased from 129 to 113 cm (–12.4%). The wounds on this leg had healed with the skin care by his nurses. With his weight loss and physical therapy training, he was now able to walk 100 m, get dressed, and perform personal hygiene without aid. His right-hand grip measured by dynamometer increased from 55.2 to 61.7 kg. He experienced less pain in his legs, and his general well-being had majorly enhanced.

His obesity-related comorbidities improved as well: his blood pressure was controlled on dual hypertensive therapy, his prediabetes resolved, and his OSA was clinically less severe. Furthermore, his liver function tests normalized, and CRP levels decreased (shown in Table 1). From a nutritional standpoint, his dietary intake was still restrictive. A single supplemental nutrition drink per day was added along with his protein powder at last follow-up. All initial vitamin deficiencies resolved with supplementation. For the management of his obesity, the patient was to continue semaglutide treatment and follow-up with short hospitalizations at our obesity center. He was also awaiting admission to a specialized rehabilitation center.

Discussion

This clinical case demonstrated the efficacy of semaglutide in a patient with extreme, disabling obesity. After 28 weeks of treatment, the patient lost 15.7% of his TBW. This is a significant amount despite using submaximal doses, and his weight was still trending down at last follow-up. The average weight loss in the STEP 1 trial was 14.9% at 68 weeks of treatment [4]. However, since none of the STEP trials included patients with BMIs ≥ 50 kg/m², it is difficult to predict therapy response in these patients [4–11]. There are unfortunately little data on the use of GLP1-RAs in patients with extreme obesity. Our literature review uncovered a single case report by Figueredo et al. [12] describing liraglutide followed by semaglutide therapy in a 37-year-old female with a weight of 314 kg and BMI of 108.7 kg/m². After 6 weeks of liraglutide treatment and 26 weeks of semaglutide treatment, the patient had lost 79.5 kg (–25.2% of TBW). More data are needed regarding the efficacy and management of GLP1-RA in patients with extreme obesity.

A second highlight of this case is the improvement of the multifocal massive lymphedema of the patient's left leg, the first description of the sort in the context of GLP1-RA treatment. General recommendations of MLL involve skin care, lymphatic massage, compression therapy, and, in most cases, surgical excision of the mass [3, 13]. In our patient, regular skin care allowed for the healing of the skin wounds associated with the lymphedema. Compression bandages could not be used given his leg's width. The decrease in his lymphedema is likely due to the overall weight loss of the patient induced by semaglutide. Whether GLP1-RAs have a direct effect on lymphedema is yet to be determined. GLP1-RAs can improve inflammation as illustrated by the decrease of inflammatory markers during treatment; perhaps this may have a beneficial effect on lymphedema [14]. For this patient, surgical resection of the lymphatic masses will be unnecessary with continued weight loss. However, if indicated, it will most likely be easier to perform due to their decreased size. Weight loss by GLP1-RA treatment before surgical excision may thus be considered in future cases of MLL.

One of the challenges of this case was managing the nutritional status of the patient [15]. Although counterintuitive, people with obesity can be malnourished for many reasons, such as an important intake of energy-dense but nutrient-poor foods and changes in nutrient metabolism caused by systemic inflammation. They also often present with multiple vitamin deficiencies, most commonly vitamins B1, B9, B12, C, D, and E [16]. Our

patient's diet was very unbalanced preadmission, leading to a macrocytic anemia, low albumin and prealbumin levels, and many vitamin deficits. He had difficulty understanding and adhering to our dietary recommendations at home, leading to the need for protein and nutrient supplementation. This case emphasizes the importance of thorough and regular nutritional evaluations and continued follow-up with dieticians in patients with obesity.

Finally, this patient's favorable evolution would not be possible without the aid of the rest of our multidisciplinary team which included nurses, physical therapists, and psychologists. The nurses' home visits made regular wound care and semaglutide injections possible, the physical therapists helped the patient boost his functional capacity, and the psychologists offered emotional support. Patients with obesity, especially when extreme, require holistic management to improve their health and overall well-being.

The main limitation of this study is that the observation was over a relatively short period of 28 weeks with submaximal doses of semaglutide; therefore its full benefits on the patient's weight loss and massive lymphedema are unknown. We also did not have details on his body composition at baseline and throughout treatment, due to the limitations of his body habitus. However, we will obtain his body composition through dual-energy x-ray absorptiometry once his weight falls below 200 kg, the maximum allowed weight for the designated machine. When the nutritional status of the patient improves, an increase in dose of semaglutide could be considered to stimulate further weight decrease. Furthermore, he may be a candidate for bariatric surgery at our specialized center. Although bariatric surgery in patients with a BMI of ≥ 70 kg/m² may be associated with increased mortality, patients can obtain significant weight loss and major improvements in their comorbidities and functional status [17].

Conclusion

To conclude, our case report shows that GLP1-RA treatment with semaglutide can be effective in treating patients with extreme obesity and MLL. To obtain these benefits, the support of a multidisciplinary team in a specialized obesity center is essential. Further research regarding the medical treatment of patients with extreme obesity and its complications is needed to optimize their management.

Statement of Ethics

Written informed consent was provided by the patient for the publication of this article and any accompanying images. The approval of this study was not required by the Ethics Committee in accordance with local guidelines.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Laurène Bosc, Marie-Amélie Barbet-Massin, Emilie Pupier, Alice Larroumet, and Blandine Gatta-Cherifi participated in the care of the patient. Joanne Nguyen collected the patient data, prepared the table and figure, and drafted and edited the manuscript. Blandine Gatta-Cherifi supervised the editing of the manuscript. All aforementioned authors as well as Marie Michelet and Maud Monsaingeon-Henry reviewed and approved the final manuscript.

Data Availability Statement

The data supporting the findings of this article are available within the text. Any inquiries regarding the data may be sent to our corresponding author.

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