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〔Case Report〕

A case of an obese, infertile Japanese woman with type 2 diabetes mellitus achieving a favorable and safe pregnancy outcome after laparoscopic sleeve gastrectomy

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Abstract

【Background】Obesity is widely known to be a major factor associated with infertility, and weight loss is often recommended to improve fertility in women of reproductive age. One treatment for morbid obesity is metabolic surgery. In obese women with infertility, metabolic surgery has been found to affect pregnancy outcomes. Furthermore, in Japan, infertility treatment has been covered by public insurance since 2022, and obesity with infertility is expected to become an increasingly important social issue. However, there are only a few reports of pregnancy and delivery after surgical weight loss in Japan.

【Case presentation】A 29-year-old woman with a history of type 2 diabetes mellitus and polycystic ovary syndrome was referred to our hospital with morbid obesity and infertility. The patient had undergone infertility treatments for two years but had not been able to become pregnant. At the first visit, her weight was 105.5 kg, and her body mass index was 39.0 kg/m^2. When six months of medical therapy failed to achieve sufficient weight loss, the patient was referred to our department for surgical intervention. A preoperative weight loss program was performed for two weeks in the hospital, and then laparoscopic sleeve gastrectomy was performed. Thirteen months after the operation, her weight had decreased to 76.0 kg, with a body mass index of 28.1 kg/m^2. No anti-diabetic agents were administered after the surgery, and there were no episodes of hyperglycemia. Infertility treatment was continued after the operation, and the patient became pregnant in the first cycle of in vitro fertilization at 12 months after the operation. The entire pregnancy course was uneventful, and a newborn of 3373 g was delivered

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by vaginal delivery at 40 weeks and 1 day of gestation, which was 20 months after the operation. There were no pregnancy complications, including gestational diabetes mellitus, pregnancy-induced hypertension, or maternal anemia.

【Conclusions】 We encountered a case in which weight loss was obtained promptly after laparoscopic sleeve gastrectomy, leading to a successful pregnancy and delivery. With proper multidisciplinary management, it is possible to become pregnant and deliver safely after surgical weight loss.

***Key words*: morbid obesity, infertility, laparoscopic sleeve gastrectomy, diabetes mellitus**

Ⅰ. Introduction

The global prevalence of obesity is increasing every year. If present trends continue, by 2025, the global obesity prevalence will exceed 21% in women over 18 years old[1]. Furthermore, obesity has been widely known to be a major factor of infertility, and weight loss is often recommended to improve fertility in women of reproductive age[2].

One treatment for morbid obesity is metabolic surgery. In obese women with infertility, metabolic surgery has been found to affect pregnancy outcomes[3-6]. Furthermore, in Japan, infertility treatment has been covered by public insurance since 2022. While obesity with infertility is expected to become an increasingly important social issue, there are only a few reports of pregnancy and delivery after surgical weight loss in Japan.

We herein report a case of pregnancy after metabolic surgery for morbid obesity with infertility along with a literature review.

Ⅱ. Case

A 29-year-old woman with a history of type 2 diabetes mellitus (T2DM) and polycystic ovary syndrome was referred to our hospital with morbid obesity and infertility. She had been gaining weight since around puberty, and her weight had reached 120 kg at 25 years old. Infertility treatments, including two instances of artificial insemination with her husband's semen (AIH), had been performed for two years, but the patient had not yet become pregnant.

At the first visit, the height, weight, and body mass index (BMI) of the patient were 164.4 cm, 105.5 kg, and 39.0 kg/m^2, respectively. She had medically taken empagliflozin and metformin for T2DM. Blood analyses revealed an increase in plasma glucose levels, HbA1c, serum triglycerides, and serum C-reactive protein levels (Table 1). After six-month medical management, the patient had not achieved sufficient weight loss and was referred to our department for surgical intervention.

When referred to our department, her weight was 101.0 kg. Plasma glucose levels and serum insulin

Table 1 Laboratory findings at the first visit

AST	13	U/L	HDL-Cho	64	mg/dL	WBC	7900	/μL
ALT	20	U/L	LDL-Cho	131	mg/dL	RBC	427×10^4	/μL
LDH	146	U/L	TG	303	mg/dL	Hb	13.2	g/dL
ALP	139	U/L	Na	139	mmol/L	Hct	39.8	%
γ-GTP	25	U/L	K	4.4	mmol/L	Plt	23.9×10^4	/μL
TP	6.8	g/dL	CRP	0.41	mg/dL			
Alb	4.0	g/dL	Glu	181	mg/dL	TSH	2.002	μIU/mL
BUN	15	mg/dL	HbA1c	6.7	%	FT3	2.82	pg/mL
Cre	0.84	mg/dL				FT4	0.96	mg/dL

levels were 191 mg/dL and 39 μIU/mL, respectively, and homeostasis model assessment of insulin resistance (HOMA-IR) score was 18.4. Computed tomography showed fatty liver. The calculated visceral fat area was 89.7 cm^2 with a subcutaneous fat area of 572.7 cm^2, measured at level of the umbilicus, and the V/S ratio was 0.18 (Fig. 1). Upper gastrointestinal endoscopy and upper gastrointestinal series revealed no abnormalities in the esophagus, stomach, or duodenum.

A preoperative weight loss program was performed for 2 weeks during hospitalization. The weight was 95.9 kg, and HOMA-IR score was 3.6 before surgery. Preoperative nutritional status was normal with Controlling Nutritional Status (CONUT) score of 0.

Laparoscopic sleeve gastrectomy (LSG) was performed under general anesthesia. The skin incisions and port size are shown in Fig. 2a. Blood vessels along the wall of the greater curvature of the stomach were dissected. A 12-mm-diameter lower gastrointestinal endoscope was inserted into the stomach to determine the resection line. Normally, a 36-Fr (12 mm) Nelaton catheter would be used, but in this case, a lower gastrointestinal endoscope of the same diameter was used because the patient had a latex allergy. The greater curvature side of the stomach was resected from 5 cm on the oral side of the pylorus to 1 cm on the anal side of the His angle, using a linear stapler with reinforced reload. The staple line on the oral side and the intersection of the staple line were reinforced with non-absorbable sutures. The operative time was 190 minutes, and there was only slight bleeding. The volume of the resected stomach was 350 ml (Fig. 2b).

Five months after the operation, her weight had decreased to 78.8 kg, with a BMI of 29.2 kg/m^2. Her nutritional status had remained normal with a CONUT score of 0. Blood analysis showed normalization of plasma glucose levels (87 mg/dL), HbA1c (5.2%), and serum CRP levels (0.05 mg/dL).

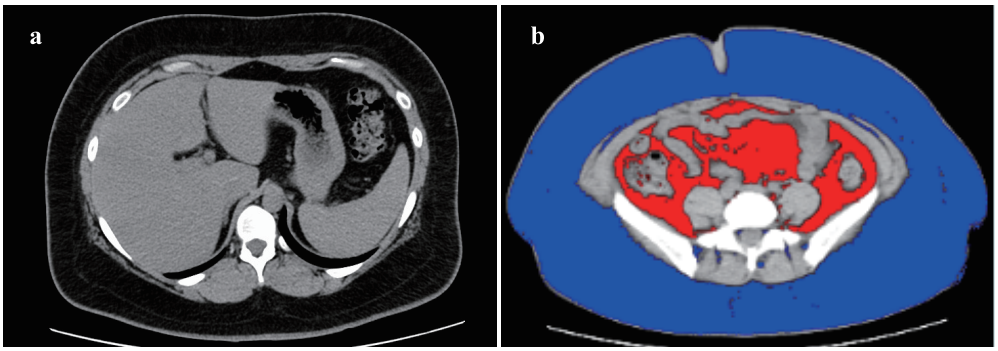

Fig. 1 Preoperative computed tomography images. a: Findings of fatty liver. **b**: Preoperative visceral fat area of 89.7 cm^2 and subcutaneous fat area of 572.7 cm^2, with a V/S ratio of 0.18.

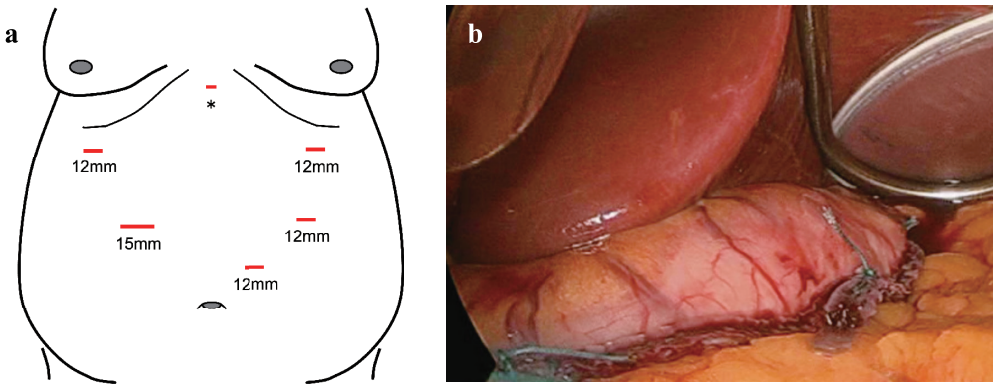

Fig. 2 Surgical schematic illustration and intraoperative photograph. a: Schematic illustration of skin incisions (red lines) with the layout and size of port shown. Shown in * is the skin incision for the Nathanson Hook Liver Retractor insertion. **b**: Intraoperative photograph with the complete gastric tube shown.

At thirteen months postoperatively, she weighed 76.0 kg and with a BMI of 28.1 kg/m^2. The HOMA-IR score was 1.5, and HbA1c was 5.5%. No anti-diabetic agents were administered after surgery, and there were no episodes of hyperglycemia.

Infertility treatment was resumed with adequate weight loss and nutritional stability achieved. Although AIH was performed both four and five months after the operation, the patient still did not become pregnant. Since she also had an ovulation disorder, in vitro fertilization (IVF) was suggested. Twelve months after the operation, the patient became pregnant in the first cycle of IVF (Fig. 3). The entire pregnancy course was uneventful, and a viable male newborn of 3373 g was delivered by vaginal delivery at 40 weeks and 1 day of gestation, which was 20 months after the operation. The maternal weight gain during pregnancy was 21.4 kg, and there were no pregnancy complications, including gestational diabetes mellitus, pregnancy-induced hypertension, and maternal anemia.

Ⅲ. Discussion

Metabolic surgery is performed for morbid obesity refractory to medical treatment and has been reported to provide better long-term weight loss than medical treatment[7]. Recent procedures commonly performed to this end include LSG, laparoscopic adjustable gastric banding, laparoscopic Roux-en-Y gastric bypass (LRYGB), and LSG with duodeno-jejunal bypass (LSG/DJB)[7]. Sleeve gastrectomy is the most frequently preformed metabolic surgery according to the Sixth IFSO Global Registry Report 2021[8], with 128382 cases (50.2% of the total) reported worldwide in the 5-year period from 2016 to 2020.

Obesity affects the sexual function through metabolic disorders of sex steroids, decreased sex hormone-binding globulin, abnormalities of adipocytokines, insulin resistance and hyperinsulinemia, and increased leptin, which interact to induce infertility[9]. Weight loss goals to improve infertility have not been established. Kort et al.[10]reported that patients who

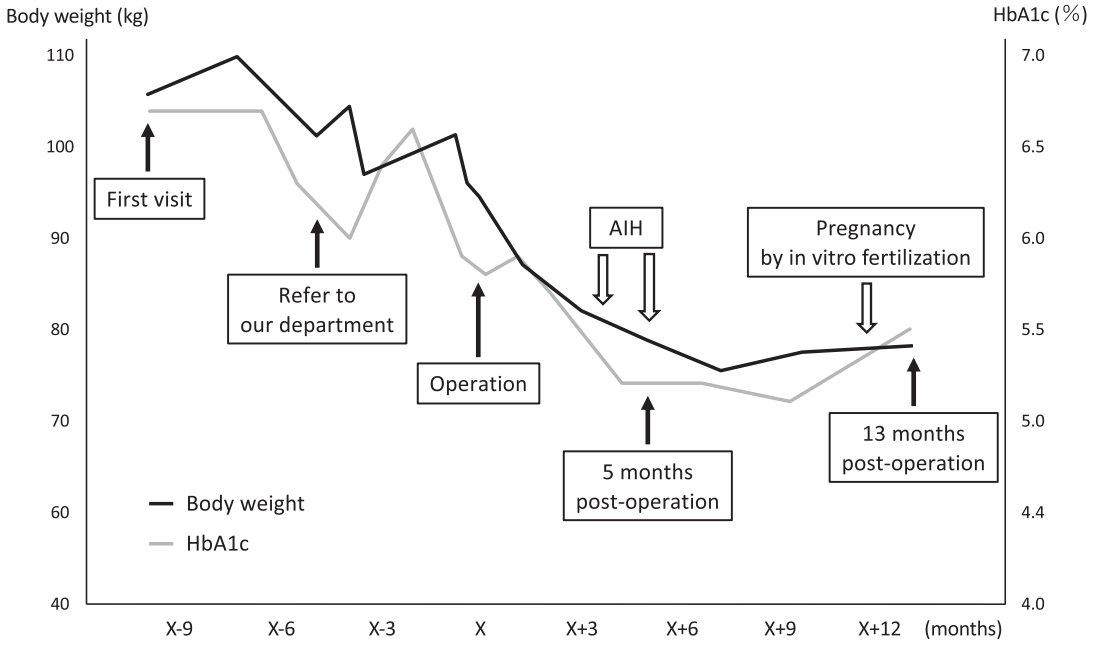

Fig. 3 Weight and HbA1c transition from the first visit to pregnancy. At the first visit, the patient's height, weight, BMI, and HbA1c were 164.4 cm, 105.5 kg, 39.0 kg/m^2, and 6.7%, respectively. After 6-month medical management, the patient was referred to surgery with a weight of 101.0 kg and HbA1c of 6.7%. A preoperative weight loss program was performed for 2 weeks during hospitalization, and preoperative weight and HbA1c were 95.9 kg and 6.6%, respectively. At 5 and 13 months postoperatively, the weight loss was 78.8 and 78.2 kg, respectively, and the percent of total weight loss from the time of surgery was 17% and 20%, respectively. Postoperative HbA1c remained below 6%. AIH was performed at 4 and 5 months postoperatively but did not achieve pregnancy, and pregnancy was achieved by IVF at 12 months postoperatively.

achieved a weight loss of 10% of their maximum weight had significantly higher pregnancy and live birth rates than those without such loss. In addition to reducing a woman's natural fertility, obesity is also associated with a patient's response to assisted reproductive technology, including IVF[11]. Bellver et al.[12]reported that the implantation rate, pregnancy rate, and live-birth rate after embryo transfer were significantly lower in the obese group (BMI ≥30 kg/m^2) than in groups with lower BMI values. A weight loss goal of ≥10% or a BMI of <30 kg/m^2 may therefore help improve infertility. In this case, IVF was not performed before weight loss, considering the low implantation rate in high BMI cases and the risk of pregnancy complications due to pregnancy with obesity. AIH was unsuccessful even after surgery, which may be due to acquired tubal factors. Although it is unclear whether weight loss contributed to getting pregnant in this case, we believe that weight loss before IVF was effective in reducing the risk of complications during pregnancy.

One of the clinical factors that can affect the outcome of pregnancy is the time interval from surgery to conception. A period of 12-18 months between surgery and conception is recommended by several reports, as maximal weight loss is observed and the risk of malnutrition for both the mother and the fetus is increased during this period[3,4]. Although the timing of resumption of fertility treatment is unclear, it is preferable to resume treatment once adequate weight loss and nutritional stability have been achieved.

Excessive weight gain during pregnancy increases the risk of pregnancy complications, including gestational diabetes mellitus and pregnancy-induced hypertension, while insufficient weight gain can affect fetal growth and increase the risk of small-for-gestational-age neonates[3]. The IOM guidelines [13]recommend an adequate weight gain of 7-11.5 kg for overweight (BMI 25-29.9 kg/m^2) and 5-9 kg for obesity (BMI ≥30 kg/m^2), however, there is no standard especially after metabolic surgery. Furthermore, in Japan, no unified standard for BMI ≥25 kg/m^2 is available. In this case, the patient was not strictly restricted to avoid malnutrition, and was allowed to gain weight if pregnancy complications did not appear. This resulted in excessive weight gain. It is necessary to consider the balance between malnutrition and the risk of pregnancy and perinatal complications for proper weight control.

Recent studies have shown that metabolic surgery, including gastric banding, sleeve gastrectomy, and Roux-en-Y gastric bypass, reduces the risk of gestational diabetes mellitus, Caesarean section, macrosomia, and large-for-gestational-age neonates[4]. However, it has also been reported that there is an increased risk of maternal nutritional deficiencies, low birthweight neonates, and small-for-gestational-age neonates with such procedures[4]. Rottenstreich et al.[5]reported the same results in their LSG group, but there are limited reports among purely LSG patients. Watanabe et al.[6]reported the impact on pregnancy and perinatal outcomes according to the surgical procedure at a single institution. Their study found no cases of maternal anemia, preterm birth, or Caesarean section after LSG. Interestingly, malabsorptive procedures, including LRYGB and LSG/DJB, with the most effective weight loss also had a relatively high frequency of maternal anemia and low birth weight. There may be some risk of maternal and fetal malnutrition after weight loss induction by metabolic surgery, so a continued careful nutritional assessment is required during pregnancy.

In the present case, LSG, which is currently covered by public insurance in Japan, was selected. The patient achieved sufficient weight loss relatively rapidly and was able to deliver her child without pregnancy complications with multidisciplinary follow-up.

Ⅳ. Conclusions

We herein report a case in which weight loss was obtained promptly after LSG, leading to a successful pregnancy and delivery. To ensure a safe pregnancy, it is important to follow up patients frequently before and after pregnancy with multiple departments, including surgery, internal medicine, gynecology, and obstetrics.

Contributors

Y. M, H. H, M. K, H. S, Y. K carried the surgical treatment. H. O responsible for drug treatment. N. N was in charge of infertility treatment. Y. K, K. H evaluated the medical images. Y. N wrote the manuscript under the supervision of R. O, H. H and H. M. All authors read and approved the final manuscript.

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Conflict of interest

H. M. is a member of the Editorial Board of the Chiba Medical Journal.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. This is not human research. This is not animal research.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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