

Original article : Case report

A case where a radical surgery was performed laparoscopically for progressive colorectal cancer complicated by morbid obesity after the reduction in body weight by sleeve gastrectomy

Takeshi Togawa¹⁾, Yuki Ozamoto¹⁾, Akeo Hagiwara²⁾

1) The Second Department of Surgery, Kusatsu General Hospital, Shiga, Japan

2) Faculty of Life and Medical Sciences, Doshisha University, Kyoto, Japan

Abstract

We experienced the case of progressive colorectal cancer complicated by morbid obesity (body mass index [BMI] 52.0 kg/m²). The stage of cancer progression was defined as the level where radical surgery could be applied as the standard therapeutic strategy. However, in view of the difficulties in surgery due to morbid obesity and risk of complications after surgery, chemotherapy and weight reduction treatment were conducted in advance. Fortunately, the chemotherapy before surgery successfully controlled the progression of cancer. However, as there was a limit to weight reduction through only nutritional guidance and exercise guidance, laparoscopic sleeve gastrectomy was performed in advance of the cancer surgery. As a result, further weight loss was achieved and type-2 diabetes and apnea syndrome, which are linked to obesity, were improved. Then, the radical surgery of colorectal cancer could be safely performed laparoscopically. In the case where a cancer patient is complicated by morbid obesity and required to lose weight rapidly and definitely, bariatric surgeries including laparoscopic sleeve gastrectomy can become powerful tools.

KEY WORDS: neoadjuvant chemotherapy, morbid obesity, weight reduction before surgery, colorectal cancer, laparoscopic sleeve gastrectomy and bariatric surgery

Introduction

Generally speaking, obese people tend to have stronger glycolytic stress than lean people. Performing surgery on obese patients is more difficult than on lean patients, so the same operator may have different results with surgical precision. In the case of morbidly obese patients with BMIs greater than 35 kg/m² in particular, unexpected dangers may occur in surgery. In this case, the author *et al.* conducting surgery on a patient with Stage IIIa progressive colorectal cancer complicated with morbid obesity, BMI of 52.0 kg/m². The guidelines for colorectal cancer treatment¹⁾ in Japan show surgery for the purposes of radical cure and post-operative adjuvant chemotherapy, therefore, chemotherapy before surgery is unusual. However, because of the difficulties in surgery caused by morbid obesity and the risks caused by complications, chemotherapy and body-weight reduction were conducted before surgery. Fortunately, chemotherapy was successful. However, because there was a limit to weight reduction though only nutritional guidance and exercise

guidance, it did not lead to a safe body weight for surgery. Therefore, before the surgery of cancer, laparoscopic sleeve gastrectomy was performed, and five months after, radical surgery of colorectal cancer was successfully conducted laparoscopically. This case is introduced as an example that bariatric surgery was effective for the case where radical surgery for progressive cancer was difficult due to morbid obesity.

Case

Patient:

Male 52 years old.

Main complaint:

Positive fecal occult blood test.

Previous diseases:

Diabetes, hypertension and sleep apnea syndrome.

Correspondence to: Takeshi Togawa, MD
The Second Department of Surgery, Kusatsu General Hospital
1660 Yabase-cho, Kusatsu, Shiga, 525-8585 Japan
Tel. : +81-77-563-8866 FAX:+81-77-565-9313
E-mail: ttogawa@qb4.so-net.ne.jp
Co-authors: Ozamoto Y, kujira735@hotmail.com ;
Akeo Hagiwara A, ahagiwara@mail.doshisha.ac.jp

Family history:

Nothing special.

Current medical history:

Positive fecal occult blood test was discovered at another hospital. Progressive cancer was detected in the sigmoid colon with colonoscopy.

Condition at initial visit:

Body height: 173.3 cm, body weight: 156.2 kg and BMI: 52.0 kg/m²

Morbid obesity was observed.

Results of physical examination at initial visit:

Carcinoembryonic antigen (CEA) showed a slightly high value of 8.5 ng/mL. Mild anemia was observed. He was being treated for diabetes, taking an oral diabetes agent (will be described later) and the value for HbA1c [NGSP] was 7.0% (*Table 1*).

Abdominal computed tomography (CT) scan:

Remarkable obesity was observed. Both visceral fat and subcutaneous fat abounded and cellulitis was observed in

subcutaneous fatty tissue. An enlarged mesenteric lymph node was observed and the metastasis of colon cancer was suspected (*Fig. 1-A, B, C*).

Colonoscopy:

An elevated lesion in the sigmoid colon was observed (*Fig. 2-A, B*), it was revealed to be well differentiated adenocarcinoma by biopsy pathological diagnosis.

From the above, this case was diagnosed as T2N1M0 Stage IIIa sigmoid colon cancer, morbid obesity (BMI 52.0 kg/m²), diabetes and hypertension. Diabetes could be relatively well controlled by using four oral diabetes agents (voglibose 0.1 mg/day, glimepiride two mg/day, Metgluco® metformin 750 mg/day, Liovel® combined agent [alogliptin 25 mg/pioglitazone 15 mg]) and hypertension by using three antihypertensive agents (amlodipine five mg/day, carvedilol 2.5 mg/day and Preminent® combined agent [Losartan potassium 100mg/hydrochlorothiazide 12.5 mg]).

Table 1. Results of biochemical examination of blood test at initial visit.

Hb	9.4	g/dL
Ht	33.9	%
MCV	70	fL
MCH	19.3	pg
MCHC	27.7	%
T-Bil	0.6	mg/dL
GOT	12	IU/mL
GPT	13	IU/mL
ALP	182	IU/mL
LDH	204	IU/mL
γ-GTP	14	IU/mL
BUN	16.4	mg/dL
CRE	0.77	mg/dL
PT	13.1	sec
PT%	75	%
PT-INR	1.15	
APTT	34.2	sec
D-dimmer	3.7	μg/mL
HbA1c [NGSP]	7	%
CEA	8.5	ng/mL

Hb, hemoglobin; Ht, hematocrit; MCV, mean corpuscular volume; MCHC, mean corpuscular hemoglobin; MCH, mean corpuscular hemoglobin concentration; T-Bil, total bilirubin; GOT, glutamic oxaloacetic transaminase; glutamic pyruvic transaminase; ALP, alkaline phosphatase; LDH, lactate dehydrogenase; γ-GTP, γ-glutamyltransferase; BUN, blood urea nitrogen; CRE, creatinine; PT, prothrombin time; PT%, percent prothrombin time; PT-INR, international normalized ratio of prothrombin time; APTT, activated partial thromboplastin time; NGSP, National Glycohemoglobin Standardization Program; CEA, carcinoembryonic antigen.

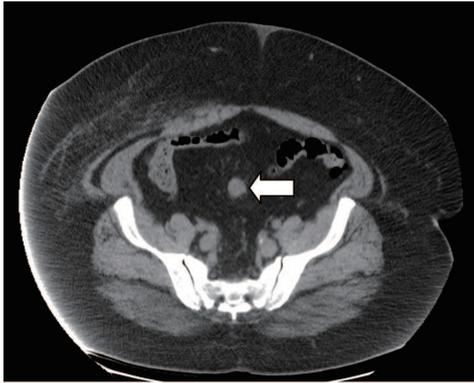


Fig. 1-A



Fig. 1-B

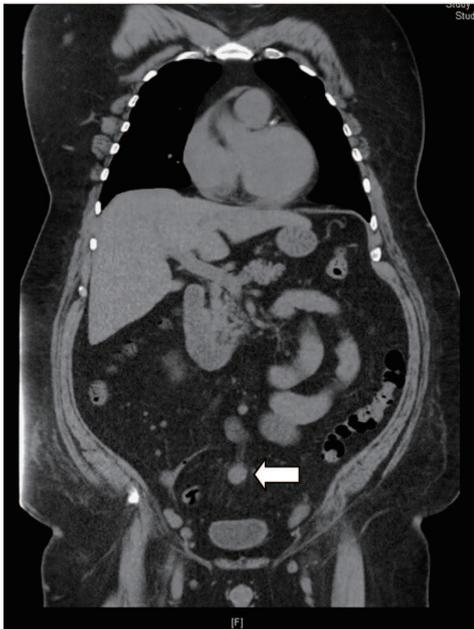


Fig. 1-C

Fig. 1-A, B, C. Abdominal CT scan.

Remarkable obesity was observed. Both visceral fat and subcutaneous fat abounded, and cellulitis was observed in subcutaneous fatty tissue. The identification of a primary tumor of sigmoid colon cancer is difficult. An enlarged lymph node was observed (arrow), and it was considered to be a metastasis of cancer. CT, computed tomography.

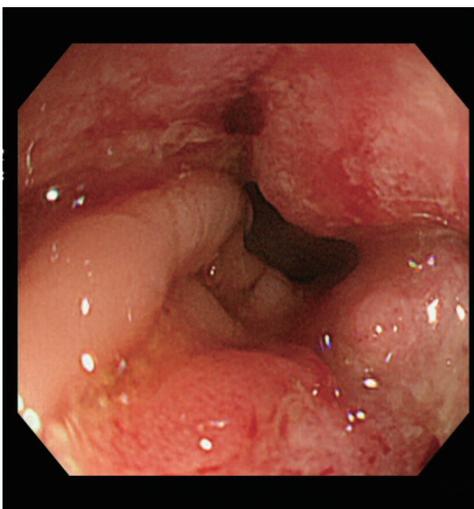


Fig. 2-A

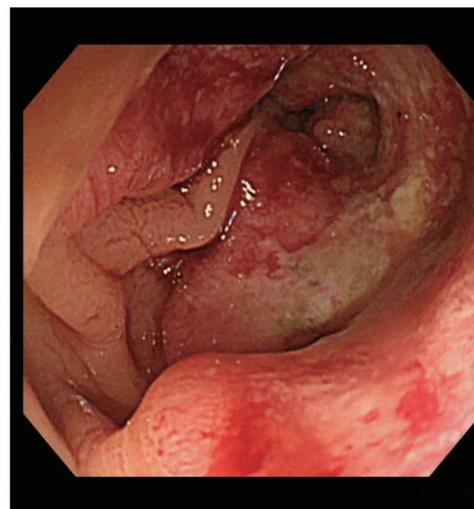


Fig. 2-B

Fig. 2-A, B. Colonoscopy images.

In large intestine endoscope images, an elevated lesion was observed in the sigmoid colon. It was pathologically diagnosed as well differentiated adenocarcinoma.

Specific process of treatment due to the complication of morbid obesity

Determination of treatment plan:

If the treatment of this case was conducted by standard care procedures in accordance with the guidelines for colorectal cancer treatment in Japan, a surgery would have been conducted for the purpose of radical treatment, and after that, a post-operative adjuvant chemotherapy would have been conducted. However, due to the morbid obesity associated with very thick visceral fat and subcutaneous fat, it was presumed to be very difficult to conduct surgery. In the case of laparoscopic surgery, there were fears that the heavy abdominal wall may not be elevated, even by sending air to abdominal cavity, and that at the head-down position, the maintenance of anesthesia may become difficult due to the elevation in airway pressure. Laparotomy was also predicted to be difficult to secure in the operative field due to the very thick subcutaneous fat. The risk of failure of sutures was also expected to be higher than in ordinary cases. It was possible that with the failure of sutures, the salvage treatments including drainage and stoma construction would be impossible due to thick subcutaneous fat.

As described above, it was judged to be impossible to carry out a safe surgery by either way of laparotomy or laparoscopic surgery. As a result, it was determined to reduce body weight as much as possible while chemotherapy was being implemented before surgery and then perform radical surgery. The patient gave enough informed-consent after discussions were made concerning that it was possible that the cancer would progress during the periods of chemotherapy and weight reduction before surgery, and if that happened, the opportunity of a radical cure would be lost.

Chemotherapy before surgery:

In this case, if the amounts of drugs for chemotherapy were calculated based on body surface area, they became very large; because this, chemotherapy was started with a lower dose of drugs calculated based on ideal body weight, and the amounts were increased little a little while the modest side effects were being confirmed. For the first time, mFOLFOX6 therapy was started. After it was confirmed that the RAS gene was a wild type, the therapy was switched to panitumumab + mFOLFOX6. However, because an oxaliplatin allergy was expressed during the course of the therapy, it was switched to panitumumab + FOLFIRI. As a reference, mFOLFOX6 therapy combines fluorouracil and *l*-leucovorin and oxaliplatin is given at the same time, and FOLFIRI therapy combines fluorouracil and *l*-leucovorin, and irinotecan is given at the same time.

The metastatic lymph nodes were remarkably reduced due to the chemotherapy for eight months and the level marker of the tumor was normalized. During this period, body weight was reduced to 125 kg and BMI to 41.3 kg/m². However, the condition where the surgery of sigmoid cancer could be safely conducted had not been achieved yet. Further deduction of body weight through nutritional guidance and exercise guidance were considered to be difficult. The patient gave enough informed-consent after discussions were made again, and it was decided to perform laparoscopic sleeve gastrectomy, for the purpose of further body weight loss.

Laparoscopic sleeve gastrectomy and course after surgery:

Under general anesthesia and laparoscopically, the entire length of omentum from the part of three cm from the pyloric ring of the greater curvature of the stomach to his angle was cut off. Then, the stomach at the side of greater curvature was resected using linear staplers and made it into a stomach tube of small diameter at the side of the smaller curvature (**Fig. 3**). Bougie of 45Fr. was used. No complications were observed after surgery and enough nutritional guidance was provided. The patient was discharged from hospital two weeks after surgery.

Five months after the laparoscopic sleeve gastrectomy, the body weight and BMI were reduced to 97 kg and 32.3 kg/m², respectively. No distal metastasis of colorectal cancer was recognized by the abdominal CT scan, the metastatic lymph nodes were reduced in size and became fussy, and both visceral fat and subcutaneous fat remarkably decreased (**Fig. 4-A, B**). By a large intestine endoscopy, it was confirmed that the primary tumor of the sigmoid colon was observed as an ulcer scar (**Fig. 5-A, B**). The respiratory function test before the start of treatment recognized high-level restrictive abnormalities such as % vital capacity (%VC) at 45.7% and percentage of 1.0 second forced expiratory volume of Gaensler (FEV 1.0%-G) at 80.47%; however, spirogram was normalized as “VC86.2% and FEV1.0%-G84.094% (**Table 2**). Due to sleep apnea syndrome, continuous positive airway pressure (CPAP) had been required; however, apnea hyponea index (AHI) was improved from 91.4 at the time of initiation of treatment, to 1.0 before the surgery of the colon cancer (**Table 2**). Along with the decrease of body weight, oral diabetes drugs became unnecessary and HbA1c[NGSP] was normalized at 5.0% (**Table 2**). As safe surgery was judged as possible, it was decided to perform a radical surgery of sigmoid colon cancer.

Radical surgery for sigmoid colon cancer and post-operative course:

A high anterior resection with D3 dissection was conducted under general anesthesia and laparoscopically. Although the patient was in a steep head-down position and pneumoperitoneum, it did not elevate airway pressure or cause a problem to anesthetic management. As the result of investigation of the resected specimen, it was feared that a part at the side of the inlet was not resected enough, since the tumor became non-palpable due to chemotherapy, intestinal tract and mesenterium were resected for five cm more. There was no problem in the course after surgery and the patient was discharged from hospital.

Findings in resected specimen:

The elevation of primary focus disappeared and became an ulcer-like legion (**Fig. 6**). An enlarged lymph node pointed out by the abdominal CT scan before surgery became scar-like. In the physiological and histological findings in the resected specimen, well differentiated and moderately differentiated adenocarcinoma was recognized as well as their infiltration beyond the proper muscle layer in very few parts. The metastases were recognized in two regional lymph nodes.

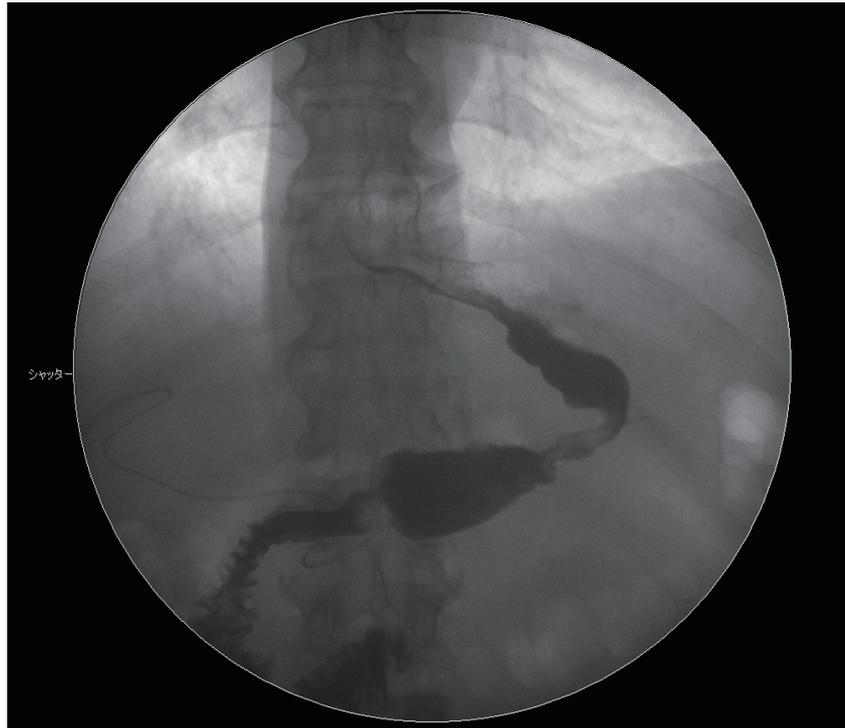


Fig. 3. Upper gastrointestinal tract X-ray examination.

The image of the remaining stomach after laparoscopic sleeve gastrectomy is shown. The stomach was made into a tube of a small diameter. Bougie of 45Fr was used for resection.



Fig. 4-A



Fig. 4-B

Fig. 4-A , B. CT scan images.

Five months after the laparoscopic sleeve gastrectomy, the body weight and BMI were reduced to 97 kg and 32.3 kg/m², respectively. No distal metastasis of colorectal cancer was recognized by abdominal CT scan, and the metastatic lymph nodes were reduced in size and became fuzzy (arrow). Both visceral fat and subcutaneous fat remarkably decreased. BMI, body mass index; CT, computed tomography.

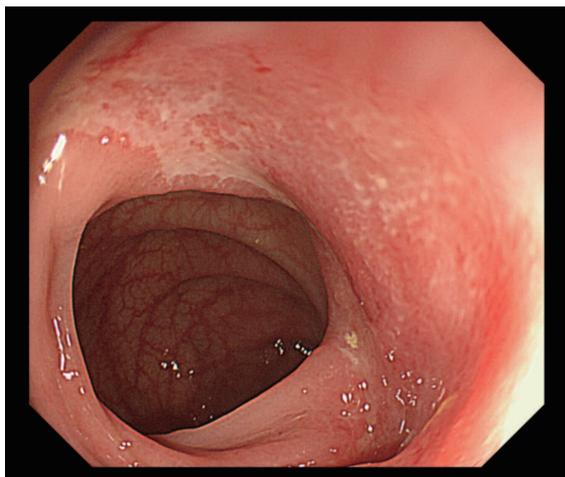


Fig. 5-A

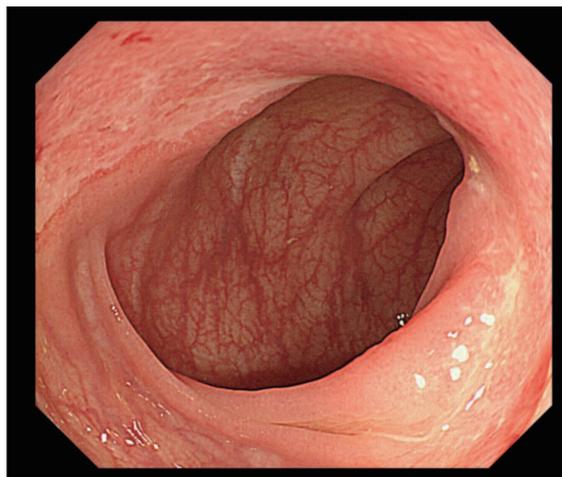


Fig. 5-B

5-A ,B. Colonoscopy images.

By a colonoscopy, the primary tumor in the sigmoid colon changed to an ulcer scar.

Table 2. Changes in data due to weight reduction.

	Start time of treatment	Before laparoscopic sleeve gastrectomy	Before colon cancer surgery
BMI (kg/m ²)	52.0	41.8	32.3
HbA1c [NGSP] (%)	7.0	6.9 (drug free)	(drug free)
%VC	45.7	79.5	86.2
FEV1.0%-G	80.47	78.94	84.04
AHI	91.4		1.0

BMI, body mass index; NGSP, National Glycohemoglobin Standardization Program; VC, vital capacity; FEV1.0%-G, percent of one second forced expiratory volume of Gaensler; AHI, apnea hypopnea index.

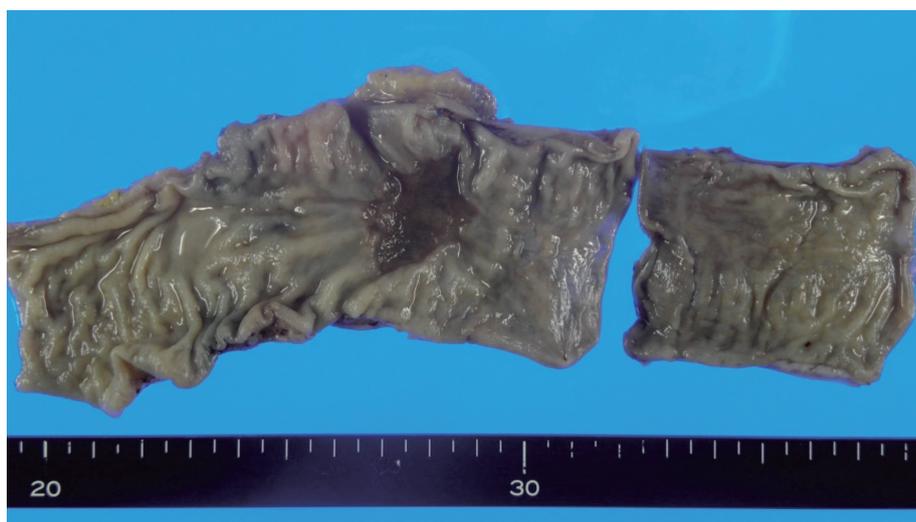


Fig. 6. Findings in the resected colon specimen.

The elevation of the primary tumor disappeared and became an ulcer-like lesion. As the tumor became non-palpable because of chemotherapy, a part at the side of the inlet was not resected enough; therefore, intestinal tract and mesenterium were resected 5 cm more.

Discussion

Recently, along with a westernized diet, morbid obesity and metabolic syndrome have become serious problems. Obesity itself not only causes various diseases including diabetes, hypertension, and sleep apnea syndrome, but also leads to various problems in medical practices due to its physical particularity²⁾, and the risks caused by surgery and anesthesia³⁻⁶⁾ are high.

The definite treatment methods for the improvement of morbid obesity are bariatric surgeries⁷⁾. The cases of BMI of 35 kg/m² or more, or BMI of 32 kg/m² or more with serious obesity complications, are defined as morbid obesity to which bariatric surgery should be applied⁸⁾. This case was a progressive colorectal cancer complicated with morbid obesity, meeting the above condition. No physician would consider that the surgery can be safely conducted on the patient with an extreme BMI of 52.0 kg/m², which is considered to be involved in great difficulties and risks by either way of laparotomy or laparoscopic surgery, so that a highly precise surgery cannot be expected. The risk for complications including failure of sutures after surgery is higher than usual, and at that time, great difficulties will arise for their treatments. Because of this, the possibility was considered that the patient cannot be saved when complications occur after surgery. Therefore, a treatment plan was determined to reduce body weight first, and during that time, conduct chemotherapy before surgery. Fortunately, in this case, the chemotherapy before surgery could successfully control the progress of cancer, and at the same time, the weight reduction treatment including bariatric surgery was also successful. However, because it was possible that the chemotherapy would not be successful and the opportunity of the radical cure of cancer would be lost, a cautious informed consent from the patient is necessary.

The fact that the amounts of intra-abdominal fat and subcutaneous fat affect the difficulty of surgery is empirically well known by surgeons; however, it is difficult to evaluate the degree of difficulty numerically. Generally, BMI and a visceral fat area (VFA) by abdominal X-ray CT measuring method are used as indicators of difficulty. Recently, reports show that VFA tends to be focused on more than BMI^{5,6,11)}. However, the level of difficulty of actual surgical technology also depends upon the length of the torso and the narrowness of the pelvis. Therefore, it is not appropriate to express the difficulty in surgery caused by obesity with a single parameter. There is a report that obesity does not affect the difficulty of laparoscopic surgery or the complication after surgery¹²⁾; however, in this report, BMI was ≥ 30 kg/m². Therefore, it was considerably different from the 52 kg/m² measurement of the case experienced by the authors. Although the surgery of a radical cure of colon cancer of this case was safely conducted laparoscopically, it was difficult due to the large amount of visceral fat compared with patients with average bodies. It is believed that if the surgery were conducted without bariatric treatment being performed before surgery, it would have been very dangerous.

It is known that type-2 diabetes related to obesity can be remarkably improved by bariatric surgery^{13,14)}. In this case, although four oral diabetes agents had been administered, the diabetes was improved so that HbA1c was normalized without oral diabetes agents owing to the bariatric treatments, including laparoscopic sleeve gastrectomy; all these treatments contributed to the reduction of surgery risk.

What was most remarkable in the course of this case

was the improvement of respiratory function caused by body weight reduction. *Fig. 7-A, B* and *C* show the changes of thoracoabdominal X-ray images caused by body weight reduction. Lung field remarkably expanded with body weight reduction. Although high-level restrictive abnormalities were observed by a respiratory function test before the start of treatment, the spirogram was normalized before colon cancer surgery when weight reduction advanced, and apnea hypopnea index (AHI) was dramatically improved (*Table 2*). The respiratory function was remarkably impaired due to a high-degree of obesity, and the risk for general anesthetic management also increased. In order to perform the surgery of sigmoid colon cancer laparoscopically, a steep head-down position is required, which further increases risks caused by the elevation of airway pressure. Because the laparoscopic sleeve gastrectomy is conducted in the head-up position, conversely, the airway pressure due to body position during surgery does not elevate. The risk of general anesthesia for laparoscopic sleeve gastrectomy in the condition where high-degree obesity has not been fully resolved is considered to be lower in the case of sigmoid colon cancer conducted in the head-down position, which supported the strategy to precedently perform bariatric surgery.

As a result of searching the reported cases where surgery was conducted for the purpose of a radical cure of cancer after bariatric surgery for patients with cancer and complicated with morbid obesity, just like this case, there were two papers, as far as was searched. One paper was reported by Szymanski *et al.*¹⁵⁾, where a laparoscopic gastric banding surgery was conducted for a morbid-obesity patient with a BMI of 51 kg/m², and after body weight was reduced, a rectal cancer surgery and hepatic metastasis resection were performed. However, this is a case where the cancer was found after bariatric surgery and not a case where bariatric surgery was conducted for the purpose of safely performing cancer operation. Another study was reported by Gianos *et al.*¹⁶⁾ and it consists of four reports where, for the purpose of safely conducting cancer surgery for the patients with early-stage malignancy complicated with morbid obesity, laparoscopic sleeve gastrectomy was conducted. It includes one case of small-intestinal carcinoid, two cases of kidney tumors and one case of prostate cancer. There were no similar reports in Japanese. As a case where it was successful that, for the purpose of safely performing radical surgery of progressive cancer complicated with morbid obesity, laparoscopic sleeve gastrectomy was conducted before surgery, this case that we experienced is probably the first reported case in Japan.

It is known that after curative resection of colorectal cancer, it is possible that new colorectal cancer or adenoma can occur from the remaining large-intestinal mucosa. Therefore, when a surgical therapy of colorectal cancer is conducted, the countermeasure against the new colorectal cancer developing after surgery is also important. It is known that in the case of obesity, in particular, the risks of developing various cancers are high^{17,18)}, and it is well known that the overweight status and amount of visceral fat correlate with the risk of development of colorectal cancer¹⁹⁻²²⁾.

Hypernutrition and undernutrition possibly affect endocrine secretion and the immune system and induce carcinogenesis. In the case of human obesity, T-cell number reduction, the lowering CD4 and CD8, and the lowering of lymphocyte transformation test reaction are reported, and the lowering of the immune system is suggested²³⁻²⁵⁾. In an experiment of mouse obesity, the lowering of the number of



Fig. 7-A Before the therapy.

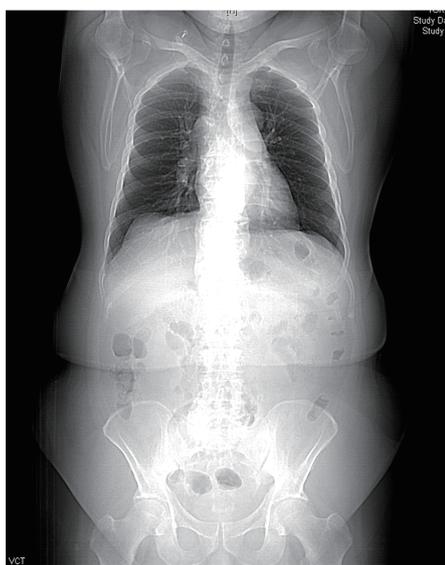
Fig. 7-B
Before the laparoscopic sleeve gastrectomy

Fig. 7-C Before the colon cancer surgery.

Fig. 7.

Lung field remarkably expanded with body weight reduction. Although high-level restrictive abnormalities were observed by respiratory function test before the start of treatment (A), spirogram was normalized before colon cancer surgery (C) when weight reduction advanced, and apnea hypopnea index (AHI) was dramatically improved from 91.4 at the start time of treatment to 1.0 before colon cancer surgery.

natural kill cells (hereinafter referred as to “NK cell”) and their activities are known²⁶⁾, and in human obesity also, NK cell function and others checking and inhibiting carcinogenesis possibly decline. Furthermore, as for the relationship between diabetes and colorectal cancer, it is reported that diabetes increases the risk of colorectal adenomas²⁷⁾, it is also recognized that elevated blood glucose, or glycative stress, itself correlates with the generation of colorectal cancer and colorectal adenomas²⁸⁻³³⁾. As mentioned above, in the case of surgery for colorectal cancer of obese patients and obese patients complicated with diabetes carrying high risk of generation of colorectal cancer, it will become a significant surgical medical plan to perform bariatric surgery for obesity as a countermeasure against the generation of new colorectal cancer after surgery.

In the future, the number of cancer patients complicated with morbid obesity similar to this case will increase in Japan. In cases where urgent and assured weight reduction is required for the purpose of treatment of malignant tumors complicated with morbid obesity, bariatric surgery will

become a powerful tool for that purpose.

Conclusion

Chemotherapy and bariatric surgery including laparoscopic sleeve gastrectomy were successfully conducted before surgery for colon cancer complicated with morbid obesity obstructive to safe and radical surgery. As the result of success in weight reduction before surgery, it became possible to safely conduct laparoscopic colon cancer surgery. Bariatric surgery is useful for malignant tumors complicated with morbid obesity.

Conflict of interest application

There are no matters relating to conflict of interest in performing this research.

References

- 1) Watanabe T, Itabashi M, Shimada Y, et al. Japanese Society for Cancer of the Colon and Rectum (JSCCR) Guidelines 2014 for treatment of colorectal cancer. *Int J Clin Oncol*. 2015; 20: 207-239.
- 2) Sebbane M, Claret PG, Lefebvre S, et al. Predicting peripheral venous access difficulty in the emergency department using body mass index and a clinical evaluation of venous accessibility. *J Emerg Med*. 2013; 44: 299-305.
- 3) Qiu Y, Liu Q, Chen G, et al. Outcome of rectal cancer surgery in obese and nonobese patients: A meta-analysis. *World J Surg Oncol*. 2016; 14: 23.
- 4) Murphy C, Wong DT. Airway management and oxygenation in obese patients. *Can J Anaesth*. 2013; 60: 929-945.
- 5) Watanabe J, Tatsumi K, Ota M, et al. The impact of visceral obesity on surgical outcomes of laparoscopic surgery for colon cancer. *Int J Colorectal Dis*. 2014; 29: 343-351.
- 6) Tanaka K, Miyashiro I, Yano M, et al. Accumulation of excess visceral fat is a risk factor for pancreatic fistula formation after total gastrectomy. *Ann Surg Oncol*. 2009; 16: 1520-1525.
- 7) Sjöström L, Narbro K, Sjöström CD, et al. Swedish Obese Subjects Study. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med*. 2007; 357: 741-752.
- 8) Guidelines Committee, Japanese Society for Treatment of Obesity. JSTO guidelines for safety, quality, and excellence in bariatric surgery (2013 edition). http://plaza.umin.ne.jp/~jsto/gakujyutsu/updatesurgery_guideline_2013.pdf (in Japanese)
- 9) Ballian N, Lubner MG, Munoz A, et al. Visceral obesity is associated with outcomes of total mesorectal excision for rectal adenocarcinoma. *J Surg Oncol*. 2012; 105: 365-370.
- 10) Hagiwara M, Miyajima A, Hasegawa M, et al. Visceral obesity is a strong predictor of perioperative outcome in patients undergoing laparoscopic radical nephrectomy. *BJU Int*. 2012; 110: E980-984.
- 11) Seki Y, Ohue M, Sekimoto M, et al. Evaluation of the technical difficulty performing laparoscopic resection of a rectosigmoid carcinoma: Visceral fat reflects technical difficulty more accurately than body mass index. *Surg Endosc*. 2007; 21: 929-934.
- 12) Leroy J, Ananian P, Rubino F, et al. The impact of obesity on technical feasibility and postoperative outcomes of laparoscopic left colectomy. *Ann Surg*. 2005; 241: 69-76.
- 13) Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: A systematic review and meta-analysis. *JAMA*. 2004; 292: 1724-1737.
- 14) Halperin F, Goldfine AB. Metabolic surgery for type 2 diabetes: Efficacy and risks. *Curr Opin Endocrinol Diabetes Obes*. 2013; 20: 98-105.
- 15) Szymanski D, Durczynski A, Strzelczyk J. Two-staged surgery for metastatic liver tumor in morbidly obese individual-left hemihepatectomy following placement of laparoscopic adjustable gastric band. *Obes Surg*. 2011; 21: 267-271.
- 16) Gianos M, Abdermur A, Szomstein S, et al. Laparoscopic sleeve gastrectomy as a step approach for morbidly obese patients with early stage malignancies requiring rapid weight loss for a final curative procedure. *Obes Surg*. 2013; 23: 1370-1374.
- 17) Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: A systematic review and meta-analysis of prospective observational studies. *Lancet*. 2008; 371: 569-578.
- 18) Rose DP, Komninou D, Stephenson GD. Obesity, adipocytokines, and insulin resistance in breast cancer. *Obes Rev*. 2004; 5: 153-165.
- 19) Gunter MJ, Leitzmann MF. Obesity and colorectal cancer: epidemiology, mechanism and candidate genes. *J Nutr Biochem*. 2006; 17: 145-156.
- 20) Larsson SC, Wolk A. Obesity and colon and rectal cancer risk: A meta-analysis of prospective studies. *Am J Clin Nutr*. 2007; 86: 556-565.
- 21) Moghaddam AA, Woodward M, Huxley R. Obesity and risk of colorectal cancer: A meta-analysis of 31 studies with 70,000 events. *Cancer Epidemiol Biomarkers Prev*. 2007; 16: 2533-2547.
- 22) Pischon T, Lahmann PH, Boeing H, et al. Body size and risk of colon and rectal cancer in the European Prospective Investigation Into Cancer and Nutrition (EPIC). *J Natl Cancer Inst*. 2006; 98: 920-931.
- 23) Fink S, Eckert E, Mitchell J, et al. T-lymphocyte subsets in patients with abnormal body weight: Longitudinal studies in anorexia nervosa and obesity. *Int J Eat Disord*. 1996; 20: 295-305.
- 24) Tanaka S, Inoue S, Isoda F, et al. Impaired immunity in obesity: Suppressed but reversible lymphocyte responsiveness. *Int J Obes Relat Metab Disord*. 1993; 17: 631-636.
- 25) Nieman DC, Henson DA, Nehlsen-Cannarella SL, et al. Influence of obesity on immune function. *J Am Diet Assoc*. 1999; 99: 294-299.
- 26) Tian Z, Sun R, Wei H, et al. Impaired natural killer (NK) cell activity in leptin receptor deficient mice: Leptin as a critical regulator in NK cell development and activation. *Biochem Biophys Res Commun*. 2002; 298: 297-302.
- 27) Elwing JE, Gao F, Davidson NO, et al. Type 2 diabetes mellitus: The impact on colorectal adenoma risk in women. *Am J Gastroenterol*. 2006; 101: 1866-1871.
- 28) Platz EA, Hankinson SE, Rifai N, et al. Glycosylated hemoglobin and risk of colorectal cancer and adenoma (United States). *Cancer Causes Control*. 1999; 10: 379-386.
- 29) Nilsen TI, Vatten LJ. Prospective study of colorectal cancer risk and physical activity, diabetes, blood glucose and BMI: Exploring the hyperinsulinaemia hypothesis. *Br J Cancer*. 2001; 84: 417-422.
- 30) Trevisan M, Liu J, Muti P, et al. Markers of insulin resistance and colorectal cancer mortality. *Cancer Epidemiol Biomarkers Prev*. 2001; 10: 937-941.
- 31) Saydah SH, Loria CM, Eberhardt MS, et al. Abnormal glucose tolerance and the risk of cancer death in the United States. *Am J Epidemiol*. 2003; 157: 1092-1100.
- 32) Colangelo LA, Gapstur SM, Gann PH, et al. Colorectal cancer mortality and factors related to the insulin resistance syndrome. *Cancer Epidemiol Biomarkers Prev*. 2002; 11: 385-391.
- 33) Saydah SH, Platz EA, Rifai N, et al. Association of markers of insulin and glucose control with subsequent colorectal cancer risk. *Cancer Epidemiol Biomarkers Prev*. 2003; 12: 412-418.