



Laparoscopic sleeve gastrectomy for morbid obesity and Klinefelter syndrome: clinical report on two patients, with long-term follow-up

Emanuela Bianciardi¹ · Paolo Orsaria² · Cinzia Niolu¹ · Alberto Siracusano¹ · Paolo Gentileschi²

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Abstract

Introduction Klinefelter syndrome (KS) can appear as a wide spectrum of clinical manifestations, with no guidelines for appropriate treatment. We present the first study of bariatric surgery (BS) with a 48-month follow-up, for the management of two patients affected by obesity and KS.

Cases presentation The first patient was a 32-year-old man with diagnosis of Klinefelter mosaicism (46 XY/47, XXY), Body Mass Index (BMI) of 50 kg/m², metabolic syndrome and Binge Eating Disorder (BED). He underwent a Laparoscopic Sleeve Gastrectomy (LSG) with weight loss (BMI = 38 kg/m²) and improvements to his metabolic profile at 48 months. The second patient was a 44-year-old man with KS (47, XXY), BMI of 49 kg/m², Obstructive Sleep Apnea Syndrome and BED. He underwent a banded LSG. After 48 months, he showed a satisfactory weight loss (BMI = 32 kg/m²) and amelioration of comorbidities.

Conclusion In patients with KS, LSG demonstrated long-term beneficial effects for weight loss and amelioration of comorbidities. An interdisciplinary approach is mandatory, since it leads to adherence to follow-up programs and mental health well-being.

Keywords Bariatric surgery · Binge eating disorder · Klinefelter syndrome · Body image dissatisfaction · Metabolic syndrome · Obesity · Interdisciplinary approach

Introduction

Klinefelter syndrome (KS) is the most common sex chromosome disorder causing primary hypogonadism in males, affecting 1 in 660 men. Since it has a wide spectrum of clinical manifestations, which may include small testes, hypergonadotropic hypogonadism, gynecomastia, cognitive delays, azoospermia and metabolic syndrome, KS is a subject of interest for various scientists, with differing specialties [1]. Individuals with KS may suffer from modification to

body composition, primarily through an increase in truncal fat and a decrease in muscle mass. Overall evidence suggests that visceral obesity is strongly associated with the metabolic effects of insulin resistance, such as impaired glucose metabolism and unfavorable lipid profile [1]. Patients with KS have an increased risk of cerebrovascular and endocrine disease, obesity, metabolic syndrome and type II diabetes. KS is, therefore, associated with an increased morbidity and mortality, from many different diseases, resulting in the loss of approximately 2 years in life span. In spite of the postulated efficacy of testosterone supplementation in preventing the metabolic syndrome, affected males have an increased mortality risk, corresponding to a significantly reduced median survival rate, due to the consequences of the many comorbidities such as the abdominal obesity [2].

To our knowledge, bariatric surgery (BS) in the setting of sex chromosomal aberration and metabolic syndrome has never been documented, even if these two diseases can often occur in the same patient. Currently, we found only one report describing a BS candidate with KS, obesity

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✉ Emanuela Bianciardi
emanuelabianciardi@libero.it

¹ Chair of Psychiatry, Department of Systems Medicine, University of “Tor Vergata”, Via Montpellier 1, 00133 Rome, Italy

² Department of Surgery, Obesity Unit, University of Rome “Tor Vergata”, Rome, Italy

(BMI = 60 kg/m²) and metabolic syndrome, in which BS was suggested but not yet performed [3].

We describe two cases of patients with KS and obesity, who underwent Laparoscopic Sleeve Gastrectomy (LSG) with a follow-up of 48 months.

Case reports

Case number 1

A 32-year-old man with KS mosaicism (46 XY/47, XXY) presented with a BMI of 50 kg/m² (height 1.68 m, weight 141 kg). Over the last 15 years he had developed an unfavorable change in body composition, increased abdominal adiposity and hypercholesterolemia. He suffered from the toxicity of testosterone replacement therapy on plasma lipids and apolipoproteins profile. Total cholesterol, calculated LDL-cholesterol, triglyceride and C-reactive protein (CRP) increased significantly after androgen treatment. Supplementation with testosterone was interrupted and statins were started. KS contributed to the occurrence of increased body fat and metabolic dysfunctions, preventing a satisfactory biological response from diet and pharmacological therapy.

An interdisciplinary work-up was started.

A psychiatrist with training relevant to obesity performed the psychosocial–behavioral evaluation. A semi-structured interview was conducted evaluating eating behaviors, weight and dieting history, motivation for BS, weight loss expectations, mental health history, substance and alcohol use [4]. Psychometric instruments were administered. Hamilton Rating Scale for Depression (HAM-D) and Beck Depression Inventory-Second Edition (BDI-II) were performed to measure current depressive symptoms. Body Shape Questionnaire (BSQ) was performed to measure body image dissatisfaction. Bulimia Test Revised (BULIT-R), Binge Scale Questionnaire (BiSQ), Eating Attitude Test (EAT-26), and Eating Disorder Inventory-2 (EDI-2) were administered to assess eating disorder symptoms. At the end of the evaluation, a final written report was produced. It included a brief summary of the relevant findings of the interview, the recommendations about both pre and post-surgical psychosocial intervention and the clearance to BS. According to Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) criteria, a diagnosis of Binge Eating Disorder (BED) was established. Moreover, a severe degree of body image dissatisfaction was found. Fluoxetine 60 mg/day and a weekly psychological therapy, with cognitive–behavioral approach, were started. After 6 months of treatment, the binge-eating symptoms improved (i.e., binge eating episodes switch from six per month to once/twice per month) as did the psychological status. Subsequently, the patient was

cleared for surgery and psychiatric follow-up was scheduled monthly.

Based on the multi-disciplinary work-up, LSG was selected as the procedure of choice. The patient experienced no post-operative complications. He was discharged on the 3rd day post-surgery.

One year after surgery fluoxetine was stopped. Notwithstanding that at 24-month follow-up he did not experience binge-eating episodes, an emerging craving for sweet foods, episodes of grazing and increased consumption of junk food were reported.

Table 1 summarizes change in psychometric instruments scores from baseline to 24 months after surgery. There was a subjective improvement in depressive symptoms and body image dissatisfaction.

The patient rated his weight loss result at 48 months, as satisfactory. The reduction of the BMI was from 50 to 38 kg/m², the percentage of Total Weight Loss (%TWL) was 23.6%, the percentage of the Excess Weight Loss (%EWL) was 40%.

Table 2 summarizes the improvement of metabolic parameters from pre-surgery and after 6, 12, 24 and 48 months of follow-up. Despite the beneficial results in BMI, biological response to adverse changes in total cholesterol levels was still not satisfactory.

Case number 2

A 44-year-old man with KS (47, XXY) presented with a BMI of 49 kg/m² (height 1.81 m, weight 160 kg). Since childhood, he had suffered from obesity. He was affected by BED and a bipolar spectrum disorder treated with Valproate 600 mg and Fluoxetine 20 mg/day. A heavy smoker, he presented with Obstructive Sleep Apnea Syndrome. An interdisciplinary work-up was started. A semi-structured interview and psychometric instruments were administered. The diagnosis of BED (three binge episodes/week) was confirmed, highlighting two major concerns: a tendency towards irritable mood and a history of poor adherence to treatment. Patient's eating pattern was characterized by a tendency to night eating and a craving for sweet foods. He was cleared for surgery with the recommendation of psychological pre-operative support. Since the patient was, already, under mental health therapy, and with the agreement of his psychiatrist, he continued the treatment at his local mental health center. Follow-up, with the psychiatric staff of the bariatric unit, was scheduled at one, 6, 12, 24, and 48-month post-surgery. He attended only one of the five, scheduled post-operative check-ups, at 36 months.

He underwent a banded LSG using a silastic Ring, with no post-operative complications. He was discharged on the 3rd post-operative day with a scheduled follow-up. After

Table 1 Change in psychometric instruments scores from baseline to 4 years after surgery

	Pre-surgery	6 months	12 months	24 months	36 months	48 months
Case report 1						
<i>HAM-D</i>	5	–	4	2	–	–
<i>BDI-II</i>	14	–	13	9	–	–
<i>BSQ</i>	189	–	150	114	–	–
<i>BiSQ</i>	9	–	2	1	–	–
<i>BULIT-R</i>	87	–	58	48	–	–
<i>EAT-26</i>	26	–	26	14	–	–
<i>EDI-2 DT</i>	12	–	–	10	–	–
<i>EDI-2 B</i>	12	–	–	0	–	–
<i>EDI-2 BD</i>	9	–	–	10	–	–
<i>EDI-2 I</i>	5	–	–	4	–	–
<i>EDI-2 P</i>	1	–	–	5	–	–
<i>EDI-2 ID</i>	4	–	–	8	–	–
<i>EDI-2 IA</i>	6	–	–	4	–	–
<i>EDI-2 MF</i>	4	–	–	7	–	–
<i>EDI-2 A</i>	9	–	–	9	–	–
<i>EDI-2 IR</i>	8	–	–	8	–	–
<i>EDI-2 SI</i>	6	–	–	6	–	–
Case report 2						
<i>HAM-D</i>	11	–	–	–	4	–
<i>BDI-II</i>	23	–	–	–	22	–
<i>BSQ</i>	153	–	–	–	119	–
<i>BiSQ</i>	11	–	–	–	11	–
<i>BULIT-R</i>	91	–	–	–	63	–
<i>EAT-26</i>	29	–	–	–	32	–
<i>EDI-2 DT</i>	12	–	–	–	7	–
<i>EDI-2 B</i>	12	–	–	–	4	–
<i>EDI-2 BD</i>	16	–	–	–	4	–
<i>EDI-2 I</i>	22	–	–	–	8	–
<i>EDI-2 P</i>	3	–	–	–	4	–
<i>EDI-2 ID</i>	7	–	–	–	13	–
<i>EDI-2 IA</i>	18	–	–	–	23	–
<i>EDI-2 MF</i>	7	–	–	–	8	–
<i>EDI-2 A</i>	9	–	–	–	9	–
<i>EDI-2 IR</i>	13	–	–	–	12	–
<i>EDI-2 SI</i>	12	–	–	–	12	–

HAM-D Hamilton Rating Scale for Depression (Hamilton M, 1980), *BDI-II* Beck Depression Inventory-II (Beck AT, 1972), *BSQ* Body Shape Questionnaire (Cooper PJ et al., 1986), *BiSQ* Binge Scale Questionnaire (Hawkins RC and Clement PF, 1980), *BULIT-R* Bulimia Test Revised (Thelen MH et al., 1991), *EAT-26* Eating Attitude Test (Garner D and Garfinkel PE, 1979), *EDI-2* Eating Disorder Inventory-2 (Garner DM, 1991). Subscales: *DT* drive for thinness, *B* bulimia, *BD* body dissatisfaction, *I* ineffectiveness, *P* perfectionism, *ID* interpersonal distrust, *IA* interoceptive awareness, *MF* maturity fears, *A* asceticism, *IR* impulse regulation, *SI* social insecurity

48 months, there was a reduction of the BMI from 49 to 28 kg/m², the %TWL was 42%, the %EWL was 77%.

Table 2 summarizes the improvement of metabolic parameters from pre-surgery and after 12, 36- and 48 months of follow-up. He attended the psychiatric follow-up at 3-year post-surgery, where it was revealed that, without the guidance of any provider, he had stopped taking his medications

2 years after surgery. At 36 months after surgery, he presented at least two/three episodes of vomiting per week, considered a failure, by dint of patient's attempts at binge eating as discussed below [5]. He reported a decreased preference for sugars, difficulties in swallowing red meat, episodes of night eating, overeating and eating too fast. Table 1 summarizes change in psychometric instruments scores

Table 2 Change in blood levels of metabolic parameters scores from baseline to 4 years after surgery

	Pre-surgery	6 months	12 months	24 months	36 months	48 months
<i>Case report 1</i>						
Fasting blood sugar level	114	85	89	76	–	90
Cholesterol	336	328	326	270	–	235
LDL	232	265	252	203	–	171
HDL	34	37	32	43	–	46
Triglycerides	352	129	209	120	–	92
<i>Case report 2</i>						
Fasting blood sugar level	81	–	86	–	90	76
Cholesterol	240	–	185	–	179	170
LDL	165	–	123	–	118	114
HDL	40	–	33	–	32	33
Triglycerides	174	–	145	–	145	116

Fasting blood sugar level (mg/dl); Cholesterol (mg/dl); LDL, low-density lipoprotein cholesterol (mg/dl); HDL, high-density lipoprotein cholesterol (mg/dl); Triglycerides (mg/dl)

from baseline to 36 months after surgery. The results supported the improvement in body image dissatisfaction and the remission of the insomnia thanks to the amelioration of sleep apnea.

Discussion

In both patients, BS was effective in long-term weight loss and the amelioration of metabolic parameters. Psychological adjustment after surgery was different in each case. KS is a sex chromosomal disorder resulting in increased mortality from many causes, including metabolic diseases. Androgen deficiency is a risk factor in the development of type 2 diabetes, hypertension and cardiovascular disease. However, testosterone replacement therapy, alone, may not be helpful in improving the metabolic profile [6]. From childhood, patients with KS may develop an increase in body fat concentrated in the truncal region. In a cross-sectional study among patients with KS, 44% had metabolic syndrome, whereas insulin sensitivity was decreased [7]. Epidemiological studies on mortality and morbidity in KS showed an increased risk of dying from diabetes or being hospitalized (SMR 5.8; 95% CI, 3.4–9.3) [1, 8]. The association between KS and metabolic syndrome with truncal obesity and diabetes mellitus is, therefore, widely documented in the literature. Strong evidence is provided about the increase of the mortality risk in patients with KS and obesity. In view of this, our results are compelling, since BS was an appropriate treatment for both patients.

In individuals with severe obesity, BS is the most effective treatment, providing sustained weight loss and amelioration of comorbidities from metabolic syndrome [9–11]. Moreover, weight loss is associated with an increased level of testosterone [1]. This report is, to date, the first experience

of BS in patients with KS. Both patients experienced a satisfactory reduction of BMI at 48 months with beneficial results in alterations to body composition and metabolic index. We noted that the decrease of plasma cholesterol level is still not satisfactory in one patient. Furthermore, psychological adjustment from baseline to 2/3 years after surgery was different in each patient. It is worth noting that both individuals suffer from psychiatric disorder. This finding is in line with literature reporting a high rate of psychiatric morbidity in patients with KS [1]. Specifically, both cases were diagnosed with BED.

Despite a less favorable %TWL, the first patient improved substantially in all the psychiatric domains measured. Although he developed a craving for sweet foods and a tendency to eat junk food, overall, his psychosocial status recovered. As of now, he has a stable job and he is of a mind to get married.

Conversely, the second patient reached a satisfactory %TWL but the psychopathological status worsened. He developed a maladaptive purging behavior. The episodes of vomiting may be caused by either the pre-existent BED or by the patient's poor adherence to the post-operative dietary requirements. Moreover, he underwent a banded LSG which has a side effect of vomiting, still, the clinical records supported the assumption that the patient developed a post-surgery eating disorder. In fact, vomiting initiated 2/3 months after surgery instead of immediately after the operation. The weight did not decrease too rapidly, there was no impairment of vital signs or generalized worsening of physical status that would have supported the hypothesis of a complication of LSG. Finally, he was aware of uncontrolled overeating and had a deep desire to avoid regaining lost weight. This patient was not treated with additional psychological support before surgery by the bariatric staff (i.e., psychiatrist with training relevant to BS). An ad hoc psychological support was not

provided, since he was under the care of the local community mental health team. We recognized that, by delegating the role of providing the perioperative care to his therapist, we failed to build a doctor–patient relationship that could have improved adherence to the treatment [12]. In fact, this may have facilitated the patient to underestimate the role of tailored behavioral treatments, resulting in a vulnerability to eating disorders after BS. Since both patients suffered from BED and showed different post-operative outcomes, we can assume that in those with psychiatric morbidity, psychological management is mandatory for BS to be effective.

Conclusion

KS symptoms vary widely among patients, with a growing body of research endeavoring to develop recommendations and guidelines for appropriate treatment [13]. In patients with a long-term history of metabolic disorders, such as obesity, an effective therapeutic approach is an essential requirement. In this report, individuals with sex chromosome disorder and metabolic syndrome were successfully treated by BS, making it an effective strategy in achieving long-term improvement of comorbidities and weight loss. The interdisciplinary approach was crucial for mental well-being and adherence to follow-up.

What is already known on this subject?

KS, the most frequent chromosomal disorder in males, can appear as a wide spectrum of clinical manifestations with no standardized set of guidelines for appropriate treatment. KS patients have an increased risk of cerebrovascular disease and endocrine and/or metabolic disease, especially obesity, metabolic syndrome and type II diabetes mellitus. KS is, therefore, associated with an increase in morbidity and in mortality from many different diseases.

What this study adds?

We present the first experience reporting the use of bariatric surgery in the management of two patients affected by severe obesity and KS, with a 48-month follow-up. Currently, no case reports or series regarding metabolic surgery in the setting of Klinefelter status exist. LSG proved an effective treatment in achieving long-term weight-loss while improving comorbidities.

Author contributions PG was responsible for the conceptualization of this manuscript. EB and PG evaluated the two patients; PG performed the surgical procedures; EB, PO and PG wrote the manuscript, EB, PG, CN and AS reviewed the manuscript.

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Compliance with ethical standards

Conflict of interest The authors declare no conflict of interests.

Ethical approval The study was approved by the Institutional Ethic Review Committee of the University of Rome “Tor Vergata”.

Informed consent Both patients were informed and agreed with their case reports.

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