

Secondary azoospermia after sleeve gastrectomy: a case report

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Objective: To report the first case of secondary azoospermia after sleeve gastrectomy.

Design: Case report.

Setting: Academic male infertility clinic.

Patient(s): A 33-year-old man with secondary azoospermia and primary testicular failure with testosterone deficiency after laparoscopic sleeve gastrectomy.

Intervention(s): Hormonal therapy with anastrozole for 10 months and diagnostic testicular biopsy.

Main Outcome Measure(s): Semen analyses and testicular histopathology.

Result(s): Non-obstructive azoospermia persisted at 20 months after surgery despite hormonal therapy with anastrozole. Testicular histopathology revealed the presence of Sertoli cells only.

Conclusion(s): Although further research is need to determine the relationship between sleeve gastrectomy and secondary infertility, men should be informed of the potentially deleterious effects of this surgery on semen parameters. (*Fertil Steril Rep*® 2021;2:245–8. ©2021 by American Society for Reproductive Medicine.)

Key Words: Azoospermia, bariatric surgery, sleeve gastrectomy, testosterone deficiency

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Obesity is a well-recognized public health crisis in the United States. Obese men have a higher risk of infertility associated with hypogonadism, impaired sperm quality, erectile dysfunction, and diminished sexual quality of life (1). Bariatric surgery, which includes Roux-en-Y gastric bypass and sleeve gastrectomy, is an effective treatment option for long-term weight loss (2). Since 2013, sleeve gastrectomy has surpassed gastric bypass as the most commonly performed bariatric surgery, likely due to its favorable safety profile with similar weight loss efficacy (3). Although weight loss and lifestyle modifications are associated with improvements in reproductive hormone parameters, an expanding body of research demonstrates the potential

deleterious effects of bariatric surgery on semen parameters (4, 5).

Data examining the relationship between bariatric surgery and postoperative semen parameters is conflicting. A 2019 meta-analysis revealed that most studies on bariatric surgery with available follow-up data failed to include semen parameters in their results, but the analysis of 3 studies with available semen analysis data revealed no significant change in the postoperative semen parameters (4). In contrast to this meta-analysis, a new multi-institutional prospective cohort—BARIASPERM—noted a significant decrease in total sperm count after 12 months of postoperative follow-up among men who underwent either gastric bypass or sleeve gastrectomy (6). Similarly, there are several case reports (7, 8) encompass-

ing a total of 7 patients which implicate that Roux-en-Y gastric bypass surgery is the cause of secondary azoospermia. All of the patients who developed azoospermia had previously fathered children, but only 1 of the 7 patients had available baseline data on semen parameters. Results of testicular pathologies were available for 6 of the 7 patients and demonstrated complete maturation arrest in all cases. The longest follow-up conducted in these patients with secondary azoospermia was 15 months (7, 8). A case report of a patient who underwent sleeve gastrectomy demonstrated secondary severe oligoasthenoteratozoospermia at 10 and 13 months postoperatively; the patient's semen parameters returned to normal at 24 months (9). In the published literature, secondary azoospermia—the most concerning presentation from a male fertility perspective—has only been previously described after gastric bypass. Here, we present the first reported case of secondary azoospermia after sleeve gastrectomy with extended clinical follow-up.

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CASE REPORT

A 33-year-old man and his 33-year-old female partner presented with secondary infertility after attempting to conceive their third child without success. His past medical history was significant for obesity, and he underwent laparoscopic sleeve gastrectomy (LSG) a year before initial clinic visit. The patient has a 14-pack year smoking history and quit 3 years before his presentation. Shortly after undergoing LSG, the patient received daily multivitamin and vitamin B12 supplementation. Vitamin D supplementation was initiated after deficiency was noted 6 months before presentation. On physical examination, the patient was afebrile, normotensive, well developed, and well nourished. The testes were firm, nontender, and mildly atrophic (14 mL) bilaterally with no palpable masses. The spermatic cord structures were normal. No varicoceles were noted on either side.

The patient developed obesity when he reached adulthood and had gradual weight gain within a period of 10 years. He was 5' 11" tall and weighed 72.5 kg at the age of 18 years, with a body mass index (BMI) of 22 kg/m². At the age of 30 years, he weighed 136.1 kg (BMI: 41.8 kg/m²). At the time of LSG, the patient weighed 157.9 kg (BMI: 48.2 kg/m²).

With regard to previous pregnancies, the couple had previously conceived 2 children. The eldest child was conceived via unassisted vaginal delivery at paternal age of 24 years. Their second child was conceived at paternal age of 28 years via intrauterine insemination (IUI). Results of the semen analysis 6 years before the current presentation demonstrated normal semen concentration and motility, with the concentration at the lower limit of normal based on the 2010 World Health Organization reference ranges (Table 1, August 2012). The couple was able to successfully conceive after 1 cycle of IUI.

Four years after their initial successful IUI cycle, the patient and his wife again presented with secondary infertility at paternal age of 32 years. At this time, the patient's BMI was 48.2 kg/m². The patient's semen parameters remained unchanged and were within normal limits (Table 1, June/August/December 2016). The couple underwent 2 cycles of IUI at this time, both of which were unsuccessful. In vitro fertilization was recommended, but the pair decided to forgo any attempts of in vitro fertilization until after the patient achieved weight loss to optimize their chances of conceiving. As such, the patient underwent LSG in August 2017, at the age of 33 years, and subsequently lost 61.2 kg within 10 months. His nadir postsurgical weight was 96.6 kg (BMI: 29.7 kg/m²).

Despite the patient's successful weight loss, the couple was still unable to conceive naturally. On initial reproductive endocrinologic evaluation 8 months after surgery, he was found to have normal sperm concentration—improved from his baseline—but complete asthenozoospermia. Sperm viability testing revealed complete necrozoospermia (Table 1, April 2018). At 10 months after surgery, the patient progressed to normal-volume azoospermia. Serum testing at that time revealed primary testicular failure with testosterone deficiency and markedly elevated follicle-stimulating hormone (Table 1, June 2018). Of note, serum testosterone

specimens were appropriately drawn in the morning between 7 AM and 10 AM. The total testosterone-to-estradiol ratio was 9.6. The patient showed a positive result on Androgen Deficiency in Aging Male test (questions #4 and #8). However, he did not experience erectile dysfunction, diminished energy, or diminished libido. Genetic testing showed absence of any Y-chromosome microdeletions. Screening scrotal ultrasound revealed a diffuse, striated hyperechoic area emanating from the right testicular hilum. Scrotal magnetic resonance imaging (to further evaluate the irregular right testicular sonographic finding), abdominal and pelvic computed tomography, and chest roentgenogram showed the absence of testicular mass or metastatic disease. Serum germ cell testicular tumor markers were within normal limits. At this time, hormonal therapy with anastrozole 1 mg daily was initiated due to testosterone deficiency and diminished testosterone-to-estradiol ratio (10).

Anastrozole therapy was maintained for 4 months, but adequate androgenization based on the total testosterone level was not achieved; however, the estradiol level was reduced (Table 1). After 4 months of anastrozole therapy, right testicular biopsy was performed via an inguinal approach under ultrasound guidance to obtain a sample from the hyperechoic area. Testicular pathology revealed extensive tubular atrophy with hyalinization and scattered calcifications. Histologic examination showed the presence of Sertoli cells only with no spermatogenesis. There was no evidence of malignancy.

The couple declined attempts of concurrent testicular sperm retrieval and only desired diagnostic biopsy. The patient was maintained on anastrozole therapy for another 6 months—finally achieving adequate androgenization—but azoospermia persisted at 20 months postoperative follow-up. At the last follow-up, results of the extended testing for serum metabolic deficiencies (vitamin B12, copper, iron, zinc, and folate) were unremarkable apart from mild vitamin D deficiency despite supplementation (27 ng/mL).

DISCUSSION

To our knowledge, the patient presented herein represents the first reported case of secondary azoospermia after sleeve gastrectomy. Unlike the previously described patients with secondary azoospermia after Roux-en-Y gastric bypass who universally demonstrated maturation arrest, this patient's testicular histopathologic evaluation revealed Sertoli cells only. He presented with testosterone deficiency after surgery and was initially refractory to hormonal therapy. The patient described in this report has had the longest clinical follow-up compared with those in the existing literature with secondary azoospermia after any form of bariatric surgery. Unlike the other single case report on severe oligozoospermia after sleeve gastrectomy, our patient did not experience delayed improvement in semen parameters.

Interestingly, his overall sperm count increased from baseline while he developed complete asthenozoospermia. We hypothesize that this change is because of spermatogenic dysfunction caused by catabolic reactions after bariatric surgery (11). However, his hypothalamic-pituitary axis remained

TABLE 1

Case weight and laboratory findings.

Date	2012		2016		2017			2018				2019	
	July ^{c,d}	June ^c	August ^c	December ^c	August ^e	October	February	April	June	July	August	October	April
Weight (kg) ^a			—		157.9	131.5	117.5	—	96.6	—	100.2	102.5	109.3
Body mass index (kg/m ²) ^a			—		48.2	40.4	36.1	—	29.7	—	30.8	31.5	33.6
Semen analysis													
Volume (mL)	1.6	2.0	2.0	3.0				2.0	3.0	^f	—	3.8	3.0
pH	—	—	—	—		8.5	8.0	—			8.0	8.0	
Viability	—	—	—	—		0.0	No sperm	—			No sperm	No sperm	
Viscosity	None	None	None	None		Normal	Normal	—			Normal	Normal	
Agglutination	—	—	—	—		—	—	—			No sperm	No sperm	
Sperm count (1 × 10 ⁶)	15	16	16	17		37.7	No sperm	—			No sperm	No sperm	
Motility (%)	68	75	75	59		0.0	No sperm	—			No sperm	No sperm	
Velocity	—	—	—	—		—	No sperm	—			No sperm	No sperm	
Linearity	—	—	—	—		—	No sperm	—			No sperm	No sperm	
Morphology	—	—	—	—		—	No sperm	—			No sperm	No sperm	
Round cells	0	0	0	0		20	—	—			0.7	0.7	
Fructose	—	—	—	—		—	Positive	—			Positive	Positive	
Androgen panel													
Total testosterone ^b									248	^f	262	223	— 441
Free testosterone ^b							—				—	14.1	
Luteinizing hormone							15	24.9	25.8		—	—	
Follicle stimulating hormone							37.7	44.7	43.5		—	—	
Estradiol							25.8	8	<5		—	—	
Sex hormone binding globulin							34	29	47		—	—	

^a Weight and body mass index unknown before 2017. Care received at non-affiliated institution.

^b Serum testosterone levels obtained in the morning. Laboratory tests in August performed between 7 AM and 10 AM. Laboratory tests in April performed at 11:30 AM.

^c Pre-bariatric surgery.

^d At the time of intrauterine insemination for second child.

^e Date of lap sleeve gastrectomy.

^f Anastrozole started.

Gomez. Azoospermia after sleeve gastrectomy. *Fertil Steril Rep* 2021.

intact; the elevated levels of follicle-stimulating hormone may have led transiently to increased overall sperm production, whereas acute necrospermia/cellular death occurred concurrently after spermiation. We also demonstrated that a variety of metabolic serum parameters remained within normal limits along with persistent azoospermia. Our single-institution clinic chart review revealed 2 other patients with azoospermia after sleeve gastrectomy, but no preoperative paternity or semen parameter data were available for these patients; thus, the impact of surgery was impossible to determine.

Previous meta-analysis results indicate that bariatric surgery is associated with improvements in male reproductive hormone profiles (4, 12, 13). Specifically, in men, studies have shown an increase in free and total testosterone levels and a decrease in estradiol levels. By contrast, our patient's postsurgical hormone profile demonstrated testosterone deficiency. Although there were no presurgical hormone parameters available for review to assess for change from his presurgical baseline, he did not have normal testosterone and estradiol levels postoperatively.

In 2019, the American Association of Clinical Endocrinologists, The Obesity Society, American Society for Metabolic and Bariatric Surgery, Obesity Medicine Association, and American Society of Anesthesiologists coauthored an update to their clinical practice guidelines for the perioperative evaluation of bariatric surgery patients. The guidelines address fertility and reproductive health concerns only for women, which include recommendations regarding contraception and pregnancy (13). An American Society for Metabolic and Bariatric Surgery 2017 position statement on the impact of obesity and obesity treatment on fertility concluded that there is lack of evidence to determine the effect of medical or surgical obesity treatments on either female or male fertility potential (12).

There are currently no consensus recommendations with regard to men's reproductive health in the setting of bariatric surgery. Fertility counseling for these patients may be modeled after the approach to patients who will undergo chemotherapy for cancer. Although it seems that azoospermia rarely occurs after bariatric surgery, it may be nonetheless beneficial to discuss the potentially deleterious effects on fertility potential and the option for presurgical sperm cryopreservation during the preoperative evaluation. With further follow-up, our patient may yet regain spermatogenic function. Further research is needed with long-term follow-up to determine the incidence of and risk factors for secondary azoospermia after bariatric surgery.

In conclusion, we report the first case of secondary azoospermia after sleeve gastrectomy. Given the increasing utilization of bariatric surgery in the United States, this report highlights the importance of further investigation in this area to truly quantify the effect of bariatric surgery on the male reproductive potential. Until more research elucidates the full impact of bariatric surgery on semen parameters and reproductive hormones, men should be informed of the potentially adverse consequences of bariatric surgery on semen parameters.

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