Digestive Diseases and Sciences
https://doi.org/10.1007/s10620-022-07711-5

DDS–SIRC COOPERATIVE CONFERENCES

Stemming the Leak: A Novel Treatment for Gastro-Bronchial Fistula

F. M. Mongardini[1] · C. Cacciatore[1] · A. Catauro[1] · F. Maglione[1] · F. Picardi[1] · A. Lauro[1,2] · C. Gambardella[1] · A. Allaria[1] · L. Docimo[1]

Accepted: 7 September 2022

Abstract
Laparoscopic sleeve gastrectomy (LSG) is a commonly used procedure in bariatric patients that often has excellent results. Despite its advantages, LSG is burdened by specific intraoperative and postoperative early and late complications. One of the life-threatening complications is gastric fistula, usually treated with a multidisciplinary surgical–endoscopic approach. In case of failure of the latter, alternative nonoperative techniques such as the use of autologous stem cells truly represents an innovative possibility, with only few cases described in literature. Here, we report the case of a 25-year-old man with post-LSG broncho-gastric fistula treated with application of autologous stem cells after the failure of the conventional surgical/endoscopic approach.

Keywords Sleeve gastrectomy · Gastro-bronchial fistula · Mesenchymal stem cells · Endoscopic treatment · Abdominal and thoracic surgery

Abbreviations

LSG	Laparoscopic sleeve gastrectomy
GBF	Gastro-bronchial fistula
SES	Stricturotomy and septoplasty
RYGB	Roux-en-Y gastric bypass
SEPS	Self-expandable plastic stent
MSCs	Mesenchymal stem cells

Case Report and Evolution

In April, 2017, a 25-year-old patient underwent LSG for obesity (BMI 40 kg/m^2). He came to our attention in September of the same year with fever ≥ 38° C, tachycardia, productive cough, hemoptysis, left retro-scapular pain, worsening general status, and excessive weight loss. Laboratories were notable for leukocytosis with neutrophilia and left shift.

He underwent an urgent CT scan with intravenous contrast, showing a 25 mm leak at the level of the gastric metallic suture line. A direct communication was shown between the gastric lumen and a 51 × 38 mm fluid collection located in the left subphrenic area, extending up to the anterior pararenal space and to the upper pole of the left kidney. Multiple enlarged lymph nodes at splenic and pancreatic hilum, likely reactive, were detected. Moreover, the above-mentioned cavity communicated through a 12 mm diaphragmatic opening with another left intrapulmonary fluid collection, compressing the left lung (Fig. 1a–c).

CT scan suggested a type 3 gastro-bronchial fistula [1]. After a multidisciplinary evaluation (bariatric surgeon, thoracic surgeon, endoscopist, and anesthesiologist), a three-step surgical/endoscopic hybrid approach was considered. A central venous catheter was placed to ensure adequate hydration, nutritional support, and proper antibiotic administration.

Initially, the patient underwent surgical laparotomy in order to drain the abscess in the abdominal cavity. According to a nutritional counseling, a nasal-jejunal tube was positioned under intraoperative endoscopic guidance. Later, successful drainage of the pulmonary abscess was achieved after several operative bronchoscopies, allowing direct antibiotic instillations (2 ml gentamicin) (Fig. 2a, b). The bronchial tract of the fistula was treated with fibrin glue.

A profile of Federico Maria Mongardini is available at https://doi.org/10.1007/s10620-022-07712-4.

✉ F. M. Mongardini
f.mongardini@gmail.com

[1] General, Mini-invasive, Oncological and Obesity Surgery Unit, University of Campania "Luigi Vanvitelli", Naples, Italy

[2] Department of Surgical Sciences, Sapienza University of Rome, Rome, Italy

Published online: 17 October 2022

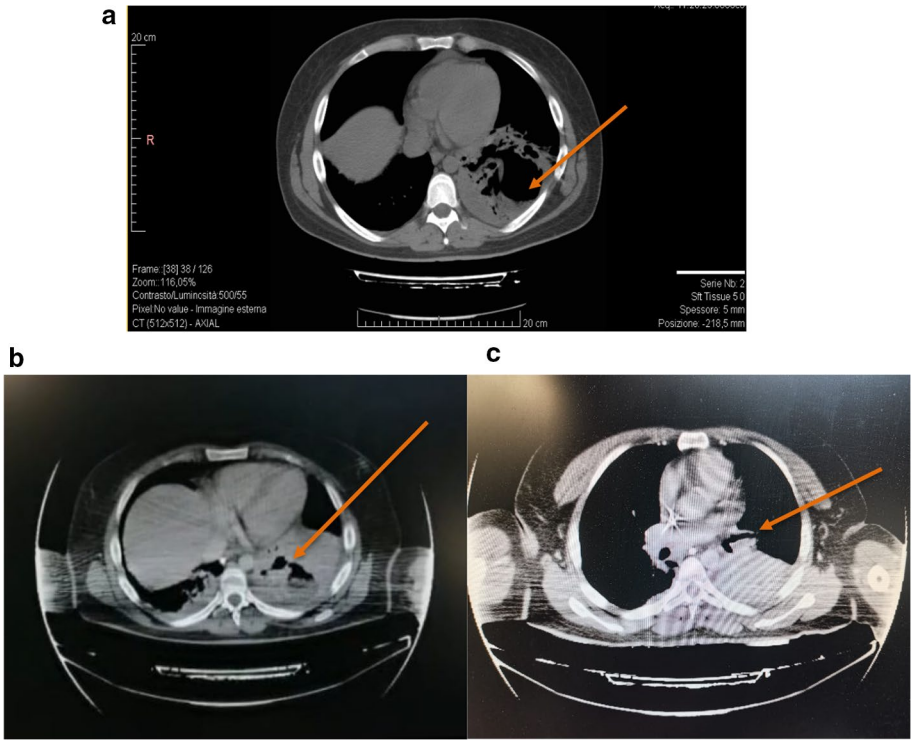

Fig. 1 **a–c** CT of the left fluid lung collection (red arrow—**b**) due to gastro-bronchial fistula (red arrow—**a** and **c**)

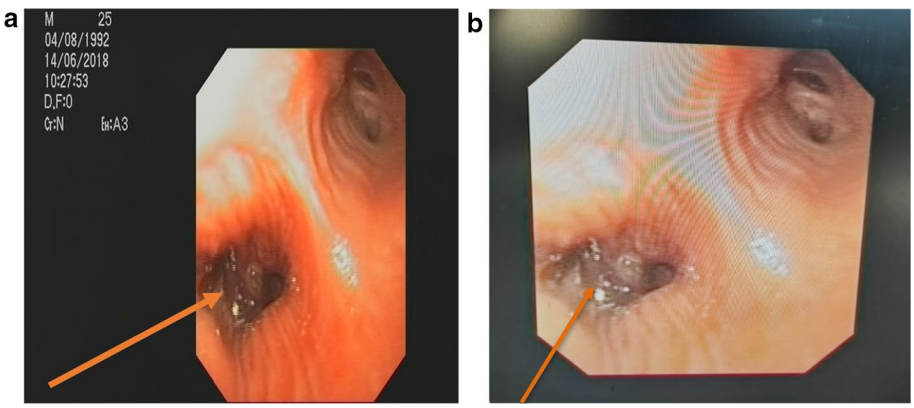

Fig. 2 **a** and **b** bronchoscopic view of the gastro-bronchial fistula (red arrow)

Eventually, the patient underwent operative gastroscopy after complete clinical stabilization and the fluid collections had been successfully drained (Fig. 3).

The gastroscopy was carried out in the operating room under orotracheal intubation. A self-expanding esophago-duodenal endoprosthesis was introduced along a guidewire. The distal end of the endoprosthesis was placed in the duodenal arch, while the proximal extremity was placed in the esophagus (30 cm from the upper dental arch) (Fig. 4).

Unfortunately, the prosthesis migrated distally during the third postoperative day, necessitating endoscopic extraction (Fig. 5).

After further multidisciplinary evaluation, the team decided that the best option was autologous stem cell grafting. This procedure was carried out in the operating room under general

Fig. 3 Gastro-bronchial fistula view (red arrow) during gastroscopic exam

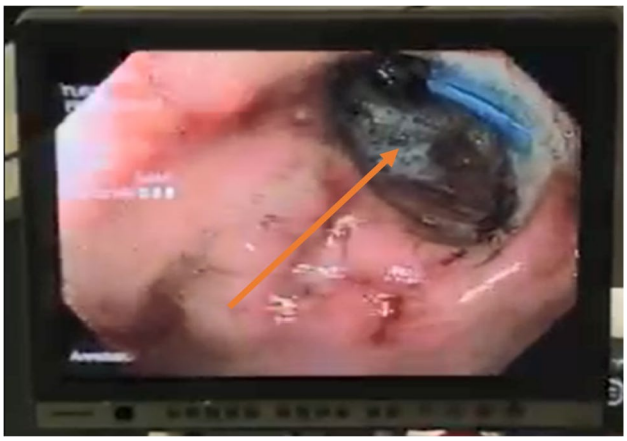

Fig. 4 Endoprosthesis placement (red arrow) during gastroscopy

Fig. 5 Endoprosthesis device after removal

anesthesia. The left lung was excluded, performing a single lung intubation. The grafting required an abdominal-thoracic approach: a bronchoscopy was carried out in order to inject the stem cells (LIPOGEMS®) in the bronchus involved by the gastro-bronchial fistula; endoscopy enabled the injection of the stem cells on the margin of the fistula using a 4 mm needle (Fig. 6).

The patient was discharged after 18 days with complete resolution of the fistula and the absence of any sign of infection or pulmonary disease. He was followed up for 8 months with serial CT scans and outpatient clinical evaluations, with gradual improvement of his clinical condition with complete radiological *restitutio ad integrum* (Fig. 7).

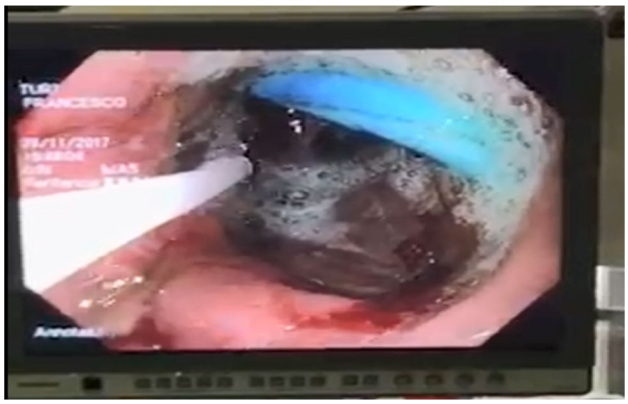

Fig. 6 Endoscopic injection of stem cells (LIPOGEMS®)

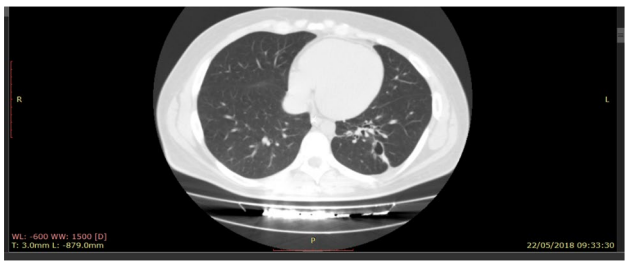

Fig. 7 Follow-up CT, with *restitutio ad integrum* (red arrow)

Discussion and Conclusions

LSG is a relatively new and evolving surgical technique indicated in the treatment of morbid obesity. Despite its advantages, LSG is fraught by specific intraoperative and postoperative complications such as staple-line bleeding, leaks, fistulae, and gastric strictures.

Gastric fistulae, mostly located at the level of the angle of His, occurs in 0.9–2.6% of the cases following bariatric surgery, reaching an 8% rate after repeat surgery [2]. The majority of gastric fistulae and leaks are due to ischemia of the gastric wall near the staple line rather than dehiscence of the staple line itself [3]. Gastric fistula is a severe life-threatening complication that can incur prolonged hospitalization necessitating the involvement of numerous specialists such as surgeons, anesthesiologists, radiologists, and endoscopists for adequate treatment. An early-onset fistula, defined as occurring during the first seven postoperative days, is usually high output and generally requires immediate surgical treatment, whereas late fistulae, which appear after the seventh postoperative day, generally have a less severe clinical course due to lower output. In the latter case, most authors suggest conservative treatment, although late-onset fistulae can have severe complications

as well [4]. A fistula lasting several months or longer can be complicated by gastro-cutaneous fistula, gastro-pleural fistula, gastro-bronchial fistula, or pylephlebitis.

The clinical presentation of gastro-bronchial fistula includes cough while swallowing, fever, dyspnea, hemoptysis, and recurrent pneumonia, which can culminate in acute respiratory distress [5–7]. Moeller and Carpenter classified gastro-bronchial fistulae in 1985, describing them as rare complications of esophageal, splenic, or anti-reflux surgeries [8–11]. Few cases of post-LSG GBFs have been comprehensively described and, due to this lack of data on GBFs, there is no consensus on the treatment of this rare complication [12]. To date only 75 cases have been reported in literature [3, 5, 6, 11, 13–25] (Table 1).

In order to select the optimal therapeutic solution, a multidisciplinary consultation is required [17]. Due to the complexity of the care of these patients, it is important to use a variety of approaches ranging from endoscopic therapy up to second-look surgery [26, 27], with each case requiring individualized treatment [16]. GBF patients are commonly in overall poor medical condition, with chronic pulmonary infection and malnutrition commonplace, requiring conservative treatment with antibiotics, nutritional support, and particular attention to electrolytes and fluid balance prior to any specific treatment. These considerations generally favor nonoperative treatments such as radiological drainage, placement of covered stents, and fibrin glue endoscopic injection, that lower morbidity with superior results in the medium and long term [23].

Campos et al. [14] suggested universal endoscopic treatment of gastro-bronchial fistulae with near-universal success, with a mean of 4.5 endoscopic procedures per patient and a mean length of treatment of 4.4 months. The endoscopic approach usually entails widening the lumen along with a combination of self-expandable plastic stents and stricturotomy plus septoplasty. Likewise, Al-Lehibi's case report [21] gives an account of GBF endoscopic therapy through a combination of over-the-scope clips and fully covered metallic stents. Nevertheless, endoscopic procedures are not always 100% successful [22]; while Campos et al. [14] reported a success rate with endoscopic treatment of 93.3%, Guillaud et al. [11] reported that complementary surgical treatments were necessary in 69% of their patients.

Our literature review (Table 1) suggests that a surgical approach is required in most cases [24, 25]. In cases of higher complexity and severity of the fistula, surgical therapy with a combined thoracic and abdominal approach [19, 28] appears to have superior results. In the series described by Rebibo et al. [13], outcomes of surgery for gastro-bronchial fistulas were improved when pre-operative intensive nutritional support was provided and abdominal plus thoracic procedures were combined. In contrast to the series reported by Campos et al. [14], all patients were treated successfully without an extended length of stay. Nevertheless, as stated in the multicenter study by Marie et al. [20], surgical management of GBFs incurs high morbidity and risk of failure, particularly when thoracic surgery occurs prior to the complete recovery from the abdominal leak.

Several papers reported the use of autologous stem cells for the treatment of GI fistulas [29–31]. The immunomodulatory and anti-inflammatory effects of mesenchymal stem cells have been extensively used for the treatment of intestinal and broncho-pleural fistulas, but they have never been used thus far for the treatment of gastro-bronchial fistula. To the best of our knowledge, this is the first case in the literature of a GBF that developed after LSG and was successfully treated using autologous stem cells. Lipogems® (Lipogems International SpA, Milan, Italy) is a disposable medical class IIA device for the closed-loop processing of liposuction of adipose tissue intended for autologous implantation. The micro-fragmented adipose tissue retains the structural properties and microarchitecture of the original tissue: scaffold (adipose tissue and stromal structure), cells (endothelium, pericytes/MSCs), and growth factors (cytokines and chemokines). The preservation of this microarchitecture is essential to support normal cellular function during both healing and tissue repair processes. The aspiration by syringe of a small amount of fat tissue from the donor site is the first part of this procedure (Fig. 8): a skin incision is made under local anesthesia. Klein® solution is subsequently injected into the subcutaneous fat tissue of the donor site. This tissue is first gathered and then treated with the Lipogems® device in a closed low-pressure cylindrical system in order to obtain fluid and uniform products that contain a high number of pericytes/MSCs.

The entire procedure requires a single surgical procedure and minimal manipulation in a closed and aseptic system through immersion in a physiological solution, in order to minimize traumatic effects on the cellular products. The procedure involves a progressive volumetric reduction of fat clusters and the elimination of pro-inflammatory oil and blood residues, improving handling and post-engraftment transplantation with effective and faster revascularization of the graft [29–31].

In our case, after the failure of both surgical and endoscopic approaches, the use of a minimally invasive treatment with autologous stem cells facilitated complete healing of the GBF within 18 days with the complete radiological *restitutio ad integrum* after 8 months. The use of autologous stem cell transplantation is a promising procedure that should be considered among the treatments for GBF, although larger comparative studies are needed to address potential safety issues.

Table 1 Treatment and outcome of post-LSG GBFs reported in literature

Author [reference]	Patient with GBF (F = female; M = male)	Procedures (Pts = patients)	Outcome	Average time from LSG
Fuks D. (2009) Obes. Surg. [5]	1 F	8 months of conservative management, 4 percutaneous drainages, 3 covered stent placements; after 4 months of stents removed, 9 months of conservative management; then total gastrectomy with intrathoracic esophagojejunostomy, left inferior lobectomy, reconstruction of diaphragm using latissimus dorsi flap	Lymphorrhea, dorsal haematoma; after 12 months of follow-up no complication	3 days
Campos J.M. (2011) Obes Surg. [14]	5 (3 F- 2 M)	Balloon dilation, SES	No complication, average 6 months (2–10) for healing	Average 6–7 months (1–30)
Sakran L. (2012) Obes. Fact. [18]	5 (3 F – 2 M)	3 pts: left lower lobectomy + total gastrectomy (2), RYGB (1). Two pts: endoscopic procedure	2–6 months for healing	Average 11 days (2–28)
Abraham A. (2012) Bmj Case Report [3]	1 F	Endoscopic SEPS + ablation of the fistulous tract	No signs of leak	20 months
Rebibo L. (2014) Surg. Obes. Relat. Dis [13]	6 (5 F – 1 M)	Endoscopic procedures; combined abdominal-thoracic surgical procedures (abdominal 1 step: total gastrectomy with esophagojejunal anastomosis or 60 cm RYGB. Thoracic 2 step: lung and diaphragm resection via left postero-lateral thoracotomy)	No postoperative deaths 4 postoperative complications (66.6%), including 2 Clavien grade III b postoperative fistulas (33.3%) treated with surgery	Average 136 days (99–238)
Barboza Besada E. (2013) Rev. Gastroenterol. Peru' [24]	1 F	Endoscopic procedure and then roux-en-y reconstruction after total gastrectomy	No improvement with endoscopic techniques; no signs of leak after surgery	Not available
Albanopoulos K. (2013) Surg. Obes. Relat. Dis [19]	2 F	1: RYGB and removal of fistulous tract 2: endoscopic stent placement	1: Free of symptoms after 3 months 2: After several months the stent was removed due to chronic enterocutaneous fistula and severe pneumonia. Drainage of a left pleural effusion with a transcutaneous catheter, sepsis, died 18 days later	1–10 days 2–6 days
Alharbi Sr. (2013) Ann. Thorac Med [6]	1 M	CT-guided percutaneous drainage of the left subphrenic collection; endoscopic covered stent; nasal-jejunostomy feeding	Healed	4 months
Guillaud A. (2015) Obes. Surg. [11]	13 from 5 centers (11 F–2 M)	Combined thoraco-abdominal surgery with gastrojejunal anastomosis ($n = 5$) or total gastrectomy ($n = 1$), multiple endoscopic treatment and thoracic surgery ($n = 3$), endobronchial valve ($n = 1$), total gastrectomy and abdominal drainage ($n = 1$), and transorificial intubation with thoracic surgery or drainage ($n = 2$)	Healed	Average: 129 days (14–277)

Table 1 (continued)

Author [reference]	Patient with GBF (F = female; M = male)	Procedures (Pts = patients)	Outcome	Average time from LSG
Guerrero Silva L.A. (2015) Cir Cir. [23]	1 F	Endoscopic clips; esophageal prosthesis in PTFE and fibrin; left thoracotomy and drainage tube placement for hemopneumothorax	Healed	14 days
Greilsamer T. (2017) Surg. Obes. Relat. Dis [17]	1 F	Postero-lateral left thoracotomy through the sixth intercostal space for left subcostal lobectomy; then total gastrectomy through a left subcostal incision with roux-en-y limb and a jejunostomy	No postoperative complications	5 years
Ben Nun A. (2018) World J. Surg [22]	13 (10 F–3 M)	After endoscopic procedure: 7 laparoscopic wash and drainage; 6 CT-guided subphrenic drainage. Then thoracoabdominal approach: primary repair of gastric sleeve or gastro-esophagostomy; Roux-en-y total gastrectomy	No postoperative complications 3 months: oral feeding 4 years:1 diaphragmatic hernia (left thoracotomy and surgical repair with mesh)	Average 14 months (7–36)
Saliba C. (2019) Am J Case Rep. [15]	1 F	RYGB	Healed	2 months
Al-Lehibi A. (2019) Saudi J Med Med Sci. [21]	1 M	Endoscopic over-the-scope clips and covered stent	12 weeks: the stent was removed 12 months: no recurrence	2 weeks
Marie L. (2020) Obes. Surg. [20]	21 from nine centers: 18 F—3 M	4 exclusive endoscopic procedure (pigtail and drainage); 5 endoscopic + thoracic surgery (drainage and endobronchial valve), 5 exclusive combined surgery, 8 endoscopy + digestive surgery (4 drainages, 1 conversion to RYGB, 1 total gastrectomy with esophagojejunal anastomosis), 2 endoscopic + combined surgery (1 drainage)	Healing time: 7 months	Average 124 days (7–760)
Badia Closa J. (2020) Obes. Surg. [25]	1 F	RYGB + resecting fistula	No postoperative complication 9 months: no complication	1 year
Sabawi M. (2021) Case Rep Radiol [16]	1 M	Resection of the fistula and gastrojejunal anastomosis	No postoperative complication	2 months

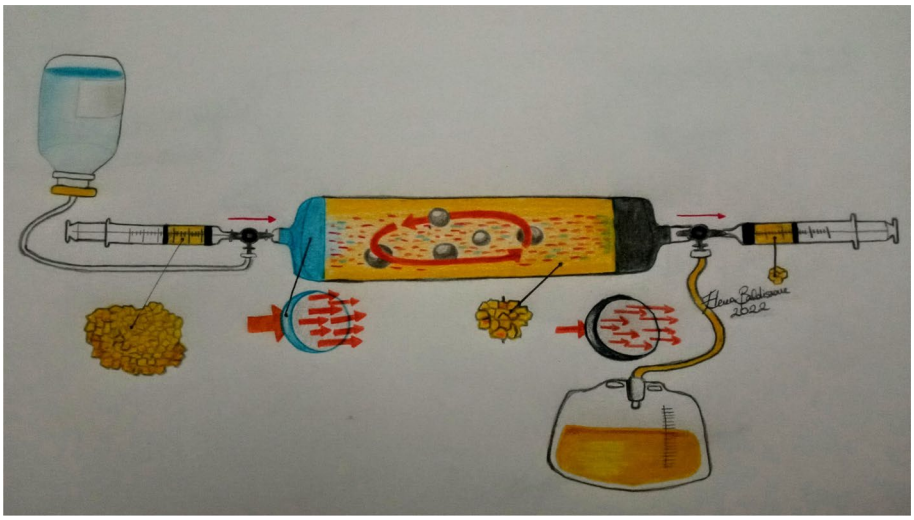

Fig. 8 Schematic of the Lipogems® device (drawing by Ms. Elena Baldissone)—see text for details

Key Messages

- GBF can represent a surgical complication after bariatric surgery.
- Endoscopic and surgical treatment of GBFs are usually but not always effective.
- The use of autologous stem cells appears to be a simple and effective salvage therapy for GBFs after bariatric surgery that have failed conventional nonoperative and operative therapies, although its overall effectiveness and safety requires larger studies.

Acknowledgments We wish to thank Ms. Elena Baldissone for the English editing and the drawing.

Declarations

Conflict of interest The authors have no conflicts of interest to declare regarding this case presentation.

References

1. Al Hajj G, Chemaly R. Fistula Following Laparoscopic Sleeve Gastrectomy: A Proposed Classification and Algorithm for Optimal Management. *Obes Surg.* 2018;28:656–664.
2. Campos JM, Siqueira LT, Meira MR et al. Gastrobronchial fistula as a rare complication of gastroplasty for obesity: a report of two cases. *J Bras Pneumol* 2007;33:475–479.
3. Abraham A, Virdi RP, Rajan D, et al. Gastrobronchial fistula following laparoscopic sleeve gastrectomy. **BMJ Case Rep** 2012 Sep 12;2012:bcr2012006789.
4. Boru CE, Angelis F, Iossa A et al. Persistent Fistula after Sleeve Gastrectomy: A Chronic Dilemma. *Chirurgia (Bucur)* 2019;114:790–797.
5. Fuks D, Dumont F, Berna P et al. Case report-complex management of a postoperative bronchogastric fistula after laparoscopic sleeve gastrectomy. *Obes. Surg.* 2009;19:261–264.
6. Alharbi SR. Gastrobronchial fistula -a rare complication post laparoscopic sleeve gastrectomy. *Ann Thorac Med.* 2013;8:179–180.
7. Moeller DD, Carpenter PR. Gastrobronchial fistula: case report and review of the English literature. *Am J Gastroenterol.* 1985;80:538–541.
8. Miwa K, Takamori S, Hayashi A et al. Gastrobronchial fistula after esophagectomy. *Eur J Cardiothorac Surg.* 2004;25:460.
9. Gaensler EH, Jeffrey RB Jr, Noonan CD. Gastrobronchial fistula: an unusual complication of Nissen fundoplication. *Gastrointest Radiol.* 1988;13:6–8.
10. Jeganathan R, Pore N, Clements WD et al. Gastrobronchial fistula—a complication of splenectomy. *Ulster Med J.* 2004;73:126–128.
11. Guillaud A, Moszkowicz D, Nedelcu M et al. Gastrobronchial fistula: a serious complication of sleeve gastrectomy. Results of a French multicentric study. *Obes Surg.* 2015;25:2352–2359.
12. De Dominicis F, Dhahri A, Verhaeghe P et al. Treatment of a chronic fistula after sleeve gastrectomy by a Roux-en-Y limb. *J Visc Surg* 2010;147:71–74.
13. Rebibo L, Dhahri A, Berna P et al. Management of gastrobronchial fistula after laparoscopic sleeve gastrectomy. *Surg. Obes. Relat. Dis.* 2009;19:261–264.
14. Campos JM, Franca Pereira E, Evangelista L et al. Gastrobronchial fistula after sleeve gastrectomy and gastric bypass: endoscopic management and prevention. *Obes Surg.* 2011;21:1520–1529.
15. Saliba C, Nicolas G, Diab S et al. Gastrobronchial fistula following a laparoscopic sleeve gastrectomy. *Am J Case Rep.* 2019;20:31–35.
16. Sabawi M, Alhasson A, Abualruz AR et al. Gastrobronchial fistula: a rare complication of postlaparascopic sleeve gastrectomy—a case report and literature review. *Case Rep Radiol.* 2021;2021:6641319.
17. Greilsamer T, Mahe PJ, Blanchard C et al. Late gastrobronchial fistula postsleeve gastrectomy. *Surg Obes Relat Dis.* 2017;13:1088.
18. Sakran N, Assalia A, Keidar A et al. Gastrobronchial fistula as a complication of bariatric surgery: a series of 6 cases. *Obes Facts.* 2012;5:538–545.
19. Albanopoulos K, Tsamis D, Leandros E et al. Gastrobronchial fistula as a late complication of sleeve gastrectomy. *Surg Obes Relat Dis.* 2013;9:e97–e99.
20. Marie L, Robert M, Montana L et al. A French National Study on Gastropleural and Gastrobronchial Fistulas After Bariatric Surgery: The Impact of Therapeutic Strategy on Healing. *Obes Surg.* 2020;30:3111–3118.

21. Al-Lehibi A. Endoscopic Management of Gastrobronchial Fistula after Laparoscopic Sleeve Gastrectomy: A Case Report. *Saudi J Med Med Sci* 2019;7:106–109.
22. Ben Nun A, Simansky D, Rokah M et al. Surgical Treatment of Gastro-Pulmonary Fistula Following Bariatric Surgery: Possible and Safe. *World J Surg.* 2018;42:1792–1797.
23. Guerrero-Silva LA, López-García S, Guardado- Bermúdez F, et al. Fístula Gastrobronquial: Complicación Mayor De Manga Gástrica. **Cir Cir.** 2015;83: 46–50 [Article in Spanish].
24. Barboza Besada E, Barboza Beraùn A, Castillo-àngeles M et al. Gastrobronchial fistula post sleeve gastrectomy. *Rev Gastroenterol Peru* 2013;33:157–161.
25. Badia-Closa J, Luna A, Montmany S et al. Esogastro-Pleuro-Bronchial Fistula: an Unusual Complication After Sleeve Gastrectomy. *Obes Surg.* 2020;30:4122–4123.
26. Cuadrado Ayuso M, Franco Herrera R, Lago Oliver J et al. Successful management of laparoscopic sleeve gastrectomy leak with negative pressure therapy. *Obes. Surg.* 2017;27:2452–2453.
27. Leeds SG, Burdick JS. Management of gastric leaks after sleeve gastrectomy with endoluminal vacuum (E-Vac) therapy. *Surg. Obes. Relat. Dis.* 2016;12:1278–1285.
28. Devbhandari MP, Jain R, Galloway S et al. Benign gastro-bronchial fistula –an uncommon complication of esophagectomy: case report. *BMC Surg* 2005;5:16.
29. Wankhade D, Shen M, Kolhe R et al. Review Article Advances in Adipose-Derived Stem Cells Isolation, Characterization, And Application in Regenerative Tissue Engineering. *Stem Cells Int.* 2016;2016:3206807.
30. Spinelli MG, Lorusso V, Palmisano F et al. Endoscopic repair of a vescicouterine fistula with the injection of microfragmented autologous adipose tissue (Lipogems®). *Turk J Urol.* 2020;46:398–402.
31. Tremolada C, Ricordi C, Caplan AI et al. Mesenchymal Stem Cells in Lipogems, a Reverse Story: from Clinical Practice to Basic Science. *Methods Mol Biol.* 2016;1416:109–122.