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LETTER TO THE EDITOR

Gastrointestinal Stromal Tumors After Laparoscopic Gastric Bypass for Morbid Obesity: a Diagnostic and Therapeutic Challenge

J. A. Fernández[1,2] · M. D. Frutos[1,3] · J. J. Ruiz-Manzanera[1] · A. Navarro[1] · G. Torres[1,2] · T. Soria[1,2]

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Introduction

Gastrointestinal stromal tumors (GISTs) are the most common mesenchymal neoplasms of the gastrointestinal tract, 60% of them being localized in the stomach [1]. Risk of recurrence stratification systems for these tumors is based on tumor diameter, mitotic index, location, and tumor rupture [2]. Most GISTs show mutations in KIT or PDGFRA that are targeted by the selective tyrosine kinase inhibitor imatinib mesylate (Glivec™, Novartis Pharmaceuticals) [3]. This drug can be used as an adjuvant treatment to reduce the rate of recurrence in high-risk patients improving dramatically their prognosis [3].

Laparoscopic gastric bypass (LGBP) is one of the most common procedures for the surgical treatment of morbid obesity [4]. The rate of gastric tumors in the excluded stomach is low, and only a few isolated cases have been reported, most of them being adenocarcinomas [5–10]. The diagnosis of GISTs in the excluded gastric remnant is anecdotic [11]. The impossibility to explore the gastric remnant by means of upper gastrointestinal endoscopy (UGE) and the absence of symptoms makes the diagnosis of these tumors difficult and late [11]. We present two cases of GISTs localized in the gastric remnant after LGBP years earlier, one of them previously published by our group [11]. To our knowledge, those are the only cases of GISTs after LGBP reported in the literature.

Case Report

Case No. 1 A 53-year-old female underwent LGBP in 2012 (BMI, 52 kg/m^2). One year later, the patient underwent laparoscopic surgery for acute purulent appendicitis, being note a left adnexal mass. A computerized tomographic scan (CT scan) identified a left adnexal cystic teratoma and, incidentally, a heterogeneous mass of 10 × 12 × 10 cm with ill-defined margins on the inferior margin of the excluded stomach (Fig. 1). Percutaneous fine needle aspiration (PFNA) revealed findings consistent with spindle cell CD117(+) gastric GIST. Surgery confirmed a tumor originating on the greater curvature of the excluded stomach, being performed an open gastrectomy of the residual stomach plus resection of the left ovarian teratoma. She developed a postoperative collection that required radiologic drainage. Pathology revealed a 10-cm-sized spindle cell gastric GIST, CD117/DOG-1 (+) with 3 mitosis/50HPF. Mutation was located at c-KIT E11. The patient was treated during 3 years with adjuvant imatinib (400 mg/day). Six years later, she is alive and free of recurrence.

Case No. 2 A 54-year-old male patient underwent LGBP in 2003 (BMI, 54 kg/m2). Sixteen years later, he is admitted to the hospital due to abdominal pain and palpable mass in the left upper quadrant. A CT scan revealed a 16 × 11 cm well-

✉ J. A. Fernández
jaferher@outlook.com

M. D. Frutos
mfb25s@gmail.com

J. J. Ruiz-Manzanera
jjrmanzanera@hotmail.com

A. Navarro
alvaronavarrobarrios@gmail.com

G. Torres
gtorressalmeron@gmail.com

T. Soria
tesoco@gmail.com

[1] Servicio de Cirugía General y del Aparato Digestivo, Hospital Clínico Universitario "Virgen de la Arrixaca", Carretera Madrid-Cartagena sin número (El Palmar), 30120 Murcia, Spain

[2] Unidad de Sarcomas, Hospital Clínico Universitario "Virgen de la Arrixaca", Murcia, Spain

[3] Unidad de Cirugía Bariátrica, Hospital Clínico Universitario "Virgen de la Arrixaca", Murcia, Spain

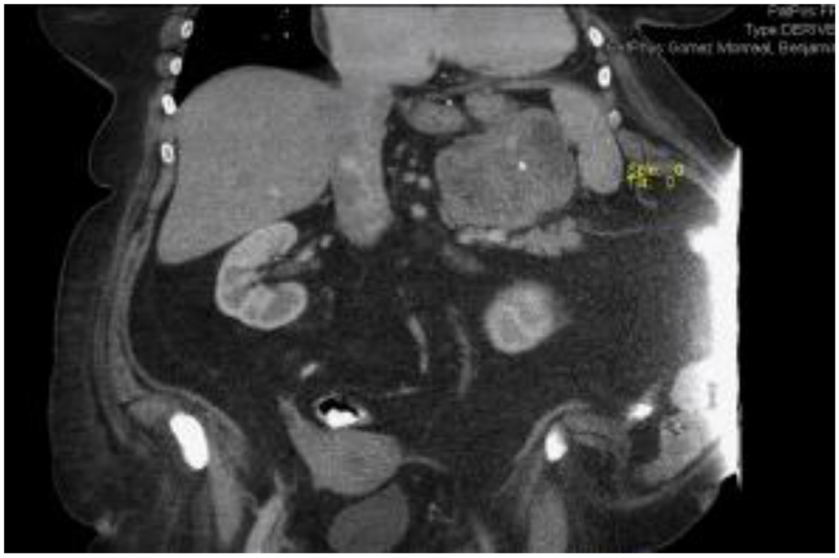

Fig. 1 CT scan showing and heterogeneous tumor dependent on the gastric remnant and in close contact with the splenic hilum

defined heterogeneous mass located in the gastric remnant (Fig. 2). Percutaneous biopsy revealed findings consistent with spindle cell gastric GIST CD117(+). Surgery confirmed a tumor originating on the greater curvature of the excluded stomach (Fig. 3), being performed an open wedge gastric resection. He developed a postoperative collection that required radiologic drainage. Pathology revealed an 18 × 12-cm-sized spindle cell gastric GIST, CD117/DOG-1 (+) with 7 mitosis/50HPF. Mutation was located at c-KIT E11. The patient is under treatment with adjuvant imatinib for 3 years.

Discussion

Malignant tumors in the remnant stomach are uncommon after LGBP, being reported in few isolated cases [5–10]. In this setting, GIST diagnosis is extremely rare [11]. Bariatric surgery appears to reduce the rate of gastric cancer according to studies comparing obese patients subjected to surgery (24/100,000) with those who are not (306/100,000) [12]. By contrast, the incidence of GISTs in obese patients undergoing bariatric surgery [13–17] is greater than that in the general population (0.8% vs 0.0006–0.0015%, respectively) [18, 19]. In the case of GISTs, the majority of the cases are diagnosed incidentally during surgery or after the pathological analysis of the surgical specimen in the case of gastrectomies. Most if not all GISTs diagnosed during bariatric surgeries are incidental small (< 2 cm) or micro (< 1 cm) GISTs [13–17].

Are these tumors new onset ones or missing ones? We cannot rule out the possibility that these tumors grow in the gastric remnant after bariatric surgery (as in case no. 2), but the relatively short time lapse observed between bariatric surgery

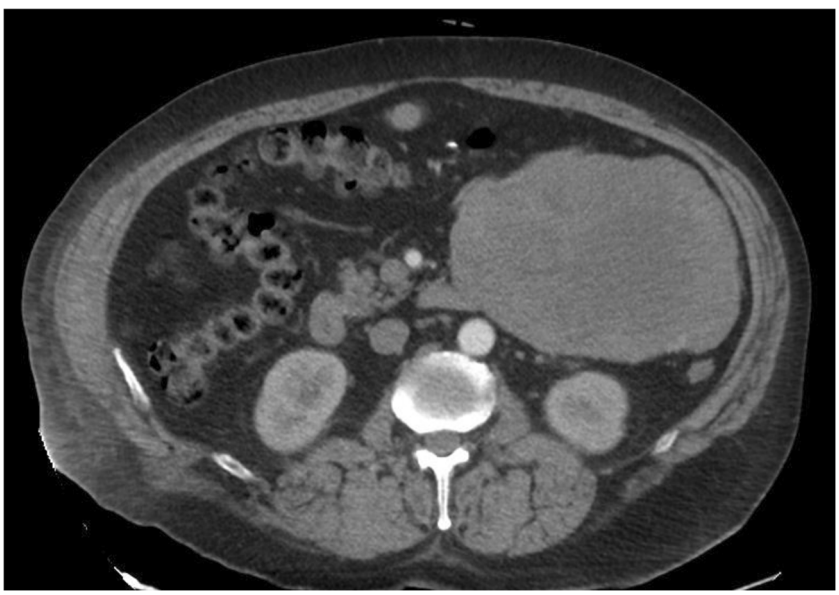

Fig. 2 CT scan of case no. 2 showing a well-defined heterogeneous mass if the left upper quadrant extending to left iliac fossa measuring 16 × 11 cm

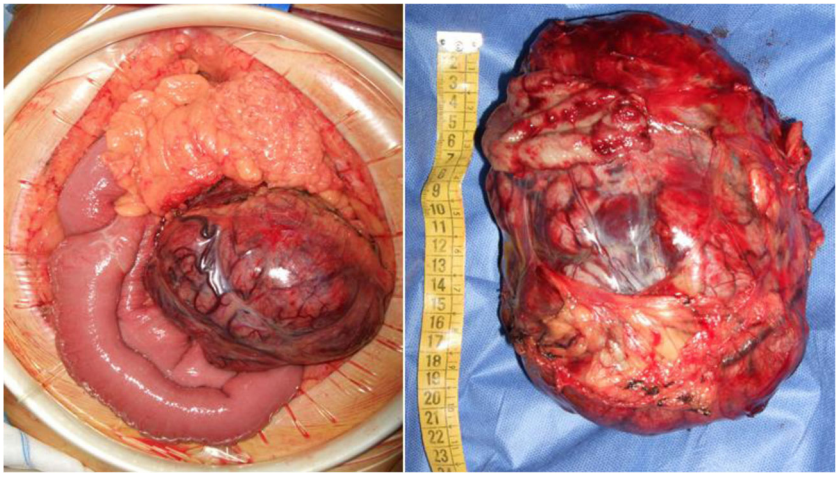

Fig. 3 Intraoperative image of case no. 2 showing the GIST arising under transverse colon and originating in the gastric remnant

and GIST diagnosis in case no. 1 makes us to consider that it was a tumor already existed during bariatric surgery but not diagnosed. Despite preoperative work-up, most if not all GISTs related to bariatric surgeries are diagnosed during surgery or after histopathological analysis [13–17]. It can be argued that the use of a preoperative UGE as a part of the routine preoperative work-up facilitates the diagnosis of these tumors but this issue is strongly debated [20–24]. Preoperative UGE allows us to diagnose pathologies such as esophagitis, gastric and duodenal ulcers, and malignancies [20–24]. Despite this, in the case of GISTs, their diagnostic scope and utility are low because they are submucosal with an exophytic pattern of growing. As CT scan is not included as a routine diagnostic tool in the preoperative work-up of these patients, its diagnosis is almost impossible [19–23]. On the other hand, the diagnosis of GISTs intraoperatively can be challenging as most of these tumors are small sized and can be hidden in adipose tissue and sometimes located in the posterior gastric wall [12–16]. In the case of LGBP, gastrectomies are not performed so the possibility of a pathological diagnosis is lost.

Complete surgical R0 resection without lymphadenectomy is the standard surgical treatment of GISTs [1–3]. As in our cases, if the tumor grows in the gastric remnant after LGBP, an open, preferably due to the size of the tumors, or a laparoscopic gastrectomy (wedge or full) can be easily performed. In the case of GISTs located in the gastric pouch, we are obligated to resect it and reconstruct the digestive tract by means of an esophagojejunostomy [13–17].

Nevertheless, these tumors, if present in the first surgery or not, are not diagnosed early due to the absence of symptoms and the impossibility to explore the gastric remnant, so when finally diagnosed, they are big sized as the two cases described.

According to the available risk stratification systems [2], both tumors were classified as high risk of recurrence, being indicated the use of adjuvant imatinib during at least 3 years in an attempt to reduce the recurrence rate [3]. This drug is taken orally usually at a dose of 400 mg or 800 mg per day depending on the mutation encountered (KIT exon 11 and KIT exon 9, respectively) [3]. One important issue is that gastrectomy impacts on absorption and thus imatinib plasma concentrations [25, 26]. LGBP patients are essentially gastrectomized patients, so despite an appropriate drug intake, plasma levels can be low. Several studies suggested that low plasma concentrations could explain some cases of suboptimal response or treatment failure [25, 26], being considered that plasma imatinib through levels between 760 and 1100 ng/ml is optimal and related with a good response [25, 26]. Our recommendation is to measure imatinib plasma levels every 6 months to assure a minimum threshold.

Conclusion

The occurrence of GISTs in the gastric remnant after LGBP is extremely rare. The absence of symptoms and the impossibility to explore the excluded stomach delay its diagnosis making GISTs, when diagnosed, big sized. Surgical R0 resection is the mainstay treatment. Imatinib adjuvant treatment is indicated in high-risk patients, but gastrectomy impairs its absorption lowering its plasma levels.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

Declaration of Ethical Approval All the procedures carried out in studies with human participants were in accordance with the ethical standards of the institutional and/or national research committee and the Declaration of Helsinki of 1964 and its subsequent modifications or comparable ethical standards.

Declaration of Informed Consent The informed consent was obtained from all the individual participants included in the study.

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