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CASE REPORT

Carcinoid Tumors and Morbid Obesity

Cláudio Corá Mottin · Ricardo Pedrini Cruz · Gustavo Gomes Thomé · Alexandre Vontobel Padoin

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Abstract Carcinoid is a rare gastrointestinal tumor, with an incidence varying from 1 to 2.5 per 100,000 in the general population. In this article, we report an elevated incidence of carcinoid tumor in an obese population, showing the importance of performing an endoscopic procedure before bariatric surgery.

Keywords Carcinoid tumor · Gastric carcinoid · Duodenal carcinoid · Morbid obesity · Bariatric surgery · Neuroendocrine tumor

Introduction

The first carcinoid tumor described was in 1867 by Langhans [1]. Oberndorfer coined the term *karzinoide* in 1907 to distinguish these neoplasms from carcinomas [2]. Carcinoid is a rare gastrointestinal tumor, but the most common gastrointestinal endocrine tumor [3–6]. They are more frequently found in the gastrointestinal tract (66.9%) [4, 5]. Within the gastrointestinal tract, most carcinoid tumors occur in the small intestine (39.3%), colon and rectum (33.9%, except appendix), appendix (17.8%), and stomach (5.9%) [5].

An incidence varying from 1 to 2.5 per 100,000 population has been reported for all carcinoid tumors [4, 6–10]. Gastric carcinoids account for less than 1% of all carcinoid tumors and less than 2% of all gastric neoplasms [3, 4, 8, 10]. Recently, an increased incidence of gastric carcinoids has been noticed [3–5, 11, 12] without a corresponding increase in survival, despite utilization of the latest available therapies [3]. The reason for the recent increase is unclear, and probably multifactorial. Changes in diet, environmental exposures, and longer life expectancy may play a role. Increased upper endoscopy screening has also contributed to the high detection of gastric carcinoids [3, 4, 11–13].

We analyzed 838 patients who underwent bariatric surgery for the treatment of morbid obesity from 2000 to 2007. An endoscopic procedure was performed in all these patients, where three cases of carcinoid tumor were discovered and described below.

Case Reports

Case 1

A 55-year-old white male with a BMI of 50.4 kg/m^2, sleep apnea, cholelithiasis, and liver steatosis, was scheduled to undergo bariatric surgery. An endoscopic procedure performed before surgery removed a carcinoid polyp in the duodenum. His preoperative levels of gastrin were 14.1 pg/ml (normal between 13–115 pg/ml). The patient denied symptoms of carcinoid syndrome. Sleeve gastrectomy with cholecystectomy was performed to allow further endoscopic duodenal follow-up. During surgery, four small nodules were found in the liver, and a partial hepatectomy was also done. Pathology revealed biliary adenoma, confirmed by immunohistochemistry. He is now 6 months postoperative, has a BMI is 35 kg/m^2, and no longer suffers from sleep apnea. Follow-up examinations showed no sign of any tumor.

C. C. Mottin (✉) · R. P. Cruz · G. Gomes Thomé · A. V. Padoin
Centro da Obesidade Mórbida, Hospital São Lucas da Pontifícia Universidade Católica do Rio Grande do Sul,
Av. Ipiranga, 6690/302,
Porto Alegre 90610-000 Rio Grande do Sul, Brazil
e-mail: claudiomottin@terra.com.br

Case 2

A 41-year-old white woman with a BMI of 45.2 kg/m^2 was scheduled to undergo bariatric surgery. The patient had a history of digestive bleeding (enterorrhagia), and menorrhagia. A preoperative endoscopic procedure showed a 6-cm carcinoid tumor in the large gastric curvature. The patient had no symptoms of carcinoid syndrome. Computed tomography (CT) and colonoscopy were unremarkable, and transvaginal ultrasound revealed a 1.3×1.7 cm myoma in the posterior wall of the uterus. A subtotal gastrectomy with hysterectomy and liver biopsy was performed, without any other lesion found during the procedure. Seven months after surgery, her BMI is 28.47 kg/m^2.

Case 3

A 32-year-old white woman with a BMI of 44.4 kg/m^2, and with Turner syndrome and hypothyroidism, was scheduled to undergo bariatric surgery. A preoperative endoscopic procedure showed multiple small polyps in the stomach body, some with central ulcerations. Biopsy revealed them to be carcinoid tumors. Immunohistochemistry with anti-chromogranin A (LK2H10), anti-Ki-67 (HB11) and anti-synaptophysin antibodies confirmed a well-differentiated neuroendocrine tumor. The patient denied any gastrointestinal symptoms. Her preoperative gastrin levels were 798 pg/ml. During surgery, para-esophageal and small gastric curvature lymphadenopathy was seen. Subtotal gastrectomy and regional lymphadenectomy were performed. Pathology confirmed carcinoid tumor in two lesions, the larger measuring 0.4 cm, involving the mucosa and submucosa. Lymph nodes did not show any lesion. Eight months later, her BMI is 30.3 kg/m^2, her gastrin level is under 10, and she has no complaints.

Discussion

Although rare, carcinoid appears to be more frequent among obese patients. Keshishian [6] et al. noticed a high incidence of carcinoid in obese patients (1.5%) compared to the general population. This has raised suspicion about the influence of obesity in the pathogenesis of tumors [14, 15], including carcinoid. In fact, like carcinoid tumors, obesity has increased over the years.

Our analysis evidenced a carcinoid tumor incidence of 0.358%, (358 per 100,000 in obese people) higher than the general population (1–2 per 100,000 people). Among these three carcinoid tumors, two were gastric, and one duodenal. Only two had gastrin measured, and only one had elevated serum gastrin levels. Although the relationship between carcinoid tumor and morbid obesity has not yet been established, it is possible that metabolic effects of obesity can be related to this higher incidence.

The pathophysiology of carcinoid is thought to be that tumors arise from neuroendocrine cells that secrete multiple hormones and other biogenic products [4, 6, 13, 16]. Regarding the pathogenesis of the majority of gastric carcinoids, it is believed that these tumors develop from the enterochromaffin-like (ECL) cells. Gastrin release from antral G-cells stimulates histamine secretion from ECL cells (mediating acid secretion from adjacent parietal cells) and their growth [11, 13, 17]. Most gastric carcinoid tumors arise from fundal ECL cells, driven to proliferate by elevated gastrin levels [3, 17–19]. ECL cell hyperplasia may be reversible if the hypergastrinemia is abolished. Because of that, antrectomy (excision of the majority of the G cells) has been performed in patients with type 1 carcinoid [11, 20]. However, there are some reports describing tumors that grow beyond the point of gastrin dependence and become autonomous [18].

Gastric carcinoids may be divided into two main groups, tumors associated or unassociated with ECL cells. The ECL cell group may be subdivided into three forms: type 1 (associated with atrophic gastritis), type 2 (associated with gastrinoma and MEN 1), and type 3 (without predisposing conditions). Type 4 carcinoids (non-ECL carcinoids) include other endocrine cell tumors. They may be located in any part of the stomach, while ECL cell carcinoids are situated in the gastric corpus or fundus. The biologic behavior and prognosis vary considerably in relation to type. Type 1 is the most common type accounting for 68 to 83%. Types 1 and 2 (both associated with hypergastrinemia) are usually multicentric, measuring 1 cm or less, without specific hormonal symptoms, and they are predominantly limited to the mucosa/submucosa (more than 90% of the cases showing low malignant potential) and rarely metastasize. Type 3 and type 4 carcinoids usually are solitary, larger and often highly malignant [3, 11, 13, 16, 17, 19].

Gastric carcinoid tumors are often asymptomatic, being usually found incidentally, and their clinical presentation is quite variable [3, 11, 13]. The most common symptoms described are abdominal pain and gastrointestinal bleeding. Typical carcinoid syndrome (attacks of flushing, watery stools, bronchoconstriction, hypotension and edema) can also occur, being associated more frequently with liver implants [7, 13].

Diagnostic tools include upper endoscopy, endoscopic ultrasound, CT scans, and somatostatin-labeled scintigraphy. Chromogranin A has been described as a biochemical marker in patients with gastric carcinoids, used for disease diagnosis and monitoring [3, 13, 16]. Many articles have described upper endoscopy as an important tool in bariatric surgery [21–26]. After surgery, the gastric remnant becomes inaccessible to conventional endoscopic examinations, denoting

the importance of the endoscopic procedure before bariatric surgery.

The prognosis of carcinoids depends on the organ involved, subtype, and extent of disease. Reviewing data from the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (NCI) from 1973 to 1999, Modlin et al. [5] showed an increase in 5-year survival rate, from 59.5 (1973–1991) to 67.2% (1992–1999) for all carcinoid tumors, regardless of site.

The treatment of gastric carcinoids depends on the subtype and size of the lesion. The treatment proposed for most type 1 gastric carcinoids includes initial endoscopic mucosal resection (EMR) if lesions are smaller than 1 cm, do not extend beyond the submucosa, and are fewer than five. Antrectomy is considered for more than five tumors with a maximum diameter of 10 mm, and for tumors larger than 10 mm (regardless of number, where in this case surgical excision of tumors larger than 10 mm is necessary). If tumors recur, total, subtotal, or partial gastrectomy with or without antrectomy may be performed. With antrectomy, the patient can return to normogastrinemia, ceasing the stimulation of ECL cells (potentially resulting in tumor regression or resolution). If total gastrectomy is not performed, an endoscopic examination once or twice a year is advised [3, 11, 13, 17]. Furthermore, in some cases, major reduction in hypergastrinemia did not prevent development of ECL carcinoids [18–20]. Because of the difficult access to the gastric remnant for follow-up, we prefer to remove it surgically, while the gastric pouch remains accessible to endoscopic exam.

This is another article associating carcinoid tumor with morbid obesity. Keshishian et al. were the first to describe this elevated association. We believe that obesity may play a role in the pathogenesis of carcinoid tumors, denoting the need for meticulous preoperative evaluation in this population. Several reports have emphasized the importance of performing a preoperative endoscopic procedure in bariatric surgery. Further clinical reports are necessary to corroborate these findings.

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