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Preoperative Endoscopic Tattooing for Laparoscopic Subtotal Gastrectomy as a Conservative Approach in Type 1 Neuroendocrine Tumor: A Case Report and Review

Veronica Salais, Jose Coronado A, Cesar Lopez A and Carlos Perzabal T*

Division of Internal Medicine/Gastroenterology, Ciudad Juarez Medical Specialty Center, Mexico

Abstract

Background: Neuroendocrine tumors are rare lesions most usually found incidentally in endoscopic procedures manifested as submucosal lesions or small polyps. Incidence is reported around 1-2 cases for every 1,000,000. Most of type 1 neuroendocrine tumors are found as small polyps located at either fundus or gastric corpus.

We present a case of a 48-year-old male with history of arterial hypertension, with severe megaloblastic anemia and melena for which endoscopic procedure was solicited. Endoscopic findings were atrophic gastritis and two small gastric polyps Paris Isp and Is. Pathology reported Type 1 neuroendocrine tumor. Due to the absence of metastasis or locoregional invasion, conservative management was done via laparoscopic subtotal gastrectomy with previous endoscopic submucosal tattoo delimiting the distal and proximal borders of disease. In conclusion an optimal treatment for type 1 neuroendocrine tumors is controversial. Conservative management is an accepted conduct in cases where local disease is confirmed. One way to better optimize the surgical treatment is to be able to better identify the affected gastric areas via endoscopic marking.

Keywords: Neuroendocrine type 1 tumor; Atrophic gastritis; Endoscopic tattoo; Laparoscopic gastrectomy

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Correspondence:
Veronica Salais, Division of Internal Medicine/Gastroenterology, Ciudad Juarez Medical Specialty Center, Avenue of the Americas 201, Margaritas, 32300 Ciudad Juarez, Chihuahua, Mexico, Tel: + 52-614-1955265;
E-mail: vero_bjs@msn.com

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Abbreviations

GNETs: Gastric Neuroendocrine Tumors; ECL cells: Enterochromaffin-like Cells; NETs: Neuroendocrine Tumors; WHO: World Health Organization; ENETS: European Neuroendocrine Tumor Society; NEC: Neuroendocrine Carcinoma; CgA: ChromograninA; NCCN: National Comprehensive Cancer Network; ER: Endoscopic Resection; CT: Computer Tomography; HPF: High Power Field

Introduction

Neuroendocrine Tumors (NETs) are rare neoplasms that arise from the peripheral neuroendocrine system dispersed in various organs [1].

The 2010 WHO classification [2] endorsed the European Neuroendocrine Tumor Society (ENETS) grading system, which is based on the mitotic count and Ki67 index of NETs [3]. As a result, NETs are classified as NET G1, NET G2, Neuroendocrine Carcinoma (NEC), mixed adenoNEC, and hyperplastic and preneoplastic lesions, based on their histological proliferation and differentiation. Tumors classified as G3 by the ENETS criteria correspond to NEC in the 2010 WHO classification of NETs. These classification and staging systems are useful in predicting prognosis as well as in therapeutic decision-making (Table 1).

Gastric Neuroendocrine Tumors (GI-NETs) have a reported incidence of only 1 to 2 cases/1000,000 [4]. These are neoplasms derived from the Enterochromaffin-like Cells (ECL cells) of the gastric mucosa. They are rare lesions with an indolent behavior and neuroendocrine differentiation. Although uncommon, their diagnosis is increasing, due to the widespread use of upper digestive endoscopy [5].

Type 1 gastric NETs, which represent 70% to 80% of all gastric NETs, occur more frequently in females [6] and are associated with chronic atrophic gastritis. In this condition, serum gastrin rises in response to gastric achlorhydria. The elevated gastrin, in turn, stimulates neuroendocrine cell hyperplasia in the stomach and development of multifocal polypoid NETs. Most are grade 1

Table 1: Histological grading of gastrointestinal neuroendocrine neoplasms.

ENETS Grading	Mitotic Index (x10 HPF)	Ki-67 Proliferation index	WHO Classification 2010
G1	<2	<2%	NET G1 (Carcinoid)
G2	2-20	3-20%	NET G2
G3	>20	>20%	NEC G3; large cell or small cell type

tumor with stage I disease and no mortality with prolonged follow-up [7]. In immunohistochemical staining, NETs cells are positive for ChromograninA (CgA), synaptophysin, vesicular monoamine transporter 2, and somatostatin receptor 2A [8].

Unlike other gastrointestinal NETs, which may cause carcinoid syndrome, gastric NETs are typically nonfunctional and may be diagnosed incidentally, or as part of the work-up for non-specific abdominal pain, anemia, or upper gastrointestinal bleeding [9].

The majority of type I GNETs present as small, multiple tumors, located in the gastric body or fundus, and limited to the mucosal or submucosal layers of the stomach wall. Since most type I GNETs are G1 tumors, the metastatic risk is very low, and the prognosis is excellent [10].

Four types of gastric NETs have been proposed and recognition of the type is important for defining the diagnostic approach and treatment. Most of type 1 NETs are smaller than 20 mm in size. Conservative management and endoscopic surveillance is adequate for well differentiated, multifocal gastric carcinoids (type 1 or type 2 gastric NETs) that are less than 10 mm to 20 mm in diameter, unless they show angioinvasion, infiltrate the muscular wall, or have a proliferation rate above 2% [11].

The National Comprehensive Cancer Network (NCCN) guidelines [12] recommend simple surveillance or Endoscopic Resection (ER) for tumors that are smaller than 20 mm in size, and without features of invasion of muscularis propria or metastasis, regardless of the tumor number. On the other hand, the ENETS guidelines recommend ER for the treatment of type I GNETs, with surgical resection to be considered only if invasion extends beyond the submucosa, or if lymph nodal or distant metastasis is present [13].

Currently, there are no randomized data comparing an aggressive endoscopic approach to more conservative strategy, and we believe that the malignant potential cannot be predicted by size and invasiveness only, but clinical classification (hypergastrinemia present or not) and WHO grading are also crucial for decision of treatment strategy [14,15].

Materials and Methods

We present the case of a 48-year-old male with history of systemic arterial hypertension who begins his condition one week prior to hospital admission presenting with melena, asthenia, adinamia, generalized paleness, severe megaloblastic anemia, exploration does not detect adenomegalies, upper endoscopy with polypectomy and biopsy is performed, reporting atrophic gastritis and multiple gastric polyps PARIS Isp. Pathology reported moderately differentiated invasive adenocarcinoma. Due to disagreement on endoscopic findings *vs.* pathologic diagnosis, it is decided to perform a new study for diagnostic confirmation, obtaining endoscopic images and histopathological report which confirmed gastritis atrophy, PARIS Isp gastric polyps as well as 0.2 cm infiltrating adenocarcinoma with neuroendocrine change, which is corroborated by immunohistochemistry with AE1/AE3 markers, Chromogranin, Ki-67, and synaptophysin. Diagnosis of grade 1 neuroendocrine tumor is confirmed coexisting with chronic gastritis and glandular atrophy. CT scan is performed to assess the extent of the disease where the stomach is reported with discrete thickening of the mucosa at the background level, without evidence of focalized or distant lesions (Figure 1).

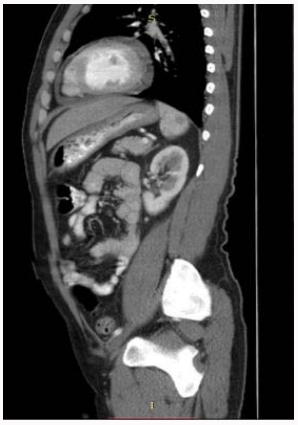

Figure 1: Sagittal section of thoracoabdominal tomography which shows thickening of the gastric mucosa.

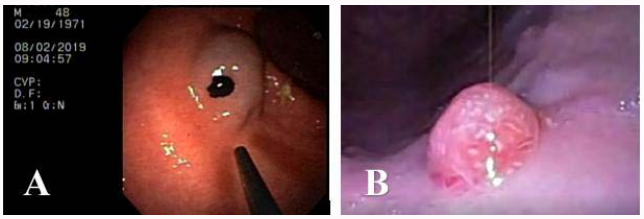

Figure 2: A: In this image endoscopic tattoos are identified at the level of greater curvature in the gastric antrum and in the greater curvature in the background; **B:** Gastric polyp.

Due to the lack of endoscopic ultrasound in our region, surgical evaluation solicited new endoscopy with placement of submucosal tattoos delimiting the area of appearance of polypoid tumors that is shown in (Figure 2) for surgical treatment with subtotal gastrectomy and gastro jejunum laparoscopic anastomosis with satisfactory post-operative evolution.

Results

The surgical technique of the treatment used is described below.

Diagnostic laparoscopy was started, and endoscopic tattoos were identified at the level of greater curvature in the gastric antrum and greater curvature in the background. Release of short gastric vessels is performed, minor curvature is released by electrofulguration, hemostasis is corroborated (Figure 3).

Linear stapling is performed at the prepyloric region level; second stapling is performed at the gastric body level, continuing with exploration at the Treitz angle, up to 40 cm (Figure 4). Opening of

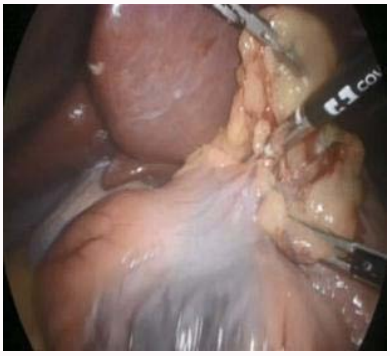

Figure 3: Identification and release of short vessels in minor curvature of the stomach by electrofulguration.

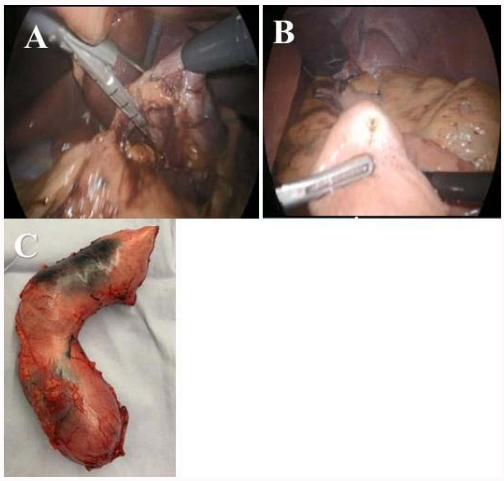

Figure 4: A: Linear stapling in prepyloric region and gastric body; **B:** Gastric pouchet opening and jejunal loop with posterior gastrojejunal anastomosis; **C:** Post-surgical piece of subtotal gastrectomy with gastrojejuno anastomosis performed via laparoscopy where submucosal tattoos are observed that were used as a guide for gastric resection.

the gastric and jejunal loop pouchet was performed, proceeding to perform a gastrojejunal anastomosis (Figure 4).

It is reinforced with Lembert points with Ethibond, a leak test is performed with methylene blue, corroborating its non-existence.

Subsequently, a histopathological report of a post-surgical specimen was obtained, in which the following was observed: well-defined neuroendocrine tumor grade 1 (G1) with radial, distal and proximal surgical limits free of injury as well as lymphovascular invasion.

Discussion & Conclusion

Neuroendocrine tumors are rare entities for which it is essential to have a high index of suspicion in order to carry out a correct diagnostic and therapeutic approach according to what is established in the clinical guidelines. Their management is based on the tumor subtype and histological features, the extent of locoregional spread, and the presence of metastasis. In the case presented, the diagnostic and therapeutic approach was discussed by our interdisciplinary team since the initial report of gastric adenocarcinoma was not consistent which the clinical presentation and endoscopic findings. Also, in areas where endoscopic ultrasound is hard to perform, imaging and surgical valuation becomes important in defining the extent of invasion. Therefore, we opted for a subtotal gastrectomy with the help of endoscopic tattooing in order to limit the resection area. This being a useful technique to offer patients a better quality of life as well as a speedy recovery.

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