

Primary hepatic gastrinoma, extremely rare case presentation and its surgical resolution, in a third level hospital in Mexico

Gastrinoma hepático primario, presentación de caso extremadamente raro y su resolución quirúrgica, en un hospital de tercer nivel en México

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Abstract

The gastrinomas are rare functional neuroendocrine neoplasms, most are localized to the duodenum (70-90%) or the pancreas (2-30%), but less common ectopic sites have been reported. The primary hepatic gastrinoma is extremely rare, with less than 40 cases reported in the medical literature. Its low incidence and its non specific clinical presentation make it a difficult disease to diagnose. Providing a timely diagnosis the patient can be treated by surgical resection with high chances of success. The objective of this paper is to describe a case of primary hepatic gastrinoma in Mexico, successfully treated by right liver segmentectomy.

Keywords: Primary hepatic gastrinoma. Surgical treatment. Segmentectomy.

Resumen

Los gastrinomas son neoplasias neuroendocrinas funcionales raras, y la mayoría se localizan en el duodeno (70-90%) o en el páncreas (2-30%), pero también existen otras localizaciones ectópicas poco comunes. El gastrinoma hepático primario es extremadamente raro, con menos de 40 casos reportados en la literatura médica. Su baja incidencia y su presentación clínica inespecífica lo convierten en una enfermedad difícil de diagnosticar. Al realizar un diagnóstico oportuno puede ser tratado mediante resección quirúrgica con altas posibilidades de éxito. El objetivo de este trabajo es presentar un caso clínico de gastrinoma hepático primario en México, tratado de manera exitosa mediante segmentectomía hepática derecha.

Palabras clave: Gastrinoma hepático primario. Tratamiento quirúrgico. Segmentectomía.

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Introduction

The Zollinger-Ellison Syndrome was described for the first time in 1955 by two surgeons: R.M. Zollinger and E.H. Ellison¹. This is the second most common functional neuroendocrine neoplasm, and it is also considered one of the neuroendocrine tumors (NET) harder to treat². This is due to the hypersecretion of gastrin produced by a tumor called gastrinoma³.

These tumors are rare functional neuroendocrine neoplasms with an annual incidence, in most geographical areas, of 0.5-1/1,000,000 inhabitants/year, approximately. The incidence is greater in men than in women and the average age of appearance is between 45 and 50 years of age. In spite of the fact that these tumors have slow growth, around 60-70% of the cases are malignant and 25% have a rapid growth⁴. They can occur sporadically (75%) or as part of the multiple endocrine neoplasia type 1 syndrome (25%)⁵.

The primary hepatic gastrinoma is a rare disease, with less than 40 cases reported in medical literature, and as it is located in an organ where metastases are common, its diagnosis is very challenging⁶.

A clinical case is presented with primary hepatic gastrinoma through surgical resection in a third level hospital in Mexico, with immediate satisfactory results and after 8 months of monitoring, as well.

Clinical case

50-year-old male, without relevant family or personal pathological history. His ailment starts with epigastric pain and heartburn of 2 years of progress, and at 6 months from the condition onset, chronic diarrhea and occasional emesis also appear. Moreover, he has presented a weight loss of 10 kg in a 12-month time.

During the initial physical examination, he only focuses on the pain to the epigastric and right hypochondrium palpation. There are no lesions nor visceromegaly identifiable through palpation, no information of peritoneal irritation, and the rest without anything else worthy of remark.

During his study protocol, he was subjected to four panendoscopies conducted by different operators and in different institutions, all of them with histopathology reports (HPR). The findings and their respective HPR were the following:

- Findings suggestive of esophageal candidiasis, erosive bulboduodenitis, chronic gastritis. HPR: esophagus biopsy with Barrett's mucosa without dysplasia, cardiac mucosa without dysplasia.

- Esophagitis grade II, superficial gastritis, normal duodenum. HPR: esophagus biopsy with chronic esophagitis.
- Esophageal moniliasis, minimal gastritis and duodenitis. HPR: esophagus biopsy with chronic esophagitis, gastric biopsy with minor chronic gastritis not associated to *Helicobacter pylori*.
- Chronic gastric duodenitis. HPR: gastric biopsy with non-atrophic gastritis, without metaplasia or dysplasia, and no evidence of malignant cells in the studied tissue. A colonoscopy is also performed, finding an image consistent with spastic colon.

After deciding to perform a simple computed tomography (CT) with double contrast, a thickening is found in the distal third of the esophagus and in the gastroesophageal junction. In segment VII of the liver there is a 49 mm nodular lesion, with regular, clear, and homogeneous borders, with density in simple phase of 15-35 UH (Fig. 1), and the rest of the study with no alterations. Due to the results of the CT scan, a percutaneous biopsy of the liver tumor is collected (Fig. 2), and it reports a neuroendocrine tumor moderately differentiated of grade 2, CK7-negative, CK20-negative, CEA negative, HEP-PAR1 negative, synaptophysin positive, chromogranin A positive and Ki-67 positive (5%).

A scintigraphy is also performed with octreotide-Tc-99m that shows a hyperenhancing lesion in the right lobe of the liver (Fig. 3). No abnormal areas are found in the rest of the whole body analyzed. The protocol is finished with a whole-body positron emission computed tomography (PET), finding a liver lesion in segment VI-VII, hypodense, with an increase in the metabolism (Fig. 4), and diffuse increase of metabolism in the esophagus and the gastric corpus.

With the NET result, serum tests of 5-hydroxyindoleacetic acid, chromogranin A and gastrin are performed with the following results: 2.2 mg/24 h, 33.9 nmol/l y 7715 pg/ml, respectively. This confirms the diagnosis of primary hepatic gastrinoma.

The patient is subjected to surgery, finding a liver of normal size, with the presence of a tumor in segment VII of approximately 7 cm in diameter. The rest of the segments show no alterations. A right posterior segmentectomy is performed (segments VI and VII). The patient presents an appropriate course and is discharged on the fourth day after surgery.

The HPR of the surgical piece reported a 6.4 cm NET of intermediate grade (G2), widening of surgical margin free from neoplasm, synaptophysin positive,



Figure 1. Simple computed tomography of the abdomen, axial section. There is a nodular liver lesion in segment VII, hypodense, with regular and clear shape.

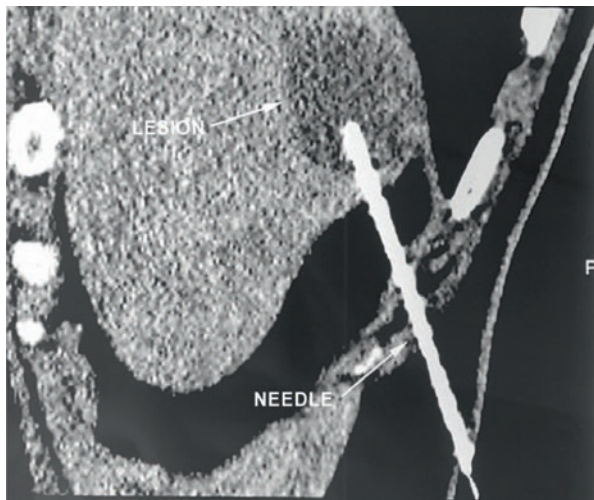


Figure 2. Percutaneous biopsy. The arrows point to the circumscribed liver lesion and the needle used to take the biopsy.

chromogranin positive, CD56 positive, Ki-67 positive (5-7%), P53 positive and cytokeratin positive (Fig. 5).

Presently, after 8 months from the intervention, the patient presents asymptomatic. The ultrasound and abdominal CT scan show no alterations and the serum gastrin test results are within normal parameters (< 115 pg/ml).

Discussion

Gastrinomas are rare neoplasms usually located in "the gastrinoma triangle": an imaginary anatomical region demarcated in its upper portion by the convergence of the cystic duct and the hepatic duct; in the middle by the junction of the pancreas head and neck; and in the lower area by the junction of the second

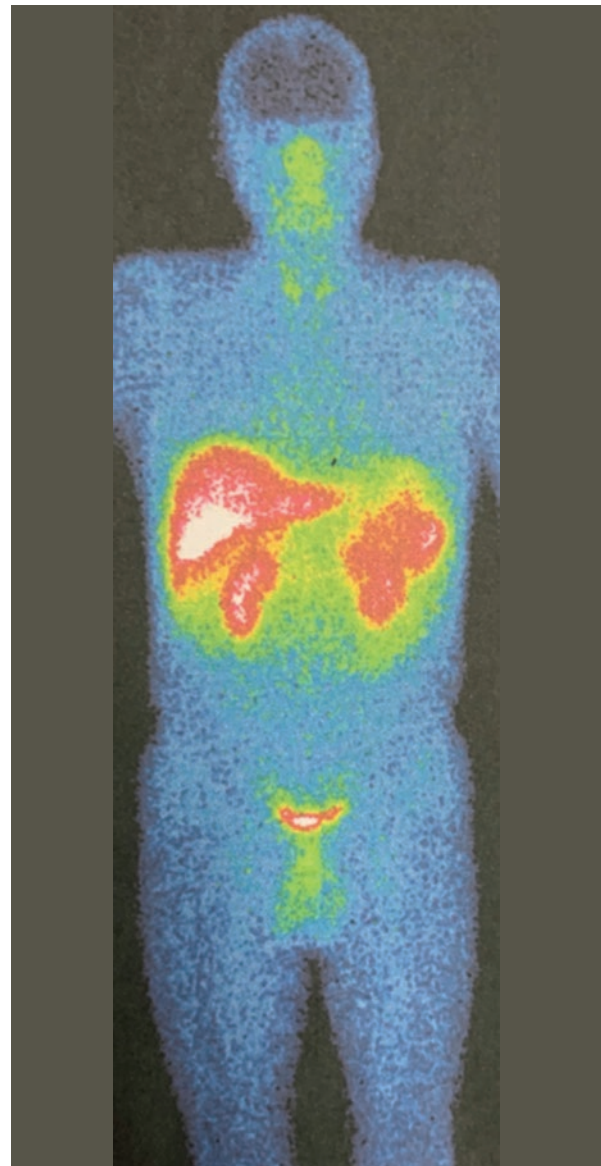


Figure 3. Scintigraphy. Coronal section that shows an uptake increase in the right lobe of the liver.

and third duodenum portions⁷. Most gastrinomas occur in the duodenum (70-90%) or in the pancreas (2-30%). However, there are other rare ectopic locations, such as the ovary, the stomach, the lymph nodes, the heart, the liver, and the bile ducts². Only 5.6% has been reported to be extrapancreatic, extraduodenal or extranodal⁸. As the liver is an organ where NETs usually tend to present metastasis, and as there are less than 40 cases of primary hepatic gastrinoma⁶ reported in medical literature, a thorough search must be conducted to rule out tumors at other sites. This is the reason this patient was subjected to several studies for diagnostic purposes that ruled out

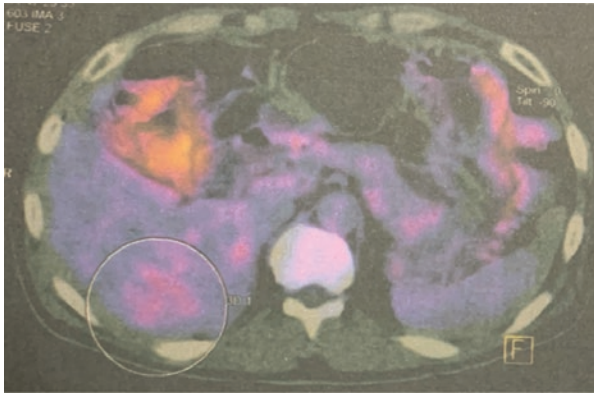


Figure 4. Positron Emission Tomography. There is an increase in the metabolism of the lesion located in the right lobe of the liver

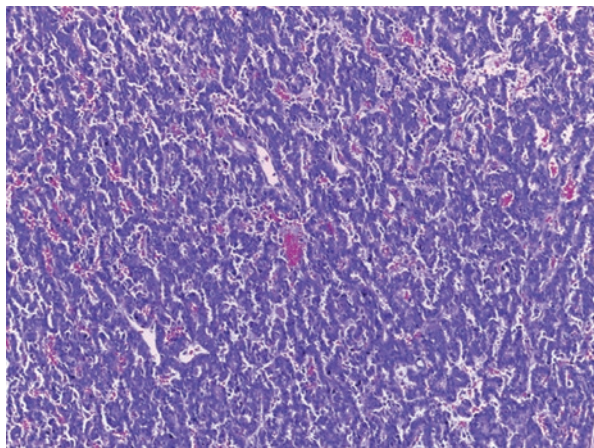


Figure 5. Microphotography with zoom in the lesion, in which there are trabeculas and pseudo glands, with homogeneous nuclei and eosinophilic cytoplasm.

a second malignant lesion, eliminating at first instance the possibility of a neoplasm in the gastroesophageal junction due to the thickening found in the CT scan.

The clinical symptoms of this tumor are associated with gastrin hypersecretion, producing a gastric acid increase. This is the cause of onset for Zollinger-Ellison syndrome, which is characterized by an acid peptic disease and disorders of gastrointestinal motility⁹. The most common presentation of this syndrome is abdominal pain (75%) and chronic diarrhea (73%)⁶, just as it happened with our patient.

In some papers, it has been reported that the scintigraphy tends to be more sensitive than any other imaging method for the identification of a gastrinoma¹⁰. It successfully locates NETs in up to a 78-86% of cases, and it has become the imaging study of choice for patients with a suspicion of gastrinoma⁷. On the other hand, during the last years, the PET has

revolutionized the screening protocols to search for neoplasms, given its ability to visualize metabolic activity. Both exams were employed for this patient, and their results confirmed a primary hepatic NET, conclusively ruling out a possible secondary lesion in another organ. After the serum tests and due to the extremely high values of gastrin found, the diagnosis of primary hepatic gastrinoma was concluded.

The importance of a timely diagnosis and treatment consists in that 65% of gastrinomas present a malignant course⁷. Besides, the symptoms presented by the patients significantly affects their quality of life.

The gastric hypersecretion of the Zollinger-Ellison syndrome may be treated generally with proton pump inhibitors or with anti-secretory medication. However, surgery is the only healing treatment for gastrinomas⁵. In spite of the few cases reported of primary hepatic gastrinoma, the surgical resection must be the treatment of choice. Surgery is the only possibility for cure, with a success rate of up to 86%, presenting normal gastrin values early after the surgery in 60% of the cases. The 15-year survival rate in patients who had surgery is 98%, versus 74% in those who had not⁶.

In this patient, it was decided to conduct a complete resection of the tumor with right posterior liver segmentectomy, obtaining neoplasm free margins. This provides the patient with a healing treatment, increasing his long-term survival rate and enhancing his quality of life.

Conclusions

Primary hepatic gastrinoma is an extremely rare tumor, with very few cases reported around the world. Abdominal pain, diarrhea, vomit, and weight loss are some of the symptoms that undermine the patients' daily life. In order to get to the diagnosis, it is necessary to have an imaging study that show the tumoral liver lesion, to conduct a biopsy of said lesion with PHR compatible with NET, to conduct extension studies that rule out neoplastic lesions in other organs, and to present high serum values of gastrin. As it is a tumor with high probabilities of presenting a malignant course, surgical resection is the priority.

This case shows us that with an appropriate and timely treatment both life expectancy and its quality can be enhanced for these patients.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical disclosures

Protection of people and animals. The authors declare that no experiments have been made on human beings or animals for this research.

Data confidentiality. The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Right to privacy and informed consent. The authors have received an informed consent from the patients and/or subjects referred to in this article. This document is in possession of the corresponding author.

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