Case Report

Somatostatin receptor molecular imaging in a misdiagnosed gastrinoma case

ABSTRACT

Gastrin-secreting tumors, hypergastrinemia and severe ulcer disease form the trademarks of Zollinger-Ellison syndrome (ZES). We report a case of gastrinoma, in a patient who was misdiagnosed for almost five years. The case emphsizes the the special role of functional imaging in the personalized approach to the patient with suggestive symptomatology for NETs. Taking into account that in 80 to 100% of cases of gastroenteropancreatic (GEP) NETs are expressing somatostatin receptors, the functional imaging with radiolabeled somatostatin analogues can be used in order to improve its diagnosis, respectively the treatment of GEP NETs. In the approach to the patient with tremendous digestive symptomatology, physicians from different specialties should evaluate NETs specific markers and then insist on structural-functional complementarity, avoiding the waste of time and high cost of repeated structural investigations. The conclusion of our study is that functional imaging is mandatory in the diagnostic algorithm of gastrinoma.

Keywords: Functional imaging, gastrinoma, hypergastrinemia, neuroendocrine tumors, somatostatin receptor scintigraphy

INTRODUCTION

Zollinger–Ellison syndrome (ZES), first described in 1955, can be sporadic or can appear in the context of a multiple endocrine neoplasia type 1.[1] Gastrin release from gastrinoma is followed by a gastric acid hypersecretion, responsible for ZES.[2] ZES is an association between gastrinoma, hypergastrinemia, and severe ulcer disease, located thrice more frequently in the duodenum than in the pancreas.[3] We present a case of a possible gastrinoma, which was initially misdiagnosed, where functional imaging had a key role in the diagnosis.

CASE REPORT

A 44-years-old male was hospitalized for the evaluation after a long history of unexplained significant weight loss, abdominal pain episodes, diarrhea, and vomiting of more than 4 years. He has no reported family history of malignancy. Medical history included diabetes mellitus diagnosed 4 years ago, abdominal pain syndrome, diarrhea, vomiting, hematemesis, and melena episodes throughout this period, culminating with numerous surgical events (liver abscess and cholecystectomy, repeated perforated duodenal ulcers, and perforated jejunal ulcer treated through segmental enterectomy). In his medical file, four times higher values

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Submitted: 12-Feb-2020, **Revised:** 08-Apr-2020, **Accepted:** 01-May-2020, **Published:** 22-Aug-2020

Access this article online	
Website: www.wjnm.org	Quick Response Code
DOI: 10.4103/wjnm.WJNM_16_20	

How to cite this article: Stolniceanu CR, Grierosu IC, Matovic M, Stefanescu C. Somatostatin receptor molecular imaging in a misdiagnosed gastrinoma case. World J Nucl Med 2020;19:417-20.

of gastrin (481 pg/mL) and 12-fold chromogranin A (CgA) values (1200 ng/mL) were found.

The differential diagnosis of gastrinoma was considered, but repeated structural imaging, did not confirm the presence of a tumor or tumor metastases. The structural imaging investigations (ultrasound, computed tomography [CT] and magnetic resonance imaging [MRI]) revealed hepatomegaly, visible intrahepatic ducts (IHD) in the left lobe of the liver, chronic pancreatitis with an enlarged pancreas, and dilated Wirsung duct (Wd), with peritoneal bursitis. Upper digestive tract endoscopy with biopsy yielded unremarkable results: superficial ulceration and chronic nonspecific duodenitis. The patient underwent a barred esophago-gastro-duodenal scan that revealed thickened gastric folds with polypoid aspect, deformed edematous bulb, and gastroesophageal reflux.

False-positive increased biochemical markers (as presented in discussion) were all excluded from the study.

At the time of presentation, physical examination revealed an ill-looking man with a body mass index of 18 and a 80% Karnofsky scale. Significant laboratory findings included accentuated hepatic cytolysis and increased neuroendocrine tumor (NET) markers compared to the values from 2 years ago: ten times higher values of gastrin (1000 μg/mL) and thirty times higher values of CgA (3005 ng/mL).

The patient imaging assessment started again with the structural imaging evaluation: abdominopelvic CT [Figure 1], MR cholangiopancreatography (MRCP), and MR enterography, which again did not show any evidence of pancreatic tumor. MRCP revealed dilatation of the IHD, a dilated hepatic duct, and an enlarged pancreas with cystic areas. MR-enterography did not reveal any pathological elements at the intestinal level: nonhomogeneous cephalic pancreas aspect suggestive of chronic pancreatitis, a dilated Wd, at the cephalic level.

After exhaustive workup, and with the continuing suspicion of gastrinoma, somatostatin receptor scintigraphy (SRS) was indicated. For an optimal imaging of the abdominal cavity, the patient was prepared using a light diet and a mild laxative starting the evening before. Study design: dynamic scintigraphy (60 images, 1 image/s, 128 × 128 matrix), spot scintigraphy (10 min/image, 256 × 256 matrix), whole-body scintigraphy (matrix 256 × 1024, 6 cm/min bed movement), and single-photon emission computed tomography (SPECT) (128 × 128 matrix, 132 images) were acquired early, 2, 4, and 24 h after 10.57 MBq/kg ^{99m}Tc-Tektrotyde iv dose. For each hot area, regions of interest were defined, uptake was quantified (counts/pixel), and indices were calculated: I_1 = Tumor/liver, I_2 = Tumor/spleen, I_3 = Tumor/lung, I_4 = Tumor/right thigh. Uptake kinetics [Figure 1] and tumor heterogeneity graphs were analyzed [Figure 2]. We diagnosed a very intense uptake, Krenning scale Grade 4, and limited tumor burden score, with possible pancreatic localization, confirming the presence of somatostatin receptors (SR) and advocating the presence of NET [Figure 1a, c – CT, b, d – SRS and Figure 3]. Our scintigraphic findings, correlated with the higher NET marker values, supported our diagnosis of possible gastrinoma on the pancreas.

DISCUSSION

Gastrinoma incidence is 1–3/million population/year, and the delay between first symptoms and diagnosis is about 5 years.[4,5] Increased gastrin and CgA levels alone commonly do not establish the diagnosis of a gastrinoma because high

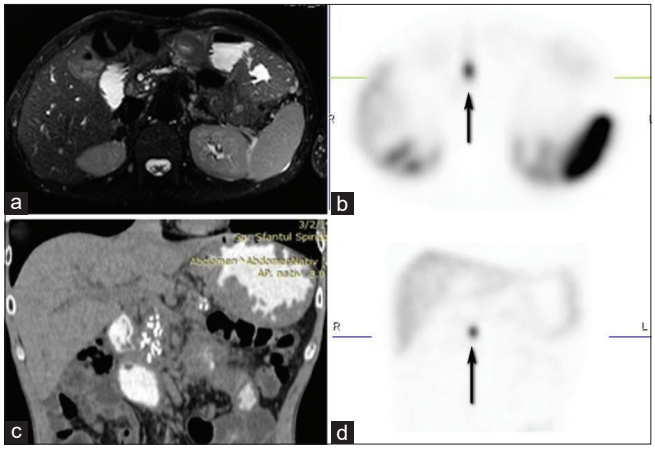

Figure 1: The different imaging techniques in a 44-years-old male with a neuroendocrine tumor. Computed tomography scan of the thorax (a and c); ^{99m}Tc tektrotyde scintigraphy (b and d)

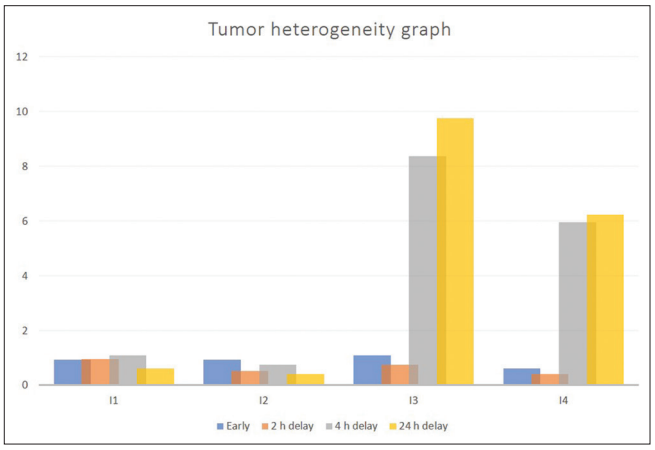

Figure 2: Heterogeneity graph. Evolution of uptake indices (I1 = Tumor/liver, I2 = Tumor/spleen, I3 = Tumor/lung, I4 = Tumor/right thigh): early, 2, 4 and 24 h

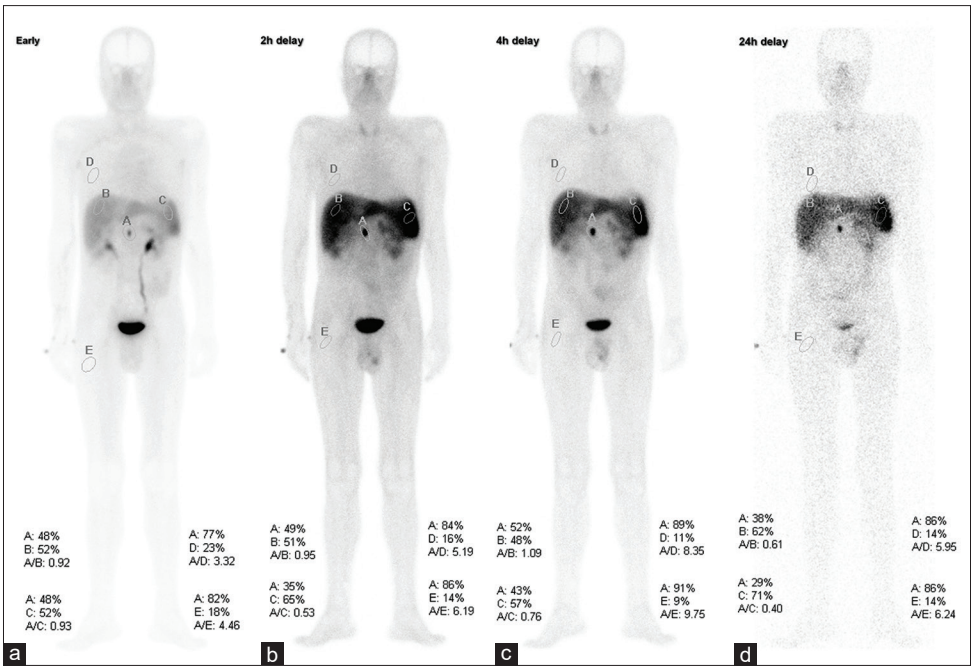

Figure 3: Intense uptake, Krenning scale Grade 4, limited tumor burden score, with possible pancreatic localization, confirming the presence of somatostatin receptors and advocating the presence of NET. Uptake indices early (a), at 2 h (b), 4 h (c), 24 h (d). A-Tumour ROI; B-Liver ROI; C-Spleen ROI; D-Lung-ROI; E- Right tight-ROI

levels can be usually found in conditions unrelated to NETs, such as chronic atrophic gastritis or proton-pump inhibitor therapy.[5] Furthermore, there are other causes of elevated CgA levels, such as reduced kidney function, hypertension, different rheumatoid arthritis, and active inflammatory bowel disease.[6]

While clinical and laboratory findings can be suggestive for gastrinomas, structural images (CT and MRI) and functional images (SRS) are required for localization and evaluating of primary tumor and metastases, definitive diagnosis however being established by the pathologist report. Small functional NETs can often pose a diagnostic challenge, and sometimes, multiple imaging modalities are required to locate tumor. In our case, the false-negative image of chronic pancreatitis could be explained by the use of noncontrast MRI because the small lesion would have been visible only in the arterial phase.

SRS, especially SRS-SPECT, with a sensitivity of 78%–88% (87.5% for ^{99m}Tc hydrazinonicotinyl-Tyr3-Octreotide) and a specificity of 85.7%–97%, has a well-established role in finding subtle functional pancreatic NET that are not seen on structural scans.[5,7]

Moreover, different SRS positron emission tomography molecules, such as ^{68}Ga-DOTA-peptide, with a mechanism of action similar to SRS-SPECT tracers, with a wider and better affinity for SR, could be extremely useful for superior lesion targeting, particularly for tumors with low SR expression, with a range for sensitivity of 74.3%–99.9%.[8,9]

Despite the evidence of ulcers, ZES should be considered, principally because of our patient's history and hypergastrinemia. In this case, there were no imaging data, except for SRS, to support the diagnosis.

The medical practitioners have to be aware of certain signs as well as increased values of NET markers. Special attention must be given to the tumors located in the pancreas, considering their greater potential of malignancy.

CONCLUSION

SRS imaging represents a mandatory step in the personalized approach to NET patients. Functional metabolic imaging helped establish the diagnosis of gastrinoma, making curative surgical treatment possible and improving the quality of the patient's life.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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