Preoperative detection of gastrointestinal neuroendocrine tumors using endoscopic ultrasonography

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ABSTRACT

Objective: almost 30% of gastroenteropancreatic neuroendocrine tumors (GEPET) escape preoperative identification using standard imaging techniques. The goal of this retrospective study is to present our cumulative experience in the assessment of GEPET by preoperative endoscopic ultrasonography (EUS), and to compare it with a literature review.

Patients and methods: thirty-seven patients with suspected specific hormonal syndromes were sequentially examined with US, CT, MRI, angiography, OctreoScan, and radial and sectorial EUS. Sixteen were males (43%) and 21 were females (57%), with a mean age of 61 years (interval: 40-84 a). Of all 37 patients, 27 had 19 endocrine tumors in the pancreas and 14 tumors in their gastrointestinal tract. No tumors were demonstrated in 10 patients, hence they were used as a control group. Of all 37 patients, 24 were operated on or had histological samples collected, with the presence of 26 GEPET (10 carcinoids) being confirmed in 22 patients.

Results: EUS sensitivity and diagnostic accuracy were 81% and 78%. Specificity was 80%. All these values were similar to the mean values obtained from the literature review.

Three pancreatic rumors smaller than or equal to 1 cm (insulinomas) were detected, which had escaped diagnosis with previous US, CT, and MRI studies.

An echoendoscopic examination of the pancreas could not be completed in two cases (5%), a pancreas carcinoid and an already gastrectomized double pancreatic gastrinoma.

Conclusion: EUS is a good preoperative technique for GEPET detection, and may likely be superior to other imaging techniques in the assessment of small tumors. EUS may study the depth and extension of this type of neuroendocrine lesions, thus facilitating endoscopic tumorectomy or polypectomy.

PATIENTS AND METHODS

Patients

Thirty-seven patients with suspected specific hormonal syndromes (carcinoid syndrome, Zollinger-Ellison syndrome (ZES), glucagonoma, insulinoma, somatostatinoma, VIPoma, and non functional carcinoid tumor; one of them, specifically a patient with ZES, had a type I multiple endocrine neoplasia) were sequentially studied with US with or without color Doppler, CT, MRI, OctreoScan, angiography, and EUS.

Sixteen were males (43%) and 21 were females (57%) with a mean age of 61 years (range: 40-84 years).

Of all 37 patients, 27 had 19 tumors in the pancreas, and 14 in their gastrointestinal tract (33 tumors).

Of all 37 patients 24 were operated on or had histological material collected, with the presence of 26 GEPETs (12 pancreatic, 14 gastrointestinal –10 carcinoids) being confirmed in 22 patients.

In 10 patients (only 2 operated on, all with long-term follow-up) no tumors were demonstrated, and these were used as a control group.

Method

EUS was initially performed using an Olympus GF-UM3/ Aloka EUM3 unit with a 7.5-MHz transducer and a 30-35-mm focal length, which allows the exploration of structures within 10 cm with a resolution of 3 mm. EUS was then carried out with an Olympus GF-UM20/EUM20-30 unit with a 7.5- and 12-MHz transducer including a 2-mm biopsy-aspiration channel. Focal length is 25-30 mm, and depth is 8 cm. More recently a radial Olympus GF-UM Q130 unit with a 7.5- and 20-MHz transducer and a 2.2-mm channel was used, as was a sectorial Olympus GF UCT160-OL5 unit with a 7.5-MHz transducer, 3.7-mm channel, and Olympus 22 G puncture needles.

Four EUS-FNAPs were performed as per the usual technique.

Exploration methodology included all VI standard positions accepted at the EUS meeting held in Stockholm in 1982 (2,3), with the stomach, duodenum, pancreas, and liver being examined.

Pancreatic neuroendocrine lesions are seen as hypo- or isoechogenic, homogeneous, well-delimited areas (Figs. 1 and 2).

Lesions in the gut are hypoechogenic, and are included in the first layers. Echoendoscopic suspicion led to excision (tumorectomy or polypectomy) in most cases (carcinoid tumors) (Figs. 3 and 4).

Statistical method

Precision (P), sensitivity (S), specificity (Sp), PPV, and NPV were all analyzed using standard formulas for all operated on and/or histologically confirmed tumors.

RESULTS

The ultrasonographic pattern obtained by EUS was similar to that of US: rounded, homogeneous, hypo- or isoechogenic, well-encapsulated masses or nodules with hypo- or isoechogenic borders and a maximum diameter of 0.4 to 5.0 cm. Three pancreatic tumors equal to or smaller than 1 cm were identified, which had escaped detection previously with US, CT, and MRI. The smallest tumor detected was 4-mm in size.

Sensitivity and diagnostic precision were 81 and 78%, respectively. PPV was 95%. Sensitivity was higher for digestive tract neuroendocrine tumors (85%) versus pancreatic neuroendocrine tumors (75%).

The tumor but not its precise location were detected in two cases: in one it was presumably detected in the head-body, and was in fact in the tail of the pancreas; the second tumor was thought to be in the head of the pancreas, and was in fact in the duodenum.

Two false positive cases were seen among the 10 controls, and thus specificity was 80%.

No echoendoscopic study of the pancreas could be successfully performed for 2 patients (5%), both with pancreatic lesions –in a carcinoid case because of exploration intolerance, and in a ZES because of a gastrectomized dual pancreas gastrinoma. All gastrointestinal neuroendocrine tumors could be appropriately identified despite their small size, and endoscopic biopsy and/or polypectomy procedures ensued.

DISCUSSION

Almost 30% of GEPETs escape preoperative localization with the usually employed modern imaging techniques (US, CT, MRI, OctreoScan, etc.) (1). Endoscopic ultrasonography (EUS) or echoendoscopy is one of the more recently introduced diagnostic techniques to study the pancreatic ultrasonographic pattern with frequencies of 7.5 and 12 MHz. Intrapancreatic neuroendocrine tumors are usually small (insulinomas are smaller than 1 cm in size), and only non-secreting or non-functional growths are usually big (greater than 4 cm). Lesions are hypo- or isoechogenic, well delimited, and resemble adenopathies; a differential diagnosis with mucinous tumors such as adenocarcinoma is required for cystic or irregular lesions.

The duodenum will be explored from the genu superior. These tumors usually exhibit an ultrasonographic pattern similar to that of leiomyoma involving the 2nd and 3rd layers, while leiomyoma usually affects the 4th layer. Exclusion of metastatic adenopathies is important.

Heyder (4) and Bolondi (5) were first to localize and diagnose insulinomas using EUS.
Lightdale et al. (7) detected endocrine tumors with EUS in 77% of cases, one in the duodenal wall and the rest in the pancreas. In five patients with CT and a negative A they detected small pancreatic tumors 0.5-2 cm in size.

Rösch et al. (9,12) studied 37 cases with 39 endocrine tumors that remained undetected with US or CT, and which had a mean size of 1.4 cm. EUS showed a precision and sensitivity of 82%, and a specificity of 95%.

We (23) have studied 20 cases, 6 without tumors and 14 patients with 22 endocrine tumors (16 operated). Sensitivity was 75%, and specificity was 83%. These values were superior to those obtained with other imaging techniques in the multicenter study by Rösch et al. (12), and in our literature review (7-23). Mean sensitivity was 81% (higher for insulinomas versus gastrinomas), and mean specificity was 85%. Also, results currently obtained with 37 cases were superior to those from our historic series. We believe that EUS is nowadays superior to the remaining imaging techniques particularly in the diagnosis of small tumors.
We detected three pancreatic tumors (insulinomas) smaller than or equal to 1 cm in size, which had not been diagnosed with US, CT, or MRI. The smallest detected case was 4 mm in size. We thought that the diagnostic strategy should be as follows: US-CT-MRI-O as first-line tests, EUS or A as second-line tests for non-located tumors, and finally EUS-assisted laparotomy or laparoscopy. Two tumors were also identified each in one patient, but their precise location was missed. EUS could not be fully carried out in 5% of cases: in one case because of test intolerance; in the other because the patient was gastrectomized.

In conclusion, we think that EUS is a good preoperative technique for GEPET detection, and will possibly be superior to other imaging techniques, including helical CT, for small-size tumors; hence it must become a primary technique for the diagnosis location, and staging of these rare tumors, even for their histopathologic diagnosis (24-28). Santo et al. (28) studied 76 cases, and performed an FNAP in 96% of them, with a precision of 94%.

REFERENCES