Role of Endoscopic Ultrasound in Evaluation of Pancreatic Neuroendocrine Tumors - Report of 22 Cases from a Tertiary Center in Iran

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Abstract

Background: The pancreatic neuroendocrine tumor (pNET) is relatively rare and generally felt to follow an indolent course. EUS has an important role in detection of pNET. This is a review of clinical and radiological presentation and pathologic reports of 22 patients with pNET. Patients and methods: In this study we analyzed clinical and radiological presentations and pathologic reports of all relevant cases who were referred to Taleghani hospital for 3 years since 2008. Results: A total of 22 patients 28-74 years old (mean=49) were enrolled between 2008 and 2011. Among the total, 13 (59%) were male, 9 (41%) were female and 16 (72.7%) had functional tumors. The results of CT were negative in 12 (54%) cases but EUS was capable of detecting the lesions in these patients, cysts being found in 4 (19%) patients. Conclusion: EUS is a highly sensitive procedure for the localization of functional pNETs and especially insulinomas. Nonfunctional tumors were detected in more advanced and late stages and cystic lesions were more common in this group.

Keywords: pNET - EUS - CT - diagnosis

Introduction

The pancreatic neuroendocrine tumor (pNET) is relatively rare and generally felt to follow an indolent course. Annual incidence of pNET between 2000 and 2004 was 0.312/100000, comprise <2% of all pancreatic tumors with average age of 60 years at the time of diagnosis. only 14% had localized disease, 22% had regional disease and 64% presented with distant metastases (Yao et al., 2008).The most common site of the tumors was body and tail of pancreas due to more accumulation of islands in these area (Tijeras-Raballand et al., 2012). pNET secret hormones including insulin, gastrin, glucagon, VIP, somatostatin, and classified as “functional” (F-pNET) or “nonfunctional” (NF-pNET) based on the presence or absence , respectively ,of specific clinical syndrome associated with hormone oversecretion (Tijeras-Raballand et al., 2012).

Overall sensitivity of CT for detection of pancreatic neuroendocrine tumors is 64-82% but sensitivity for lesions smaller than 1 cm is low. MRI has a good quality imaging with sensitivity of 90%. However this technology may not be available and its commentary is operator dependent (Noone et al., 2005). These two modalities are capable for detection of major part of pancreatic neuroendocrine tumors but small functional neuroendocrine tumors may be missed. In contrast, EUS can detect small lesions especially insulinoma in measuring of 0.2-0.5 cm in size (Rosch et al., 1992). Average size of insulinoma at the time of diagnosis is about 1-6 cm and 90% of them are less than 2 cm (Akerstrom, 2007) that is in the capability of EUS.

Surgery is only curative treatment in primary stages, also has an effective role in advanced stages including liver metastases. Other treatment methods are chemotherapy, RFA, transarterial chemoembolization (TACE), anti angiogenic therapy and selective internal radiotherapy (SIR) (Ellehalt et al., 2009).

The goal of this study is evaluation of clinical and radiological presentation and pathologic reports of 22 patients with neuroendocrine tumors who were referred to Taleghani Hospital for three years since 2008.

Materials and Methods

During three years 22 patients with pancreatic neuroendocrine tumors were referred to Taleghani Hospital and clinical and radiological presentation and pathologic reports were retrospectively evaluated. All the patients underwent EUS and CT-scan. Samplings with EUS-FNA or CT-guided or during operation were taken and according to clinical symptoms were classified into
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mass was seen in the head of the pancreas. Evaluations sent for surgery, interestingly intraoperative strong suspicion to insulinoma according to biochemical evaluations but without any success in detection of lesion but due to detection of lesions but EUS was capable for this purpose and all of these patients except one had functional tumors. One patient was glucagonoma. All of the patients except one who had insulinoma with multiple lesions in the body and head of pancreas had primary solitary lesion.

Results

Among the 22 evaluated patients 28±74 years old (mean=49), 13 (59%) were male and 9 (41%) were female, 16 (72.7%) were classified as having functional tumors versus 6 (26.7%) who were classified as having non functional tumors. Among the patients with functional tumors, 14 were insulinoma ,one was VIPoma and one was glucagonoma. All of the patients except one who had insulinoma with multiple lesions in the body and head of pancreas had primary solitary lesion.

Among the 14 patients with insulinoma, 8 (57%) had lesion in the head of pancreas, 8 were male and 6 were female and all of the lesions were well differentiated.

The patients with functional tumors in comparison to non functional tumors were in the less advanced stages. The most common site of tumors was head of pancreas but 6 patients had lesion in the body of pancreas. The average time between onsets of symptoms up to diagnosis of the disease was 19 months (3-48 months). In the group of non functional tumors only one of them presented with tarry stool and during work up a mass was detected in the head of pancreas but others presented with significant weight loss, sweating, anorexia, fever and intermittent abdominal pain. All of the patients underwent EUS and CT-scan except one patient that EUS was not performed. In the 12 patients CT-scan had not any success in detecting the lesions but EUS was capable for this purpose and all of these patients except one had functional tumors. One of the patients underwent two times EUS and CT-scan without any success in detection of lesion but due to strong suspicion to insulinoma according to biochemical evaluations sent for surgery, interestingly intraoperative sonography also was normal but during operation a 1.5 cm mass was seen in the head of the pancreas.

Among the total 22 patients only four was diagnosed with EUS-FNA sampling, four (19%) had cystic lesion that one was functional. 15 patients underwent surgical resection, 13 were insulinoma, and two were nonfunctional tumors. Among the patients with insulinoma 10 patients underwent enucleation, three patients underwent partial pancreatectomy. One patient with multiple lesions in the head and body underwent radiofrequency ablation. Five patients had liver metastases that one of them was functional tumor and others were nonfunctional tumors that due to inoperability treated with long acting octreotide and chemoembolization was done for three patients with good response in two patients and fair response in one patient.

Discussion

In this study that was performed in a tertiary center during three years 14 insulinoma were reported. In a report from Johns Hopkins medical institutions during 47 years (Phan et al., 1998) 122 patients with pNETs were reported. In another study only 20 patients with functional pNETs who were undergone surgery were reported during 25 years (Matthews et al., 2002). The number of reported insulinoma in our center is significant in comparison to other centers. This was because our institution is a tertiary referral center for pancreatic malignancies.

Non functional tumors were reported as 15-67% in different studies. In our study, 6 (27.2%) patients classified as having non functional tumors.

Halfdanarson and et al have previously reported on 1483 patients with pNETs since 1973-2000 their study provided that the majority of patients (90%) had non functional tumors that may be due to exclusion of benign insulinoma (the most common pNET s) (Koppel and Heitz, 1988).

Furukawa and et al have reported 16 patients with non functional tumors and only two patients had liver metastases (Furukawa et al., 1998).

In our study 6 patients had non functional tumors that four patients had liver metastases, in the other hand among the five patients with liver metastases 4 (80%) were non functional that may be due to late diagnosis and detection of tumors in the more advanced stages.

The majority of functional tumors were insulinoma with the same prevalence in both sexes (8 male, 6 female).

According to literature review 75% of insulinoma and glucagonoma are located in the body and tail of pancreas left to the superior mesenteric artery (SMA) (Howard et al., 1990) while in our study 57% of tumors were located in the head of pancreas and more than 90% were solitary beta cell with exception of one patient who had insulinoma with multiple lesions.

Macroscopically these tumors had not any certain capsule and generally were solid. None of our patients classified as having MEN.

Cystic tumors compose less than 5% of pNETs (Adsay, 2008). Preceding studies have reported 2-10% (Fernandez-del and Warshow, 1995; Le Bodic et al., 1996: 1998; Brugge et al., 2004) but in a recent study 9-21% (Jani et al., 2008) were reported. Due to great vascular supply
of pNETs cystic degeneration is uncommon (Li Destri et al., 2006). In our study among the 4 (19%) patients with cystic lesions 3 were nonfunctional. Iacona and al were reported two cystic pNETs that both of them were non functional and preoperative diagnosis of them were mucinous pancreatic tumor (Iacono et al., 1992).

Among the total 22 patients in 13 patients CT scan was unable to detect lesions and only EUS was capable for this purpose, that all except one were functional, 10 (76%) were insulinoma, one was VIPoma and one was glucagonoma. In the pa tient with glucagonoma CT scan and MRI were unable to detect lesion. In all but one tumor size were less than 2 cm.

According to Kang et al. (2006) EUS sensitivity for detection of insulinoma was 66%, while Anderson et al. (2000) and Tamm et al. (2007) have reported 90% sensitivity for EUS. EUS is an operator dependent modality.

In one study EUS detected pNETs in all cases (100%), whereas the CT detection rate was 77%. Furthermore, among those with multifocal pNETs, the extent of pancreatic involvement was underestimated by CT imaging in three cases. As a result, the decision to undergo surgery was changed in 36% of patients and the extent of surgery required was changed in 50% of patients. In our study no inferences can be made about the efficacy of EUS in impacting the role of surgery because of the small numbers of patients and the retrospective, descriptive study design. However, because pNETs are rare (estimates of one per 100,000 population), to accumulate more cases would require years, during which time imaging technology and surgical techniques would most certainly change. A multicentre review would be the best way to investigate whether EUS truly impacts surgery. Many pNETs are vascular lesions and often enhance to the same degree as adjacent pancreatic tissue, thereby evading detection by contrast CT. Although all pNETs have somatostatin receptors, the elusive tumors are small and there is variable binding of somatostatin in them. Therefore, current indium-based scintigraphy is unable to detect the small lesions with variable somatostatin binding due to a lack of resolution (Lam, 2008).

In the patients with insulinoma, the sensitivity of somatostatin receptor scintigraphy (SRS) is 50% (Tamm et al., 2007).

Most studies of the accuracy of EUS focused on functional pNETs that were determined by biochemical work ups. EUS is a good modality for detection of functional pNETs, because 90% of insulinoma located in the pancreas and 75% of them are less than 1.5 cm.

Previous studies of the performance of EUS in detection of islet cell tumors demonstrated 82% sensitivity and 92% specificity (Rosch et al., 1992). After that multiple studies of the accuracy of EUS published especially in insulinoma (Schumacher et al., 1996; Anderson et al., 2000; Ardengh et al., 2000; Zimmer et al., 2000; Gouya et al., 2003) with detection rate of 79-94% .in a recent study 52 patients underwent EUS for detection of insulinoma (according to clinical and laboratory data) that sensitivity was 89.5% and accuracy of 83.7% according to surgical finding . Sensitivity of EUS for detection of lesion ns in the head, body and tail of the pancreas respectively was 92.6%, 78.9% and 40% (Sotoudehmanesh et al., 2007). This study support previous studies that EUS is the most sensitive modality for detection of lesions in the head and body of pancreas in comparison to tail of pancreas. Probable pitfalls in EUS are related to very small and multiple insulinoma and pedunculated lesions in the tail of pancreas (Kann et al., 2003).

In our study the sensitivity of EUS for detection of pNETs was 95%. Our results are similar to the study of Khashab and et al in Johns Hopkins that CT was unable for detection of lesions less than 2 cm that probability of insulinoma is more than other lesions, so EUS is a primary sensitive test for detection of insulinoma (Khashab et al., 2011).

In our study the average time between the onset of symptoms and detection of lesions was 19 months and in Myo clinic study this time was less than 18 months (Service et al., 1991).

Evaluation of these 22 patients that is the first Iranian case series of pNETs demonstrated that non functional tumors were detected in more advanced stages and cystic change is more common in this group. In comparison to other modalities EUS has a high valuable role in detection and localization of pNETs and is a primary sensitive test for detection of functional tumors especially insulinoma.

References


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