Indications and outcomes of endoscopic ultrasound in Tanta-Egypt: Initial experience

Welcome letter from Editor-in-Chief

Welcome to the Int J Cancer and Biomedical Research (IJCBR)!

It is with great pleasure that I write this editorial to welcome you to the IJCBR. This journal provides a platform for publication of original and reviews research articles, short communications, letter to editor, thesis abstract, conference report, and case studies. These types of publication are directed at the interface of the fields of cancer and biomedical research.

The IJCBR relies on a distinguished expert of the Advisory and Editorial Board Members from the top international league covering in depth the related topics. They timely review all manuscripts and maintain highest standards of quality and scientific methodology and ethical concepts. Meanwhile, we take all possible means to keep the time of the publication process as short as possible.

I take this chance to welcome your contributions to the IJCBR and have every expectation that it will soon become one of the most respected journals in both the fields of cancer and biomedical research.

Mohamed L. Salem,
Editor in Chief
**Indications and outcomes of endoscopic ultrasound in Tanta-Egypt: Initial experience**

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**Background:** Endoscopic ultrasound (EUS) is valuable in the diagnosis and staging of gastrointestinal tumors and some extra-luminal malignancies. **Aim:** This study aimed to describe the initial experience with EUS and fine-needle aspiration (FNA) and the indications and outcomes of patients at the Tanta University Teaching Hospital. **Subjects and Methods:** This is a cross-sectional descriptive survey study analyzing 70 EUS cases seen at Tanta University Teaching Hospital from January to December 2019. FNA was performed for 61 patients. A provisional cytopathology diagnosis was made by on-site and the final cytology/histopathology report was given after immunostaining and review of slides. **Results:** The major indications for EUS were pancreatic, gastric, and ampulla of Vater lesions. EUS revealed pancreatic masses in 27, cysts in 1, and chronic pancreatitis in 1 case. Gastric masses were seen in 13, polyps in 5, and varices in 3 cases. Ampulla of Vater lesions were masses in 5, common bile duct (CBD) distal end stones in 3 cases, and one case proved normal. The final diagnosis of pancreatic lesions was adenocarcinoma in 25, cyst in 1 case, mucoepidermoid tumour in 1 case, neuroendocrine tumour in 1 case and chronic pancreatitis in 1 case. Gastric lesions were gastrointestinal stromal tumors (GIST) in 8, and adenocarcinoma in 5 cases, while 3 cases of polyps were hyperplastic, one inflammatory and one tubulovillous adenomatosis. Celiac axis block was done for 6 cases. No major complications were recorded. **Conclusion:** The major indications for EUS were pancreatic, gastric and ampulla of Vater lesions, while the main outcomes were pancreatic adenocarcinoma, gastric GIST, adenocarcinoma and ampullary adenocarcinoma.

**Keywords:** Celiac axis block, Cytopathology, Endoscopic ultrasound, Fine needle aspiration, Pancreatic lesions

**INTRODUCTION**

Endoscopic ultrasound (EUS) is characterized by high resolution which presents perfect and exceedingly meticulous images of the gastrointestinal (GI) wall and nearby structures up to 4-5 cm (Strohm et al., 1980, Bhutani, 2000). It has many indications but is mostly used to detect and stage GI lesions originating from deep layers, as well as some extra-luminal masses, including pancreatic cancers (Brugge 1998, Byrne and Jowell 2002). EUS has been highly used to determine the nature, detect the layer of origin and allow for sampling of bulging gastric lesions determined by conventional endoscopy specially when arising from below the mucosa (Strohm et al., 1980, Byrne and Jowell, 2002).

Other indications of EUS include chronic pancreatitis, pancreatic lesions in the form of masses or cysts, and gall bladder masses (Brugge, 1998; Bhutani, 2000). Evaluation of lesions outside the gastrointestinal tract (GIT), such as mediastinal lymph nodes enlargement of unknown cause is an indication of EUS (Byrne and Jowell 2002). Another advantage of EUS is the estimation of the degree of fibrosis through detection of tissue stiffness by EUS tissue elastic.
imaging (Deprez, 2013, Saftoiu and Vilmann, 2013).

EUS-guided fine needle aspiration (FNA) biopsy is a meticulous, safe procedure used to differentiate between benign and malignant lesions; determine tumor stage and apply histological confirmation of malignancy needed to select the best line of treatment including; chemotherapy, radiotherapy, or even surgery (Hawes, 2010; Dumonceau et al., 2011).

The present study was conducted to determine common indications for requesting EUS and to describe the diagnoses made after endoscopic ultrasound/fine-needle aspiration and cytology (FNAC), the indicated therapeutic procedures and prognosis for cases seen at the Tanta University Teaching Hospital in 2019.

SUBJECTS AND METHODS

This is a cross-sectional descriptive survey study of the initial EUS experience at the Tanta University teaching hospital during the period from January 2019 to December 2019. Institutional ethical committee approval was obtained before the start of the study and informed consent was signed by every patient before enrolment. The study was registered on clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT03267355).

All patients referred for EUS were screened for study participation. The patients were referred for one of the following indications: (1) detailed imaging and FNA of mediastinal, gastric, ampullary, or pancreatic lesions (2) staging of previously diagnosed gastric and pancreatic cancers for TNM classification. Patients too ill (hypoxemic/hypotensive) to undergo the procedure safely or having unacceptable sedation risks and those with large upper esophageal tumors preventing the advancement of the scope/EUS probe were excluded.

A detailed history was taken from every patient, previous investigations (upper GIT endoscopy, chest or abdominal CT) were reviewed and the procedure was explained to the patients. Indications were documented as per the site of pathology, including lymph node, pancreas, stomach, ampulla of Vater, esophagus, and mediastinum. A comprehensive clinical and laboratory pre-procedure assessment including PT and INR was performed for each patient. Patients were instructed not to ingest any food or drink for 8 hours before the procedure.

An experienced endosonographer aware of the patients’ clinical history performed the procedure using a Pentax EG-3870UTK with a Hitachi system EUS linear scope. Patients were given conscious sedation using midazolam/nalophen. EUS findings were recorded against indications as enlarged lymph nodes, tumor staging or normal.

TNM classification was used for staging of esophageal, gastric, ampullary and pancreatic tumors which were detected by EUS (Amin et al. 2017). Fine-needle aspiration cytology (FNAC) was performed as determined by the EUS findings using 22 gauge needles (ECH O 3-22 Cook Medical Echotip Ultra with HDFNA G 31521 22 ga USA), five to fifteen passes were performed by moving the needle back and forth within the target using the fanning or the capillary technique as needed.

Smearing technique

Immediately after the FNA specimens were obtained, two to four smears were prepared using positively charged slides, fixed immediately in 95% ethanol and stained with Haemotoxylin and Eosin (H&E). Any excessive material, including the needles used in aspiration, was submitted in 50% ethanol (ethanol/water, 1:1) for cell block preparation (Skipper and DeStephano, 1989).

A histopathologist attended each procedure and air-dried slides were reviewed for adequacy of tissue and provisional cytopathological diagnoses were made. The obtained cytological diagnoses were classified into benign and malignant.

Cell blocking

After preparation of the smears, the syringes and needles used for the fine-needle aspirates were rinsed in 10 ml of 50% ethanol in a container. Any residual tissues or clots in the hub of needles used for aspiration were removed meticulously in the laboratory with the help of another needle and rinsed in 50% ethanol. The whole specimen was centrifuged in
a 10 ml disposable centrifuge tube at 4,000 rpm for 6 minutes to create a single pellet (Hecht S 2013).

Nathan alcohol formalin substitute (NAFS) consisting of 9 parts of 100% ethanol and 1 part of 40% formaldehyde was prepared freshly then the deposit was fixed in it. After 45 minutes of fixation, re-centrifugation was done for 6 minutes. These pellets detached themselves or were removed easily with a disposable Pasteur pipette following centrifugation. The cell pellets were covered with crayon paper, placed in a cassette, and kept in 80% ethanol until ready for processing in the automatic tissue processor. The cell blocks were embedded in paraffin and sectioned at 4 μm thickness (Hecht, 2013).

**Staining**

Routine H&E staining was performed for all cell block sections. According to the manufacturer’s instructions for the kits, Immunohistochemical staining using LCA monoclonal mouse anti-human antibody clone 2B11 + PD7/26 (Code no. M0701, Dako), polyclonal rabbit anti-human C-kit (code no. A4502, Dako), Monoclonal rabbit chromogranin A antibody (SP12)(code no. MA5-14536, Thermofisher scientific) or monoclonal mouse cytokeratin 7 antibody clone OV-TL 12/30 (code no.MA1-06316, Thermofisher Scientific) for identification or phenotyping of tumor cells using the streptavidin-biotin method was done after the provisional cytopathological diagnosis. Further investigations and work-up like ERCP with stenting, surgical and/or oncology consultation were done when desired. Therapeutic procedures were performed when indicated, including coeliac axis block and aspiration of a pancreatic cyst.

EUS guided coeliac axis block was done by FNA needle which was prepared by flushing the device with 0.9% saline solution. After removal of the stylet, a syringe with 5 ml of saline solution was attached to the hub of the needle. The needle assembly was passed through the biopsy channel and advanced under direct EUS visualization to a position immediately alongside and anterior to the aorta. Aspiration was performed, and if no blood was seen, 4 cc Bupevacain, 2 cc Triamcinolone and 20 cc of absolute alcohol were injected at the base of the celiac trunk (central injection).

Pancreatic cyst EUS guided aspiration was performed by the FNA needle while the endoscope tip was positioned in the duodenum. The needle was inserted into the center of the cyst, the stylet withdrawn, and the vacuum applied. The fluid was aspirated and the cyst thoroughly emptied, after which a sample was taken from the cyst wall for cytopathological analysis.

**Statistical analysis**

The statistical data are reported as the mean ± standard deviation (SD), frequencies (number), and percentages when appropriate. Percentages and frequencies were determined for various variables (indications, diagnosis, and treatment modalities). All statistical analyses were performed using the computer program SPSS (Statistical Package for the Social Science; SPSS, Chicago, Illinois, USA) version15 for Microsoft Windows.

**RESULTS**

In total, 81 patients were screened for study participation and 11 were excluded. Of those excluded, 8 had failures in exclusion criteria, and 3 declined to participate. Thus, seventy patients underwent EUS during the study period; 45 (64.3%) were males and 25(35.7%) females. Age ranged from 32 to 69 years with a mean of 50.87±9.87 years. The mean procedure time was 37±10.2 minutes (range 22-65 min).

The indications for patients’ referral for EUS are shown in Table 1. The most frequent indication of EUS in this study was abnormal pancreatic imaging (mass lesion, fullness or prominence of the pancreatic head on ultrasound or CT abdomen) in 41.43% of cases. Gastric lesions were the second major indication in 30% of the cases followed by ampullary lesions in 12.85% cases. EUS findings of the patients are shown in Table 2. The pancreatic lesions were masses in 27, cyst in 1, and chronic pancreatitis in 1 patient (Fig. 1). Gastric lesions were masses in 13, polyps in 5, and varices in 3 patients. Ampullary lesions were found to be masses in 5, stones of the distal common bile duct (CBD) in 3, and one
patient referred for a suspected enlargement of the ampulla of Vater was proved to be normal by EUS (Figure 2).

FNAC was performed for 61 patients out of 70. The nine patients for whom FNAC was not done were: 3 with gastric varices, 3 with CBD stones, and 3 with normal EUS findings for whom the clinically suspected pathology was not found (one patient with suspected enlargement of the ampulla of Vater and 2 patients with abdominal pain who were diagnosed with irritable bowel syndrome (IBS).

### Table 1. Indications for EUS

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<thead>
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<th>Indication</th>
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<tr>
<td>Stomach</td>
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</tr>
<tr>
<td>Ampullary lesions</td>
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<td>12.86</td>
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<tr>
<td>Mediastinum</td>
<td>3</td>
<td>4.28</td>
</tr>
<tr>
<td>Esophagus</td>
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<td>2.86</td>
</tr>
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<tr>
<td>Left suprarenal mass</td>
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<tr>
<td>Splenic focal lesion</td>
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<td>1.43</td>
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<tr>
<td>Abdominal lymphadenopathy</td>
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<tr>
<td>Abdominal pain</td>
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<td>2.86</td>
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<tr>
<td><strong>Total</strong></td>
<td>70</td>
<td>100</td>
</tr>
</tbody>
</table>

FNAC/cytopathology diagnosis of the lesions is shown in Table 3. Pancreatic lesions were adenocarcinoma in 23 patients, and one patient of each of the following: simple cyst, mucocoeplidermoid tumour, neuroendocrine tumour, and chronic pancreatitis (Figure 3). As regards the TNM classification of pancreatic adenocarcinoma; T stage was from T1 to T4 and N and M stages of most cases were N0 and M0.

Of the 13 gastric masses, 8 proved to be gastrointestinal stromal tumors (GIST) (Fig. 4), and 5 adenocarcinomas, the other gastric lesions detected were polyps; hyperplastic in 3, inflammatory in 1, and tubulovilous adenomatosis in 1 patient. The staging of the 8 GIST tumors revealed: 2 high risk (T2N1M1 and T2N0M0) and 6 low risk (T1N0M0). All five gastric adenocarcinoma patients were found to be of stage (T3N1M1).

The five ampullary masses proved to be periampullary adenocarcinoma. Out of the 3 mediastinal masses, there was one lymphoma (Figure 5), one anaplastic carcinoma and a case of sarcoidosis. Treatment modalities of the patients are shown in Table 4. Treatment was indicated for 69 patients out of 70, as the case with suspected enlargement of the ampulla of Vater which proved normal by EUS needed no treatment apart from patient reassurance.

EUS-guided therapeutic interventions were few. EUS guided coeliac axis block was done to treat abdominal pain associated with pancreatic cancer in 5 patients and chronic pancreatitis in one case. Also, EUS guided complete aspiration of a pancreatic cyst located in the head of the pancreas was successfully done for one patient and complete resolution of the cyst was achieved. There were no major complications recorded by this study. Minor intraluminal bleeding after FNAC was reported in two (3%) patients out of 61, and transient hypotension after EUS guided coeliac axis block in one (16.6%) out of 6.

### DISCUSSION

EUS is used to get images of lesions originating from any layer of the GIT and also from all around organs to a depth of about 5 centimeters (Bhutani, 2000). Pancreatrico-biliary and mediastinal lesions are important indications of EUS too. FNA guided by EUS is needed to differentiate between benign and malignant lesions and to estimate the malignant lesions’ stage before surgical intervention, chemotherapy or radiotherapy (Strohm et al., 1980; Brugge, 1998; Byrne and Jowel, 2002).

The main indication of EUS in this study was the assessment of pancreatic lesions (41.42%) with pancreatic adenocarcinoma being the major underlying etiology (35.71%). This is similar to another study in USA, in which EUS was performed for 7614 cases and the authors concluded that evaluation of the pancreas accounts for approximately 40% of the indications for EUS (D'Souza et al., 2016). On the other hand, another study reported that pancreatico-biliary lesions (29.6%) were the second indication for EUS after esophageal lesions (30.7%) in a study including 526 Australian patients (Kalade et al., 2006).

The most valuable execution of EUS in hepatobiliary disease is to visualize and stage pancreatic and distal biliary neoplasms and to perform the same session EUS ultrasound-
Indications and outcomes of endoscopic ultrasound...

guided fine-needle aspiration in the same session for cytologic diagnosis (Hussain et al. 2009). EUS/FNA is minimally invasive and very definitive in getting tissue samples for the diagnosis of solid pancreatic tumors. EUS is indispensable in guiding biopsy needles into lesions that cannot be identified by CT/MRI because of its small size or surrounded by high vascularity which makes safe percutaneous biopsy impossible (Hewitt et al., 2012). The second most common indication for EUS in our study was the assessment of gastric lesions, accounting for (30%) of all the EUS cases carried out.

Table 2. EUS findings

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<tr>
<th>Indication</th>
<th>EUS findings</th>
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<td>Pancreas (n=29)</td>
<td>Mass</td>
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<td></td>
<td>Cyst</td>
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<td>Chronic pancreatitis</td>
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<td>1.43</td>
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<tr>
<td>Stomach (n=21)</td>
<td>Mass</td>
<td>13</td>
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</tr>
<tr>
<td></td>
<td>Polyps</td>
<td>5</td>
<td>7.14</td>
</tr>
<tr>
<td></td>
<td>Varices</td>
<td>3</td>
<td>4.28</td>
</tr>
<tr>
<td>Ampullary lesions (n=9)</td>
<td>Mass</td>
<td>5</td>
<td>7.14</td>
</tr>
<tr>
<td></td>
<td>Common bile duct stones</td>
<td>3</td>
<td>4.28</td>
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<td></td>
<td>Normal</td>
<td>1</td>
<td>1.43</td>
</tr>
<tr>
<td>Mediastinum (n=3)</td>
<td>Mass</td>
<td>3</td>
<td>4.28</td>
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<tr>
<td>Esophagus (n=2)</td>
<td>Mass</td>
<td>2</td>
<td>2.86</td>
</tr>
<tr>
<td>Miscellaneous (n=6)</td>
<td>Left suprarenal mass</td>
<td>1</td>
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<tr>
<td></td>
<td>Splenic focal lesion</td>
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<td>1.43</td>
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<td></td>
<td>Abdominal lymphadenopathy</td>
<td>2</td>
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</tr>
<tr>
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<td>Normal</td>
<td>2</td>
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<tr>
<td>Total</td>
<td></td>
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</table>

Table 3. Final diagnosis on fine-needle aspiration and cytology/cytopathology

<table>
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<tr>
<th>FNAC</th>
<th>Diagnosis</th>
<th>No</th>
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<tr>
<td>Pancreas (n=29)</td>
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<td></td>
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<td></td>
<td>Mucoepidermoid tumour</td>
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<td>Neuroendocrine tumour</td>
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<td>1.43</td>
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<td>Stomach (n=18)</td>
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<td></td>
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<td>Hyperplastic polyps</td>
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<td>Anaplastic carcinoma</td>
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<td>Sarcoidosis</td>
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<tr>
<td>FNAC/Cytopathology not done/indicated (n=9)</td>
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<td></td>
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<td>Total</td>
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EUS: endoscopic ultrasound; GIST: gastrointestinal stromal tumour.
## Table 4. Patient treatment modalities

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<td><strong>ERCP (n=21)</strong></td>
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<td>Palliative stent insertion for pancreatic adenocarcinoma</td>
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<td>Stone removal from the distal end of CBD</td>
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<td>Esophageal leiomyomas</td>
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<td>Mediastinal metastatic lymphadenopathy (anaplastic carcinoma)</td>
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<td>Pancreatic adenocarcinoma</td>
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<td>Chronic pancreatitis</td>
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<td><strong>Others (n=10)</strong></td>
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</tbody>
</table>

EMR: endoscopic mucosal resection; ERCP: endoscopic retrograde cholangio-pancreatography; EUS: endoscopic ultrasound; CBD: common bile duct; GIST: gastrointestinal stromal tumour; IBS: irritable bowel syndrome.
Figure 1. 1A) FNA of pancreatic cancer. 1B) Large pancreatic head mass. 1C) Pancreatic cyst. 1D) CBD stent and FNA inside a pancreatic mass. 1E) Central necrosis inside a large pancreatic mass.
Figure 2: 2A) CBD stones. 2B) CBD stent through an ampullary mass. 2C) Dilated CBD due to ampullary mass.

Figure 3: 3A) Cell block from pancreatic mass showing malignant glands suggesting adenocarcinoma (H&E x400). 3B) Cell block showing positive cytokeratin 7 immunostaining in adenocarcinoma (streptavidin-biotin x400). 3C) FNAC from pancreatic mass showing groups of small monotonous cells suggesting pancreatic neuroendocrine tumor (H&E x400). 3D) Cell block showing positive chromogranin-A immunostaining of pancreatic neuroendocrine tumor (streptavidin-biotin x400).

Figure 4: 4A) FNAC from gastric mass showing large atypical spindle cells suggesting GIST (H&E x400). 4B) Cell block showing positive C-kit immunostaining of neoplastic spindle cells (streptavidin-biotin x400).
Indications and outcomes of endoscopic ultrasound...

Gastric GIST and adenocarcinoma were the most frequent findings. (Hussain et al., 2009) reported that growth of stomach (11%) was the third common indication for EUS referral in a study including 189 Pakistani patients and gastric malignant tumors were the main underlying etiology.

EUS is more suitable than CT in the establishment of the extent of wall invasion by gastric carcinoma. It can also reveal extra-gastric spread and local lymph node involvement that could be missed by CT. The accuracy of EUS for detecting the depth of invasion is 83-88% compared with 35% for CT. For detecting lymph node metastasis, EUS is 66-72% accurate compared with CT at 45% accuracy (Ho, 2003). EUS can differentiate carcinoma from lymphoma and is a most helpful technology for the assessment of possible GIST lesions that have a submucosal localization making them difficult to biopsy on conventional endoscopy. Recent studies have devised characteristics for discriminating features suggestive of benign or malignant behavior in GIST (Chak et al., 1997; Palazzo et al., 2000).

In our study, EUS guided coeliac axis block was performed for 6 cases to treat abdominal pain associated with pancreatic cancer in 5 cases and chronic pancreatitis in one case. According to a meta-analysis; the percentage of patients with pancreatic cancer pain for whom pain relief was attained by EUS-guided coeliac axis block was 80% (Puli et al., 2009). Moreover, the estimates for pain relief among chronic pancreatitis patients’ consequent to EUS-guided coeliac axis block have been reported to be 51% to 59% (Puli et al., 2009; Kaufman et al., 2010).

Some side effects were recorded in a previous study, as 3% of cases had minor intraluminal bleeding after FNAC and 16.6 % of cases had transient hypotension after EUS guided coeliac axis block. (Voss et al., 2000). Other studies revealed transient diarrhea and hypotension after EUS guided coeliac axis block in (4%-15%) and (1%) of cases respectively (Sakamoto et al., 2011; Leblanc et al., 2013). The high percentage of transient hypotension after the coeliac axis block in our study may be attributed to the small number of cases.

CONCLUSION

The major indications for EUS were pancreatic, gastric and ampulla of Vater lesions, while the main outcomes were pancreatic adenocarcinoma, gastric GIST, adenocarcinoma, and ampullary adenocarcinoma. Therapeutic procedures were few in this study. No major complications were recorded.

CONFLICT OF INTEREST

Authors declare that they have no conflicts of interest.

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Amin MB, Edge S, Greene F, Byrd DR, Brookland RK, Washington MK, Gershenwald JE, Compton CC, Hess KR, Sullivan DC, Jessup JM, Brierley JD,


Egyptian Association for Cancer Research (EACR)
http://eacr.tanta.edu.eg/

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