Abstract

Objective: Endoscopic ultrasound-guided fine-needle aspiration cytology (EUS-FNAC) is a precise and safe technique that provides both radiological and pathological diagnosis with a better diagnostic yield and minimal adverse events. EUS-FNAC led to the remarkable increase in the detection rate of incidentaloma found during radiologic staging or follow-up in various malignancy or unrelated conditions. Aims: We did this preliminary study with an aim to evaluate the role of EUS-FNA in diagnosing and classifying adrenal lesions, clinical impact, and compare the outcome with the previously published literature. Materials and Methods: We included 32 consecutive cases (both retrospective and prospective) of EUS-guided adrenal aspirate performed over a period of 3.3 years. The indications for the aspirate in decreasing order were metastasis (most common carcinoma gall bladder) > primary adrenal mass > disseminated tuberculosis > pyrexia of unknown origin. On EUS, 28 cases revealed space occupying lesion or mass (two cases bilateral) and four cases revealed diffuse enlargement (two cases bilateral) with a mean size of 21 mm. Results: The cytology reports were benign adrenal aspirate (43.8%), metastatic adenocarcinoma (15.6%), histoplasmosis (9.4%), tuberculosis (9.4%), round cell tumor (6.2%), adrenocortical carcinoma (3.1%), and descriptive (3.1%). Three cases (9.4%) yielded inadequate sample. The TNM staging was altered in 22.23% of the cases by result of adrenal aspirate. Conclusions: EUS-FNA of the adrenal gland is a safe, quick, and sensitive and real-time diagnostic technique, which requires an integrated approach of clinician, endoscopist, and cytopathologist for high precision in diagnosis. Although the role of EUS-FNA for right adrenal is not much described, we found adequate sample yield in all the four patients that underwent the procedure.

Keywords: Adrenal, endoscopic ultrasound, fine needle aspiration cytology, incidentaloma

Introduction

Endoscopic ultrasound-guided fine-needle aspiration cytology (EUS-FNAC) has emerged as a precise and safe technique that enables real-time visualization and onsite cytological examination to characterize not only the luminal gastrointestinal tract lesions but also the periluminal and abluminal organs such as pancreas, liver, kidney, adrenal glands, and both mediastinal and intra-abdominal lymph nodes for quick and more accurate diagnosis. It has advantage over other simple imaging techniques as it provides both radiological and pathological diagnosis of the lesions. It is a simple, very sensitive, cost effective and safer procedure in comparison to previously used techniques with per-cutaneous approach (non-diagnostic yield about 14%), which enables timely optimal management of the disease. The adverse event rate in EUS-FNA is 0.01%, which is much lesser in comparison to earlier used conventional computer tomography (CT) or trans-abdominal ultrasound guided per-cutaneous approaches (adverse events 0.4–12%).

Since the advent of EUS technique, incidentally detected adrenal masses (incidentaloma) found during radiologic staging or follow-up in various malignancy and or unrelated conditions is more frequently diagnosed and characterized. However, no well-defined criteria have been formulated to differentiate between benign and malignant adrenal lesions.

The aim of this preliminary study was to evaluate the role of EUS-FNA in diagnosing and classifying adrenal lesions, clinical impact, and compare the outcome with the previously published literature.
clinical impact, and compare the outcome with the previously published literature [Table 1].

**Materials and Methods**

This study was done in a single tertiary care centre over a period of 3.3 years including both retrospective and prospective cases between January 2013 and April 2016. A written informed consent was obtained from the relative of each patient after explaining the procedure and related complications. A combination of anaesthetic agents including intravenous midazolam (0.1 mg/kg) and Propofol (1 mg/kg) was given as per standard recommendations based on body weight and age of the patients for conscious sedation under cardio-respiratory monitoring.

Linear EUS was performed using (Olympus GF-UCT180, Tokyo, Japan) with a longitudinal convex ultrasound transducer and an ultrasound scanner in all patients. The left adrenal gland was identified by tracing descending aorta till celiac axis then rotating the scope clockwise with slight withdrawal. A trans-duodenal approach was followed to visualize right adrenal gland with endoscope in the long position along the greater curvature of the stomach. The right adrenal gland was identified between the upper pole of the right kidney and the inferior vena cava after visualizing these landmarks.

EUS-FNA was performed using a 22 gauge, 8 cm needle (Cook-Medical, Winston-Salem, NC; United States). Minimum two passes were done often avoiding suction. The aspirated material was smeared immediately and kept in 95% alcohol as well as air dried by a trained pathologist with rapid on-site evaluation (ROSE) for adequacy of the sample. ROSE was performed by keeping slide in Toluidine blue stain in a coplin jar for 30 seconds followed by washing in running tap water and examination under microscope. In selected cases with enough material, cell block preparation were also done. Post-procedure, patients were monitored in the recovery room for at least 60 min before discharge.

Three stains Giemsa, hematoxylin and eosin, and papanicolaou were routinely used as per the standard guidelines in all the cases along with special stains in case of infective etiologies such as Ziehl–Neelsen (ZN), periodic acid-Schiff (PAS) and silver methenamine (SM). Also, in selected cases Immunocytochemistry (ICC) was performed on smear/cell block sections as per the requirement. For ICC on smears, slides were kept in cold acetone overnight. Next day, slides were washed thrice in Tris buffer followed by peroxide and protein blocking. Primary antibody was applied without performing antigen retrieval. Later, slides were washed in Tris buffer solution than HRP conjugated secondary antibody was applied and subsequently 3,3’-Diaminobenzidine (DAB), counterstaining with hematoxylin and mounting was done. However, standard procedure was followed in cell block immunohistochemistry. ICC was contributory in two cases of poorly differentiated metastatic carcinoma (Pan CK, Thermo-Fisher; RTU) and a case of adrenocortical carcinoma (synaptophysin and Inhibin-A, Thermo-Fisher; RTU).

**Results**

Over a period of 3.3 years between January 2013 and April 2016, about 1500 EUS-FNA were performed in the department out of which adrenal aspirate comprised 2.13% (32 cases) [Table 2]. Two cases were managed by trans-abdominal ultrasound guided FNAC. The main indication for adrenal aspirate was metastasis 50% (16/32) followed by primary adrenal mass 28.13% (9/32), 12.5% (4/32) disseminated tuberculosis and 9.37% (3/32) cases of pyrexia of unknown origin. The clinical diagnosis in decreasing order were carcinoma gall bladder (10/32), carcinoma pancreas (4/32), adrenal mass/retroperitoneal mass (6/32), disseminated tuberculosis (4/32), unknown primary (2/32) and one case each of carcinoma lung, cholangiocarcinoma, carcinoma stomach, periampullary carcinoma, lymphoma and chronic liver disease.

The mean age was 53.8 years with a slight male predominance and male:female ratio of 1.2:1. On EUS, 28 cases revealed space occupying lesion (SOL) or mass lesion (two cases bilateral), and four cases showed diffuse

**Table 1: Previous studies and their outcomes evaluating the role of endoscopic ultrasound-guided fine-needle aspiration of the adrenal gland**

| Year | Author (Ref no) | No of patients | Adverse outcomes | Conclusion |
|------|-----------------|----------------|-----------------|------------|
| 2004 | Jhala et al.[9]  | 24             | None            | 29% positive for malignancy |
| 2007 | De Witt et al.[10] | 38            | None            | 24% non-diagnostic |
| 2009 | Bodger et al.[11] | 40            | None            | 70% showed alteration in TNM staging |
| 2010 | Eloubeidi et al.[12] | 59            | None            | 100% adequacy, 37% malignant, altered shape predict metastasis |
| 2011 | Schuurbers et al.[13] | 85            | None            | Sensitivity 86%, NPV 70%, false negative 2 cases, metastasis 62%, benign aspirate 29% |
| 2013 | Uemura et al.[14] | 11            | None            | Effectiveness 100%, 36% metastasis |
| 2015 | Puri et al.[15] | 21            | None            | 100% diagnostic, PUO 57% |
| 2016 | Present study   | 32            | None            | 90.63% adequacy, BAA 43.75%, metastasis 15.6%, histoplasma 9.37%, TB 9.37% |

TNM: Tumor node metastasis, NPV: Negative predictive value, PUO: Pyrexia of unkown origin, BAA: Benign adrenal aspirate, TB: Tuberculosis
Table 2: Summarizing clinical details, indications, endoscopic ultrasound findings, radiological, and cytological diagnosis

| SN | Age | Sex | Indication | Adrenal side | EUS image | Size (mm) | Echogenicity | Clinical diagnosis | EUS diagnosis | FNAC report |
|----|-----|-----|------------|--------------|-----------|-----------|-------------|-------------------|---------------|-------------|
| 1  | 58  | F   | Mets       | Right        | Mass      | 30×25     | Hypoechoic  | Ca GB            | Mets          | ACC         |
| 2  | 55  | M   | Mets       | Left         | SOL       | 10×10     | Hypoechoic  | Ca lung          | Mets          | BAA         |
| 3  | 44  | M   | Adrenal mass | Left        | Mass      | 12×10     | Heteroechoic | Adrenal mass     | Incidentaloma | BAA         |
| 4  | 58  | M   | Mets       | Left         | Mass      | 20×15     | Hypoechoic  | Ca stomach       | Mets          | Inadequate  |
| 5  | 53  | M   | TB         | Left         | B/L Mass  | 40×27     | Hypoechoic  | TB               | TB            | Histoplasma |
| 6  | 59  | F   | PUO        | Left         | Mass      | 15×15     | Hypoechoic  | lymphoma         | TB            | TB          |
| 7  | 58  | M   | PUO        | Left         | SOL       | 8.5       | Hypoechoic  | Incidentaloma    | Inadequate    | BAA         |
| *8 | 40  | M   | RP mass    | Right        | -         | 35×25     | -           | RP mass          | -             | Descriptive |
| 9  | 52  | M   | PUO        | Left         | SOL       | 43×17     | Hypoechoic  | TB               | TB            | Histoplasma |
| 10 | 60  | F   | Mets       | Left         | SOL       | 18×11     | Hypoechoic  | Ca GB            | Mets          | BAA         |
| 11 | 70  | M   | Mets both  | B/L SOL      | 10×10     | Hypoechoic | Ca pancreas | Mets             | Mets          | BAA         |
| 12 | 51  | F   | Mets       | Left         | Mass      | 10×10     | Hypoechoic  | Unknown primary  | Mets          | BAA         |
| 13 | 63  | F   | Mets TB    | Left         | SOL       | 20×10     | Hypoechoic  | Disseminated disease | Mets/B | TB |
| 14 | 47  | M   | Infectious | Left         | B/L diffuse enlarged | 40×30 | Hypoechoic | CLD etiology | Histoplasma/TB | Histoplasma |
| 15 | 16  | F   | TB         | Left         | mass      | 25×15     | Hypoechoic  | Disseminated TB  | TB            | TB          |
| 16 | 85  | F   | Mets       | Left         | B/L diffuse enlarged | 30×20 | Hypoechoic | Mets           | Mets/ histoplasm/TB | PDAdca |
| *17| 55  | M   | RP mass    | Right        | -         | 40×30     | -           | Suprarenal mass  | -             | PDAdca      |
| 18 | 60  | M   | Mets       | Left         | SOL       | 10×10     | Hypoechoic  | Ca GB            | Mets          | BAA         |
| 19 | 65  | M   | Mets       | Left         | SOL       | 14×10     | Hypoechoic  | Ca GB            | Mets          | Inadequate  |
| 20 | 70  | F   | Mets       | Left         | SOL       | 10×10     | Hypoechoic  | Ca GB            | Mets          | BAA         |
| 21 | 84  | M   | Mets       | Left         | SOL       | 10×7      | Hypoechoic  | Ca HOP           | Mets          | BAA         |
| 22 | 50  | M   | Adrenal mass | Left        | SOL       | 10×10     | Hypoechoic  | Ca GB            | Mets          | BAA         |
| 23 | 30  | F   | Adrenal mass | Right        | Diffuse enlargement | 70×60 | Heteroechoic | Suprarenal mass | RP mass       | Round cell tumor |
| 24 | 40  | F   | Mets       | Left         | SOL       | 10×7      | Hypoechoic  | Ca GB            | Mets          | BAA         |
| 25 | 65  | M   | Adrenal mass | Left        | SOL       | 10×10     | Hypoechoic  | Ca HOP           | Mets          | BAA         |
| 26 | 55  | F   | Adrenal mass | Left        | SOL       | 10×10     | Hypoechoic  | Disseminated cholangiocarcinoma | Mets | BAA |
| 27 | 55  | F   | Adrenal mass | Left        | SOL       | 10×10     | Hypoechoic  | Ca HOP           | Mets          | Adca        |
| 28 | 34  | F   | RP mass    | Left         | Diffuse enlargement | 62×42 | Heteroechoic | RP mass         | RP mass       | Round cell tumor |
| 29 | 40  | F   | Mets       | Right        | Mass      | 10×10     | Hypoechoic  | Ca GB            | Mets          | Adca        |
| 30 | 65  | M   | Mets       | Left         | SOL       | 8×8       | Hypoechoic  | Ca GB            | Mets          | BAA         |
| 31 | 45  | M   | Mets       | Left         | SOL       | 7×7       | Hypoechoic  | PACA             | Mets          | Adca        |
| 32 | 38  | M   | Adrenal mass | Left        | SOL       | 11×7      | Hypoechoic  | Ca GB            | Mets          | BAA         |

EUS: Endoscopic ultrasound, FNAC: Fine needle aspiration cytology, f: Female, m: Male, mets: Metastasis, Ca: Carcinoma, SOL: Space occupying lesion, GB: Gall bladder, ACC: Adrenocortical carcinoma, BAA: Benign adrenal aspartate, TB: Tuberculosis, B/L: Bilateral, PUO: Pyrexia of unknown origin, RP: Retropertitoneal, CLD: Chronic liver disease, PD: Poorly differentiated, Adca: Adenocarcinoma, HOP: Head of pancreas, *Transabdominal ultrasound guided

enlargement (two cases bilateral) [Figure 1a-i]. The overall mean size of the adrenal lesion was 21 mm, while based on nature of pathology the mean size of adrenal was 10.64 mm in benign adrenal aspartate, 31.3 mm in infective etiology, and 32.4 mm in malignant lesions. On EUS, 27/30 cases were hypoechoic while in 3 cases they were heteroechoic. Three cases (9.37%) yielded inadequate sample. The cytology was reported as: benign adrenal aspartate (14/32), metastatic adenocarcinoma (5/32), histoplasmosis (3/32), tuberculosis (3/32), round cell tumor (2/32), adrenocortical carcinoma (1/32), and descriptive (1/32).

Cytomorphological spectrum
In tubercular adrenitis, smears were largely necrotic with occasional collection of epithelioid histiocytes [Figure 2a]. The ZN staining showed characteristic acid-fast bacilli [Figure 2b]. In histoplasmosis, the aspirates revealed both intracellular (both within cortical cells and histiocytes) and extracellular...
clusters and scattered small yeast form of histoplasma with narrow-based budding, and occasional epithelioid cell granuloma. These yeasts were highlighted by SM and PAS stain and showed negative shadow in ZN stain [Figure 2c-f].
The round cell tumor aspirates were richly cellular comprising of monomorphic round to oval cells displaying mainly hyperchromatic nuclei, occasional nuclear moulding and overlapping, scant to moderate amount of cytoplasm, and indistinct cell borders and marked vacuolization artefacts in the background (Figure 3a-c).

Metastatic adenocarcinomas aspirates were variably cellular and showed tight to loosely cohesive cell clusters of atypical cells with moderate nuclear pleomorphism, hyperchromatic to vesicular nuclei, high N:C ratio, occasional prominent nucleoli, and moderate amount of eosinophilic cytoplasm without focal mucinous changes (Figure 3d-f).

In most of the benign adrenal aspirates, smears were scant to moderately cellular containing cortical cells with maintained N:C ratio in a hemorrhagic background with abundant vacuolization artefacts (Figure 3g and h). In addition, many aspirates also showed benign intestinal epithelial cells (Figure 3i).

ICC showed synaptophysin and inhibin-A positivity in adrenocortical carcinoma (Figure 3j and k) and pan-cytokeratin (Figure 3l) positivity in two cases of poorly differentiated metastatic carcinoma.

**Discussion**

EUS is a real time high resolution imaging modality that has significantly increased the detection of adrenal incidentaloma especially in patients with known primary malignancy. Although EUS-FNA introduced about 2 decades ago, but in India this technique came lately and more so available only in tertiary care centres. Adrenal gland is one of the common sites of metastasis in lung and gastro-intestinal cancers. It is very important to differentiate between primary benign/malignant lesions and metastasis for the proper management and staging of a case. Although conventional radiological techniques such as CT scan and MRI are useful modalities to rule out involvement of adrenal in different
malignancies, but false positive and negative results were observed in about 10% of the cases. EUS-FNA is a highly accurate technique with a good adequacy in comparison to earlier per-cutaneous methods. It has an advantage of providing real-time diagnosis in some cases due to incorporation of ROSE by expert pathologist. Also, the rate of adverse events associated with the per-cutaneous approach are much higher; 0.4–12% in comparison to 0.01% in EUS-FNA procedure. In our study, none of the cases showed any procedure-related complications. In this series, adequacy of yield was 90.63%, which is comparable to previously published literature.

Of the 18 patients including two with unknown primary evaluated for metastasis, five (27.78%) showed malignant lesion which is comparable to 29% positivity in series by Jhala et al. and TNM staging altered in 22.23% of the cases. One case of carcinoma gall bladder revealed a second primary of the adrenal (adrenal cortical carcinoma) instead of metastasis. Incorporation of ancillary technique like ICC has proven very helpful in cytopathology. In this series, three cases (two cases of poorly differentiated metastatic carcinoma and one case of adenocortical carcinoma) were conclusively diagnosed based on the results of ICC.

Size of the adrenal gland alone is not a very sensitive and specific criterion. In our study, the mean size of adrenal was 10.64 mm in benign adrenal aspirate, 31.3 mm in infective etiology, and 32.4 mm in malignant lesions. Matinez et al. reported a higher median adrenal diameter in benign lesions in comparison to malignant aspirates, while Eloubeidi et al. found an opposite result in their series.

Adrenal incidentalomas are mostly non-functional (>90%) with a low (<10%) risk of being malignant, and the cumulative risk of malignant transformation is less than 1:1000. About 2% of the incidentalomas shows a metastatic tumor. In our series, 14/32 (43.75%) cases showed a benign aspirate and 8/32 (25%) malignant lesions. In 2/3 of the patients with a known malignancy undergoing evaluation for staging, if an adrenal lesion is detected show metastatic tumor commonly from carcinomas of lung, gall bladder, stomach, kidney, breast, and lymphomas.

As most of the lesions were hypoechoic irrespective of etiologies, a confirmatory diagnosis is challenging based on only adrenal image findings in EUS. However, a complete assessment involving thoraco-abdominal organs, different group of lymph nodes along with clinical presentations have a much higher cumulative potential to improve certainty of the diagnosis. Further coupling FNAC, cell block preparation, and use of ancillary techniques ensure an accurate diagnosis in majority of the cases. In this series, EUS imaging alone made a correct diagnosis/differential diagnosis in about 1/3rd of the cases.

Kievit et al. suggested that adrenal incidentaloma has important bearing on the life expectancy of patients, which can be decreased by a mean period of 12 months, if the tumor is undiagnosed or inappropriately treated.

EUS has a potential to identify a normal or minimally enlarged left adrenal gland in almost all the patients compared with only a 69% by trans-abdominal ultrasound. Reversely, for right adrenal lesions trans-abdominal ultrasound is a much better technique compared to EUS. A limited literature is available explaining the role of EUS-FNA in right adrenal lesion and its utility is still questionable. In our series right adrenal aspiration was done in six patients (trans-abdominal ultrasound = 02, EUS = 04), all of which revealed adequate sampling with the diagnosis of malignant pathology in four cases.

Decision on the adequacy of yield and onsite examination by a trained cytopathologist is of utmost importance, which reduces number of non-diagnostic samples and turnaround time of the endoscopic procedure. In our institute, an integrated approach with the active engagement of treating physician, endoscopist and trained pathologist is followed to maintain the high yield and minimum turnaround time for reporting of a case.

Limitations of the study are small number of patients, lack of follow-up which restrain the further elucidation of exact nature of lesion reported as benign adrenal aspirate. No correlation with other imaging modalities like positron emission tomography, CT scan, and MRI limits the appropriate outcome of study. In two cases with right adrenal lesions, a trans-abdominal ultrasound approach was used.

To conclude, EUS-FNA of the adrenal gland is a safe, quick, and sensitive and real-time diagnostic technique, which requires an integrated approach of clinician, endoscopist, and cytopathologist for high precision in diagnosis. Although role of EUS-FNA for right adrenal is not much described, we found adequate sample yield in all the four patients underwent the procedure.

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**Conflicts of interest**

There are no conflicts of interest.

**References**

1. Pfau PR, Chuk A. Endoscopic ultrasonography. Endoscopy 2002;34:21-8.
2. Jhala NC, Jhala DN, Chhieng DC, Eloubeidi MA, Eltoum IA. Endoscopic ultrasound-guided fine-needle aspiration. A cytopathologist’s perspective. Am J Clin Pathol 2003;120:351-67.
3. Saboorian MH, Katz RL, Chansangavej C. Fine needle aspiration cytology of primary and metastatic lesions of the adrenal gland: A series of 188 biopsies with radiologic correlation. Acta Cytol 1995;39:543-51.
4. Lumachi F, Borsato S, Brandes AA, Boccagni P, Tregnaghi A, Angelini F, et al. Fine-needle aspiration cytology of adrenal masses in noncancer patients: Clinicoradiologic and histologic correlations in functioning and nonfunctioning tumors. Cancer 2001;93:323-9.
5. Mody MK, Kazerooni EA, Korobkin M. Percutaneous CT-guided biopsy of adrenal masses: Immediate and delayed complications. J Comput Assist Tomogr 1995;19:434-9.
6. Welch TJ, Sheedy PF 2nd, Johnson CD, Johnson CM, Stephens DH. CT-guided biopsy: Prospective analysis of 1,000 procedures. Radiology 1989;171:493-6.
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7. Arellano RS, Garcia RG, Gervais DA, Mueller PR. Percutaneous CT-guided radiofrequency ablation of cell carcinoma: Efficacy of organ displacement by injection of 5% dextrose in water into the retroperitoneum. AJR Am J Roentgenol 2009;193:1686-90.

8. Grumbach MM, Biller BM, Braunstein GD, Campbell KK, Carney JA, Godley PA, et al. Management of the clinically inapparent adrenal mass ("incidentaloma"). Ann Intern Med 2003;138:424-9.

9. Jhala NC, Jhala D, Eloubeidi MA, Chhieng DC, Crowe DR, Roberson J, et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy of the adrenal glands: Analysis of 24 patients. Cancer 2004;102:308-14.

10. DeWitt J, Alsatie M, LeBlanc J, McHenry L, Sherman S. Endoscopic ultrasound-guided fine-needle aspiration of left adrenal gland masses. Endoscopy 2007;39:65-71.

11. Bodiger U, Vilmann P, Clemensen P, Galvis E, Bach K, Skov BG. Clinical impact of endoscopic ultrasound-fine needle aspiration of left adrenal masses in established or suspected lung cancer. J Thorac Oncol 2009;4:1485-9.

12. Eloubeidi MA, Black KR, Tamhane A, Eltoum IA, Bryant A, Cerfolio RJ. A large single-center experience of EUS-guided FNA of the left and right adrenal glands: Diagnostic utility and impact on patient management. Gastrointest Endosc 2010;71:745-53.

13. Schuurbers OC, Tournoy KG, Schoppers HJ, Dijkman BG, Timmers HJ, de Geus-Oei LF, et al. EUS-FNA for the detection of left adrenal metastasis in lung cancer. J Cancer 2011;73:310-5.

14. Uemura S, Yasuda I, Kato T, Doi S, Kawaguchi J, Yamauchi T, et al. Preoperative routine evaluation of bilateral adrenal glands by endoscopic ultrasound and fine-needle aspiration in patients with potentially resectable lung cancer. Endoscopy 2013;45:195-201.

15. Puri R, Thandassery RB, Choudhary NS, Kotecha H, Misra SR, Bhagat S, et al. Endoscopic ultrasound-guided fine-needle aspiration of the adrenal glands: Analysis of 21 patients. Clin Endosc 2015;48:165-70.

16. Frilling A, Tecklenborg K, Weber F, Kuhl H, Stamatis G, Broedisch C. Importance of adrenal incidentaloma in patients with history of malignancy. Surgery 2004;136:1289-96.

17. Viidik J, Haak HR. Diagnosis and treatment of adrenal incidentaloma. A cost-effectiveness analysis. Endocrinol Metab Clin North Am 2000;29:69-90.

18. Dietrich CF, Wehrmann T, Hoffmann C, Herrmann G, Caspary WF, Seifert H. Detection of the adrenal glands by endoscopic or transabdominal ultrasound. Endoscopy 1997;29:859-64.

19. Chang KJ, Katz KD, Durbin TE, Erickson RA, Butler JA, Lin F, et al. Endoscopic ultrasound–guided fine-needle aspiration. Gastrointest Endosc 1994;40:694-9.

20. Binmoeller KF, Thul R, Rathod V, Henke P, Brand B, Jabusch HC, et al. Endoscopic ultrasound-guided, 18-gauge, fine needle aspiration biopsy of the pancreas using a 2.8 mm channel convex array echoendoscope. Gastrointest Endosc 1998;47:121-7.

21. Jhala D, Eloubeidi M, Chhieng DC, Frost A, Eltoum IA, Roberson J, et al. Fine needle aspiration biopsy of the islet cell tumor of pancreas: A comparison between computerized axial tomography and endoscopic ultrasound-guided fine needle aspiration biopsy. Ann Diagn Pathol 2002;6:106-12.

22. Erickson RA, Sayage-Rabie L, Beissner RS. Factors predicting the number of EUS-guided fine-needle passes for diagnosis of pancreatic malignancies. Gastrointest Endosc 2000;51:184-90.

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