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Research Article

Endoscopic Ultrasound Guided Fine Needle Aspiration of Incidentally Detected Adrenal Gland Lesions

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Abstract

Objective- *Adrenal glands are easily approachable for fine needle aspiration (FNA) by endoscopic ultrasound (EUS) due to proximity. There is lack of data on EUS guided FNA of incidentally detected adrenal gland masses. The aim of this study was to assess the diagnostic yield and safety of EUS-FNA for incidentally detected adrenal lesions.*

Methods- *This prospective observational study was conducted between June 2018 to May 2021. Data related to demography, laboratory parameters, EUS and FNA cytology of consecutive patients who came for EUS for other indications but found to have incidental adrenal mass, were prospectively collected.*

Results- *Fourteen patients (median age 55, range 27-88 years, 13 males) were enrolled during the study period. Endoscopic ultrasound guided FNA was done from the left adrenal mass in 13 patients and from the right adrenal in one patient. Technical success was obtained in all the patients. Median number of passes were 2 (range 1-4), and all procedures were done with 22 G needle. Adequate cellularity was achieved in all 14 samples. The cytological diagnosis was tuberculosis in 7(50%), carcinoma in 6(42.85%) and non-specific chronic inflammatory cells observed in one (7.14%) patient. So, a definite diagnosis was made in 13 (92.86%) patients. None of the patient developed any post procedure complications.*

Conclusions-*Tuberculosis and carcinoma are the most common diagnosis in incidentally detected adrenal lesions. EUS guided FNA is safe and an efficacious method for the diagnosis of incidentally detected adrenal lesions.*

Key words- *Endoscopic ultrasound; Adrenal lesions; Tubercular; Malignant*

Introduction

Adrenal gland enlargement has been observed in many benign and malignant pathologies. Benign causes like tuberculosis and fungal infections require prompt diagnosis and treatment.[1] Among the malignant etiologies, metastasis from lung is common.[2] An adrenal mass may represent a benign adrenal adenoma without any prognostic implications. On computed tomography (CT) scan for lung cancer patients an isolated adrenal mass was found in 10% of cases. The adrenal involvement in 32% of these cases was due to metastases, the remaining 68% were benign adenomas, this shows that imaging characteristics alone are unreliable to differentiate benign and malignant adrenal lesions.[2] Ultrasound or CT guided fine needle aspiration (FNA) of adrenal masses was the choice of diagnostic test earlier, but the diagnosis remains uncertain in up to 14% cases with adverse events in up to 12% patients.[3-6] Endoscopic ultrasound (EUS) guided FNA from adrenal gland is a less invasive and highly accurate method with least adverse events and complications.[7,8] Endoscopic ultrasound allows both detailed imaging as well as FNA of the adrenal gland and because of the proximity of the ultrasound transducer to the adrenal gland it may even detect small lesions not visible on transabdominal imaging. Endoscopic ultrasound with a detection rate of 98% as compared to 69% in transabdominal ultrasound has been shown to be superior to transabdominal ultrasound in visualising the left adrenal gland.[7,8] There are limited published data on the EUS-FNA of incidentally detected adrenal lesions. Therefore, we aimed to study the diagnostic yield and safety of EUS-FNA for incidentally detected adrenal lesions in patients who underwent EUS for other indications.

Methods

In this prospective observational study, data of consecutive patients who underwent linear EUS and incidentally detected adrenal mass were recorded in the Gastroenterology department of SMS Hospital, Jaipur during a period of three years from June 2018 to May 2021. All the patients who underwent EUS during this period were screened for adrenal mass and all patients with age >18 years with incidentally detected adrenal mass on EUS were included. Patients with age <18 years, thrombocytopenia (platelets <50000/cmm), coagulopathy (international normalized ratio [INR] >1.5), already diagnosed adrenal mass, pregnancy and severe cardiopulmonary diseases were excluded. Enrolled study patients underwent a detailed clinical examination followed by laboratory tests including complete blood count (CBC), liver function tests (LFT), renal function tests (RFT), erythrocyte sedimentation rate (ESR), serum electrolytes,

acid base analysis, and Mantoux test (in suspected tuberculosis patients) along with demographic details. Each study patient also underwent chest radiography, abdominal and/or chest contrast-enhanced computed tomography (CECT) scan for further etiological work up. Informed consent in writing was obtained from each patient and the study protocol confirmed to the ethical guidelines of the 2000 declaration of Helsinki as reflected in priori approved by the appropriate institutional ethics committee.

Procedure

The procedure was done by linear echoendoscope (GF-UCT180, Olympus, Tokyo, Japan) under conscious sedation using midazolam (3 to 5 mg intravenously). The left adrenal gland was found by tracing the descending aorta to the celiac trunk and then rotating the echoendoscope clockwise; the left adrenal gland seen as a seagull shaped structure. Right adrenal gland identified in the second part of the duodenum with the echoendoscope in the long position along the greater curvature of the stomach. The inferior vena cava or the right kidney was traced, and the right adrenal gland was identified between the upper pole of the right kidney and the inferior vena cava. The left adrenal was selected for the FNA in the presence of bilateral adrenal masses. Data related to size, location, appearance (echogenicity, presence or absence of necrosis), number of needle passes, the result of FNA, and procedure related complications were recorded. Once the appropriate puncture site was identified, a puncture was made by an EUS-FNA needle (Echo-1-22, Cook Endoscopy, NC and USA) guided by real-time EUS imaging with doppler. A total of 10–15 to and fro movements of the needle were done in the adrenal tissue after removing the stylet. The acquired material in the needle was sprayed on the slides bit by bit with help of stylet. Two slides from each pass were immediately fixed in absolute alcohol and rest were air dried. The number of needle passes were operator dependent. Suction was applied using a 10-cm3 vacuum syringe during the second pass if the first pass yielded pus-like or inadequate material. The pathologist analyzed the slides within 24 hours. The adequate specimen was defined if there was an adequate number of representative cells from the mass acquired. The specimens with necrosis or granulomas were also stained for fungal and Ziehl Neelsen (ZN) stain. Diagnosis of adrenal tuberculosis (TB) was made on the basis of caseating granulomas in the presence of acid-fast bacilli or, positive culture for Mycobacterium tuberculosis or positive gene Xpert in the EUS-FNA specimens. Diagnosis of adrenal malignancy was based on cytology and immune-cytochemistry (ICC). Flow cytometry was not used in any patient.

Statistical Analysis

Statistical analysis was accomplished using statistical package for social sciences (SPSS) version 22.0 for Windows (SPSS, Chicago, IL, USA). Study data were demonstrated as absolute numbers and percentage for categorical variables and±mean standard deviation (SD) or median and ranges for continuous variables, as appropriate.

Result

A total of 390 patients underwent EUS for various indications during the study period, out of them 14(3.6%) patients had adrenal mass as incidental finding. These 14 patients (median age 55, range 27-88 years, 13 males) underwent EUS-FNA specimens from adrenal mass as described. Baseline demographic, laboratory and EUS features are shown in table 1. The FNA was done from the left adrenal in 13 patients and from the right adrenal in one patient (figure 1). Technical success was achieved in all 14(100%) patients. Adequate cellularity was also observed in all 14(100%) samples as shown in figure 2-4. Median number of needle passes were 2(range 1-4) and all the procedure were done with 22 G needle as described in procedure. The cytological diagnosis was tuberculosis in 7(50%), carcinoma in 6(42.85%) and non-specific chronic inflammatory cells observed in one (7.14%) patient. So, a definite diagnosis was made in 13(92.86%) patients. None of the patients developed any post procedure complications.

These 7(50%) patients diagnosed with tuberculosis had a history of prolonged fever for more than 4 weeks, anorexia and cough. Out of these 7 patients, 5 patients had positive findings on chest X-ray in the form of infiltrates, opacities, cavities or fibrosis while two patients had only adrenal involvement. On further investigations ultrasonography abdomen and CT chest and abdomen also supported the EUS findings. The remaining 7(50%) patients underwent EUS-FNA for anorexia, weight loss and mediastinal or lung mass on CT chest. Out of these 7 patients 6 were diagnosed to have carcinoma and one had non-specific chronic inflammatory cells. One out of fourteen patients had unilateral right adrenal mass on EUS which was diagnosed as metastatic adenocarcinoma. The median enlargement of adrenal gland on short axis was 2.3 cm (range 1.6-4.5cm). EUS showed hypo echoic homogenous mass in 12(85.8%) and asymmetric enlargement of one limb in 2(14.2%) patients. On EUS the associated mediastinal or lung mass was observed in 4(28.5%) study patients. The malignant lesions were metastatic from lung carcinoma in 5

patients, metastasis from unknown primary in one patient. 7 out of 14(50%) were had tubercular histology. In tubercular patients all had caseating granulomas in the aspirate, and two patients had positive of acid-fast bacilli (AFB) stain. In three patients gene Xpert was positive. All seven patients with suspected tuberculosis had a positive Mantoux test. In one patient EUS-FNA of adrenal mass had chronic inflammatory cells. All tubercular patients received the standard anti-tubercular therapy. Patients diagnosed with lung carcinoma had disseminated malignancy were referred to oncology department for further management.

Parameter (Median/range)	Total study patients (n=14)
Sex Male/Female (n)	13/1
Age (years)	55(27-88)
Haemoglobin (gm/dl)	10.2(8.8-11.6)
Total leucocyte counts (10^3/cumm)	9.62 (4.62-12.8)
Platelets (10^5/ml)	2.82(1.30-4.88)
Serum albumin (gm/dl)	3.1(2.8-3.7_
ALT (U/l)	52.26(44.46-110.50)
AST (U/l)	58.30(46.50-106.60)
ESR (mm/hour)	46(12-96)
Adrenal mass size (in cm)	2.3 (1.6-4.5)
Location of mass (Left/Right)	13/1
Clinical Features n(%)	
Pain abdomen	5(35.7)
Fever	8(57.1)
Anorexia	12(85.7)
Cough	5(35.7)

(ALT- Alanine aminotransferase; AST- Aspartate aminotransferase; ESR- Eryhrocyte sedimentation rate)

Table 1 – Demographic, Laboratory and Clinical features of study patients

Figure 1- Endoscopic ultrasoound image of right adrenal mass

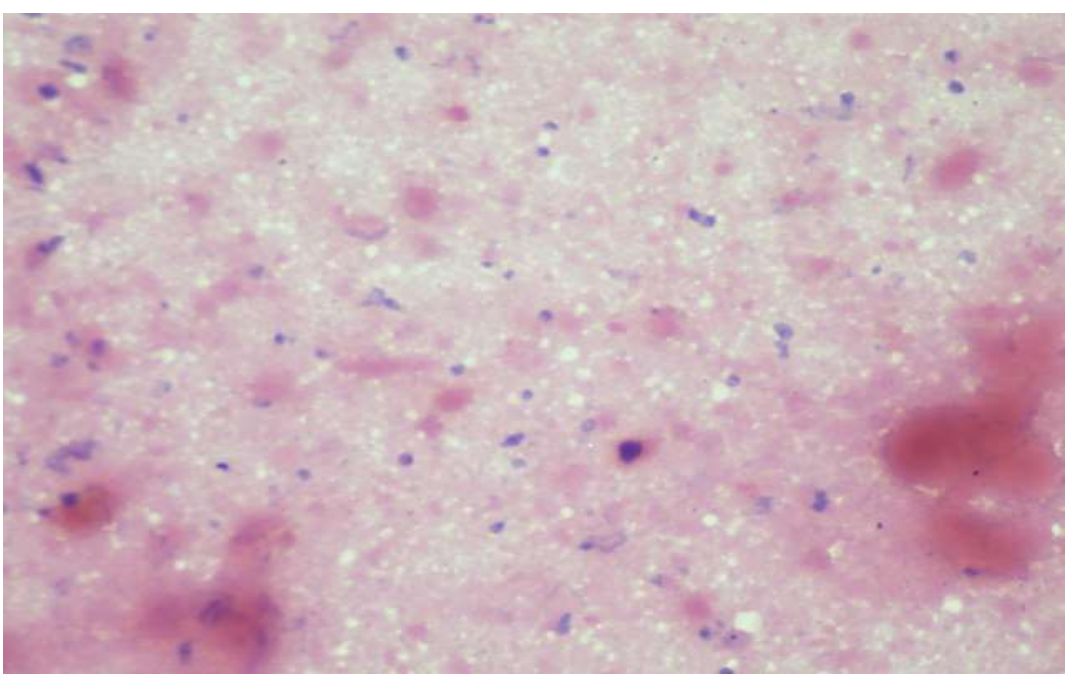

Figure 2- Histopathology slides of left adrenal mass showing single atypical cell with hyperchromatic nuclei and irregular nuclear membrane suggestive of metastatic malignant neoplasm.

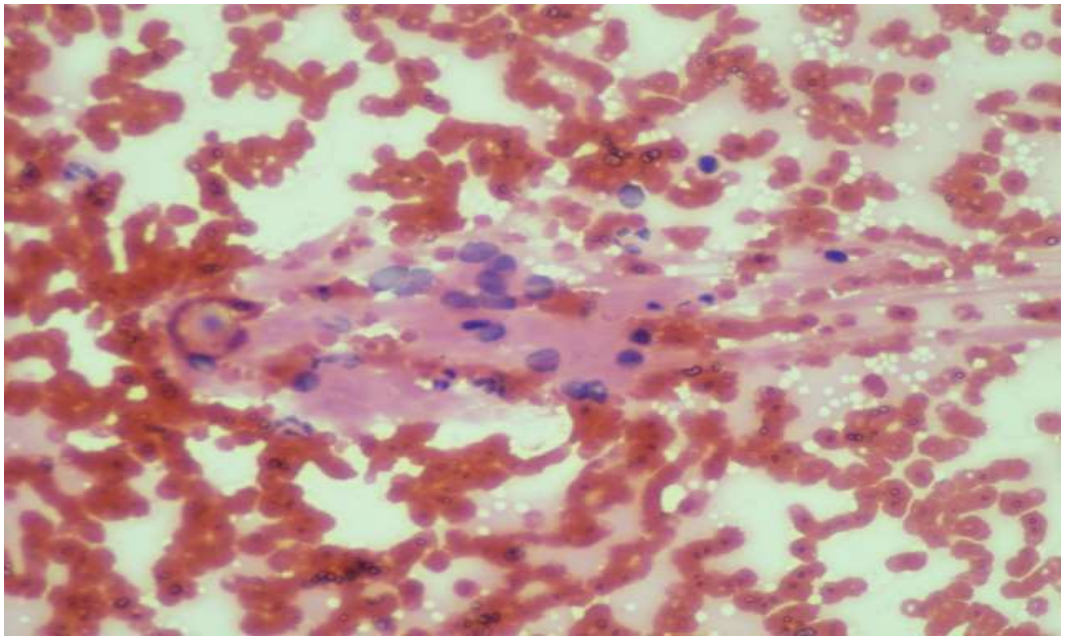

Figure 3- Histopathology slides of left adrenal mass showing small cluster of cells with nuclear overlapping and overcrowding, nuclear membrane irregularity suggestive of metastatic adenocarcinoma.

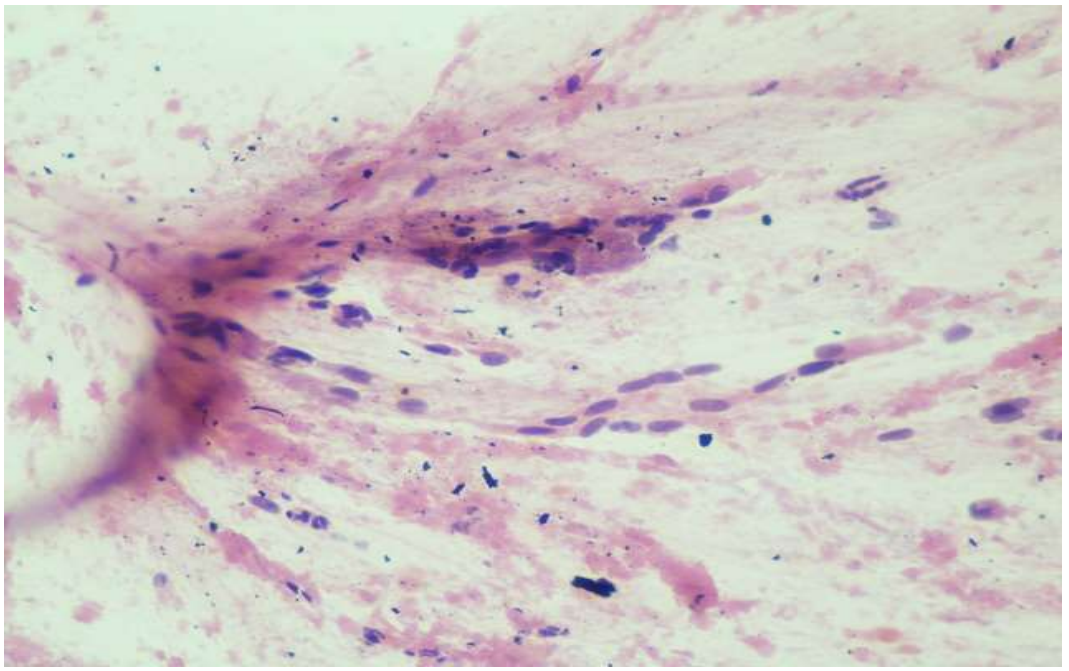

Figure 4- Histopathology slides of left adrenal mass showing epitheloid cells, langerhen's giant cells with scanty caseous necrotic material suggestive of granulomatous inflammation, favouring tuberculosis.

Discussion

Our study revealed incidentally detected adrenal mass in 3.6% patients who underwent EUS for other indications. Technical success and adequate cellularity were observed in all patients. The cytological diagnosis was tuberculosis in 7(50%), carcinoma in 6(42.85%) and non-specific chronic inflammatory cells observed in one (7.14%) patient. So, a definite diagnosis was made in 13(92.86%) patients. None of the patients developed any post procedure complications. So, EUS-FNA is safe and effective procedure for etiological diagnosis for adrenal masses. A previous study published on EUS-FNA from adrenal gland in patients of pyrexia of unknown origin in 52 patients also revealed EUS-FNA is safe and effective method for evaluating etiology in these patients. In this study tuberculosis was observed in 69.2% patients.[9] In CT staging about 75% of adrenal masses identified are metastatic lesions that could be from malignancy involving lung, breast, stomach, kidney, skin, or lymphatic system.[10-12] An unsuspected adrenal mass undetected on imaging (adrenal incidentinoma) ranges from 0.2 to 7%.[13,14] Most of these incidentally found lesions are non-functioning adenomas, but 2% cases can be metastatic so, patients with a high index of suspicion for malignancy are often referred for percutaneous biopsy.[15,16] Ultrasonography or CT guided FNA or biopsy has traditionally been the modality of choice for sampling of the adrenal glands. However, these techniques, yield non-diagnostic samples in up to 14% of patients and are associated with adverse events in 0.4-12% patients.[7,17-19] A study on 59 patients of adrenal mass revealed EUS-FNA is minimally invasive and a safe approach to document or exclude malignancy.[16] Another study on 119 patients, who underwent diagnostic EUS, during which the left adrenal gland was routinely examined. Out of these 119 patients, 12 underwent EUS as a part of lung cancer staging and only 2 patients had left adrenal masses detected on CT while on EUS, left adrenal mass was detected in 2 more patients which were not visualized on CT. The overall prevalence of a left adrenal mass was 3.4%; while in patients with confirmed lung cancer the prevalence was 33.3%.

This study also revealed that EUS-FNA appears safe and useful for the evaluation of left adrenal masses.[20] The EUS-FNA of the left adrenal gland is safe and accurate as compared with the percutaneous approach because the only organ traversed by the needle is the gastric wall. EUS identified the left adrenal gland in 98% cases and the right adrenal gland in only 30% of the cases. EUS-FNA of the right adrenal gland is rather difficult because of the retrocaval location of the right adrenal gland.

Percutaneous FNA of the right adrenal gland is technically easy than the left side, so the role of EUS-FNA is less crucial in this setting.[21]

In our study 4 (28.5%) patients of mediastinal or lung mass had incidentally detected adrenal mass which were positive for malignancy. These results are similar with an earlier published study which revealed the chances of adrenal lesions to be metastases are higher in the presence of an underlying cancer, so screening of adrenal should be done in all EUS examination of mediastinal and lung masses.[22] In our study 50% patients had tubercular aetiology who had symptoms of prolong fever, anorexia and cough, these findings are similar to the earlier published study.[9] In our study EUS-FNA of the adrenal gland had 100% technical success and there were no significant post procedure complications. Now-a-days EUS-FNA is commonly used and is a more accurate and safe procedure with fewer complications than percutaneous biopsies for diagnosing of adrenal lesions as described in various studies.[7,9,19,23] The strength of our study is that we described safety and efficacy of EUS FNA in incidentally detected adrenal masses, as there is a lack of data in the literature on this topic. The limitation of our study is small sample size and lack of onsite by a cytopathologic availability because of that we could not establish a definite diagnosis in one of the patients. Further randomized controlled studies are required which compare EUS with percutaneous US and/or CT guided FNA of the adrenal glands to prove the safety and efficacy of the technique. In conclusion tuberculosis and carcinoma are the most common diagnosis in incidentally detected adrenal lesions. EUS guided FNA is a safe and efficacious method for the diagnosis of incidentally detected adrenal lesions.

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