

Original Article

Endoscopic ultrasound guided aspiration cytology — a useful diagnostic tool

Nadira Mamoon, Sajid Mushtaq, Muhammad Usman Rathore
Department of Histopathology, Armed Forces Institute of Pathology, Rawalpindi.

Abstract

Objective: To evaluate the diagnostic utility of endoscopic ultrasound guided fine needle aspiration cytology in the diagnosis of mediastinal and abdominal lesions

Methods: Endoscopic ultrasound guided aspiration cytology was carried out on a total of 155 cases during the study period. The lesions were categorized according to the site of needle biopsy. Clinical impression and provisional diagnoses were compared with the final cytological diagnoses and the percentage of inadequate/non diagnostic smears was calculated.

Results: Out of 155 cases, 18 cases (11.5%) were reported as inadequate while a definite diagnosis was given in the remaining cases (88.5%). The mean patient age was 49 ± 14.0 years. There were 105 (68%) males and 50 (32%) females. The most common site biopsied was mediastinal lymph nodes followed by pancreas. The most frequent diagnosis was adenocarcinoma mostly of pancreas followed by chronic granulomatous inflammation of mediastinal and abdominal lymph nodes. The average number of passes made was 3. The size of the lesions ranged from 0.6 cm to 25 cm with mean size of 3 cm as measured by endoscopic ultrasound probe.

Conclusion: Endoscopic ultrasound guided aspiration cytology is a useful procedure in the evaluation of deep seated lesions of gastrointestinal tract (GIT), abdominal cavity and mediastinum.

Keywords: Endoscopic ultrasound, fine needle aspiration cytology, mediastinum, abdominal cavity (JPMA 61:367; 2011).

Introduction

A wide variety of inflammatory, reactive and neoplastic lesions can occur in the abdominal and mediastinal cavities. They are detected as space occupying lesions by visualization through endoscopy or by ultrasonographic imaging.¹⁻³ However these imaging techniques are not useful in the exact diagnosis of these pathologic processes or differentiation between inflammatory process, benign and malignant lesions.⁴⁻⁶

Endoscopic ultrasound (EUS) which involves fiberoptic endoscopy with endoluminal ultrasound; when

combined with needle aspiration of the lesions through the endoscope can lead to direct sampling of the lesion leading to definite diagnosis.⁷⁻¹¹ Endoscopic ultrasound guided fine needle aspiration cytology (EUS-FNA) is a safe and accurate procedure which is practiced in various parts of the world.¹² However this technique is not very common in Pakistan. It was started at Gastroenterology department of Military Hospital Rawalpindi in 2005 and since then has gained tremendous popularity.

In this study we evaluated the diagnostic yield of

endoscopic ultrasound guided needle cytology of mediastinal and abdominal lesions.

Material and Methods

All consecutive cases EUS-FNA received at Armed Forces Institute of Pathology, Rawalpindi from January 2007 to December 2008 were included in the study. The EUS-FNA was performed at the endoscopy unit of Gastroenterology Department, Military Hospital (MH), Rawalpindi. Pancreatic, hepatic, gastric, oesophageal, mediastinal and other abdominal lesions were sampled. The main indications of EUS-FNA in these cases were a space occupying lesion, a mass or mediastinal or abdominal lymphadenopathy detected on CT scan of abdomen or chest.

EUS was performed on an outpatient basis. The patients were placed in left lateral decubitus position and with patients under conscious sedation a linear echoendoscope (model GIF 160 Olympus Linear U/S scope) was used to evaluate the mediastinal and abdominal lesions. After the lesion was identified, colour flow and Doppler sonography were performed to exclude intervening vascular structures, vascular lesions and to choose a vessel free needle tract.

All the FNAs were carried out using 22 gauge needle equipped with a stylet that had a tight fit within the needle to minimize contamination by the gastrointestinal tract (GIT). The catheter that contained the needle was then inserted through the working channel of the endoscope. When the tip of the catheter was visualized, the needle was advanced from the catheter sheath, through the wall of the bowel into the target lesion under ultrasound guidance. The stylet was removed when needle was within the target lesion and aspiration biopsy was performed by moving the needle back and forth for 5-10 seconds. The needle was then retracted. No suction was applied during the biopsy. If additional passes were needed, the stylet was reinserted into the needle and the steps were repeated. This procedure was stopped after confirmation of adequacy of material obtained by on site cytological examination of the smears by a pathologist from Armed Forces Institute of Pathology, Rawalpindi of registrar level.

The aspirate was placed on glass slide and two smears were prepared from a single aspirate by placing another slide over it and spreading the aspirate on the slides. Both air dried and alcohol fixed smears were prepared. Air dried smears were stained with Diff-Quik stain and reviewed immediately by the cytopathologist to confirm the adequacy of the material and to render a provisional diagnosis at that time. Wet fixed smears were placed in 95% alcohol for 15-20 minutes and then air dried. These slides along with air dried slides were then submitted at AFIP, Rawalpindi along with a proforma containing clinical details, endoscopic ultrasound findings and clinical diagnosis as well as provisional

cytological diagnosis.

At AFIP, the wet fixed smears were stained with Haematoxylin and Eosin (H&E) or Papanicolaou (PAP) stain. The final cytological diagnosis was based on the examination of both air dried and wet fixed smears.

Cell block was made in 45 cases and histopathological examination followed by immunohistochemistry was also carried out in 6 cases.

The cases were evaluated for adequacy, site of biopsy, number of passes, size of the lesion, clinical impression, provisional and final cytological diagnosis. The term Inadequate or non-diagnostic aspirate was reserved for those smears in which the cellularity was not sufficient to characterize the lesion or in which the cells were not representative of the target lesion.

Results

During the year January 2007-December 2008, 155 cases of EUS-FNA were received at AFIP, Rwp. 105 patients were males and 50 were females. Their ages ranged from 12 to 85 years and the mean age was 49 ± 14 years.

The most common site of FNA was mediastinal lymph nodes constituting 68 (44%) cases, followed by pancreas in 36 (23%) cases. Other sites included abdominal lymph nodes, stomach, ampullary region, lung, liver etc. The site wise distribution of cases is shown in Figure-1.

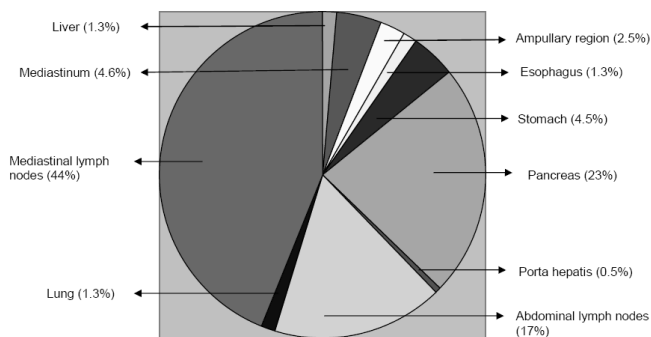


Figure-1: Site wise distribution of EUS-FNA.

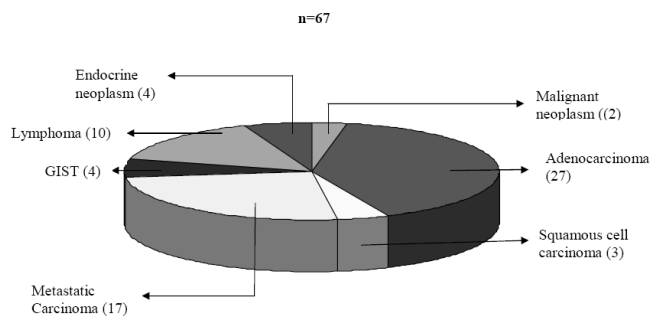


Figure-2: Frequencies of neoplastic lesions.

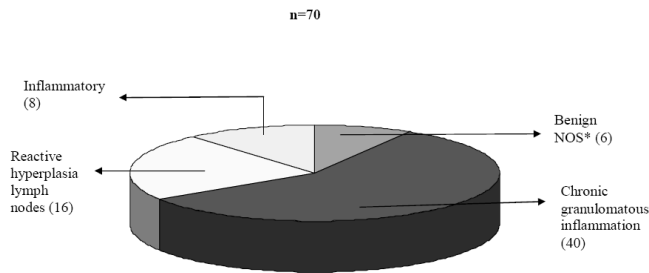


Figure-3: Frequencies of non-neoplastic lesions.

The average number of passes made was 3 with a minimum of 1 pass and maximum of 10 passes. The number of passes was documented in 118 cases. The size of the lesion was documented in 110 cases. The average size of the lesions was 3 cm (\pm 2.6) with a minimum of 0.6 cm and maximum of 25 cm.

Out of 155 cases, 18 (11.5%) were reported as inadequate. Out of the remaining 137 cases, 67 (43%) were reported as neoplastic lesions (Figure-2); the most common being adenocarcinoma mainly of pancreas in 27 cases. Eight cases were of intermediate or undetermined malignant potential including 4 GISTs all from the stomach and 4 endocrine neoplasms, 2 from mediastinum and 2 from pancreas.

Seventy (45%) lesions were reported as benign of non-neoplastic nature. The most common among non-neoplastic lesions was chronic granulomatous inflammation in 40 cases of abdominal and mediastinal lymph nodes followed by reactive hyperplasia of lymph nodes in 16 cases. Frequencies of non-neoplastic lesions are summarized in Figure-3.

The correlation of final cytological diagnoses with the

Table-1: Correlation of site of FNA with final cytological diagnosis.

Final cytological diagnosis	Site of FNA									Total	
	Mediastinal LNs**	Lung	Abdominal LNs**	Porta hepatis	Pancreas	Stomach	Liver	Ampulla	Mediastinum		Esophagus
Inadequate/non diagnostic	9		5		2	1	1				18
Benign (NOS)*					4		1	1			6
Malignant neoplasm		1						1			2
Squamous cell carcinoma									1	2	3
Reactive hyperplasia lymph node	11		5								16
Chronic granulomatous inflammation	34	1	5								40
Metastatic carcinoma	7		8						2		17
Adenocarcinoma				1	23			1	2		27
GIST						4					4
Lymphoma	6		3			1					10
Inflammatory/ Abscess	1				5	1		1			8
Endocrine neoplasm					2				2		4
Total	68	2	26	1	36	7	2	4	7	2	155

*NOS- Not otherwise specified.

** LNs - Lymph nodes.

Table-2: Correlation of provisional diagnosis with final cytological diagnosis.

Final cytological diagnosis	Provisional diagnosis							Total
	Reactive/ Inflammatory	Chronic granulomatous inflammation	Carcinoma/ malignant	Metastatic carcinoma	GIST	Lymphoma	Benign	
Inadequate/non diagnostic	4	3	4	2	1	4		18
Benign (NOS)*	1		3	1			1	6
Malignant neoplasm			2					2
Squamous cell carcinoma			3					3
Reactive hyperplasia lymph node	7	2		6		1		16
Chronic granulomatous inflammation		33	2	2		2	1	40
Metastatic carcinoma			4	13				17
Adenocarcinoma			27					27
GIST		1			3			4
Lymphoma			1			8	1	10
Inflammatory/abscess	3	1	3		1			8
Endocrine neoplasm			3	1				4
Total	15	40	52	25	5	15	3	155

*NOS- Not otherwise specified.

site of FNA is summarized in Table-1. Of 68 mediastinal lymph nodes sampled, chronic granulomatous inflammation was diagnosed in 34 mediastinal lymph nodes followed by reactive hyperplasia in 11 cases. Twenty six abdominal lymph nodes were sampled with metastatic carcinoma diagnosed in 8 cases. Twenty three cases of adenocarcinoma were diagnosed in total of 36 pancreatic aspirates.

Fifty-eight cases were provisionally diagnosed as benign/non neoplastic and 97 cases as malignant/neoplastic by the on site pathologist at the time of performing FNA. When these were correlated with the final cytological diagnosis the number of false positive cases reported on provisional diagnosis was 32 whereas 2 cases proved to be false negative (Table-2).

No complication was observed following EUS-FNA in any case except minimal discomfort at the time of needle puncture.

Discussion

Endoscopic ultrasound (EUS) is a rapid, safe, economical and accurate diagnostic procedure that can be used in the assessment of various neoplastic and non-neoplastic diseases involving gastrointestinal tract (GIT), abdominal cavity and mediastinum.¹³ For gastrointestinal tract lesions, EUS is particularly helpful in identifying the origin of the lesion whether it is arising from the wall or is extrinsic and compressing the lumen from outside.^{14,15} EUS can also identify the layer of the bowel wall from which the lesion arises and it also provides information on the extent and borders of the lesion. However, definitive differentiation between benign and malignant lesions using EUS alone is usually not possible. Therefore tissue sampling for EUS-FNA is required to establish a conclusive diagnosis.

Advantages of the technique include its utility in patients with inoperable lesions, and in whom surgery is contraindicated due to some reason such as fitness for anaesthesia. With diagnoses like tuberculosis, inflammatory lesion, lymphoma etc treatment can be started on the basis of cytological diagnosis. There are few limitations including very small lesions, inaccessible lesions, vascular lesions, calcifications, cavitating and necrotic lesions.

As the diagnosis is rapidly available on EUS-FNA, appropriate medical or surgical therapy can also be started earlier, at times avoiding unnecessary and often invasive diagnostic surgical procedures. In lesions requiring surgical procedures, operative time is reduced as intraoperative evaluation is not required.

Moreover as this procedure is performed on an outpatient basis, surgical mortality, morbidity and patient hospitalization is reduced thereby benefiting the patient and health care system.¹⁶

In our study the diagnostic yield was 88.5% with non diagnostic aspirates yielded in 18 cases. The factors contributing to inadequate or non diagnostic aspirates include non-cooperative patients, very small lesion, necrotic centre of the lesion, sampling error leading to tissue sampling from the inappropriate site, haemorrhagic lesions and cytological error due to poor sample quality, preparation or interpretation.

It is also important to note that in this study, the most common site of EUS-FNA was mediastinal lymph nodes (68) followed by pancreas (36) and abdominal lymph nodes (28). Sampling of mediastinal lymph nodes is difficult and requires invasive surgical procedures such as thoracotomy or thoracoscopy. Similarly sampling of pancreatic lesions is also very difficult. EUS-FNA thus provides an alternate safe, rapid and non invasive method of sampling these lesions.

Another advantage of EUS-FNA is that it is very effective method for detecting and sampling very small lesions of pancreas so that early diagnosis is possible in pancreatic neoplasms. It has been shown that EUS alone is more sensitive than CT scan and magnetic resonance imaging in detecting very small lesions of pancreas, especially when they are smaller than 3 cm.¹⁷ In our study also, the mean size of lesions was 3 cm with a minimum of 0.6 cm sampled from pancreatic lesion.

The use of stylet during advancement of the biopsy needle through the bowel wall minimizes the plugging of the needle tip with GI tract epithelium. Because our target lesions were within or close to GI tract, GI tract epithelium was not considered a contaminant. The presence of GI tract mucosal fragments in EUS-FNA specimens of GI tract lesions is less critical than in specimens of lymphadenopathy, because these benign GI tract mucosal fragments can be mistaken for metastatic carcinoma.¹⁸⁻²⁰

There was a significant number of false positive (32) diagnosis made on preliminary examination at the time of EUS when compared with the final cytological diagnosis. Keeping this in mind it may be prudent to restrict the pathologist to commenting on the adequacy alone rather than attempting to make a diagnosis. If a provisional diagnosis is to be rendered than careful examination of the slides at the time of EUS is essential which requires expertise and experience.

Cell block should be made in every possible case as it proves very helpful in establishing the final diagnosis in cases where adequate tissue was obtained. Similarly immunohistochemistry can be applied on the cell block in difficult cases.

Follow up of these patients and confirmation of our diagnoses with the histological diagnoses after surgical treatment could not be carried out because the patients undergoing EUS-FNA came from different hospitals.

Surgical treatment if rendered also took place in different set ups and all the histopathology samples were not sent to at AFIP, Rawalpindi.

Conclusion

In conclusion, our observations suggest that EUS-FNA is a reliable and effective procedure with adequate yield in the diagnosis of neoplastic and non-neoplastic lesions of GI tract, abdominal cavity and mediastinum.

(The clinical aspect of this collaborative work has been published in the Journal of the college of Physicians and Surgeons Pakistan 2009, Vol 19: 223-227).

References

1. Fleischer AC, Muhletaler CA, James AE Jr. Sonographic assessment of the bowel wall. *AJR Am J Roentgenol* 1981; 136: 887-91.
2. Morgan CL, Trought WS, Oddson TA, Clark WM, Rice RP. Ultrasound patterns of disorders affecting the gastrointestinal tract. *Radiology* 1980; 135: 129-35.
3. Chhieng DC, Jhala D, Jhala N, Eltoun I, Chen VK, Vickers S, et al. Endoscopic ultrasound-guided fine needle aspiration biopsy; A study of 103 cases. *Cancer* 2002; 92: 232-9.
4. Heintz A, Mildenerger P, Georg M, Braunstein S, Junginger T. Endoscopic ultrasonography in the diagnosis of regional lymph nodes in esophageal and gastric cancer - results of studies in vitro. *Endoscopy* 1993; 25: 231-5.
5. Kaufman AR, Sivak MV Jr. Endoscopic ultrasonography in the differential diagnosis of pancreatic disease. *Gastrointest Endosc* 1989; 35: 214-9.
6. Vander Noot MR 3rd, Eloubeidi MA, Chen VK, Eltoun I, Jhala D, Jhala N, et al. Diagnosis of gastrointestinal tract lesions by endoscopic ultrasound guided-guided fine-needle aspiration biopsy. *Cancer* 2004; 102: 157-63.
7. Boyce GA, Sivak MV Jr, Lavery IC, Fazio VW, Church JM, Milsom J, et al. Endoscopic ultrasound in the pre-operative staging of rectal carcinoma. *Gastrointest Endosc* 1992; 38: 468-71.
8. Akahoshi K, Misawa T, Fujishima H, Chijiwa Y, Maruoka A, Ohkubo A, et al. Preoperative evaluation of gastric cancer by endoscopic ultrasound. *Gut* 1991; 32: 479-82.
9. Rosch T, Lorenz R, Braig C, Feuerbach S, Siewert JR, Schusdziarra V, et al. Endoscopic ultrasound in pancreatic tumor diagnosis. *Gastrointest Endosc* 1991; 37: 347-52.
10. Rosch T, Lorenz R, Braig C, Classen M. Endoscopic ultrasonography in diagnosis and staging of pancreatic and biliary tumors. *Endoscopy* 1992; 24: 304-8.
11. Rice TW, Boyce GA, Sivak MV. Esophageal ultrasound and the preoperative staging of carcinoma of the esophagus. *J Thorac Cardiovasc Surg* 1991; 101: 536-43.
12. Vilmann P, Saftoiu A. Endoscopic ultrasound guided fine needle aspiration biopsy: equipment and technique. *J Gastroenterol Hepatol*. 2006; 26: 1646-55.
13. Anand D, Barroeta JE, Gupta PK, Kochman M, Baloch ZW. Endoscopic ultrasound guided fine needle aspiration of non pancreatic lesions: an institutional experience. *J Clin Pathol*. 2007; 60: 1254-62.
14. Bhutani MS, Logrono R. Endoscopic ultrasound-guided fine-needle aspiration cytology for diagnosis above and below the diaphragm. *J Clin Ultrasound* 2005; 33: 401-11.
15. Caletti G, Odegaard S, Rosch T, Sivak MV, Tio TL, Yasuda K. Endoscopic ultrasonography (EUS): a summary of the conclusions of the Working Party for the Tenth World Congress of Gastroenterology Los Angeles, California October, 1994. The Working Group on Endoscopic Ultrasonography. *Am J Gastroenterol* 1994; 89: S138-43.
16. Rowley VA, Cooperberg PL. Ultrasound guided biopsy. *Interventional ultrasound*. In: *Clinics in "Diagnostic Ultrasound"*. E Vansonnenberg, editor. Vol. 21. New York: Churchill Livingstone, 1987; pp 59-76.
17. Jhala NC, Jhala D, Eltoun I, Vickers SM, Wilcox CM, Chhieng DC, et al. Endoscopic ultrasound-guided fine-needle aspiration biopsy: a powerful tool to obtain samples from small lesions. *Cancer* 2004; 102: 239-46.
18. Kedar RP, Patel VH, Merchant SA, Aggarwal V, Pandit AA. Ultrasound guided aspiration cytology--a valuable diagnostic aid. *J Postgrad Med* 1991; 37: 84-7.
19. Klapman JB, Logrono R, Dye CE, Waxman I. Clinical impact of on-site cytopathology interpretation on endoscopic ultrasound-guided fine needle aspiration. *Am J Gastroenterol* 2003; 98: 1289-94.
20. Wiersema MJ, Wiersema LM, Khusro Q, Cramer HM, Tao LC. Combined endosonography and fine-needle aspiration cytology in the evaluation of gastrointestinal lesions. *Gastrointest Endosc* 1994; 40: 199-20.