

Impact of endoscopic ultrasound-guided fine needle aspiration of small lymph nodes

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Abstract

Background: There is very limited literature on results of fine needle aspiration (FNA) of small (defined as ≤ 1 cm at long and short axis) lymph nodes, particularly in the setting of pyrexia of unknown origin (PUO). **Methods:** The study was conducted from July 2014 to December 2015 at a tertiary care center. A total of 34 endoscopic ultrasound (EUS)-guided FNAs in 33 patients were done for lymph nodes ≤ 1 cm at long and short axis and these were included in the analysis. **Results:** The study cohort comprised 33 patients; 23 males and 10 females, mean age of 58 ± 12 years. Indication of FNA was to look for malignancy ($n = 15$), PUO ($n = 16$), unexplained weight loss ($n = 1$), and presence of lymphadenopathy in prospective liver donor ($n = 1$). The FNA was taken from mediastinal nodes ($n = 20$, 14 subcarinal) and abdominal ($n = 14$, 8 at porta). The mean size of lymph nodes was 87 ± 11 mm at large axis and 68 ± 17 mm at short axis. A total of 3 (8.8%) FNAs were nondiagnostic (inadequate material). The cytopathologic diagnosis was malignancy in 8 (23.5%), granulomatous change in 8 (23.5%), and reactive lymphadenopathy in 15 (44.1%). Thus, EUS-guided FNA of these small nodes changed the management decisions in 44% of cases (one patient had tubercular lymphadenopathy at two sites). The 22-gauge EUS FNA needle was used in majority of patients ($n = 26$). There was no significant difference between pathologic (malignant and granulomatous) and reactive lymph nodes regarding size at long or short axis, ratio of long and short axis, hypoechogenicity, and sharply defined borders. **Conclusion:** EUS-guided FNA of small lymph nodes showed pathological enlargement in 44% of cases.

Key words

Axis, granulomatous, lymph node, pyrexia of unknown origin

Introduction

Small (or subcentimetric) lymph nodes are defined as short axis diameter < 1 cm (long axis may be > 1 cm in size). Often these lymph nodes are detected by current refined diagnostic modalities (computed tomography or magnetic resonance

imaging) done for some other purpose. Furthermore, multiple postmortem studies in patients with no chest infection or malignancy have shown that presence of these nodes is common.^[1-3] There is very limited literature regarding lymph nodes with both long and short axis ≤ 1 cm in size, we have defined these nodes as small nodes for purpose of the present study. These lymph nodes are difficult to fine needle aspiration (FNA) due to small size and location. Endoscopic ultrasound (EUS)-guided FNA offers real-time vision and it has been proved to be very safe from mediastinum where vascular

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structures are abundant.^[4] There is a lack of knowledge about nature of these small lymph nodes (≤ 1 cm at long and short axis), and scarce data are available in the setting of pyrexia of unknown origin (PUO). In the present study, we describe our experience of EUS-guided FNA of small mediastinal or abdominal lymph nodes in the setting of PUO or nonlung malignancy.

Methods

The study was conducted from January 2014 to December 2015 at a tertiary care center in North India (Delhi NCR). All the patients who underwent EUS-guided FNA of small lymph nodes (defined as ≤ 1 cm at both long and short axis) were included in the analysis. The study was conducted prospectively after clearance from the Institute's Review Board/Ethical Committee. A total of 476 EUS-guided lymph node FNA were done at our center in defined time period, out of which, 34 (7.1%) were done for small lymph nodes. EUS-guided FNA was done for those nodes which were not easily accessible by percutaneous ultrasound and when diagnosis could not be achieved by other easier/noninvasive methods. All the procedures were carried out in conscious sedation (midazolam). EUS-guided FNA was done using GF-UCT140 linear echoendoscope (EUS scope, Olympus, Tokyo, Japan). The primary objective of the study was to look for safety and diagnostic accuracy of EUS-guided FNA of small lymph nodes. Following data were recorded for each patient; age, sex, indication for procedure (PUO vs. malignancy), site of lymph node, echo features of lymph node, size at short and long axis, type and number of needle passes, number of slides, result of FNA, and any procedural complications. In the presence of multiple lymph nodes, node with larger size/having sharply demarcated borders/hypoechoic in nature following features was preferred for FNA. A lymph node was considered reactive when FNA showed lymphoid cells in different stages of activation in the presence of adequate cellularity and absence of granulomas/necrosis/malignant cells.

Endoscopic ultrasound fine needle aspiration procedure

A lymph node was selected based on above-mentioned criteria for FNA if feasible (avoidance of vascular structures and vital organs). A linear array echoendoscope was directly inserted into the esophagus. EUS FNA needle with stylet was introduced in working channel; Doppler was used to avoid any vascular structures in needle path. The stylet was withdrawn slightly before puncture; it was reintroduced fully after puncture of lymph node to displace any material in needle (from gastrointestinal wall). After that stylet was completely withdrawn; 10–20 to and fro movements of needle were done within lymph node. The material inside needle was pushed on slides bit by bit with help of stylet. One or two slides from each pass were immediately fixed in absolute alcohol and rest were air dried. The slides were stained with Papanicolaou, Giemsa stain, and Ziehl–Neelsen stain (wherever required).

The type of needle and method of FNA (suction, no suction, or capillary) and number of needle passes (as we do not have on-site cytopathologist facility) were operator's dependent. A different needle was used for different lymph node if needed.

Statistical analysis

The data are shown as number, percentage, and mean (standard deviation). Two groups were compared with Student's *t*-test or Fisher's exact test (nominal data). A two-tailed $P < 0.05$ was considered statistically significant. All statistical analysis was performed with SPSS, version 16 (SPSS, SPSS Inc., Chicago, IL, USA).

Results

The study cohort comprised 33 patients; 23 males and 10 females. The mean age of study cohort was 58 ± 12 years. A total of 34 lymph nodes FNA were done. Indication of FNA was to look for malignancy ($n = 15$), PUO ($n = 16$), presence of lymphadenopathy in unexplained weight loss ($n = 1$), and prospective liver donor ($n = 1$). The primary in cases of malignancy included hepatocellular carcinoma in 10 patients and FNA was done before liver transplantation to rule out metastasis, other sites of primary included carcinoma of cholangiocarcinoma ($n = 4$) and esophagus ($n = 1$). The FNA was taken from mediastinal nodes ($n = 20$, 14 subcarinal) and abdominal ($n = 14$, 8 at porta). The prospective liver donor was asymptomatic, imaging showed small lymph nodes at porta and mediastinum, and she underwent FNA from both of these sites. The mean size of lymph nodes was 87 ± 11 mm at long axis and 68 ± 17 mm at short axis. The mean ratio of long to short axis was 1.2 ± 0.29 . A total of 3 (8.8%) FNAs were nondiagnostic (inadequate material). None of the patients had any complication related to anesthesia or FNA procedure. The cytopathologic diagnosis was malignancy in 8 (23.5%), granulomatous lymphadenopathy in 8 (23.5%), and reactive lymphadenopathy in 15 (44.1%). The prospective donor had presence of granulomas in both aortopulmonary and porta lymph nodes; AFB stain was positive from AP window lymph node. The patient who presented with weight loss had azygoesophageal lymph node and FNA showed granulomas and necrosis. When patients with nondiagnostic FNA (inadequate material) were compared to patients with diagnostic FNA, there was no significant difference regarding long axis and short axis diameter. The 22-gauge EUS FNA needle was used in majority of patients ($n = 26$) and a 25-gauge needle was used in rest of the patients. Out of eight granulomatous lymph nodes, five also showed the presence of necrosis, one showed the presence of calcification, and this node was positive for AFB stain. Only one of these granulomatous lymph nodes showed the presence of patchy hypoechoic area within. A positive diagnosis (pathologic versus reactive enlargement) could be made in 18/20 of mediastinal and 13/14 of abdominal lymph nodes ($P = 0.83$). The sex ratio was equal in pathologic versus reactive node groups (10 males and 5 females in each group, 3 males had

inadequate material for diagnosis). Thus, EUS-guided of these small nodes changed the management decisions in 44% of cases (47% of FNAs, one patient had FNA from 2 sites). Representative images with cytopathological diagnosis are shown in Figures 1-3.

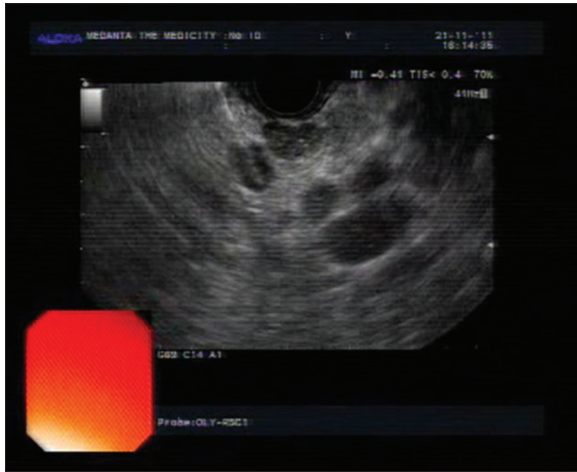


Figure 1: Malignant lymph node at porta



Figure 2: Granulomatous lymph node near azygos vein

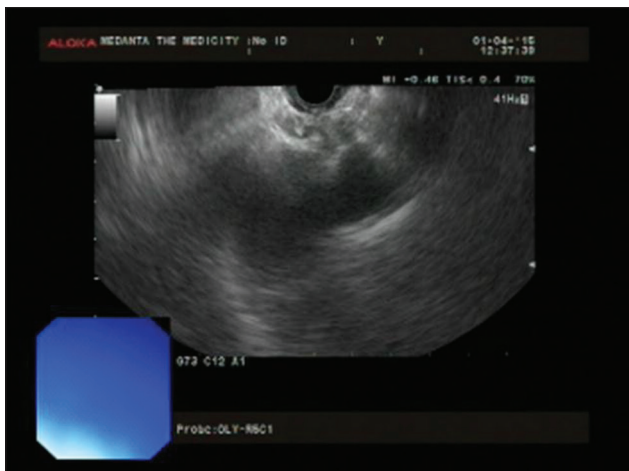


Figure 3: Granulomatous lymph node in AP window

Discussion

There is no uniform definition of small versus very small lymph nodes, for the purpose of the present study, we defined small lymph nodes as ≤ 1 cm at both long and short axis. Subcentimetric (small) lymph nodes are defined as < 1 cm at short axis, and there is a lack of literature on lymph nodes ≤ 1 cm at both long and short axis. These sub-centimetric lymph nodes (< 1 cm at short axis) were considered as benign based on several studies.^[1-3] With evolution of EUS-guided FNA, mediastinal FNA can be done very safely, and it has shown to be accurate.^[4] Few studies have shown that some of small nodes may be malignant; however, data are limited to lung carcinoma.^[5-7] There is a lack of literature on FNA results of small lymph nodes (≤ 1 cm at both long and short axis) in other indications, particularly PUO. The traditional criteria of malignant node include size > 1 cm, round shape, sharply defined border, and homogeneous/hypoechoic echo pattern.^[8] Recently, Jamil *et al.*^[9] compared 68 benign lymph nodes with 94 pathological lymph nodes. The authors showed that various echo features including echogenicity, margins, and shape were not significantly different between these groups, only size was significantly different. Tuberculosis is the most common cause of PUO in India, we recently described our experience of 53 tubercular nodes (accepted for publication in Indian Journal of Gastroenterology), the morphological features of these nodes included hypoechoic echotexture (94.5%), patchy anechoic/hypoechoic areas (30.2%), calcification (24.5%), sharply demarcated borders (34.5%), pus-like material on aspirate (18.2%), and conglomeration of lymph nodes (10.9%). The tubercular lymph nodes have a size of 2.4 ± 1.1 cm and 1.5 ± 0.7 cm at short axis. As shown in Table 1, EUS morphological criteria are not different between pathologically enlarged and reactive nodes in small nodes. Some of the features of tubercular nodes describe above such as calcification (present in only one node), patchy hypoechoic areas were also not present in small nodes. We have a major difference with other published studies as a significant proportion of sample size had PUO as indication of FNA. In these patients, granulomatous pathology was predominant cause of pathological lymph node enlargement. Our findings are similar to two other studies from India in patients with mediastinal lymphadenopathy that suggested tuberculosis in 32 out of 60 patients and 22 out of

Table 1: Comparison of pathologic and reactive lymph nodes (n=31)

Parameter	Malignant/ granulomatous change (n=16)	Reactive lymph nodes (n=15)	P
Age (years)	55.2±13.6	60.3±11.3	0.27
Long axis (mm)	89±9	85±13	0.36
Short axis (mm)	72±19	65±16	0.28
Long and short axis ratio	1.19±0.27	1.17±0.35	0.82
Hypoechoogenicity	9	7	0.72
Well-defined borders	8	5	0.47
Number of slides	10.1±4.3	12.8±3.8	0.09
Number of passes	2.07±0.59	2.5±0.94	0.14

42 patients.^[10,11] We did not encounter any complication during this study. A meta-analysis of 32 studies of mediastinal lymph node FNA by Puli *et al.* showed complication rate of 0–2.3% across studies.^[4] Our study has limitations in the form of no follow-up of patients with granulomatous change as PUO patients are referred from other hospitals or other departments for purpose of EUS-guided FNA. We do not want to suggest that all lymph nodes seen in mediastinum or abdomen should be sampled in asymptomatic patients (as they are present in normal individuals also). We suggest that small lymph nodes should be sampled when it is indicated like in our series (for PUO or to confirm malignant lymphadenopathy and thus avoiding futile surgeries). The unnecessary (futile) surgery could be avoided in almost half of patients with malignancy in current series. Although sample size is small in the present study, these truly small (≤ 1 cm at both long and short axis) nodes are uncommon at presentation to clinicians as reflected by total number of FNAs done by us in defined study period. In conclusion, we shown that small lymph nodes are pathologically enlarged in significant percentage of patients and they should be sampled whenever clinically indicated. Pathological features cannot differentiate between reactive and pathological small lymph nodes.

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Conflicts of interest

There are no conflicts of interest.

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