Irregular Echogenic Foci Representing Coagulation Necrosis: a Useful but Perhaps Under-Recognized EUS Echo Feature of Malignant Lymph Node Invasion

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Abstract

Background and Aims: Coagulation necrosis has been described in malignant lymph nodes. Our aim was to determine if coagulation necrosis in mediastinal lymph nodes imaged by EUS could be used as a useful echo feature for predicting malignant invasion. **Methods and Design:** Patients with known or suspected lung cancer who had undergone mediastinal lymph node staging by EUS. **Setting**: Tertiary Care university hospital. **Participants and Intervention:** An expert endosonographer blinded to the final diagnosis, reviewed the archived digital EUS images of lymph nodes prior to being sampled by FNA. LNs positive for malignancy by FNA were included. The benign group included lymph node images with either negative EUS-FNA or lymph nodes imaged by EUS but not subjected to EUS-FNA, with surgical correlation of their benign nature. **Results**: 24 patients were included. 8 patients were found to have coagulation necrosis. 7/8 patients had positive result for malignancy by EUS-FNA. One patient determined to have coagulation necrosis had a non-malignant diagnosis indicating a false positive result. 16 patients had no coagulation necrosis. In 6 patients with no coagulation necrosis, the final diagnosis was malignant and in the remaining 10 cases, the final diagnosis was benign. For coagulation necrosis as an echo feature for malignant invasion, sensitivity was 54%, specificity was 91%, positive predictive value was 88%, negative predictive value was 63% and accuracy was 71%. **Conclusion**: Coagulation necrosis is a useful echo feature for mediastinal lymph node staging by EUS.

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Key words

Endoscopic ultrasound – endosonography – lung cancer – lymph node – echo feature – coagulation necrosis – metastases.

Introduction

Endoscopic ultrasound (EUS) with fine needle aspiration (FNA) has become an important modality for locoregional lymph node staging in gastrointestinal and pulmonary cancers [1-9]. It is important to determine whether the lymph nodes visualized by EUS are benign or represent metastatic malignant invasion. This can be determined by assessing the echo features of lymph nodes [10] as well as by EUS guided fine needle aspiration [1-9, 11, 12]. Traditionally four echo features have been considered to be highly predictive of malignant invasion. These four features include size of > 1 cm, round shape, hypoechogenicity, and distinct margins [10].

A recently published study by Roberts et al [13] described a new endosonographic sign of coagulation necrosis in malignant mediastinal lymph nodes. Coagulation necrosis within a lymph node on EUS was described as an ill-defined, rounded, non-shadowing echogenic area within a lymph node. This was differentiated from the linear non-shadowing, hilar echogenic structure that may be seen in the centre of benign lymph nodes on ultrasound. Coagulation necrosis on EUS imaging of lymph nodes has not been the main focus of any EUS studies prior to the report by Roberts et al [13]. Therefore, the purpose of our study was to evaluate the utility and accuracy of this newly described feature of coagulation necrosis during EUS imaging of mediastinal lymph nodes.

Methods

This was a retrospective study. The study included patients from May 2002 to June 2005 who had undergone radial or linear EUS imaging with 7.5 MHz of the mediastinum for lymph node staging in patients with known non-small cell lung cancer with already a tissue diagnosis or mediastinal lymphadenopathy with suspected lung cancer and no tissue

diagnosis. The study was conducted after Institutional Review Board approval for review of archived digital EUS images and other clinical or pathological data on the included subjects. Images of those patients were included that had a positive EUS guided FNA of a mediastinal lymph node to create the malignant lymph node group. All the patients in this group with positive EUS guided FNA had non-small cell lung carcinoma. The benign lymph node group included patients with negative EUS guided FNA of lymph nodes with subsequent surgery confirming their benign nature or lymph nodes imaged by EUS but not subjected to EUS FNA with subsequent confirmation of their benign nature by surgery. Only those patients whose archived EUS images were available (with confirmed cytopathology or histopathology by EUS FNA or surgery) for retrospective blinded evaluation and re-interpretation were included. Archived videos of EUS exams were not available to us at the time of the study.

An advanced EUS fellow retrieved the archived images with knowledge of the clinical and pathological details of the subjects. He then selected representative images of patients with malignant and benign lymph nodes based on the criteria described above. The images were coded and de-identified. A single expert endosonographer (MSB) then analyzed the EUS images in a blinded fashion with malignant and benign lymph node images presented to the endosonographer in random order. EUS images of 24 subjects were available based on the criteria described above.

Results

On image analysis of 24 patients, EUS images of lymph nodes of 8 patients (33%) were considered to have coagulation necrosis as scattered non-shadowing echogenic areas within a lymph node (Figs. 1, 2). When the endosonographer was unblinded to the pathologic results, 7 of these 8 patients had positive EUS FNA for malignancy (all with non-small cell lung carcinoma). In only 1 of these 8 patients considered to have coagulation necrosis by the endosonographer, this echo feature was a false positive sign for malignancy as this was a benign lymph node. Among 16 patients with no coagulation necrosis of lymph nodes (Figs. 3, 4), 6 were malignant and the other 10 were benign (Fig. 5). The overall sensitivity of coagulation necrosis as a predictor of malignant invasion of lymph nodes was 54% and the specificity was 90%. The results from the study are summarized in Table l.

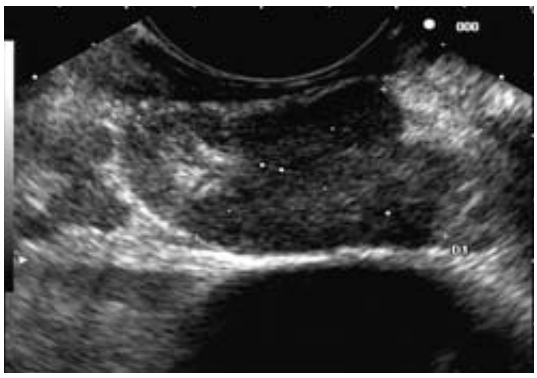

Fig 1. Linear EUS of a malignant mediastinal lymph node in non-small cell lung cancer with a non-central echogenic area consistent with coagulation necrosis.

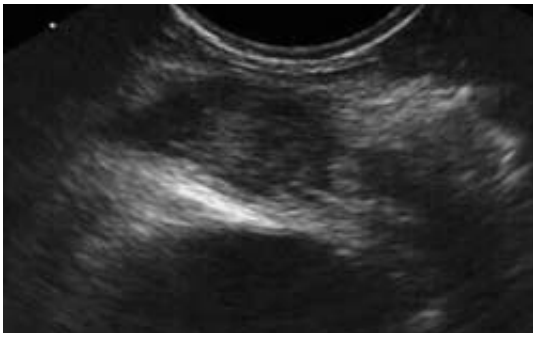

Fig 2. Linear EUS of a malignant mediastinal lymph node in non-small cell lung cancer with scattered non-central echogenic areas consistent with coagulation necrosis

Fig 3. Linear EUS image of a large mediastinal lymph node with echogenic areas within the lymph node. EUS guided transesophageal FNA confirmed the presence of metastatic non-small cell carcinoma of the lung.

Fig 4. Linear EUS image of a benign mediastinal lymph node that was negative for coagulation necrosis.

Discussion

The study was an evaluation of a newly described echo feature of malignant invasion of lymph nodes described as coagulation necrosis by Roberts et al [13] and recognized as

Table I. Summary of results

Coagulation necrosis	Final malignant diagnosis	Final non-malignant (benign) diagnosis
Present	7	1
Absent	6	10

Sensitivity 0.54; Specificity 0.91; Positive predictive value 0.88; Negative predictive value 0.63; Accuracy 0.71

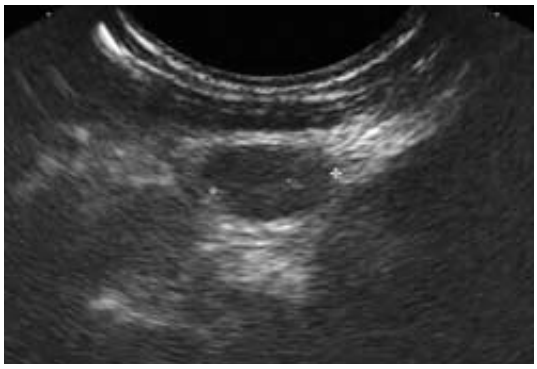

Fig 5. Linear EUS image of a benign mediastinal lymph node that was negative for coagulation necrosis. An isoechoic to mildly echogenic central, linear structure is seen that does not represent coagulation necrosis but normal hilum.

ill defined, non-shadowing echogenic areas within a lymph node. This was an application and extension of previously described literature on ultrasound of neck lymph nodes during staging of head and neck cancer [14, 15]. Coagulation necrosis in malignant lymph nodes is manifested by cell swelling or cell rupture, denaturation and coagulation of cytoplasmic proteins, and breakdown of organelles with often preservation of the general tissue architecture despite the death of its constituent cells. Ahuja and Ying [15] have shown that the hilum of a normal lymph node is a linear, echogenic, non-shadowing structure. On the other hand a malignant lymph node with coagulation necrosis shows an ill defined, non-shadowing, echogenic area in the lymph node. Sakai et al [14] in a study of in-vivo and in-vitro ultrasound images of cervical metastatic malignant lymphadenopathy with histopathologic correlation showed that echogenic region within a lymph node on ultrasound imaging was caused by coagulation necrosis. In fact, the image analysis in the study by Roberts et al [13] was done by a radiologist experienced in staging head and neck cancer with transcutaneous ultrasound who was blinded to the malignant or benign nature of the lymph node.

In our study, coagulation necrosis was found in 33% of analyzed lymph nodes (8/24). The sensitivity of coagulation necrosis as an echo feature of malignancy was 54% with a specificity of 91%. This implies that malignant lymph nodes have this echo feature only about 54% of the time but when present it is highly predictive of the possibility of malignant invasion. When we compared our results with those of Roberts et al [13] which included a mixed group of patients with lung and other cancers, there appeared to be consistency, as in their study there was a similarly low sensitivity of 48% but with a very high specificity of 100%.

Prior to the development of EUS guided FNA, echo features were the only method to predict the presence of malignant invasion. Patients with primary gastrointestinal tumors and patients with lung cancer may not present with similar echo features. In the study by Catalano et al [10] which analyzed the four typical echo features of lymph nodes in patients with a primary gastrointestinal tumor (esophageal cancer), when all 4 features (round shape, distinct margins, hypoechogenicity and size of > 10 mm) were present, 100% of the lymph nodes were malignant. With the advent of EUS guided FNA, we performed one of the earliest studies comparing the accuracy of EUS echo features of lymph nodes with EUS-FNA for prediction of malignant invasion in a mixed group of patients with esophageal, pancreatic, and lung cancer [11]. None of the four echo features described above by Catalano et al [10] by itself were predictors of malignant invasion. However, when all four features were present the likelihood of malignancy was 80%. More importantly, only 25% of malignant lymph nodes had all four typical echo criteria.

We found another feature apart from these four criteria which we described as scattered echogenic areas within a predominantly hypoechoic lymph node. This was actually the only feature that was statistically significant in differentiating benign from malignant lymph nodes as this finding was present in 5/16 (31%) of malignant and 0/19 (0%) of benign lymph nodes (specificity 100%). Roberts et al [13] in their recent paper describing coagulation necrosis in lymph nodes noted these results and discussed the belief that the above echo feature of scattered, echogenic areas within a lymph node described in our study in 1997 represents coagulation necrosis. We agree with this conclusion since the results of our prior study in 1997 [11], Roberts et al study in 2005 [13] and the study presented in this paper are basically describing similar findings in a mixed group of patients with lung, esophageal and other cancers. More importantly, the results also appear to be similar and consistent with moderate to low sensitivity but very high specificity (91-100%) [11, 13].

The relevance of results of our current study and prior study is further increased by the fact that we only included subjects with a positive EUS guided FNA for malignancy and surgical confirmation for benign lymph nodes and did not include just clinical follow up as a marker for benign lymph nodes. Although sensitivity of coagulation necrosis appears to be low, may be if combined with other classical echo features, one may be able to better differentiate benign and malignant lymph nodes. Even though EUS guided FNA has been shown to be much more accurate for prediction of malignancy than just echo features [11, 12], the presence of coagulation necrosis may help endosonographers preferentially select a lymph node for FNA when multiple nodes are visualized by EUS, and therefore FNA would help in clinical decision making. Furthermore, EUS-FNA may not be always possible if it requires traversing the primary

tumor in gastrointestinal luminal cancer or an area of high grade dysplasia in a segment of Barrett's esophagus. In these situations, coagulation necrosis when present can be used as a specific sign suggesting malignant invasion. However, the endosonographer using these criteria should carefully assess this finding to differentiate from the normal echogenic hilum of a lymph node as described earlier in this paper and by Roberts et al [13]. It is also important to note that what we and Roberts et al [13] are describing as coagulation necrosis are echogenic areas in lymph nodes that are non-shadowing. This should be differentiated from calcifications in lymph nodes seen in many conditions (e.g. histoplasmosis) in which there are shadowing echogenic areas consistent with a calcification and the pattern of calcification might be more diffuse.

In **conclusion**, non-linear, scattered or rounded, non-central, non-shadowing echogenic areas within a lymph node representing coagulation necrosis is a useful feature for the prediction of malignant invasion on EUS imaging of the mediastinum that can help endosonographers in selecting a lymph node for EUS FNA or predicting likelihood of metastasis where EUS FNA is not technically possible. Future areas of study related to our results include prospective confirmation of these results and confirmation of interobserver variability.

Conflicts of interest

None to declare.

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