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ORIGINAL ARTICLE

Utility and morphologic features of granulomas on rapid on-site evaluation of endobronchial ultrasonography-guided fine-needle aspiration

Shelley I. Odronic, MD, Amanda E. Maskovyak, MD, Bridgette S. Springer, CT(ASCP), Kathryn S. Dyhdalo, MD, Fadi W. Abdul-Karim, MD, Christine N. Booth, MD*

Robert J. Tomsich Pathology and Laboratory Medicine Institute, Cleveland Clinic, Cleveland, Ohio

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Introduction Endobronchial ultrasonography (EBUS)-guided fine-needle aspiration (FNA) is increasingly used to sample central lung lesions and mediastinal lymphadenopathy. We investigate the utility of EBUS-guided FNA and concomitant rapid on-site evaluation (ROSE) to diagnose granulomas, the morphologic characteristics of granulomas on ROSE, and how the diagnosis of granulomas changed the clinical impression.

Materials and methods All pathologic reports and associated clinical records of patients who had EBUS-guided FNA of the lungs or mediastinal lymph nodes that yielded granulomas were reviewed with at least a 1-year follow-up after EBUS-guided FNA. All ROSE slides were rereviewed to evaluate granulomas for quantity, necrosis, and cohesion.

Results Over a 3-year period, 882 EBUS-guided FNAs were performed. One hundred and twelve patients (49% male, average age 50.8 years, range 16-83) had 161 EBUS-guided FNAs that yielded granulomas (18%). The etiologies of the granulomas were as follows: sarcoidosis (54%), infection (12%), malignancy (5%), inflammatory bowel disease–related lymphadenopathy (1%), and no specific clinical etiology (28%). Of the patients with EBUS-guided FNAs, 98 had ROSE performed (87.5%) and granulomas were seen in 70 of these patients (71%). Granulomas associated with sarcoidosis were mostly well-formed and non-necrotizing (90%). The results of the EBUS-guided FNA changed or redefined the clinical diagnosis in 79 patients (71%).

Conclusions EBUS-guided FNA with concurrent ROSE is a useful technique for the diagnosis of granulomas. The quality and quantity of granulomas detected during ROSE may suggest an etiology and help direct ancillary testing.

*Corresponding author: Christine N. Booth, MD, Cleveland Clinic, Robert J. Tomsich Pathology and Laboratory Medicine Institute, 9500 Euclid Avenue/L25, Cleveland, OH 44195; Fax: +1 2164453707.

E-mail address: boothc1@ccf.org (C.N. Booth).

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Introduction

Endobronchial ultrasonography (EBUS)-guided fine-needle aspiration (FNA) has dramatically improved the diagnostic sampling of central lung lesions and mediastinal and hilar lymphadenopathy and has proved to be an effective alternative to conventional mediastinoscopy. EBUS-guided FNAs are safe and efficacious with a diagnostic yield of 78% to 89% for malignancy.[1-4] Most previous studies have focused on the diagnosis of malignancy; however, the differential diagnosis for patients with mediastinal or hilar lymphadenopathy also mainly includes granulomatous disease. In patients with a high clinical suspicion of sarcoidosis, EBUS-guided FNA has a sensitivity of 77% to 85% for the detection of granulomas.[5-9] The utility of EBUS-guided FNA in patients regardless of pretest probability of sarcoidosis has not been previously studied. Additionally, other etiologies of granulomatous disease have not been investigated.

Rapid on-site evaluation (ROSE) performed at the time of EBUS-guided FNA allows the bronchoscopist and pathologist to assess specimen adequacy and triage material for ancillary testing, including immunohistochemistry, microbiologic cultures, flow cytometry, and molecular analysis. ROSE can avoid unnecessary delay and allow better specimen acquisition. Only 1 study has looked at the utility of ROSE for EBUS-guided FNA and found a diagnostic yield of 68.8% for any disease process.[3] No previous studies have analyzed the diagnostic yield of granulomas by ROSE for EBUS-guided FNA.

The goals of this study were to identify the etiology of granulomas detected on EBUS-guided FNA, assess the diagnostic yield of granulomas by ROSE, review the morphologic characteristics of granulomas on ROSE slides, and evaluate how the diagnosis of granulomas changed the clinical impression.

Materials and methods

After institutional review board approval, all EBUS-guided FNAs of the lung parenchyma or mediastinal lymph nodes with a final diagnosis of granulomas at the Cleveland Clinic over a 3-year period (September 1, 2008 to September 1, 2011) were retrospectively reviewed. A search of the Anatomic Pathology CoPathPlus (Cerner Corporation, Kansas City, Mo) database was performed for all pathologic material. The clinical data was obtained from the institution's electronic medical record system (Epic Systems Corporation, Verona, Wis) with at least a 1-year follow-up after EBUS-guided FNA (median follow-up: 2.5 years). The clinical impression prior to EBUS-guided FNA was determined from the pulmonology office visit note immediately before the procedure.

ROSE is routinely performed and cases subsequently signed out by board-certified cytopathologists. Lung surgical pathology specimens are diagnosed by pulmonary subspecialty surgical pathologists. A case was considered positive for infection if morphologic evidence of microorganisms was seen on any pathology specimen, the patient had a positive culture, or the patient had positive antibody titers. If there was no definitive diagnosis, the case was placed into the "no specific clinical diagnosis" category. A case was considered positive for malignancy if it had a definitive tissue diagnosis on FNA, biopsy, or resection within the follow-up period from the same location or if treatment was initiated due to high clinical suspicion.

For this study, all ROSE modified Giemsa-stained slides and cases were independently rereviewed by 2 pathologists (C.N.B., F.W.A.-K.) without prior knowledge of the diagnoses that had been rendered. Although no specific criteria for adequacy are used at our institution, there have been proposals for adequacy criteria for ROSE of EBUS-guided FNA.[1,10-12] Fine-needle aspirates of lymph nodes were considered adequate by the clinical team when a lymphoid sample was obtained on 3 separate passes. At our institution, passes are nondiagnostic when an FNA of a lesion is attempted and the material on the slides does not represent the location of the aspirate (ie, blood only). The sensitivity of EBUS-guided FNA ROSE was calculated. The negative predictive value was not calculated because negatives cases for the presence of granulomas were not screened to detect false negatives.

All slides for each case were reviewed and granulomas were quantified based on the slide with the highest number of granulomas: rare (<4 granulomas per slide), occasional (4-10 granulomas per slide), or numerous (>10 granulomas per slide). Granulomas were also rated based on quality: well-formed necrotizing, well-formed non-necrotizing, or poorly formed. Whenever a case demonstrated >1 pattern, the predominant pattern was used. Cases with multinucleated giant cells were also recorded. Discrepant results were reviewed at a dual-headed microscope and a consensus was reached.

Results

Over a 3-year period (September 1, 2008 to September 1, 2011), 882 EBUS-guided FNA procedures were performed. One hundred and twelve patients (49% male, average age 50.8 years, range 16-83) had 161 EBUS-guided FNAs that had final pathologic diagnosis of granulomas (18%; 159 lymph node and 2 lung parenchyma samples). EBUS-guided FNA was performed on 64 subcarinal lymph nodes (station 7), 42 paratracheal lymph nodes (station 4; 33 right, 7 left, 2 not specified), 27 hilar lymph nodes (station 10; 20 right, 7 left), 20 interlobar lymph nodes (station 11; 14 right, 6 left), 2 right lobar lymph nodes (station 12), 2 bronchial not otherwise specified, 1 aortopulmonary lymph node (station 5), 1 pretracheal, 1 lung lower left lobe, and 1 right lung. A mean of 1.4 lymph node stations were sampled per case (range 1-3). There was a mean of 3.2 needle passes per lymph node (range 1-10) and a mean of 4.3 needle passes per case (range 1-10).