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**Title:** Advancements in pulmonary endosonography: the new standard to diagnose sarcoidosis and assessment of its safety profile

**Issue Date:** 2016-12-06
Mediastinal abscess formation after EUS-guided FNA: are patients with sarcoidosis at increased risk?

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Gastrointestinal endoscopy, May 1, 2012, Vol 75, No 5
Sarcoidosis is a disease of unknown etiology mostly affecting young adults and presenting with mediastinal or hilar lymphadenopathy in 85% of patients. Endoscopic US-guided FNA (EUS-FNA) and endobronchial US-guided transbronchial needle aspiration (EBUS-TBNA) of intrathoracic lymph nodes is increasingly used for the diagnosis of pulmonary sarcoidosis. Complications are rare; severe procedure-related infections have been reported in only 2 patients. One patient developed mediastinitis and another a mediastinal abscess after EUS-FNA.1,2 This case series describes 5 patients with suspected sarcoidosis who developed mediastinal abscesses after EUS-FNA, necessitating surgical treatment in 4 patients.

MATERIALS AND METHODS

We retrospectively reviewed records of all patients with a final diagnosis of sarcoidosis who had undergone EUS or EBUS of mediastinal/hilar lymph nodes in two university hospitals. Between 1999 and 2011, Leiden University Medical Center (LUMC) (n=184) and Radboud University Medical Center (n=68) investigated 252 patients. Five patients (LUMC [n=3], Radboud [n=2]) developed mediastinal abscesses after EUS-FNA. One case has been reported previously.2

The LUMC and Radboud UMC are both tertiary-care hospitals, and the pulmonary departments are referral centers for mediastinal analysis with endosonography. EUS-FNA has been used as a routine test in daily clinical practice for the assessment of granulomas in patients suspected of sarcoidosis. Informed consent was obtained in all patients. Investigations were performed with the patients under conscious sedation, with 22-gauge needles, and mostly with on-site cytology, as previously described.2 Immediate complications were assessed routinely; later complications were recorded after patients’ complaints.

RESULTS

Case description

A 30-year-old man without comorbidities was referred for fatigue and arthralgia with bilateral hilar and mediastinal lymphadenopathy. On the suspicion of sarcoidosis, EUS-FNA was performed, showing coalescing, iso-echogenic, subcarinal lymph nodes (short axis 25 mm). No complications were observed during the 8 nodal aspirations showing noncaseating granulomas. Fifteen days after EUS, the patient felt retrosternal pain—increasing with breathing/swallowing—and had cough and fever. Inflammatory test parameter results were elevated, and a CT scan of the chest revealed a subcarinal mass (4.3 x 4.1 x 3.8 cm)—evidently increased compared to the before-EUS CT—with thick walls and a hypodense center, consistent with a mediastinal abscess (Fig. 1). Culture of the aspirate was positive for Streptococcus salivarius and Staphylococ-
Figure 1. Chest CT images of the subcarinal area (lymph node station 7) before EUS-guided FNA. 1, 15 days after procedure. 2, 2 days later when symptoms of dysphagia existed. 3, Hypodense centers were seen centrally in the subcarinal lymph nodes, compatible with abscess formation. The small arrows indicate the border of the enlarged subcarinal lymph nodes (2 and 3). The position of the esophagus is indicated by OE. RMB, right main bronchus; LMB, left main bronchus; LN7, lymph node station 7; OE, esophagus; HDS, hypodense centers.
*Staphylococcus aureus* but negative for *Mycobacterium tuberculosis*. The patient was admitted to the hospital and treated with intravenous antibiotics (amoxicillin / clavulanic acid, metronidazole followed by penicillin / metronidazole / flucloxacillin). Despite this regimen, the patient developed progressive dysphagia and maintained intermittent periods of fever during the following 2 days. Repeat CT showed progression of the subcarinal mass to 5.8 x 5.0 x 3.6 cm. Subsequently, a thoracotomy was performed, with drainage of the abscess. With chest tube drainage and antibiotics, clinical conditions improved in 1 week, and the patient was discharged 1 week later. Pus culture of the abscess showed *Actinomyces*, for which clindamycin treatment was administered for 4 weeks. At 2 months of follow-up, the patient had fully recovered.

**Case description**

A 49-year-old woman with a history of salpingitis and iodine-treated goiter was referred for dyspnea on exertion and arthralgia. A CT scan showing mediastinal and bilateral hilar lymphadenopathy was compatible with stage I sarcoidosis. At EUS, multiple, conflating, isoechoic, subcarinal, and lower paraesophageal lymph nodes (15 mm) were sampled 4 times. Aspirates showed granulomas without necrosis. Two days after the uneventful procedure, the patient developed fever and retrosternal pain, only to report these symptoms 10 days later. By then, inflammatory test parameter results were elevated, and a CT scan showed a large, inhomogeneous, subcarinal mass (7 x 7 cm) with septa, consistent with abscess formation. Intravenous gentamicin / metronidazole / flucloxacillin was started because her clinical condition failed to improve. Subsequently, a posterolateral thoracotomy was performed 5 days later during which necrotic nodes in the subcarinal space (10 x 6 x 4 cm) were removed, and the abscess was drained. Repeat CT showed a mediastinal-esophageal fistula with air collections. The latter was confirmed at gastroscopy and healed after antibiotic treatment. Results of Gram stains and several cultures of EUS and thoracotomy material were negative, as was polymerase chain reaction and culture for *Mycobacterium tuberculosis*. Four months after the procedure, the patient had recovered completely, aside from persistent post-thoracotomy pain.

**Case description**

The third case concerns an otherwise healthy, 36-year-old man with weight loss and cough. On CT, mediastinal and bilateral hilar lymphadenopathy was seen, together with diffuse intrapulmonary nodules compatible with stage II sarcoidosis. Subsequently, EUS was performed during which enlarged, iso-echogenic, grapelike nodes were observed (15 mm). Two aspirates from a subcarinal lymph node demonstrated noncaseating granulomas and abundant bacteria (not cultured). Directly after EUS, the patient noticed pain on swallowing, which disappeared gradually within 4 days. Six days after EUS, however, symptoms returned and were accompanied by progressive dysphagia but no fever. Inflammatory test parameter results were elevated. A CT of the thorax demonstrated enlargement of the subcarinal node from 1 to 3 cm, with a central, round, hypodense area compatible with a mediastinal abscess. Esophagoscopy ex-
cluded an esophageal-mediastinal fistula. The patient was treated with amoxicillin / clavulanic acid intravenously for 2 days, followed by oral treatment for 3 weeks, after which all symptoms and radiographic changes resolved.

Case description
A 65-year-old woman with a history of eczema and removal of the gall bladder and appendix was evaluated for fatigue. A CT scan showed mediastinal lymphadenopathy as well as multiple intrapulmonary nodules (sarcoidosis stage II). Conventional bronchoscopy including TBNA of a subcarinal node did not yield a diagnosis. Subsequently, EUS was performed, during which a subcarinal lymph node was sampled. Cytology showed reactive nodal tissue but no granulomas. Ten days after the EUS, the patient developed retrosternal pain and fever (39.9°C). Thirteen days after the EUS, the patient presented at the emergency department with persistent high fever, right upper abdominal pain, nausea, and pain on breathing. Inflammatory test parameter results were grossly elevated, and CT showed a thickened esophageal wall with air collections and an enlarged subcarinal node, suspected for an abscess. At gastroscopy, swelling of the esophageal wall was observed without signs of an esophageal rupture. The patient was judged to be critically ill with threatening sepsis and was transferred to the operating room the same day for thoracotomy. A subcarinal abscess was localized, and creamy serous fluid was found in the right hemithorax. The abscess and pleural empyema were flushed and drained. Histologic nodal resection material confirmed granulomas without necrosis. Blood cultures were positive for *Staphylococcus aureus*, and a pus culture was positive for *Streptococcus milleri* but negative for *Mycobacterium tuberculosis*. The patient was hospitalized for 22 days, including 5 days in the intensive care unit, and she was treated for 6 weeks with intravenous flucloxacillin and oral clindamycin. At follow-up, she reported persistent complaints of retrosternal pain and ructus without dysphagia, but repeat esophagoscopy showed remission of the esophageal lesions.

Case description
A 57-year-old woman with a history of uterus extirpation, asthma, and melanoma of the skin had symptoms of malaise. A CT scan showed multiple, enlarged, mediastinal, and bilateral hilar lymph nodes and multiple intrapulmonary nodules (stage II sarcoidosis). At EUS, a subcarinal node was aspirated and yielded non-caseating granulomas, consistent with sarcoidosis. One week after the procedure, the patient developed fever and retrosternal pressure. Despite treatment with antibiotics, symptoms worsened, and the patient developed chills, atrial fibrillation, and retrosternal pain, worsening when she was lying flat. Inflammatory test parameter results were elevated. A repeat CT scan showed further enlargement of the subcarinal mass, with hypodense areas compatible with a subcarinal abscess. A mediastinoscopy was performed to drain the abscess. Microbiologic analysis of the purulent material showed species of *Enterococcus faecium* and *Streptococcus*
milleri. The patient was treated with amoxicillin / clavulanic acid (2 weeks intravenous, 4 weeks oral) and recovered fully.

DISCUSSION

We report 5 patients with sarcoidosis (stage I/II) who developed mediastinal abscesses after EUS-FNA of subcarinal lymph nodes. Four patients underwent surgery in addition to antibiotic treatment. All patients recovered completely.

In recent years, several studies have demonstrated a high yield (> 85%) of EUS-FNA in assessing granulomas without necrosis in patients with suspected sarcoidosis. The occurrence of mediastinal infections after EUS-FNA is rare. In the literature, only two mediastinal infections have been reported in over 750 sarcoidosis patients undergoing endosonography for diagnostic purposes. In 1 patient, the diagnosis of mediastinitis was made, based on blood examinations and CT findings, with symptoms resolving after antibiotic treatment. The other complication is case 2 of the current article, which was reported previously. Furthermore, mediastinal abscess formation and mediastinitis occasionally have been described in relation to EUS-FNA and/or EBUS-FNA in patients with cysts, lung carcinoma, teratomas, or benign lymphadenopathy.

Because of its high diagnostic yield for assessing granulomas and very good safety profile, EUS is increasingly used as an alternative to bronchoscopy with transbronchial lung biopsies to diagnose sarcoidosis. Transbronchial lung biopsies are associated with hemoptysis and pneumothorax in 7% of cases. In our institutions, 5 of 252 patients with sarcoidosis who underwent EUS-FNA for diagnostic purposes developed mediastinal abscesses. These cases are retrospective observations from a period of over 10 years in the two institutions. For a proper risk assessment of EUS-related mediastinal abscess formation, a prospective complication registry is indicated. Although all patients fully recovered, the consequences of mediastinal abscess formation were severe, because the condition of these patients required prolonged admission, intravenous antibiotic treatment, and, most importantly, a thoracotomy. In the 5 specific cases, no risk factors such as neutropenia, immunosuppressive therapy, or relevant comorbidities were identified.

Both LUMC and Radboud UMC are referral centers for endosonography, and local investigators have extensive experience in performing endosonography in patients with sarcoidosis and lung cancer. In more than 3000 EUS procedures for mediastinal analysis—mostly in lung cancer patients—only 2 other cases of mediastinal abscess formation occurred in these two centers, both in patients with cystic lesions. Furthermore, because the single-use needle is sterile, the scopes were disinfected properly according to manufacturer instructions, and the complications occurred in two different centers with many years between the events, the most likely cause of the abscess formation is iatrogenic inoculation of the nodes with commensal
oropharyngeal flora by the needle. The organisms are introduced through the working channel of the scope while it traverses the bacteria-rich oropharynx. Bacteremia after FNA of lymph nodes by EUS and EBUS has been reported. In one study, TBNA needle washing results were positive for typical commensal oropharyngeal organisms in 35% of cases. Despite this, no patients developed clinical signs of infection in any of these studies.

It is unlikely that the infectious complications in this case series were caused by one specific virulent pathogen, because the cultured bacteria varied and included commensal oropharyngeal flora. One might speculate whether abscess formation was caused by a diminished antimicrobial response within the lymph nodes. In patients with sarcoidosis, local inflammation is caused by increased activation of macrophages and CD4-helper T cells and by increased production of cytokines (eg, interleukin-2 and interferon-gamma). Although opportunistic infections are uncommon in sarcoidosis, a locally increased infection risk may be explained partly by the observation that the population of regulatory T cells is amplified at the periphery of sarcoid granulomas.

So far, no mediastinal abscess formation after blind TBNA or EBUS-guided TBNA of mediastinal nodes from the airways has been reported. The earlier described complications call for a prospective EUS complication registry to properly evaluate whether a potential risk exists from diagnosing sarcoidosis by EUS-FNA. In the situation that patients with sarcoidosis are indeed at increased risk for developing mediastinal abscesses, the use of prophylactic antibiotic treatment should be discussed. Generally, an optimal yield for finding granulomas can be obtained by doing 4 needle aspirations, whereas further attempts do not increase the yield considerably. On-site cytology may limit the risk of complications when granulomas are found after the first puncture, and cytological examination may preempt the need for further passes. Aspirating inhomogeneous hypo-echoic nodal areas should be avoided, because they often reflect necrotic tissue, which could be a risk factor for infections, as described previously. Also, rinsing the oral cavity with an antiseptic before introducing the endoscope may reduce the chance of an infection.

Finally, after EUS, minor complaints such as dysphagia, low-grade fever, coughing, and thoracic pain should be taken seriously and followed-up closely. A low-virulence commensal pathogen introduced in a mediastinal node may not provoke systemic inflammatory symptoms immediately but may progress to a life-threatening infection if left untreated.

We argue, based on these 5 cases, that endoscopists should be aware of this potential complication and register their complications prospectively.
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References
