Pleural mesothelioma: When echo-endoscopy (EUS-B-FNA) leads to diagnosis in a minimally invasive way

Roberto Piro1 | Matteo Fontana1 | Francesco Livrieri1 | Francesco Menzella1 | Eleonora Casalini1 | Sofia Taddei1 | Federica De Giorgi2,3 | Nicola Facciolongo1

1Pulmonology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
2Pathology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Reggio Emilia, Italy
3Unit of Pathological Anatomy, University Hospital of Parma, Parma, Italy

Correspondence
Roberto Piro, Pulmonology Unit, Azienda Unità Sanitaria Locale - IRCCS di Reggio Emilia, Via Amendola 2, 42123 Reggio Emilia, Italy.
Email: roberto.piro@ausl.re.it

Abstract
Malignant pleural mesothelioma (MPM) is an asbestos-related and locally invasive tumor with poor prognosis. The acquisition of histological material is mandatory in order to establish a diagnosis. In this situation, the sampling of tissue is generally performed via a thoracoscopic pleural biopsy, either medically or surgically. The use of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) or transesophageal fine needle aspiration with an EBUS scope (EUS-B-FNA) of pleural lesions have only rarely been reported due to the theoretical limitations of tissue acquisition in such cases. We herein report a rare case of MPM successfully diagnosed via EUS-B-FNA in a 49-year-old woman with an unusual presentation characterized by solid thickening in the right mediastinal pleura.

KEYWORDS
bronchoscopy, EBUS/TBNA, EUS-B-FNA, pleural mesothelioma

INTRODUCTION
Malignant pleural mesothelioma (MPM) is a locally invasive tumor associated with exposure to asbestos,1 with a notoriously poor prognosis.2 The incidence is low but related deaths are significant, despite the fact that asbestos has been banned in several countries.3 A histological diagnosis is mandatory and is usually performed on biopsies obtained by thoracoscopy: this approach is suggested by international guidelines to obtain multiple and deep samples.1 In the last few years, important advances have occurred in both knowledge and therapy.1–6

Making a quick and minimally invasive diagnosis is difficult but important. Here, we report a case of mesothelioma diagnosis successfully and simply made via the esophagus using echo-bronchoscopy.

CASE REPORT
A 49-year-old woman with no tobacco or known asbestos exposure underwent an evaluation for fever (up to 39°C), chest tightness and arthralgia. She was in employment with no significant history of past disease. She had noticed a weight loss of about 10 kg in the last three months and had no dyspnea. Blood tests documented microcytic anemia (hemoglobin 6.7 g/dl).

Chest computed tomography (CT; Figure 1d,e) revealed solid thickening of the right pleura, with a maximum thickness in the lower paramediastinal area where the solid tissue appeared to extend into the mediastinum from the subcarinal region to the thoracoabdominal passage, coming into close proximity with the esophagus, anterior wall of the descending aorta and posterior wall of the inferior vena cava. Multiple nodular-like thickenings were present in the intrascissural area at the level of the ipsilateral large fissure and the small fissure. Some solid nodulations were also present in the right pericardiophrenic space. Positron emission tomography (PET) showed intense fixation of fluorine-18 fluorodeoxyglucose (F18-FDG) which corresponded with thickening of the right pleura, and a maximum standard uptake volume (SUV) of 13 (Figures 1a–c). The main differential diagnoses were considered to be MPM, lung cancer, lymphoma.
and a soft tissue tumor. The hypothesis of a primary pleural tumor was supported by the radiological appearance but other possibilities were investigated due to the relatively young age of the patient and the absence of a known asbestos exposure. After obtaining the patient’s consent, a transesophageal fine needle aspiration with EBUS scope (EUS-B-FNA) was performed. The choice of an endoscopic approach with EUS-B-FNA was made because of its feasibility, safety and effectiveness, and taking into consideration the proximity to the esophagus. Moreover, this region showed increased uptake on F18-FDG-PET. A conventional linear echo-bronchoscope (Olympus BF-UC190F) was used. The echo-endoscopic study confirmed the presence of solid tissue adjacent to the esophagus. Adequate tissue was obtained from the pleural mass using a 19-gauge needle (Olympus) under direct EUS guidance (Figure 2a). Three passes with the same needle were performed. The procedure ended without complications. Rapid on-site evaluation (ROSE) was not performed. On histological evaluation, the specimens obtained via EUS-B-FNA revealed confluent sheets of neoplastic cells with abundant cytoplasm and marked nuclear atypia (Figure 2b). Areas of necrosis were noted. On immunohistochemistry, the neoplastic cells were immunoreactive for calretinin (Figure 2d), Wilms’ tumor protein 1 (WT1 Figure 2c) and cytokeratin 5, whereas they were negative for p40, thyroid transcription factor 1 (TTF1) and BerEp4.

Morphological and immunohistochemical findings were indicative of epithelioid mesothelioma clinical stage IIIB (T4N1M0).

**DISCUSSION**

EBUS-TBNA has significantly changed the approach to lesions located in the mediastinum, leading to the possibility of detection and sampling of small masses and nodes. Over the last decade EBUS-TBNA has emerged as an effective tool for the diagnosis and staging of lung tumors. Indeed, dedicated needles allow these lesions to be reached in order to sample enough material suitable to perform cytological and microbiological evaluation, molecular testing and set up immunohistochemistry on cell blocks; core biopsies for histology are also possible. Expert bronchoscopists also use EBUS bronchoscopy to enter the esophagus and explore paraeosophageal lymph nodes and the left adrenal gland: this technique is called EUS-B-FNA. Echoendoscopy through the esophagus is well tolerated by patients, even in comparison with EBUS-TBNA, not causing significant onset of cough and desaturation.

The use of EUS-B-FNA and EBUS-TBNA for pleural sampling is unusual because the standard approach to pleuropathy is pleural effusion analysis followed by thoracoscopy or image-guided pleural biopsy. However, when one or more pleural lesions are near the central airways or esophagus, either EUS-B-FNA and/or EBUS-TBNA are considered and subsequently chosen because of their simplicity and safety. Indeed, compared with a thorascopic approach, it can be performed with less sedation and as an outpatient procedure, even when the general or respiratory condition of a patient is poor. The choice of needle is also important and because of the wide differential...
diagnosis in the case reported here we wanted to maximize the tissue sampling by choosing a 19-gauge needle.

To the best of our knowledge, only 13 cases of echo-endoscopic sampling of the pleura have been published to date. In several of these patients, echo-endoscopy was not the only procedure that was undertaken. While EBUS-TBNA was performed in nine of these cases, in the other four patients EUS-B FNA was performed: two patients had mesothelioma, one had lymphoma and one had metastatic renal carcinoma. It has previously been reported that a 22-gauge needle was used in eight patients and 21-gauge in one patient.

The case presented here is the second published manuscript reporting a pleural mesothelioma diagnosed only with EUS-B-FNA. It highlights echo-endoscopy as a valid diagnostic procedure for establishing the diagnosis of MPM in selected patients with a favorable location of pleural thickening. Indeed, in a proportion of cases and in the correct clinical and radiological context, a high-quality FNA can obtain a sufficient amount of material to make a firm diagnosis of mesothelioma, particularly if accompanied by a cell-block allowing immunohistochemical stains to be performed. The utility of EBUS-TBNA and EUS-B-FNA in these diseases should be perceived by interventional pulmonologists as an additional option to obtain pathological samples in a minimally invasive manner, rather than more invasive procedures. Nevertheless, the role of thoracoscopic pleural biopsies in diagnosing MPM remains undisputed due to the additional ability to stage the disease and administer immediate palliative treatment, such as pleurodesis.

CONFLICT OF INTEREST
The authors confirm that there are no conflicts of interest.

ORCID
Roberto Piro https://orcid.org/0000-0003-1046-4848
Francesco Menzella https://orcid.org/0000-0003-3950-5789
Eleonora Casalini https://orcid.org/0000-0002-8223-7137
Sofia Taddei https://orcid.org/0000-0003-1487-1192

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