Original Article

Rapid on-site evaluation with BIOEVALUATOR® during endobronchial ultrasound-guided transbronchial needle aspiration for diagnosing pulmonary and mediastinal diseases

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Abstract:

AIM: Rapid on-site evaluation (ROSE) is used widely during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). BIOEVALUATOR® is a device used for determining whether the tissues obtained by EBUS-TBNA are appropriate for a pathological diagnosis. This study describes our experience with ROSE using BIOEVALUATOR® during EBUS-TBNA for diagnosing pulmonary and mediastinal diseases.

MATERIALS AND METHODS: We retrospectively evaluated the results of 35 patients who underwent EBUS-TBNA with BIOEVALUATOR® between December 2011 and February 2013. For the diagnosis, the tissue areas were appearing white and red through BIOEVALUATOR® are considered to be appropriate and inappropriate, respectively. We examined their medical records to obtain information concerning the examination of BIOEVALUATOR® results of the patient's materials (white/red), the diagnosis yield, site and size of lymph nodes and number of needle passes.

RESULTS: The median longest diameter of 40 lymph nodes (21 #7, 13 #4R, 4 #4L and 2 #11) from 35 patients was 27.9 (range 12.4-50.6) mm and the median number of needle passes was 2 (range 1-5). The definitive diagnosis was made by EBUS-TBNA in 28 of 35 patients, by thoracotomy in one patient and BIOEVALUATOR® results were white and lymphocytes were seen in the rest six patients. The BIOEVALUATOR® results of other patients without accurate diagnosis were left indefinitive. Finally, the six patients were judged as having benign lymphadenopathy because the lymph node size on computed tomography decreased or remained stable after for at least 8 months.

CONCLUSIONS: Checking aspirated samples using BIOEVALUATOR® appears useful for determining their adequacy for pathological diagnosis.

Key words:

BIOEVALUATOR®, endobronchial ultrasound-guided transbronchial needle aspiration, rapid on-site evaluation

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a minimally invasive modality with a high diagnostic yield for not only mediastinal lymph node staging of patients with lung cancer, but also other pulmonary and mediastinal diseases.[1,2] More recently, rapid on-site evaluation (ROSE) during EBUS-TBNA allowed the deferral of additional biopsies without reducing the diagnostic yield in a randomized trial.[3] Other reports indicated that ROSE during EBUS-TBNA resulted in a low rate of non-diagnostic sampling.[4] However, Monaco *et al*. experienced some difficulty with ROSE of aspirates from EBUS-TBNA because of contamination with background material.[5]

BIOEVALUATOR® is a device used for identifying the material aspirated during EBUS-TBNA during ROSE. It is considered useful for determining whether specimens are appropriate for making a pathological diagnosis quickly. We have used BIOEVALUATOR® since December 2011. Here, we describe our experience with ROSE using the device during EBUS-TBNA for diagnosing pulmonary and mediastinal diseases.

Materials and Methods

Patients

We reviewed EBUS-TBNA cases at Okayama University Hospital between December 2011 and February 2013. Thirty-five patients underwent EBUS-TBNA using ROSE with BIOEVALUATOR® for diagnosing pulmonary and mediastinal diseases. Chest radiographs and computerized tomography (CT) before the bronchoscopic examinations revealed at least one enlarged mediastinal or hilar lymph node >10 mm along the long axis in all patients.

Procedure

First, conventional flexible bronchoscopy (BF-260 Bronchovideoscope; Olympus; Tokyo, Japan) was used for observation, using a siliconized, uncuffed tracheal tube with an inside diameter of 7.5 mm (Portex; Smiths Medical, St. Paul, MN, USA). Then, EBUS-TBNA was performed using a convex probe EBUS bronchoscope (BF-UC260F-OL8, Olympus; Tokyo, Japan). In pretreatment, 25 mg hydroxyzine pamoate were used by intramuscular injection. 5 ml of 2% lidocaine was sprayed into the pharynx and 5 ml of 2% lidocaine was administered through the channel during the procedures. The bronchoscope was inserted orally during midazolam induced conscious sedation. Patients were monitored by electrocardiogram, pulse oximetry and blood pressure without the presence of an anesthesiologist. The examination of the enlarged mediastinal lymph node stations accessible by EBUS (stations 2, 4 and 7) as well as the hilar lymph nodes (stations 10 and 11) was performed.

BIOEVALUATOR®

BIOEVALUATOR® is a device used for identifying the material aspirated during EBUS-TBNA during ROSE [Figure 1a]. This device illuminates samples from below, using a 12-V light-emitting diode [Figure 1b]. The aspirated materials are smeared on a watch glass and illuminated [Figure 1c]. By illuminating the collected specimen, tissue sample is discerned clearly. We can easily distinguish the tissue part from the other components of blood. Neither special technical properties of this equipment nor the staining method used before the examination of this equipment were needed. For the diagnosis, the tissue areas appearing white and red through BIOEVALUATOR® are considered to be appropriate and inappropriate, respectively. This device was developed by Murazumi Industrial Co. Ltd. (Osaka, Japan) in collaboration with one of the authors (HI).

Specimen handling

The aspirated materials were pushed out of the puncture needle and smeared on a watch glass and then evaluated immediately by a cytopathologist on site. More than half the smears were stained using Hemacolor® rapid staining (PROMICLOS; Tokyo, Japan) and any remaining samples were placed in 10% formalin for histological evaluation. The decision making on numbers of aspirations were decided according to BIOEVALUATOR® results and the ROSE method. For example, when we found white areas illuminated using BIOEVALUATOR® without malignant cells on ROSE, we finished aspirations. In addition, if adequate tissue was not observed after five passes from each lymph node, the procedure was terminated. The tissue diagnosis was performed by Papanicolaou staining using formalin-fixed paraffin-embedded samples.

Results

The patient's characteristics are listed in Table 1. There were 24 males and 11 females. Their median age was 66 (range 27-85) years. Forty lymph nodes were aspirated with a median of 2 (range 1-5) attempts per node, including 21 subcarinal, 13 right lower paratracheal, 4 left lower paratracheal and 2 right hilar nodes. The mean size of the enlarged lymph nodes in the long axis, as measured using CT imaging, was 27.9 (range 12.4-50.6) mm. During EBUS-TBNA, four patients experienced fever or an asthmatic attack, which were easily managed. The examination time of EBUS-TBNA defined as the time from the intubation with an intratracheal tube to the termination of ROSE with BIOEVALUATOR® of the last puncture was less than 30 min. Additional time with BIOEVALUATOR® process was less than a few minutes. Definitive diagnoses were made using EBUS-TBNA in 28 patients: 14 lung cancers (7 adenocarcinoma, 4 small cell carcinoma, 3 squamous cell carcinoma), 8 sarcoidosis and 1 case each of prostate cancer, renal cancer, neuroendocrine tumor, sarcoid reaction, tuberculous lymphadenitis and nonspecific lymphadenopathy (sensitivity 80%, specificity 100%). All the samples of the diagnosed cases contained white areas illuminated using BIOEVALUATOR®. The non-specific lymphadenopathy was confirmed at thoracotomy. Figure 2a shows an example of adequate material for pathological evaluation. The white circled areas contained cancer cells, which were confirmed using Hemacolor® rapid staining [Figure 2b] and Papanicolaou staining [Figure 2c]. Figure 2d shows inadequate material. The string-like red areas were contaminated, mostly with blood, as confirmed using Hemacolor® rapid staining [Figure 2e] and Papanicolaou staining [Figure 2f].

Table 1: Patient characteristics

Characteristics	No
Patients in total	35
Male/female	24/11
Median age (range), years	66 (27-85)
Enlarged lymph node stations (#4R/#4L/#7/#11)	13/4/21/2
Longest diameter in the lymph node (range), mm	27.9 (12.4-50.6)
Diagnosis by EBUS-TBNA	
Lung cancer	14
Prostate cancer	1
Renal cell cancer	1
Neuroendocrine tumor	1
Sarcoidosis	8
Sarcoid reaction	1
Tuberculous lymphadenitis	1
Nonspecific lymphadenopathy	1
Indefinite	7

#4L=Left lower paratracheal node, #4R=Right lower paratracheal node, #7=Subcarinal nodes, #11=N1 nodes, EBUS-TBNA=Endobronchial ultrasound-guided transbronchial needle aspiration

Pathological diagnoses could not be made in seven patients. Since the EBUS-TBNA samples for six patients contained abundant lymphocytes, we decided to follow them using CT. The pathological specimens from EBUS-TBNA examined using BIOEVALUATOR® revealed normal lymphocytes or atypical cells. An example of suitable material obtained with BIOEVALUATOR® is circled in Figure 3a. It contained lymphocytes [Figure 3b]. Ultimately, these cases were judged to be benign lymphadenopathy because the lymph node size decreased or remained stable for at least 8 months. One patient underwent a thoracotomy that found squamous cell lung cancer. We decided to perform the thoracotomy because

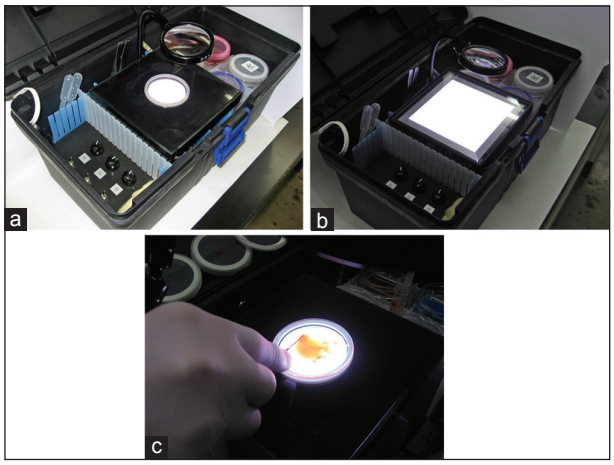

Figure 1: (a) BIOEVALUATOR® is a device used to evaluate the material aspirated during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) for rapid on-site evaluation. (b) The device illuminates the material using a 12-V light-emitting diode (LED). (c) The materials aspirated at EBUS-TBNA are smeared on a watch glass and illuminated from below using the LED

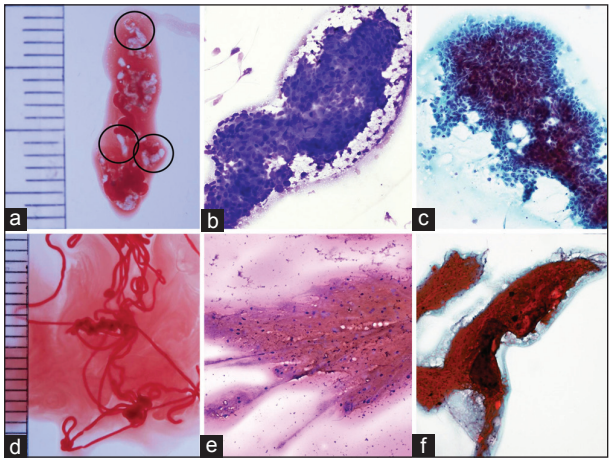

Figure 2: (a) BIOEVALUATOR® shows some adequate material for pathological evaluation (the circled white tissue). (b) Squamous cell carcinoma identified in theatre using Hemacolor® rapid stain, original magnification ×200. (c) Squamous cell carcinoma identified in theatre using Papanicolaou staining, original magnification ×200. (d) Using BIOEVALUATOR®, there are no adequate materials for pathological evaluation (red tissues are inadequate for pathological evaluation). (e and f) There was some difficulty with rapid on-site evaluation of the endobronchial ultrasound-guided transbronchial needle aspiration aspirates because of contamination by background material (e: Hemacolor® rapid stain, original magnification ×200; f: Papanicolaou stain, original magnification ×200)

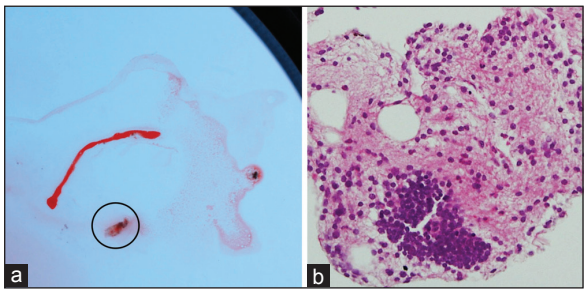

Figure 3: (a) The material in the circle was illuminated using BIOEVALUATOR®. (b) The specimens contained lymphocytes stained using Papanicolaou stain, original magnification ×200

the samples contained only red areas, which contained few lymphocytes pathologically, despite five passes with EBUS-TBNA.

Discussion

ROSE is a cytomorphological diagnostic procedure that allows an assessment of the adequacy and accuracy of the material obtained during bronchoscopy within a few minutes in or near the bronchoscopy suite (on-site) using quick staining of smears.[2] In patients with lung cancer, ROSE during EBUS-TBNA showed a low rate of non-diagnostic sampling for nodal staging.[4] In other reports, ROSE during endoscopic ultrasound-guided fine needle aspiration was useful for the diagnosis of mediastinal lymphadenopathy.[6-8] Some studies showed that EBUS-TBNA with ROSE had high accuracy for diagnosing sarcoidosis.[9,10] We showed that the use of BIOEVALUATOR® might have an additional benefit for ROSE during EBUS-TBNA.

As shown in Figure 2a, we could distinguish the tissue part from other components of samples, mostly blood. Our experience indicated that the use of BIOEVALUATOR® might improve the efficiency of determining whether the tissues obtained by EBUS-TBNA are appropriate for making a pathological diagnosis. The pathological specimens in six of the seven patients who could not be diagnosed at EBUS-TBNA revealed normal lymphocytes or atypical cells. Ultimately, the lymphadenopathy was considered benign in these six patients because the lymph node size decreased or remained stable after more than 8 months. Both the bronchoscopist and cytopathologist should be satisfied to see white areas illuminated using BIOEVALUATOR® in the EBUS-TBNA specimen because they probably contain adequate materials for diagnosis. The median number of needle passes was only two in this study. Therefore, this equipment might shorten the examination time.

This study had a few limitations. Firstly, we could not say whether BIOEVALUATOR® equipment performed with ROSE method had any contribution to ROSE method alone. If we prove its effectiveness, randomized study with or without BIOEVALUATOR® equipment should be performed. More realistically, comparison with retrospective analysis without BIOEVALUATOR® equipment or a large-scale observational study based on clinical practice may be useful. Secondary, we could not find equipment similar to BIOEVALUATOR® to the best of our knowledge. Thus, we could not discuss about the usefulness of BIOEVALUATOR® comparing with other equipment.

We performed ROSE with BIOEVALUATOR® during EBUS-TBNA. BIOEVALUATOR® might be useful for determining the adequacy of specimens for making a pathological diagnosis quickly. Further prospective study is warranted.

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