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INSTITUTIONAL REPORT

Usefulness of endobronchial ultrasound in patients with previously treated thoracic malignancy

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Abstract

Diagnosis of mediastinal/hilar lymph nodes and tumours is often challenging for patients with previously treated thoracic malignancy, especially when they have a history of thoracotomy. Endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA) has been proposed as a safe, less-invasive modality for such patients. We retrospectively evaluated the role of EBUS-TBNA in the assessment of newly developed mediastinal/hilar abnormalities in patients with previously treated thoracic malignancy. Of 79 patients who underwent EBUS-TBNA between July 2009 and July 2011, 14 patients (18%) had a history of treatment for thoracic malignancy. In all patients, malignancy was confirmed again for the newly developed mediastinal/hilar abnormalities and three of them (21%) presented with a different pathology from the previous malignancy. Out of 14 patients, 12 had a history of thoracotomy and EBUS-TBNA was a useful, less-invasive diagnostic method particularly for these patients. Out of 14 patients, 11 (79%) had a history of lung cancer and 10 of them (91%) had received surgical resection. In conclusion, we confirmed that EBUS-TBNA obtained the pathological diagnosis in a less-invasive manner in all cases. Despite the small number of cases, our results can reveal the usefulness of EBUS-TBNA particularly in patients with previously treated thoracic malignancy.

Keywords: Endobronchial ultrasound • Endobronchial ultrasound-guided transbronchial needle aspiration • Lung cancer • Malignancy • Recurrence

INTRODUCTION

Endobronchial ultrasound with transbronchial needle aspiration (EBUS-TBNA) has been proposed as a safe, less-invasive alternative to mediastinoscopy for the diagnosis of mediastinal lymph nodes and tumours. Currently, EBUS-TBNA has been widely spread all over the world as it allows us to obtain cytological confirmation about mediastinal/hilar abnormalities less invasively, without requiring general anaesthesia [1–3].

In the last decades, treatment of various malignant tumours dramatically evolved and thus the number of patients who had a history of treatment for previous malignancy has increased. In these patients, mediastinal/hilar nodal assessment is often needed to rule out tumour recurrence or another new malignancy, which is still challenging although radiological modalities, including computed tomography (CT), positron-emission tomography (PET) and combined CT/PET scan have developed [4]. A change in the size of mediastinal/hilar lymph nodes in chest CT or an increased uptake in PET scan during follow-up after treatment is generally suggestive of cancer recurrence; however, pathological confirmation is necessary for its treatment.

Mediastinoscopy is still the gold standard for the diagnosis of mediastinal abnormalities, but such surgical biopsies of the mediastinal/hilar abnormalities become more difficult when the patients have a history of previous surgical extirpation in the chest, such as lobectomy with nodal dissection [5, 6]. Furthermore, patients who have undergone mediastinoscopy for mediastinal staging at the time of primary treatment are not ideal candidates for surgical mediastinal assessment, such as with a repeat mediastinoscopy. In these cases, EBUS-TBNA would be a good option as a tool for cytological confirmation of these mediastinal/hilar abnormalities. Therefore, we evaluated the role of EBUS-TBNA in the assessment of newly developed mediastinal/hilar abnormalities in patients with previously treated thoracic malignancy in our institution.

PATIENTS AND METHODS

Between July 2009 and July 2011, EBUS-TBNA was performed for 79 patients in our department. During this study period, 14 patients (18%) had a history of treatment for thoracic malignancy. Results of EBUS-TBNA in these patients with previously treated thoracic malignancy were retrospectively analysed. Various parameters including EBUS procedures, pathological results and treatments for new lesions as well as characteristics and treatments for previous malignancy were recorded from the medical charts.

EBUS-TBNA was performed as described elsewhere [7]. In brief, EBUS-TBNA was performed with the patient under conscious sedation. The convex probe EBUS (BF-UC160F-OL8/BF-UC180F, Olympus, Tokyo, Japan) and dedicated 22-gauge needles (NA-201SX-4022, Olympus, Tokyo, Japan) were used for EBUS-TBNA. An on-site cytological evaluation by our cytopathologist was available whenever possible to confirm the quality of sampled materials and to obtain a quick cytological diagnosis. The definitive cytological diagnosis was reported later and was used for analyses in the current study.

RESULTS

In 14 patients undergoing EBUS-TBNA for mediastinal/hilar lesions with a history of previous thoracic malignancy, 14 lymph nodes, comprising 11 mediastinal and three hilar lymph nodes, were biopsied (Table 1). Median age of the patients was 74 years (range, 47–85). Nine patients were male and five were female. Previous malignancies were lung cancer in 11, oesophageal cancer in one, liposarcoma in one and solitary fibrous tumour in one.

EBUS-TBNA showed that all 14 were positive for malignancy in the mediastinum/hilum. The number of cases for EBUS-TBNA in each lymph node station was station 2R ($n = 1$), 4R ($n = 1$), 4L ($n = 2$), 7 ($n = 7$), 10 ($n = 2$) and 11 ($n = 1$). The malignant cell types from the positive results by EBUS-TBNA in 14 patients and those of previous thoracic malignancy were summarized in Table 2. In 14 patients whose mediastinal/hilar abnormalities was found malignant, cytological confirmation did not make a definitive diagnosis in one patient, requiring surgical extirpation. In details, one patient had a history of surgical resection for lung cancer 4 years ago and breast cancer 2 years ago. She developed subcarinal lymphadenopathy, which was diagnosed as adenocarcinoma by EBUS-TBNA; however, it was difficult to confirm whether the lesion was originated from lung cancer or breast cancer only from the EBUS-TBNA specimen because the amount of the specimen could not allow us to perform detailed pathological confirmation. Then, mediastinoscopy was performed and the subcarinal lesion was found to be most likely from lung cancer. In this way, the detailed pathological confirmation is sometimes difficult especially when the amount of specimens obtained from EBUS-TBNA is small. In addition, the differentiation of primary lung cancer from metastatic lung cancer originated from the breast cancer is frequently difficult.

In 11 patients with a history of lung cancer, 10 of them (91%) received surgical resection and nine patients had more than lobectomy with lymph node dissection. Furthermore, in a patient with a history of surgical treatment for previous liposarcoma located in the posterior mediastinum, posterior mediastinal mass was detected again. In another patient with a history of solitary fibrous tumour, he underwent three thoracotomies for the recurrent tumours including right upper lobectomy with lymph node dissection. In this way, 12 out of 14 patients (86%) had a history of thoracotomy with or without lymph node dissection.

In all patients, malignancy was confirmed again for the newly developed mediastinal/hilar lesions by EBUS-TBNA. Out of 14 patients, 11 revealed the same pathology as the previous malignancy, while three patients presented with a newly developed tumour with different pathology (Table 2). To be more specific, one patient with a history of complete surgical resection for posterior mediastinal liposarcoma approximately 3 years ago developed a new lesion in the posterior mediastinum, which was diagnosed as small cell lung cancer by EBUS-TBNA. Another patient with a history of right upper lobectomy for adenocarcinoma (pT1N2M0) with adjuvant chemotherapy 3.5 years ago

Table 1: Characteristics of patients previously treated with thoracic malignancy

Variable		Number
Age	47–85 years (median 74 years)	
Gender	Male	9
	Female	5
Previous thoracic malignancy	Lung cancer	11
	Liposarcoma	1
	Oesophageal cancer	1
	Solitary fibrous tumour	1
Location of newly developed mediastinal/hilar lymph nodes or tumours	2R	1
	4R	1
	4L	2
	7	7
	10	2
	11	1
Cell type of newly developed mediastinal/hilar lymph nodes or tumours	Adenocarcinoma	9
	LCNEC	1
	Squamous cell carcinoma (oesophagus)	1
	Small cell carcinoma	2
	Solitary fibrous tumour	1

LCNEC, large cell neuroendocrine carcinoma.

Table 2: Cytological results of endobronchial ultrasound-guided transbronchial needle aspiration in previously treated thoracic malignancy ($n = 15$)

Malignant cell types in previous treatment	Number	Cell type from EBUS-TBNA	Number
Lung cancer		Lung cancer	
Adenocarcinoma	9	Adenocarcinoma	7
		Small cell carcinoma	1
		Adenocarcinoma[a]	1
Adenosquamous cell carcinoma	1	Adenocarcinoma	1
LCNEC	1	LCNEC	1
Solitary fibrous tumour	1	Solitary fibrous tumour	1
Oesophageal cancer		Oesophageal cancer	
Squamous cell carcinoma	1	Squamous cell carcinoma	1
Liposarcoma	1	Lung cancer	
		Small cell carcinoma	1

EBUS-TBNA, endobronchial ultrasound-guided transbronchial needle aspiration; LCNEC, large cell neuroendocrine carcinoma.
[a]EBUS-TBNA did not confirm if adenocarcinoma was from breast cancer or lung cancer.

developed subcarinal lymph node enlargement, which was diagnosed as small cell lung cancer by EBUS-TBNA. The other patient received right upper and middle resection for adenosquamous cell carcinoma. Eleven years later, he developed a tumour with mediastinal lymphadenopathy (pT1N2M0), which was diagnosed as adenocarcinoma. These three cases were considered as newly developed lung cancer and 10 cases were considered as recurrence of a malignant tumour, although the rest one case could not be determined because the mediastinal/hilar lymph node enlargement occurred 11 years after the previous complete surgical resection.

In 14 patients diagnosed as newly developed or recurrent malignant mediastinal/hilar abnormalities, surgical resection ($n = 1$), chemotherapy ($n = 9$) and irradiation ($n = 4$) were selected and started soon after the definitive diagnosis. In a patient who performed surgical resection after EBUS, definitive histology confirmed the EBUS results. In nine patients with the diagnosis of adenocarcinoma, epidermal growth factor receptor (EGFR) mutation status was investigated and four patients (44%) were positive for EGFR mutation. In three patients, EGFR-tyrosine kinase inhibitor (TKI) was administered, resulting in tumour regression. On the other hand, in one patient, T790M mutation was also found and therefore, EGFR-TKI was stopped and radiotherapy was initiated.

DISCUSSION

New mediastinal/hilar abnormalities after primary therapy in patients with thoracic malignancy becomes more and more common as anti-tumour therapies have developed over time; however, it is still a challenge to obtain a definitive diagnosis in such patients by re-thoracotomy and/or repeat mediastinoscopy [5]. EBUS-TBNA has been established as an important, novel technique for the diagnosis of such abnormalities. Toronto group, which is now one of the leaders in the field of EBUS, reported that of 450 patients who underwent EBUS-TBNA, 77 (17%) had a history of cancer treatment, of which 44 (10%) had lung cancer [6]. Our study also showed a similar data where of 79 patients undergoing EBUS-TBNA, 14 (18%) had a history of thoracic malignancy, among which 11 (14%) had lung cancer. In 14 patients, approximately 90% of the patients had a history of thoracotomy for the treatment of previous thoracic malignancy, but pathological confirmation of mediastinal/hilar abnormalities was determined less invasively by EBUS-TBNA without any complications in all patients. In fact, mediastinoscopy can be an alternative for EBUS-TBNA only in one of 12 patients with previous thoracotomy in our study, and in the rest 11 patients, re-mediastinosocpy or re-thoracotomy should be conducted for the diagnosis if it were not for EBUS-TBNA. However, it should be kept in mind that EBUS-TBNA is likely to yield fewer samples than required for the definitive pathological confirmation. In our study, we could not make a definitive diagnosis in one patient whether the lymph node involvement was from the previous lung cancer or breast cancer, requiring mediastinoscopy for the definitive pathological confirmation.

In all cases, appropriate treatments were performed individually soon after the definitive pathological confirmation. There were three cases which showed different pathology in the newly developed mediastinal/hilar lesions from the previous malignancy. Of note is that two out of these three cases presented with small cell lung cancer. Considering the difference in chemotherapy regimen between small cell lung cancer and non-small cell lung cancer, the definitive pathological diagnosis is essential for the treatment of such patients, and therefore, EBUS-TBNA is one of the most effective diagnostic tools for these patients.

In our study, EBUS-TBNA allowed us to determine the EGFR mutation in all patients with pulmonary adenocarcinoma. The EGFR mutation is a meaningful molecular marker used to predict the response to molecular-targeted therapy using EGFR-TKI. It has been reported that they can be tested using biopsy materials from EBUS-TBNA [8, 9] and 44% of the investigated patients with pulmonary adenocarcinoma were positive for EGFR mutation in the EBUS-TBNA specimens in our study. Considering the frequency of EGFR-mutated lung cancer patients in Asian countries including Japan [10], it is clinically very important to check EGFR mutation in a newly developed mediastinal/hilar abnormality by EBUS-TBNA. Furthermore, of note is that EBUS-TBNA also detected T790M mutation, which is known as a marker resistant to EGFR-TKI [11], in one patient with enlarging subcarinal lymph nodes during EGFR-TKI treatment for EGFR-mutated lung cancer. More encouragingly, there are several reports, describing the possibility of investigation onto the mutation status of other molecular markers using EBUS-TBNA samples [12].

There are several limitations in this retrospective study. The largest limitation is the size of the study in number. Since the number of patients with previously treated thoracic malignancy undergoing EBUS was limited in our institution, it would be difficult to determine a certain decision only from this study.

In conclusion, we confirmed that EBUS-TBNA obtained the pathological diagnosis in a less-invasive manner in all cases. Despite the small number of cases, our results can reveal the usefulness of EBUS-TBNA in patients with previously treated thoracic malignancy.

Conflict of interest: none declared.

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