Contents lists available at ScienceDirect

Respiratory Investigation

journal homepage: www.elsevier.com/locate/resinv

Original article

The predictive value of endobronchial ultrasonography with a guide sheath in the diagnosis of the histologic subtypes of lung cancer

Yutaka Takeuchi, M.D.[a], *Naofumi Shinagawa, M.D, Ph.D.*[a,*], *Eiki Kikuchi, M.D, Ph.D.*[a], *Yoshihiro Matsuno, M.D, Ph.D.*[b], *Yasuhiro Hida, M.D, Ph.D.*[c], *Kichizo Kaga, M.D, Ph.D.*[c], *Satoshi Oizumi, M.D, Ph.D.*[a], *Masaharu Nishimura, M.D, Ph.D.*[a]

[a]*First Department of Medicine, Hokkaido University School of Medicine, North 15, West 7, Kita-ku, Sapporo 060-8638, Japan*

[b]*Department of Surgical Pathology, Hokkaido University Hospital, Sapporo, Japan*

[c]*Department of Cardiovascular and Thoracic Surgery, Hokkaido University Graduate School of Medicine, Sapporo, Japan*

ARTICLE INFO

Article history:
Received 4 December 2015
Received in revised form
17 May 2016
Accepted 23 May 2016

Keywords:
Lung cancer diagnosis
Pathology
Bronchoscopy
Ultrasound

ABSTRACT

Background: Recent studies have shown differential response to chemotherapy among the subtypes of non-small cell lung carcinoma (NSCLC). Therefore, to accurately differentiate between the types of lung cancer is of paramount importance. Transbronchial biopsy using endobronchial ultrasonography with a guide sheath (EBUS-GS) is a promising method for the diagnosis of NSCLC. The purpose of this study was to evaluate the consistency between the types of lung cancer histologically diagnosed by bronchial biopsy or cytologically by EBUS-GS, and the final diagnosis of the resected specimen.

Methods: A retrospective analysis was performed on 203 patients having primary lung cancers diagnosed by EBUS-GS, who subsequently underwent curative pulmonary resection at the Hokkaido University Hospital between July 2003 and December 2011. In the present study, non-small cell carcinoma was defined as non-squamous cell carcinoma, and squamous cell carcinoma (Sq) was excluded.

Results: Of the 40 cases diagnosed as Sq by EBUS-GS, 37 cases were diagnosed as Sq, and 3 cases were diagnosed as non-Sq after surgical resection. Of the 159 cases diagnosed as non-Sq by EBUS-GS, 151 cases were diagnosed as non-Sq, 6 as Sq, and 2 as small cell carcinoma after surgical resection. These results showed that the positive predictive value of EBUS-GS in the diagnosis of Sq was 93%, and its positive predictive value in diagnosing non-Sq was 95%.

Conclusions: The pathological subtyping of NSCLC using small tissue and cytology samples

Abbreviations: EBUS, endobronchial ultrasound; EBUS-GS, endobronchial ultrasonography with a guide sheath.

*Corresponding author. Tel.: +81 11 706 5911; fax: +81 11 706 7899.

E-mail addresses: y-takeuti@hokkaidoh.rofuku.go.jp (Y. Takeuchi), naofu@med.hokudai.ac.jp (N. Shinagawa), eikik@med.hokudai.ac.jp (E. Kikuchi), ymatsuno@med.hokudai.ac.jp (Y. Matsuno), yhida@med.hokudai.ac.jp (Y. Hida), kaga-hmg@med.hokudai.ac.jp (K. Kaga), soizumi@med.hokudai.ac.jp (S. Oizumi), ma-nishi@med.hokudai.ac.jp (M. Nishimura).

http://dx.doi.org/10.1016/j.resinv.2016.05.003

Please cite this article as: Takeuchi Y, et al. The predictive value of endobronchial ultrasonography with a guide sheath in the diagnosis of the histologic subtypes of lung cancer. Respiratory Investigation (2016), http://dx.doi.org/10.1016/j.resinv.2016.05.003

obtained by EBUS-GS appears to effectively distinguish between Sq and non-Sq and is therefore considered useful in making a treatment decision.

1. Introduction

Approximately 70% of patients with lung cancer are diagnosed at advanced stages and are treated with systemic chemotherapy [1]. In patients with advanced non-small cell lung carcinoma (NSCLC), the effect of new anti-cancer drugs is reported to depend on the histological subtype of NSCLC [2]. In addition, several adenocarcinoma (Ad)-exclusive or squamous (Sq)-exclusive genomic targets, such as driver mutations or fusion genes, were identified, and concurrently, molecular-targeted therapies were developed [3].

Therefore, accurate differentiation among the histological types of lung cancer has become increasingly important. Surgical specimens represent the diagnostic reference standard for patients with operable-stage lung cancers. However, the pathological subtype is often determined via the examination of small biopsy or cytology specimens for advanced-stage disease.

Bronchoscopic procedures are currently the mainstay in obtaining small biopsy or cytological specimens. Endobronchial ultrasound (EBUS) has been used for imaging guidance in the transbronchial biopsy (TBB) of peripheral pulmonary lesions; the feasibility and effectiveness of TBB using EBUS with a guide sheath (EBUS-GS) were previously demonstrated [4,5]. Furthermore, immunohistochemistry (IHC) is a powerful ancillary tool used to further classify the previously diagnosed tumors, even with small biopsy samples. In conclusion, bronchoscopy is considered an effective procedure for obtaining small specimens used in the subtyping of NSCLC to guide treatment decisions.

In this retrospective study, the role of TBB using EBUS-GS was investigated for the histological subtyping of lung cancers.

2. Patients and methods

2.1. Patients

A retrospective analysis was performed for 203 patients who had been diagnosed with primary lung cancer by bronchoscopy using EBUS-GS, and who subsequently underwent curative pulmonary resection at the Hokkaido University Hospital between July 2003 and December 2011. We previously reported the results of a study we performed on the diagnostic yield of EBUS-GS for lung cancer. The purpose of the present study was to evaluate the reliability of lung cancer subtyping using bronchoscopic specimens compared to the final histological diagnosis using surgical specimens. The patients who had no definitive diagnosis by EBUS-GS were excluded.

2.2. Ethics approval

The present study was approved by the institutional review board of the Hokkaido University Hospital (project approval number 015-0243, approval date; Nov 19, 2015), and the need for informed consent to access patient records was waived.

2.3. The bronchoscopy procedure

All patients were premedicated using 7.5 or 15 mg pentazocine hydrochloride and/or 0.5 mg atropine sulfate. Local anesthesia of the upper respiratory tract was achieved using 4% lidocaine. For peripheral lesions, a conventional flexible bronchoscope (P-260F; Olympus Medical Systems; Tokyo, Japan) was used. After the bronchoscope was inserted orally under local anesthesia into the target bronchus, an endoscopic ultrasound system equipped with a 20-MHz mechanical radial-type probe (UM-S20-17R; Olympus Medical Systems, Tokyo, Japan) with an external diameter of 1.4 mm was inserted into the guide sheath (B01–836-12; Olympus Medical Systems). The guide sheath–covered probe was then inserted through the working channel of the bronchoscope into the bronchi that led to the area suspected of containing the lesions. Endobronchial ultrasonography imaging and X-ray fluoroscopy were used to confirm that the probe and guide sheath had reached the lesions. After locating the lesions on the EBUS image, biopsy forceps and bronchial brushes were inserted via the guide sheath. Subsequently, specimens were obtained under fluoroscopic guidance for pathological and cytological analyses, and for culturing. Brushing specimens for cytological examination were smeared on two slides. The slides were fixed with methanol-acetone and stained using the conventional Papanicolaou method. Tissue specimens were fixed in 4% formaldehyde. In the present study, no cellblock specimens were prepared from the cytological materials obtained by EBUS-GS.

2.4. Pathological diagnosis

Tissue section, 4 μm in thickness, were then stained with hematoxylin-eosin. Specimens were further analyzed by performing IHC staining for thyroid transcription factor-1, napsin A, CK7, CK20, surfactant protein A, p63, synaptophysin, chromogranin A, and CD56. IHC analysis of cellblocks could not be performed because only few malignant cells were available for an antibody panel. All histological and cytological specimens were interpreted by an experienced pathologist. Suspicious findings were considered as negative in the analysis. All specimens were reviewed by certified cytopathologists, following a preliminary interpretation conducted by the laboratory technicians. The cytological and histological results were confirmed separately and independently of each other.

The histopathological diagnosis was made in compliance with the 2004 World Health Organization classification of lung tumors. Carcinomas were classified according to the World Health Organization nomenclature into Sq, Ad, adenosquamous (AdSq), NOS (not otherwise specified), small cell

Please cite this article as: Takeuchi Y, et al. The predictive value of endobronchial ultrasonography with a guide sheath in the diagnosis of the histologic subtypes of lung cancer. Respiratory Investigation (2016), http://dx.doi.org/10.1016/j.resinv.2016.05.003