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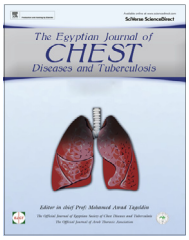

ORIGINAL ARTICLE

Synchronous invasive or preinvasive bronchial lesions detected by autofluorescence bronchoscopy in patients with lung cancer

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KEYWORDS

Lung cancer;
Synchronous;
Preinvasive bronchial lesions

Abstract *Objectives:* In support with field cancerization theory, some patients with lung cancer (LC) will also have synchronous invasive or pre-invasive bronchial lesions. In this cross sectional – analytic study autofluorescence bronchoscopy (AFB) was used to assess the prevalence of synchronous lesions in patients with LC.

Materials and methods: All patients with abnormal sputum cytology underwent white light and AFB. From 335 patients with abnormal sputum cytology referred for AFB, lung cancer was detected in 91 patients (89 male and 2 female) of age (mean ± SD), 67 ± 8 years. 77 had squamous cell carcinoma (SqCC), 13 had adenocarcinoma and one patient with small cell lung cancer (SCLC).

Results: Synchronous lesions detected in 26 (29%) patients, 25 (33%) of patients with SqCC, one with adenocarcinoma, no synchronous lesion detected in one patient with SCLC. The most severe detected synchronous lesion was adenocarcinoma in one patient, Carcinoma insitu (CIS) in 4 patients, severe dysplasia in 3 patients, moderate dysplasia in 10 patients, and mild dysplasia in 8 patients. Synchronous lesions were more frequently detected in current smokers (35%), than in ex-smokers (20%) and non-smokers (15%).

Conclusion: Synchronous preinvasive lesions are frequent in patients with LC and AFB should be included in pre-operative evaluation of these patients.

Introduction

The incidence of synchronous primary lung tumors is reported around 0.2–20% [1] and has been increasing recently due to the widespread use of imaging modalities such as multislice spiral computed tomography (CT), fluorescence endoscopy and positron emission tomography (PET) scanning. The simultaneous detection of more than one pulmonary nodule in patients with a lung cancer raises the clinical dilemma of whether these lesions represent intrapulmonary metastases that migrated

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from the same origin or the secondary primary lung tumors. The criteria proposed by Martini and Melamed [2] in 1975 for the diagnosis of synchronous multiple primary lung tumors are still commonly used and are primarily based on the histological characteristics of the tumors, location, presence or absence of carcinoma in situ, vascular invasion, metastasis and other empirical features without the biological and molecular bases [3].

Up to 10% of patients successfully treated for primary NSCLC will develop a second primary lung cancer [1]. Since diagnosis of a synchronous primary tumor may affect the diagnostic work-up and definite therapy, precise diagnostic procedures are mandatory. Lung imaging fluorescence endoscopy (LIFE) has proven better than conventional white light bronchoscopy (WLB) for visualizing premalignant lesions or early stages of lung cancer [4–6]. However, Kurie et al [7] have cast a serious doubt on the sensitivity of LIFE and state that LIFE cannot replace conventional bronchoscopy, but should be used in addition to WLB. In this study, the prevalence of preinvasive bronchial lesions in patients with lung cancer was estimated, and its impact on definite outcome of the patients was evaluated.

Patients and methods

Patients

This cross sectional – analytic study was conducted as part of Japan lung cancer (LC) early detection program, in which patients at high risk for LC underwent screening by sputum cytology; persons with abnormal sputum cytology were subjected to autofluorescence bronchoscopy.

From 335 consecutive patients at risk of LC with abnormal sputum cytology and underwent AFB examinations at Chiba University Hospital, Chiba, Japan during the period from December 1999 to December 2008, 91 patients (89 men and 2 women) were included in the current study. Patients eligible for this study had LC (non small cell lung cancer or small cell lung cancer).

Patients' median age was 68 (mean ± SD, 67 ± 8 years). A patient was considered an ex-smoker if he/she had stopped smoking for more than 1 year. All patients underwent white light (WLB) and autofluorescence bronchoscopy (AFB).

Bronchial biopsy specimens were reviewed by 2 pathologists according to the WHO 1999 criteria for pre-invasive bronchial lesions [8]. Biopsies were classified as follows: normal or inflammatory, basal cell hyperplasia (BCH), squamous metaplasia (SM), mild dysplasia, moderate dysplasia, severe dysplasia, CIS or squamous cell carcinoma [8].

Endoscopy

WLB was done using a flexible video bronchoscope (BF-240, Olympus Optical Corporation, Tokyo, Japan until January 2004, and by BF 6C260, Olympus Optical Corporation, Tokyo, Japan thereafter). WLB was first performed under local anesthesia with sedation by intravenous midazolam and oxygen inhalation. This was followed by AFB using Laser Induced fluorescent endoscopy (LIFE) (Xillix LIFE; Xillix Technologies Corp., Richmond, BC, Canada) which was applied using a fiberoptic bronchoscope (BF40; Olympus) from December 1999 to October 2001, or by autofluorescence imaging (AFI) bronchovideoscope (BF type F260, Olympus Optical Corporation, Tokyo, Japan) thereafter. Biopsy was taken from all sites that appeared abnormal at white light and/or autofluorescence bronchoscopy. Biopsies were immediately formalin fixed and paraffin embedded. All participants provided written informed consent before enrollment into the study. The study was approved by the Chiba University ethics committee.

Table 1 Demographic data and primary diagnosis.

Age (mean ± SD)	67 ± 8
Sex	
Male	89 (98%)
Female	2 (2%)
Smoking status	
Current smoker	51 (56%)
Ex-smoker	34 (37%)
Non-smoker	6 (7%)
Primary diagnosis	
Squamous cell carcinoma	77 (85%)
Adenocarcinoma	13 (14%)
Small cell carcinoma	1 (1%)

Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS software version 12) (SPSS Inc., Chicago, IL). Comparisons were made by Chi-square tests and bilateral Fisher test, with Yates correction when required. $P < 0.05$ was considered statistically significant.

Results

The current study included 91 patients, 89 male and 2 females, smoking status is shown in Table 1 and 77 patients had squamous cell lung cancer (SQCC), 13 had adenocarcinoma while one patient had small cell lung cancer (SCLL) (Table 1).

Synchronous lesions were detected in 25 patients (28%), 7 patients had mild dysplasia as the most severe synchronous lesions, 10 patients had moderate dysplasia, 3 patients had severe dysplasia, 4 patients had carcinoma in situ and one patient had adenocarcinoma as the most severe detected Table 1: demographic data and primary diagnosis synchronous lesion (Table 2).

Number of patients with synchronous lesions according to their primary lung cancer diagnosis is shown in Table 3 and the distribution of detected synchronous lesions for each lung cancer type is shown in Table 4.

Table 2 Detected synchronous preinvasive lesions.

Detected synchronous lesions	Number of patients	Percent
No synchronous lesion	66	72
Mild dysplasia	7	8
Moderate dysplasia	10	11
Severe dysplasia	3	3
Carcinoma insitu	4	5
Adenocarcinoma	1	1
Total	91	100