Original Article

Descriptive data on cancerous lung lesions detected by auto-fluorescence bronchoscope: A five-year study

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Abstract:

BACKGROUND: Auto-fluorescence bronchoscopy (AFB) has been used for the identification and localization of intra-epithelial pre-neoplastic and neoplastic lesions within the bronchus.

OBJECTIVES: To determine the applicability of AFB for the detection and localization of precancerous and cancerous lesions, in addition to analyzing the morphologic presentation, their association to histological type and the variation between genders.

METHODS: A five-year study involving 4983 patients, who underwent routine bronchoscopy [B] examination in a local tertiary teaching hospital, was done. The B examination was performed under intratracheal lidocaine, and samples were obtained using suitable approach. One thousand four hundred and eighty-five pathologically confirmed lung cancer patients were included in the study. The following parameters were studied: Morphological presentation, biopsy sites, histology. Differences between the groups were analyzed using Chi square test.

RESULT: One thousand four hundred and eighty-five patients who had hyperplasia or neoplastic lesions were further confirmed as lung cancer pathologically. Lung cancer was more commonly found in the right lung (51.58% vs. 42.82%). The lesion occurred more frequently in the upper lobe than the lower lobe (44.17% vs. 22.42%). Male patients with squamous cell carcinoma showed upper lobe involvement more commonly, while the left main bronchus was more commonly involved in female patients. Adenocarcinoma mostly involved lesion of the upper lobe. Squamous cell carcinoma and small cell carcinoma were the major proliferative types (80.15% and 76.16% respectively).

CONCLUSION: AFB is efficient in the detection of pre-invasive and invasive lung lesions. The morphological presentation is associated to the histological type. There is variation in the presentation and histology of cancerous lung lesions between genders.

Key words:

Auto-fluorescence bronchoscopy, gender, invasive lesion, lung cancer, screening

Lung cancer is a leading cause of cancer deaths in the world. The worsening of the risk factors for the disease and the aging of the population may be the two major contributors to the current status, that lung cancer has become one of the most common malignant neoplasms in China.[1,2] The majority of patients are already in a fairly advanced stage when they first seek medical attention and only 25-30% of patients can be offered therapeutic resection at most.[3] Characteristically, lung cancer arising from the bronchial mucosa (central type lung cancer) at its initial development is radiological occult. The intra-epithelial neoplastic lesions may be asymptomatic and can only be identified by bronchoscopy using light in the blue spectral region. Screening test using sputum cytology has been used with limited success.[4] Evaluation of low-dose spiral computer tomography (CT) scan as a screening tool for lung cancer is being studied,[5] and its limitations include high costs, need for repeated scanning and necessity to obtain histological confirmation with additional procedures. Bronchoscope techniques appear to be a promising tool in the early diagnosis of lung cancer in high-risk patient groups,[6] as they allow visualization of early morphological changes in the lung and taking samples for pathological confirmation.

Fluorescence bronchoscope for localization of early neoplastic changes in the bronchial mucosa was clinically introduced in the early 1980s; the method was based on the principle associated with drug-induced fluorescence using light emission from a hemotoporphyrin derivative. Autofluorescence diagnosis relies on the emission from endogenous fluorophores, following light absorption, to provide contrast between normal and abnormal tissue. Auto-fluorescence bronchoscopy (AFB) has reportedly increased the identification and localization of early neoplastic lesions of the bronchial mucosa.[6] The established applications of AFB include sputum examination; examination of patients with prolonged cough and hemoptysis; follow-up for airway recurrence after surgery; and monitoring the therapeutic effect on tracheal tumors.

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The aim of this study was to determine the applicability of AFB for the detection and localization of precancerous and cancerous lesions, in addition to analyzing the morphologic presentation, their association to histological type and the variation between genders.

Methods

Four thousand nine hundred and eighty-three patients underwent routine bronchoscopy examination during 2004 to 2009 at our department. Olympus BF-XP 260 F bronchofiber videoscope was used for the examination and EVIS LUCERA BF-260 broncho videoscope system was used. The examination was performed under local anesthesia with three subsequent sprays of 7% lidocaine each at five-minute intervals, followed by intratracheal injection of 5% lidocaine; the samples were obtained using suitable approach of forceps' biopsy, transbronchial needle aspiration and bronchial brushing with aspiration. One thousand four hundred and eighty-five patients were pathologically confirmed as lung cancer. All the pathologically confirmed cases of lung cancer were included in the study. The following parameters were studied: Morphologic presentation, biopsy sites, and histology. The case records of patients were observed for age, sex, smoking status, blood-gas, X-ray/CT, Complete Bold Count, Electro cardiogram, Prothrombin Time, and Activated Partial Thromboplastin Time.

Statistical analysis

Descriptive data were recorded for all parameters. The clinical variables including pathological and bronchoscope reporting were processed using SPSS 13.0 statistical software, and χ^2 test was done for relative frequency representation. A $P<0.05$ was considered statistically significant.

Results

Gender distribution

Among the total patients who underwent B, 3314 were male and 1669 were female. The male to female ratio for pathologically confirmed lung cancer cases was 1148:337. The incidence among male patients was significantly higher ($\chi^2 = 110.775$, $P<0.001$). The results showed 680 patients with squamous cell carcinoma (45.79%), 371 with adenocarcinoma (24.98%), 432 with small cell carcinoma (29.09%), and two with adenosquamous carcinoma (0.14%). The detection rate for squamous cell carcinoma in males (54.61%) was significantly higher than that in females (15.73%), ($\chi^2 = 158.732$; $P<0.001$). The incidence of adenocarcinoma and small cell carcinoma was higher in females (49.85% and 34.42%) than in males (13.67% and 21.28%) ($\chi^2 = 6.005$, $P=0.014$) [Table 1].

Age distribution

Pathologically confirmed cancer was highest among patients above 40 years of age. Squamous cell carcinoma and adenocarcinoma had a higher prevalence among patients older than 60 years. The male to female ratio for squamous cell carcinoma was 55.5%:58.49%; and 54.19%:46.43% for adenocarcinoma. Small cell carcinoma was more common in patients between 40 to 59 years of age (male:female ratio was 50.62%:49.14%) [Table 2].

Location of lesion

The right lung showed a higher involvement (579 males and 187 females) than the left lung (502 males and 134 females). The upper lobe was the more frequent site of lesion (522 males, 134 females) than the lower lobe (250 males, 83 females). The right upper lobe lesion (21.52%) was more common than the left upper lobe lesion (20.57%); 22.5% of female patients showed involvement of the right upper branch. Male patients with squamous cell carcinoma showed upper lobe involvement, while the left main bronchus was most commonly involved in female patients. Adenocarcinoma mostly involved lesions of the upper lobe. The right and left upper lobes were frequently involved in male patients diagnosed with small cell lung cancer, whereas female patients mostly presented with right upper, middle and left upper lobe lesions for small cell cancer. Involvement of the trachea and carina was seen in 15 patients, of which nine cases were of squamous cell carcinoma. Mixed tumor types were seen in 68 patients and involved bilateral lung fields [Table 3].

Morphologic presentation and microscopic view

One thousand and twenty-two cases of hyperplasia (68.82%) were noted, and these had multiple patterns (mainly nodular, cauliflower-like, polyploidy, and irregular); 389 cases of invasive lesion (26.2%) showed mucosal roughening, congestion, edema, erosion, necrosis, and purulent secretion under the microscope. Fifty cases of compression (3.37%) and

Table 1: Pathological type of cancer and variation between the genders

Cancer type	Squamous cell (%)	Adenocarcinoma (%)	Adeno-squamous (%)	Small cell (%)	Total (%)
Gender					
Male	627 (54.61)*	203 (13.67)#	2 (0.17)	316 (21.28)†	1148 (77.31)
Female	53 (15.73)	168 (49.85)	0 (0)	116 (34.42)	337 (22.69)
Total	680 (45.73)	371 (24.98)	2 (0.14)	432 (29.09)	1485 (100)

In comparison to females: *Squamous cell ($\chi^2 = 158.732$, $P<0.001$). #Adenocarcinoma ($\chi^2 = 143.849$, $P<0.001$). †Small cell ($\chi^2 = 6.005$, $P=0.014$)

Table 2: Pathological cancer types in subjects and distribution between age groups

Cancer type	Male (%)				Female (%)			
	<40 year	40-59 year	≥60 years	Total	<40 year	40-59 year	≥60 years	Total
Squamous cell	15 (2.39)	264 (42.11)	348 (55.5)	627	3 (5.66)	19 (35.8)	31 (58.49)	53
Adenocarcinoma	7 (3.45)	86 (42.36)	110 (54.19)	203	12 (7.14)	78 (46.4)	78 (46.43)	168
Small cell	17 (5.38)	160 (50.62)	139 (43.99)	316	8 (6.9)	57 (49.1)	51 (43.97)	116
Adenosquamous	1	0	1	2	0	0	0	0
Total	40 (3.48)	510 (44.43)	598 (52.09)	1148	23 (6.82)	154 (45.7)	160 (47.48)	337

Table 3: Morphological location, gender variation and pathological lung cancer type

Morphological location	Male					Female				
	Squamous cell	Adenocarcinoma	Adeno-squamous	Small cell	Total	Squamous cell	Adenocarcinoma	Adeno-squamous	Small cell	Total
Trachea	6 (0.96)	2 (0.99)	0	0 (0)	8 (0.70)	1 (1.89)	0 (0)	0	1 (0.86)	2 (0.59)
Carina	2 (0.32)	1 (0.49)	0	2 (0.63)	5 (0.44)	0 (0)	0 (0)	0	0 (0)	0 (0)
Left main bronchus	65 (10.37)	9 (4.43)	0	26 (8.23)	100 (8.71)	9 (16.98)	7 (4.17)	0	10 (8.62)	26 (7.72)
Left bronchus	151 (24.08)	44 (21.67)	0	65 (20.57)	260 (22.65)	7 (13.21)	26 (15.48)	0	25 (21.55)	58 (17.21)
Right main bronchus	10 (1.59)	7 (3.45)	0	2 (0.63)	19 (1.66)	1 (1.89)	3 (1.79)	0	2 (1.72)	6 (1.78)
Right upper bronchus	62 (9.89)	22 (10.84)	0	39 (12.34)	123 (10.71)	7 (13.21)	25 (14.88)	0	12 (10.34)	44 (13.06)
Right middle bronchus	41 (6.54)	5 (2.46)	0	9 (2.85)	55 (4.79)	3 (5.66)	5 (2.98)	0	7 (6.03)	15 (4.45)
Right lower bronchus	141 (22.49)	52 (26.11)	1	68 (21.52)	262 (22.82)	11 (20.75)	48 (28.57)	0	17 (14.66)	76 (22.55)
Bilateral	45 (7.18)	4 (1.97)	0	32 (10.13)	81 (7.06)	2 (3.77)	11 (6.55)	0	17 (14.66)	30 (8.9)
Total left	19 (3.03)	13 (6.40)	0	22 (6.96)	54 (4.70)	3 (5.66)	16 (9.52)	0	8 (6.90)	27 (8.01)
Total right	65 (10.37)	26 (12.81)	0	35 (11.08)	127 (11.06)	8 (15.09)	18 (10.71)	0	13 (11.21)	39 (11.57)

Figures in parenthesis are in percentage

24 cases with normal presentation (1.62%) were observed. Squamous cell carcinoma and small cell carcinoma were the major proliferative types (80.15% and 76.16% respectively) [Table 4 and Figure 1].

Discussion

Less than 15% of all patients survive five years after a diagnosis of lung cancer.[6] In the absence of a reliable screening program less than 15% of patients are diagnosed with an early Stage I cancer. In China and across the globe, 80% of patients are ineligible for surgical resection at diagnosis, mostly because of the advanced stage of cancer and also due to poor general condition. Among the methods used for the diagnosis of lung cancer, bronchoscopy serves as an important tool involved with diagnosis, staging, and management of lung cancer.[7] Technological advancements have allowed for the emergence of newer modalities to evaluate endobronchial, parenchyma, and mediastinal pathology.[8] Conventional techniques such as white light video bronchoscopy and its ancillary procedures (forceps biopsy, brush biopsy, bronchoalveolar lavage, bronchial washings, and transbronchial needle aspiration) help with accuracy in relation to tumor location, size, and type. This study aimed to evaluate the contribution of AFB in the diagnosis of lung cancer, on a hospital site, over a period of five years.

The results of our study show that out of 4983 patients, 3314 cases involved male patients, which represents that male subjects more frequently present with lesions apprehensive of lung cancer. This is supported by pathologically confirmed lung cancer in 1148 male subjects, which is in agreement with earlier findings.[9-11] Our results substantiate a 3.41 times higher possibility of lung cancer in male subjects taking AFB examination. Moreover, the incidence of squamous cell carcinoma was 54.61% in male and 15.73% in females; a possible explanation to this tendency can be the higher prevalence of smoking among male subjects in China[10-17] [Table 1].

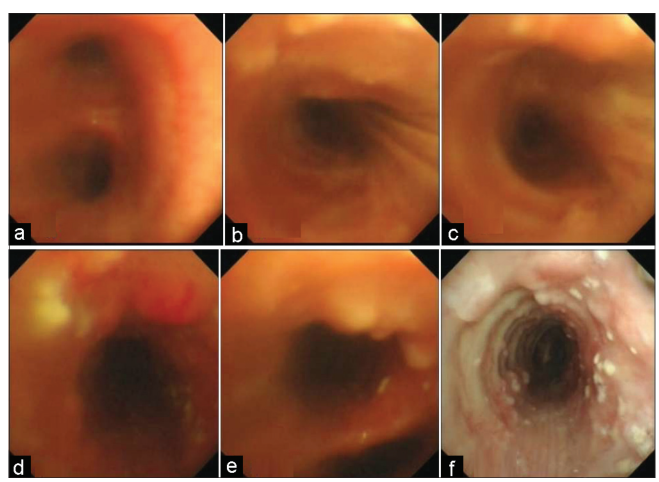

Figure 1: AFB view of lung lesions. (a) Superior view of a normal tracheal bifurcation; (b) Mild inflammation of the right main bronchus; (c) Mild inflammation of the left main bronchus; (d) Hyperemia at the right upper bronchus; (e) Exudation from the left lower bronchus; (f) Metastatic calcification of the main bronchus

Table 4: Morphological presentation and pathological lung cancer type

Morphological presentation	Squamous cell (%)	Adenocarcinoma (%)	Adeno-squamous cell (%)	Small cell (%)	Total (%)
Proliferative	545 (80.15)	147 (39.62)	1	329 (76.16)	1022 (68.82)
Invasive/infiltrative	115 (16.91)	188 (50.67)	1	85 (19.68)	389 (26.20)
Compression	10 (1.47)	24 ((6.47)	0	16 ((3.70)	50 (3.37)
Normal	10 (1.47)	12 (3.24)	0	2 (0.46)	24 (1.61)
Total	680 (100)	371 (100)	2	432 (100)	1485 (100)

Transbronchial needle aspiration (TBNA) is a minimally invasive and increasingly utilized technique to diagnose and stage lung cancer. Large case series[8,18] have reported a diagnostic accuracy of 70-95%, depending upon several factors including operator and cytopathology expertise. In the 1485 diagnosed cases of lung cancer we noted squamous cell carcinoma (45.79%), small cell carcinoma (29.09%), adenocarcinoma (24.98%), and adenosquamous carcinoma (0.14%). These findings advocate that suspicious peripheral and central airway lesions investigated with AFB have a higher chance for pathological confirmation. Hence, AFB examination should be the initial investigation once clinical features are suggestive of a mass bronchial lesion in the chest.[19] The female cases had a higher incidence of adenocarcinoma (49.85%) and small cell carcinoma (34.42%), which is in agreement with earlier findings related to the occurrence of lung cancer type in female subjects.[11,20,21] We also observed a yearly increase in the incidence of squamous cell carcinoma among female subjects, perhaps increasingly popular smoking behavior is an explanation[22,23] [Table 2].

The results show a positive relation between lung cancer incidence and old age. The high incidence of lung cancer among elderly subjects may be related to factors like smoking status, food habits, occupational exposure and infectious diseases.[20,21,24-26] Moreover, the lack of observed gender predisposition for lung cancer types among subjects more than 50 years of age supplements ours assumption that the elderly in China are predisposed to malignancy.[27] Bronchial carcinomas typically involve the main, middle and segmental bronchus. Our results show a higher incidence in the right lung and frequent involvement of the upper lobe. These findings are possibly related to the variation in vascular, lymphatic and anatomic structures. An earlier study[6] has shown a correlation between morphological abnormality and pathological types. This study found morphological patterns relative to cancer types and provided clues before the pathological confirmation was made. Our study found that adenocarcinoma presents as an invasive pattern; while squamous cell carcinoma and small cell carcinoma have a proliferative presentation under AFB [Tables 3 and 4].

Our study has certain limitations; first there is no arm of conservative follow-up. Secondly, it is a single-center study and involves a group of physicians with a similar approach. We believe that a multi-centric study will provide a better approach in the generalization of results.

In conclusion, AFB is efficient in the detection of pre-invasive and invasive bronchial cancer lesions. Our study proposes that AFB may be used in the screening of lung cancer. Though newer technologies, such as narrow band imaging, endoscopic ultrasound, endobronchial ultrasound, electromagnetic navigation, optical coherence tomography, and con-focal fluorescent laser microscopy are favorite clinical investigations in the developed world, they are yet to prove their medico-economic viability in the developing world.

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