Lung Cancer 95 (2016) 1–7

Contents lists available at ScienceDirect

Lung Cancer

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

Diffuse malignant mesothelioma and synchronous lung cancer: A clinicopathological study of 18 cases

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ARTICLE INFO

Article history:
Received 9 December 2015
Received in revised form 8 February 2016
Accepted 15 February 2016

Keywords:
Mesothelioma
Lung carcinoma
Asbestos
Cancer
Synchronous

ABSTRACT

Objectives: To examine the clinicopathologic characteristics of individuals with diffuse malignant mesothelioma (DMM) occurring concurrently with lung cancer (LC).
Materials and methods: A database of approximately 3800 patients with DMM was reviewed, from which 18 patients (0.5%) who had synchronous LC were identified. The clinicopathologic features, as well as the occupational exposure history and fiber burden analysis data were examined.
Results: The patient median age was 68 years (range 58–84 years). Of the 18 patients (14 male, 4 female), 11 (61%) had epithelial, 5 (28%) had biphasic, and 2 (11%) had sarcomatoid DMM, with the majority (16 cases; 89%) originating in the pleura and only 2 were peritoneal. Among the histologic types of LC, adenocarcinoma was most frequent (12 cases; 67%), while 5 cases of squamous cell carcinoma, and 1 case of small cell carcinoma were observed. Three patients also had a history of prior malignancy (1 with testicular seminoma and bladder carcinoma and 2 with prostate carcinoma). Fifteen patients had a positive smoking history. All but 3 had documented asbestos exposure. Three had histologic features of asbestosis. Mineral analysis performed in 8 showed an elevated asbestos fiber burden in 4 (22%). Amosite was detected in 4 patients, crocidolite in 3, and non-commercial amphiboles in 5.
Conclusion: The finding of simultaneous carcinoma of the lung and DMM is distinctly unusual. The majority of patients are male smokers with pleural epithelial DMM and lung adenocarcinoma. This study represents the largest cohort of patients reported to date with synchronous malignant mesothelioma and lung cancer, and we propose guidelines for making a diagnosis of synchronous malignant mesothelioma and primary lung cancer.

1. Introduction

Malignant mesothelioma (DMM) is a tumor of mesothelial origin that is associated with asbestos exposure [1]. Asbestos exposure is likewise associated with lung cancer (LC) and has a synergistic relationship with smoking in terms of increasing the risk of developing LC [2]. Selikoff et al. described a multiplicative model in insulators, showing that cigarette smokers exposed to asbestos have a 55-fold increased risk of developing lung cancer over those not exposed to either agent [3]. Individuals with concurrent DMM and LC have been rarely reported. We are aware of 27 published examples, most of which have been in the form of single case reports or small case series, with the largest containing 6 cases [4–16]. Two additional cases of LC co-occurring with localized malignant mesothelioma have been reported [17,18].

The purpose of the present study is to describe our experience with DMM and synchronous LC, to compare our findings with those previously reported, and to propose criteria for the diagnosis of synchronous DMM and primary LC.

2. Materials and methods

This study was approved by the institutional review board at our institution. A search of the database of approximately 3800

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http://dx.doi.org/10.1016/j.lungcan.2016.02.007
0169-5002/

DMM cases of one of the authors (VLR), comprised of professional and medicolegal consultation cases from 1982 to 2015, disclosed 18 individuals with synchronous DMM and LC. The diagnosis of DMM was based upon the gross distribution of tumor as determined by radiologic studies, observations of the surgeon at time of exploration, and/or observations of the prosector on surgical or autopsy specimens, histologic features of the tumor, and the results of immunohistochemical studies, according to the WHO classification [19]. The diagnosis of LC was also made according to the WHO classification and based upon clinical and radiographic features, histologic findings, and immunohistochemical features [19]. For each case, information was sought regarding the gender, age, smoking history, the presence or absence of pleural plaques, and occupational history. In addition, the histologic type of the LC and DMM, as well as the presence or absence of histological asbestosis was determined.

For 8 cases, lung tissue was available for analysis of mineral fiber content using the sodium hypochlorite digestion technique [20]. Digested lung tissue was collected on 0.4-micron pore size Nuclepore filters. For light microscopic analysis, the filter was mounted on a glass slide. Asbestos bodies were quantified using a magnification of 400×. Only ferruginous bodies exhibiting typical morphology with thin, translucent cores were counted as asbestos bodies [21]. Results were reported as asbestos bodies per gram of wet lung tissue (AB/g), with a detection limit of approximately 3 AB/g for a 0.3 g sample. For scanning electron microscopic (SEM) analysis, the filter was mounted on a carbon disc with colloidal graphite and then sputter-coated with gold. A JEOL JSM-6400 scanning electron microscope (JEOL, Peabody, MA) with a screen size of 22.7 × 17.3 cm was used to quantify uncoated fibers (UF) and AB at a screening magnification of 1000×. Only fibers 5 μm or greater in length with a length to width ratio of at least 3:1 and approximately parallel sides were counted. Fibers meeting these criteria were quantified by examining 100 consecutive fields, with a total area of approximately 2.37 mm^2, or until a 200 fiber-count was reached. The limit of detection is approximately 500 fibers/g for a 0.3 g sample.

The chemical composition of fibers was determined by energy-dispersive x-ray analysis (EDXA). Asbestos fibers were classified as commercial amphiboles, specifically amosite or crocidolite (AC), non-commercial amphiboles, including tremolite, anthophyllite, and actinolite (TAA), or chrysotile [20]. Tissue concentration of AC, TAA, and chrysotile was calculated in each case using the proportion of each type of fiber and the total asbestos fiber concentration. Non-asbestos mineral fibers (NAMF) were classified according to their morphology and X-ray spectra.

3. Results

3.1. Demographic data and pathologic findings

A total of 18 patients with concurrent DMM and LC were identified in a database that included 3800 cases of DMM, representing 0.5% of all cases. Data regarding these 18 cases is summarized in Table 1. There were 14 males (78%) and 4 females (22%). The median age at diagnosis was 68 years (range, 58–84 years). The types of pathologic specimens available for review included lung fine needle aspirate or core biopsy with concomitant pleural biopsy (5 patients), lung wedge biopsy/lobectomy with pleural biopsy or decortication (6 patients), extrapleural pneumonectomy (1 patient) and autopsy material (6 patients). Most patients (11 of 18; 61%) had epithelial DMM, 5 (28%) had biphasic DMM, and 2 (11%) had sarcomatoid DMM (Fig. 1A,C). Sixteen of the DMM (89%) originated in the pleura and 2 (11%) in the peritoneum. One epithelial DMM showed foci with well-differentiated papillary mesothelioma and multicys-

Table 1
Demographic features, pathologic findings, and occupational histories of patients with synchronous diffuse malignant mesothelioma and lung cancer.

Patient	Age (yrs)/gender	Specimen types	DMM type/site	LC type	Occupation	Smoking history (pack-yrs)	Asbestos exposure duration (yrs)	Pleural plaques	Histologic asbestosis
1	60/M	Lobectomy, decortication	S/Pl	SqCC	Millwright, construction worker	20	30	–	Y
2	72/M	EPP	E/Pl	ADC	U.S. Navy, construction worker, engineer	30	34	–	N
3	65/F	Autopsy	B/Pl	ADC	–	Y	–	–	–
4	64/M	Autopsy	S/Pl	SqCC	Insulator	Y	33	Y	Y
5	60/M	Lung FNA Pleural bx	B/Pl	ADC	Asbestos manufacturing	40	13	–	–
6	68/M	Lung needle bx Pleura bx	E/Pl	ADC	Laborer	NS	3	–	–
7	73/M	LobectomyPleural bx with partial rib resection	B/Pl	ADC	Shipyard worker, merchant marine	<18	9	–	N
8	74/M	Autopsy	B/Pl	ADC	Oil refinery worker	Y	–	Y	N
9	78/M	Pleural bx Autopsy	E/Pl	SCLC	Pipefitter	15	–	–	–
10	68/M	Autopsy	E/Per	SqCC	Insulator	–	20+	Y	Y
11	59/M	Lobectomy Parietal pleural bx	E/Pl	SqCC	Paper mill worker	48	14	–	N
12	71/M	Lung bx Pleural bx	B/Pl	ADC	Teacher, mechanic	56	30	Y	–
13	84/F	Lung bx Pleural bx	E/Pl	ADC	Printing press stripper, artist	45	45	–	N
14	71/F	Lung wedge bx Pleural nodule excision	E/Pl	ADC	–	–	–	–	N
15	61/M	Lobectomy Pleural bx	E/Pl	SqCC	Railroad engineer	35	33	–	N
16	63/F	Lung FNA Peritoneal bx	E/Per	ADC	–	Y	–	–	–
17	55/M	Pleural bx Autopsy	E/Pl	ADC	Pipefitter	70	36	N	N
18	73/M	Lobectomy Parietal pleura bx	E/Pl	ADC	U.S. Navy, machinist mate, construction	20	11	Y	N

Abbreviations: M, male; F, female; Pl, pleural; Per, peritoneal; bx, biopsy; FNA, fine needle aspirate; E, epithelial; B, biphasic; S, sarcomatoid; SqCC, squamous cell carcinoma; ADC, adenocarcinoma; NS, non-smoker; SCLC, small cell lung cancer; EPP, extrapleural pneumonectomy.