Spontaneous Pneumothorax and Lung Carcinoma

Should One Consider Synchronous Malignant Pleural Mesothelioma?

Trevor A. Flood, MD, Harman S. Sekhon, MD, PhD,* Jean M. Seely, MD,† Farid M. Shamji, MD,‡ and Marcio M. Gomes, MD, PhD**

Abstract: We describe the clinical and pathologic findings of a 68-year-old smoker with previous asbestos exposure who presented with spontaneous hydropneumothorax and was diagnosed with synchronous undifferentiated lung carcinoma and incidental malignant pleural mesothelioma. The synchronous occurrence of these two neoplasms is an extremely rare event with fewer than 20 reported cases in the English literature. The accurate diagnosis of synchronous tumors can be extremely challenging and the identification of a concomitant mesothelioma in our case was not made until an extensive immunohistochemical analysis was done on the resection specimen. Spontaneous pneumothorax occurs much more commonly in patients with malignant mesothelioma than with primary lung carcinomas. Consequently, although synchronous pleural mesotheliomas and lung carcinomas are infrequent, this diagnosis should be considered when a patient with a lung mass and a history of asbestos exposure presents with spontaneous pneumothorax and pleural thickening on imaging. Identification of synchronous tumors is of critical importance for determining the patient's stage and management and can have significant medicolegal implications should the patient seek compensation.

Key Words: Mesothelioma, Asbestos, Pneumothorax, Lung carcinoma.

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CLINICAL SUMMARY

A 68-year-old male former electrician with a 40-pack year smoking history presented with a 2-month history of shortness of breath and fatigue. Thoracic computed tomography demonstrated an 11.5 × 8.0 cm heterogeneous mass involving the posterior segment of the right upper lobe with an associated large hydropneumothorax (Figure 1). The mass occluded the segmental bronchus of the right upper lobe and crossed the oblique fissure to involve the superior segment of the right lower lobe. A fine-needle aspiration biopsy was positive for a nonsmall cell carcinoma with extensive necrosis. There was also associated mild visceral pleural thickening interpreted as possible metastatic spread of the lung carcinoma. Enlarged mediastinal lymph nodes were not identified. Bone scan and computed tomography scans of the head and abdomen showed no metastasis. Pleural cytology was positive for nonsmall cell carcinoma, making it a stage IIIB lung carcinoma. However, because of a bronchopleural fistula with persistent air leak that precluded chemoradiation therapy, a palliative pneumonectomy was planned. Finally, an extrapleural pneumonectomy was performed because of extensive pleural disease detected intraoperatively.

Gross examination demonstrated diffuse mild nodular thickening of the parietal pleura and a well-circumscribed lesion measuring 12.0 × 8.3 × 7.8 cm almost completely replacing the right upper lobe parenchyma with minimal extension into the right lower lobe. Approximately 90% of the lung mass was necrotic. The parietal pleura was also resected and there was focal pleural adhesion at the site of the tumor. The nonneoplastic lung parenchyma demonstrated anthracosis and emphysematous changes.

Histologic examination of the parenchymal mass showed morphologic features of an undifferentiated carcinoma, composed of large polygonal cells containing markedly pleomorphic hyperchromatic nuclei, prominent nucleoli, and abundant pale cytoplasm. Extensive necrosis and numerous mitotic figures were also present (Figure 2). There was no evidence of squamous or glandular differentiation and no mucin production. The tumor focally involved the visceral pleura at the above described site of adhesion. In addition, both the visceral and parietal pleura showed an epithelioid malignant mesothelioma with focal sarcomatoid morphology. There were microscopic foci of invasion into the lung parenchyma and into the submesothelial parietal adipose tissue (Figure 3). The two tumors collided at the site of pleural adhesion. The nonneoplastic parenchyma showed no evidence of asbestosis and no ferruginous bodies were identified.

The immunohistochemical studies confirmed synchronous malignant pleural mesothelioma and large cell undifferentiated lung carcinoma (Table 1). The pleural tumor diffusely expressed the mesothelial markers. The large cell undifferentiated carcinoma expressed epithelial antigens with ambiguous results for specific histologic subtype markers. Many undifferentiated epithelial cells coexpressed thyroid transcription factor-1 and p63 protein,

Departments of *Pathology and Laboratory Medicine, †Radiology, and ‡Surgery, The Ottawa Hospital, University of Ottawa, Ottawa, Ontario.
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Address for correspondence: Department of Pathology and Laboratory Medicine, The Ottawa Hospital, University of Ottawa, 501 Smyth Road, CCW, Room 4221, Ottawa, ON K1H 8L6. E-mail: mgomes@toh.on.ca

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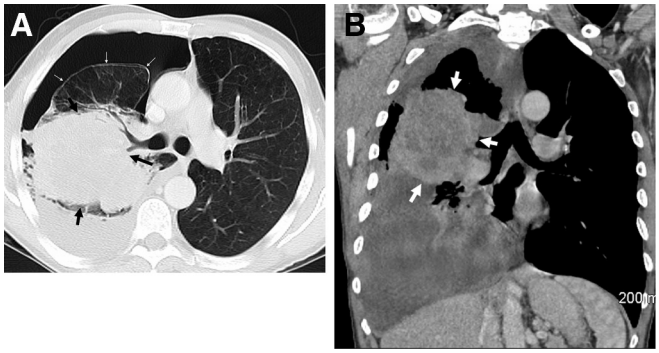

FIGURE 1. *A,* Axial computed tomography (CT) image through the upper lobes demonstrates a large mass in the right upper lobe (black arrows) obliterating the posterior segmental bronchus of the right upper lobe. There is a large right hydropneumothorax. Note the smooth visceral pleural thickening (white arrows) suggestive of visceral pleural tumor seeding. *B,* Coronal reformatted CT image obtained with contrast demonstrates the large right upper lobe tumor (white arrows) and the large right pleural effusion. No parietal pleural thickening or nodularity is identified.

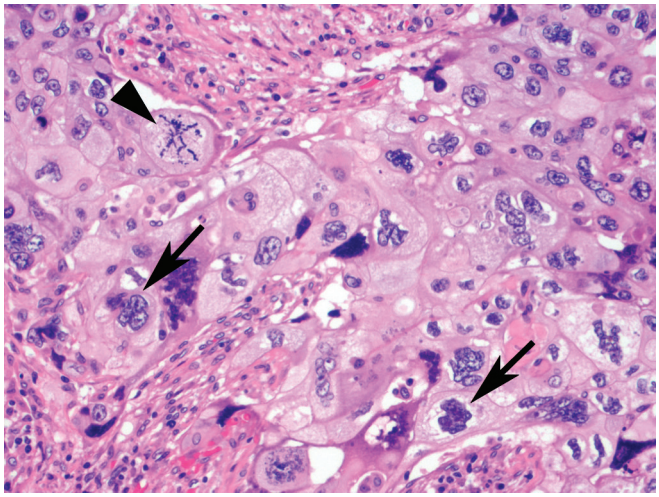

FIGURE 2. Histologic features of the undifferentiated carcinoma demonstrating large pleomorphic cells (arrows) and an atypical mitosis (arrowhead) (hematoxylin and eosin, ×200).

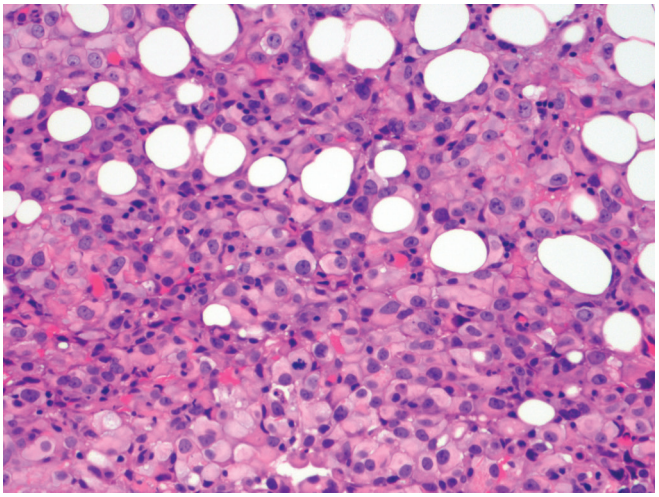

FIGURE 3. Epithelioid malignant mesothelioma invading into the submesothelial parietal adipose tissue (hematoxylin and eosin, ×200).

TABLE 1. Results of the Immunohistochemical Reactions are Shown for the Two Neoplasms

	Malignant Mesothelioma	Undifferentiated Carcinoma
Mesothelial markers		
Calretinin	+	−
CK5/6	+	+ (focal)
WT1	+	−
Epithelial markers		
MOC-31	−	+
Ber-EP4	−	+ (focal)
B72.3	−	+ (focal)
mCEA	−	+ (focal)
CD15	−	Inconclusive
Other markers		
TTF-1	−	+
p63	−	+

The mesothelial, epithelial, and other antibodies are separated into different groups.
CK5/6, cytokeratins 5 and 6; WT1, wilms tumor 1; mCEA, monoclonal carcinoembryonic antigen; CD, cluster of differentiation; TTF-1, thyroid transcription factor-1.

usually present in lung adenocarcinoma and squamous cell carcinoma, respectively.

DISCUSSION

In this case study, we have presented the occurrence of synchronous undifferentiated large cell lung carcinoma and biphasic malignant pleural mesothelioma in a 68-year-old male smoker with an occupational history of asbestos exposure. The synchronous occurrence of these two neoplasms is extremely uncommon, with fewer than 20 cases reported in the English literature.[1–7] It is well recognized that asbestos is a risk factor for both malignant mesothelioma and lung carcinoma. It has been speculated that the pathogenic mechanisms by which asbestos induces the two malignancies must be different because of the rarity of synchronous presentation.[2]

The detection of synchronous malignant pleural mesothelioma and pulmonary carcinoma is challenging because of its seldom occurrence and the confounding radiologic and morphologic features. In our case, radiographic imaging demonstrated thickening of the pleura that was interpreted as metastatic spread of an obvious nonsmall cell lung carcinoma. Similarly, the cytologic examination of the pleural effusion was reported as necrosis and malignant cells consistent with the already diagnosed nonsmall cell lung carcinoma. The identification of malignant pleural mesothelioma was made only on the resection specimen and after a thorough immunohistochemical study.

Interestingly, none of the reported cases in the literature of synchronous malignant neoplasms were diagnosed before resection or autopsy. Eleven cases were diagnosed at postmortem examination[1,3,5,7] and seven incidental tumors were identified after resection for lung cancer and/or malignant pleural mesothelioma.[2,4,6] It is clear that the existence of one neoplasm can obscure the existence of a second malignancy and can pose an extremely difficult diagnostic challenge.

In this case, the histologic dilemma was the confirmation of two different tumors versus a single advanced tumor, either mesothelioma or carcinoma, with local spreading into adjacent structures. No single marker can be used to reliably distinguish an epithelioid malignant mesothelioma from an adenocarcinoma, and a comprehensive immunohistochemical panel is mandatory to confirm the diagnosis. In our case, the pleural lesion expressed the positive "Mesothelial Markers" and was negative for "Epithelial Markers."[8] The opposite was observed in the parenchymal lesion (Table 1). Although a reduced panel can be used in the appropriate clinical setting, when facing a differential diagnosis of an extremely infrequent synchronous neoplasm and a much more common carcinoma with pleural spread, an extensive immunohistochemical analysis should be performed.

A primary lung cancer resulting in spontaneous pneumothorax is an extremely rare event that is responsible for only 0.03 to 0.05% of all pneumothoraces.[9] However, malignant pleural mesotheliomas are associated with a pneumothorax 10% of the time.[10] This data suggest that in a case of primary lung carcinoma associated with pleural thickening and spontaneous pneumothorax, the possibility of a synchronous malignant mesothelioma should be ruled out. However, to our knowledge, this is the only case where a synchronous mesothelioma and lung carcinoma presented as a spontaneous hydropneumothorax.

The majority of the literature regarding synchronous malignant neoplasms emphasizes the medicolegal aspects of an asbestos-induced mesothelioma. Compensation is assessed according to morbidity, estimates of salary loss, and reduction of life expectancy. The presence of a second malignancy is taken into consideration when this calculation is performed. Should the second malignancy also be asbestos related, further compensation could be obtained.[5] It is our view that arriving at an accurate and correct diagnosis of this rare entity is the critical step that must be achieved before pursuing a medicolegal inquisition.

CONCLUSIONS

It is clear that the accurate diagnosis of synchronous malignant pleural mesothelioma and primary lung carcinoma can be extremely challenging, with one tumor obscuring the identification of the other. In our report, cytology and thoracic imaging identified the primary lung carcinoma but were unable to detect the pleural malignant mesothelioma. The presence of mesothelioma was not detected until a complete histologic examination was performed on the resection specimen and then confirmed using immunohistochemical stains. Interestingly, the patient presented with spontaneous hydropneumothorax, a rare event that occurs relatively more frequently with malignant pleural mesothelioma than with a primary lung carcinoma. Although synchronous pleural mesotheliomas and lung carcinomas are infrequent, this diagnosis should be considered when a patient with a lung mass and a history of asbestos exposure presents with spontaneous pneumothorax and pleural thickening on imaging. More importantly, not only is the establishment of synchronous mesothelioma and lung carcinoma diagnosis critical for determining the stage and management, but it is also of paramount importance for medicolegal reasons.

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