**Elena Prisciandaro[1], Lara Girelli[1], Cristiano Rampinelli[2], Mariacristina Ghioni[3], Lorenzo Spaggiari[1, 4]**

[1]Division of Thoracic Surgery, European Institute of Oncology IRCCS, Milan, Italy
[2]Division of Medical Imaging and Radiation Sciences, European Institute of Oncology IRCCS, Milan, Italy
[3]Division of Pathology, European Institute of Oncology IRCCS, Milan, Italy
[4]Division of Oncology and Hemato-Oncology, University of Milan, Milan, Italy

# Not everything is what it seems: malignant pleural mesothelioma mimicking lung cancer

## Abstract

Malignant pleural mesothelioma usually arises from the pleural surface and progressively encases the lungs. Pulmonary involvement generally occurs at an advanced stage, while intraparenchymal nodules, in the absence of pleural lesions, constitute a less frequent presentation. We describe the case of a patient with multiple bilateral pulmonary nodules, mediastinal lymphadenopathies and left pleural effusion in the absence of pleural lesions, simulating advanced stage lung cancer. Thoracoscopic inspection did not detect any lesions. Pathological examination on one pulmonary nodule revealed malignant pleural mesothelioma. Despite its rarity, intraparenchymal malignant pleural mesothelioma should always be taken into account, when lung nodules are present, to prevent misdiagnosis and avoid delayed treatment.

**Key words:** malignant pleural mesothelioma; differential diagnosis; lung cancer; intraparenchymal mesothelioma; lung nodule

**Adv Respir Med. 2019; 87: 265–267**

## Introduction

Malignant pleural mesothelioma (MPM) is a rare malignancy, arising from the pleural surface and progressively wrapping and constricting the lungs. Typical radiological findings are diffuse pleural thickenings or nodules, associated with pleural effusion, while pulmonary lesions usually occur later in the disease course [1]. Instead, intrapulmonary growth in the absence of pleural disease represents an uncommon mode of presentation, as few examples are described in the literature. Here we report the case of a patient with multiple bilateral pulmonary nodules and left pleural effusion, in the absence of pleural lesions.

## Case report

A 67-year-old woman was admitted with dyspnoea on exertion and persistent cough. She had undergone combined chemo-radiotherapy plus splenectomy for a Hodgkin's lymphoma and triple coronary bypass surgery for myocardial infarction with papillary muscle rupture. There was no relapse of lymphoma since the end of therapy, dating back thirty-seven years. Physical examination detected left hemithorax basal hypophonesis and diminished vesicular murmur. Computed tomography (CT) showed multiple bilateral pulmonary nodules, left pleural effusion plus subaortic and subcarinal lymph nodes enlargement. There was no radiological evidence of pleural thickening (Figure 1A). $^{18}$F-Fluoro-Deoxy-Glucose Positron Emission Tomography ($^{18}$F-FDG PET) revealed an increased uptake in the pulmonary nodules and mediastinal lymph nodes (Figure 1B). Flexible bronchoscopy with endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) was then carried out on the mediastinal hypermetabolic lymphadenopathies. Cytopathology disclosed an epithelioid malignancy, suspicious of MPM. In order to rule out pleural involvement and to collect more specimens for differential diagnosis, thoracoscopic pleural biopsies were recommended. No suspicious lesions were found at pleural exploration. Pleural

**Address for correspondence:** Elena Prisciandaro, Department of Thoracic Surgery, IEO, European Institute of Oncology IRCCS, Milan, Italy; e-mail: elena.prisciandaro@unimi.it
DOI: 10.5603/ARM.2019.0065
Received: 6.08.2019

ISSN 2451–4934

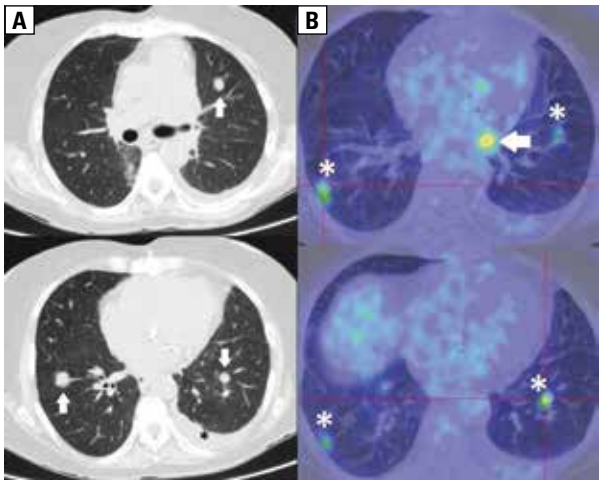


**Figure 1. A.** Computed tomography axial view showing multiple pulmonary nodules (white arrows) associated with left pleural effusion (black asterisk). A total of 13 nodules were detected, 8 in the right lung and 5 in the left lung; **B.** $^{18}$F-Fluoro-Deoxy-Glucose positron emission tomography detecting an increased uptake in the pulmonary nodules (white asterisks) and mediastinal lymph nodes (white arrow). No pleural uptake was detected

fluid cytology revealed reactive mesothelial cells, granulocytes and lymphocytes. A tumorectomy of one pulmonary nodule of the left lower lobe was then performed. Histopathological examination revealed a nodule of inflammatory cells intermingled with epithelioid atypical cells, isolated or arranged in microaggregates (Figure 2), with an immunohistochemical and molecular profile consistent with MPM. The neoplastic population was positive for epithelial markers (cytocheratin AE1/AE3 and cytcheratin 5/6), mesothelial markers (calretinin and WT-1) and negative for pulmonary antibody (TTF-1) (Figure 3). The patient started chemotherapy with combined Cisplatin and Pemetrexed, but died two months later of acute drug toxicity after the first cycle.

## Discussion

Intraparenchymal nodules in the absence of pleural lesions constitute a very rare presentation of MPM, with a prevalence of 0.6% [2]. Due to the rarity of this growth pattern, differential diagnosis represents a challenging issue. In the described case, multiple bilateral pulmonary nodules, mediastinal lymphadenopathies and left pleural effusion in a former smoker were suggestive of stage IV lung cancer [3]. On the other hand, pleural effusion might have resulted from cardiac dysfunction, given the patient's clinical history. Unexpectedly, at thoracoscopic inspection no lesions were found on the pleural surface and, even more surprisingly, pathological examination on one pulmonary nodule revealed an intraparenchymal MPM. Prognosis of this unusual variety of MPM seems to be slightly better than the "classic" form, with a survival of 28 months [2]. Our patient, unfortunately, died

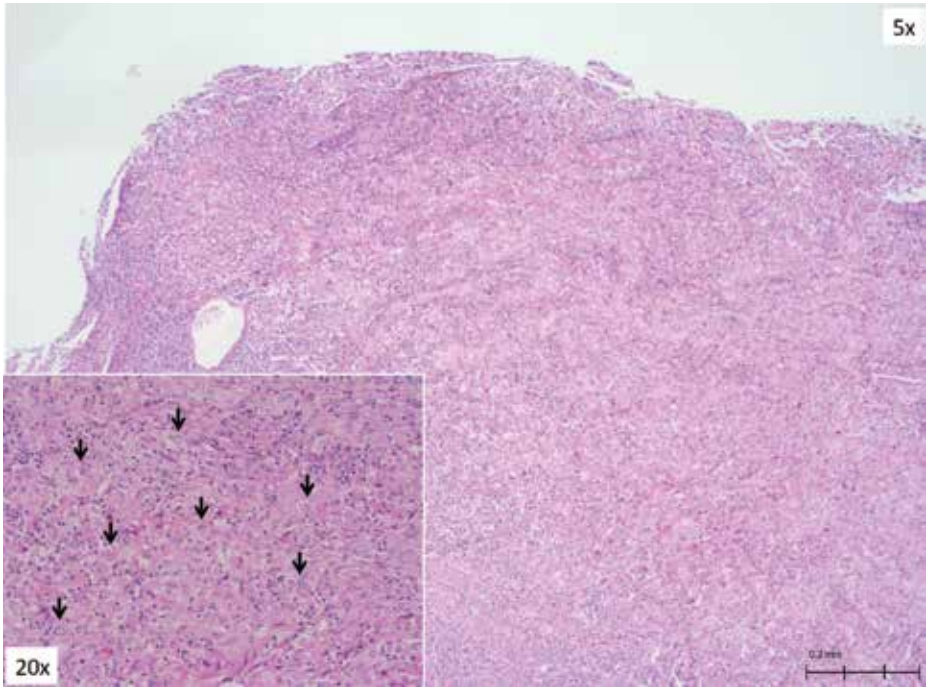


**Figure 2.** Lung nodule composed of inflammatory cells intermingled with epithelioid cells that reveal cytological atypia (black arrows)

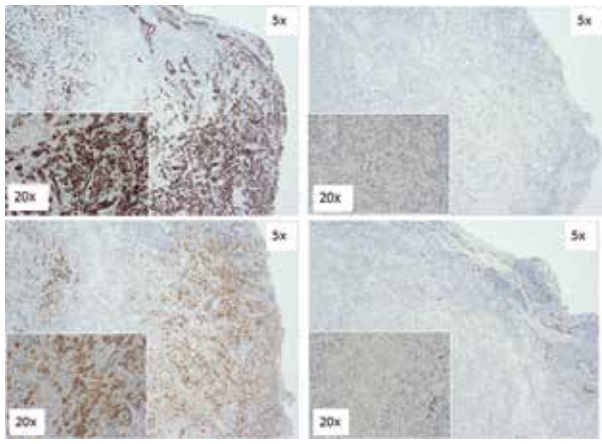


**Figure 3.** Immunohistochemical profiling of the lesion disclosed positivity (brown staining) of the atypical cells for cytocheratin AE1/AE3 (top left), WT1 (top right) and calretinin (bottom left), associated to negativity (absence of brown staining) for TTF1 (bottom right)

two months after surgery, due to acute toxicity following the second chemotherapy cycle. However, the recognition of this rare variety of MPM and its distinction from lung cancer was fundamental in order to elaborate a therapeutic approach, as, for instance, chemotherapy regimens for MPM and lung cancer are different. In conclusion, despite its rarity, intraparenchymal MPM should always be taken into account when in the presence of lung nodules to prevent misdiagnosis and avoid delayed treatment.

## Acknowledgements

The Authors' contributions: E.P. drafted the manuscript. L.G. was responsible for the critical review of important intellectual content. C.R. provided radiological images and their interpretation. M.G. was responsible for pathological analysis. L.S. was in charge of supervising the work as a whole.

All Authors gave final approval of the manuscript.

Other contributions: The Authors would like to thank Maria Giovanna Campobasso for proofreading the text and Dr. Luca Bertolaccini for his precious advice.

## Conflict of interest

None declared.

## References:

1. Nind NR, Attanoos RL, Gibbs AR. Unusual intraparenchymal growth patterns of malignant pleural mesothelioma. Histopathology. 2003; 42(2): 150–155, doi: 10.1046/j.1365-2559.2003.01555.x, indexed in Pubmed: 12558747.
2. Larsen BT, Klein JRH, Hornychová H, et al. Diffuse intrapulmonary malignant mesothelioma masquerading as interstitial lung disease: a distinctive variant of mesothelioma. Am J Surg Pathol. 2013; 37(10): 1555–1564, doi: 10.1097/PAS.0b013e3182910c82, indexed in Pubmed: 23797722.
3. Detterbeck FC, Boffa DJ, Kim AW, et al. The Eighth Edition Lung Cancer Stage Classification. Chest. 2017; 151(1): 193––203, doi: 10.1016/j.chest.2016.10.010, indexed in Pubmed: 27780786.