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A Case of Malignant Pleural Mesothelioma Presenting with Recurrent and Massive Pleural Effusion as the Main Manifestation

Ruo-Nan Yan
The First Affiliated Hospital of Henan University of Chinese Medicine
Xue-Qing Yu
The First Affiliated Hospital of Henan University of Chinese Medicine
Yuan-Yuan Wang
The First Affiliated Hospital of Henan University of Chinese Medicine
Dan-Yang Zang
The First Affiliated Hospital of Henan University of Chinese Medicine
Xiang-Yan Guo
The First Affiliated Hospital of Henan University of Chinese Medicine
Shu-Guang Yang
ysg0530_0512@126.com

The First Affiliated Hospital of Henan University of Chinese Medicine

Case Report

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Abstract

Malignant pleural mesothelioma (MPM) is a rare, malignant tumor with a dismal prognosis, often presenting with insidious and nonspecific symptoms that complicate clinical diagnosis. We report a case of a patient who experienced repeatedly massive pleural effusion over a five-year period, ultimately diagnosed via thoracoscopy and immunohistochemical analysis. We compiled the clinical data and performed a literature review to summarize the characteristics of such patients, aiming to improve clinical awareness and reduce misdiagnosis and missed diagnoses.

Introduction

Malignant pleural mesothelioma (MPM) is a rare, aggressive malignancy originating from pleural mesothelial cells and fibroblasts, often associated with asbestos exposure (1). Patients typically present with nonspecific symptoms such as chest tightness, thoracalgia, and pleural effusions, as well as imaging findings like pleural thickening. Consequently, MPM is frequently misdiagnosed as tuberculous pleurisy or pleural metastases, leading to delayed diagnosis and advanced disease at presentation. Furthermore, limited clinical experience with MPM further contributes to its poor prognosis (2). This case report describes a patient with MPM who experienced recurrent massive pleural effusions for five years before diagnosis. Through detailed clinical describe and a comprehensive literature review, we aim to enhance clinicians' understanding and awareness of MPM to reduce misdiagnosis and missed diagnosis.

Case Presentation

A 58-year-old male, employed as a cotton mill worker with a history of asbestos exposure, smoking and alcohol consumption, presented with a five-year history of recurrent pleural effusion. Five years ago, the patient developed chest tightness and shortness of breath without apparent cause, and a lung computed tomography (CT) scan at a local hospital revealed pleural effusion. Thoracentesis was performed to drain the fluid, and symptomatic treatment (details unknown) led to temporary improvement. Over the subsequent years, the patient underwent seven thoracenteses for recurrent pleural effusion, but no definitive diagnosis was established. In September 2023, the patient's symptoms of chest tightness and shortness of breath worsened again, prompting admission to Lanzhou Central Hospital. During hospitalization, the patient underwent a thoracotomy for pleural adhesion release and pleural biopsy, but it failed to yield a definitive diagnosis. Nevertheless, no further pleural effusion occurred over the subsequent six months. In April 2024, the patient went to the local hospital due to worsening chest tightness and shortness of breath. A lung CT scan revealed bilateral pleural effusions, initially misdiagnosed as severe pneumonia with respiratory failure. After receiving comprehensive anti-infective therapy, the patient temporarily improved and was discharged.

On May 12, 2024, the patient's chest tightness and shortness of breath worsened, accompanied by coughing and expectoration. The patient self-administered oral diuretics, which failed to provide relief,

prompting him to seek treatment at the First Affiliated Hospital of Henan University of Chinese Medicine. Laboratory investigations were completed after admission (Table 1), and chest axial plain and contrast-enhanced CT scan was performed. The results revealed a mass-like shadow adjacent to the right upper pulmonary hilum, with encasement of the neighboring esophagus. The inferior aspect of the mass was ill-defined against a localized pleural effusion in the mediastinal pleura, suggestive of a space-occupying lesion, and a biopsy was recommended. Additional findings included multiple inflammatory foci in the right lung, bilateral pleural and interlobar pleural effusions (partly wrapped), bibasilar atelectasis, and multiple lymph nodes in the mediastinum, some of which were enlarged (Fig. 2). Left-sided thoracentesis with tube placement on 16 May, revealed an exudative effusion (Table 1). Cytology showed numerous metamorphosed mesothelial cells, a small number of lymphocytes, with no malignant tumor cells. On May 21, 2024, the patient underwent thoracoscopic lung biopsy via the left axillary line (7th-8th intercostal space), intraoperative finding extensive fibrous tissue in the pleural cavity, with markedly dilated and tortuous vessels on the pleural surface that bled readily on manipulation. Based on the pathological and immunohistochemical analysis confirmed a diagnosis of MPM (Fig. 3). Pemetrexed and cisplatin chemotherapy was proposed, but the patient and family declined due to financial constraints, opting for palliative symptom management. On May 28, 2024, the patient and their family strongly expressed a desire to be discharged. After comprehensive counseling regarding the potential risks of early discharge, the patient was discharged against medical advice (AMA) with detailed instructions for ongoing care.

To better visualize the clinical course, we present key milestones in chronological order, including symptom onset, disease progression, and MPM diagnosis (Fig. 1).

MPM: Malignant pleural mesothelioma. On May 24, 2024, the patient was diagnosed with MPM at The First Affiliated Hospital of Henan University of CM, based on pathological and immunohistochemical analysis.

(A-F) Lung window; (G-L) Mediastinal window.

Multiple patchy opacities are seen in the right lung, with scattered small nodules present in the left lung. The right upper hilum is enlarged and accompanied by a mass, which demonstrates mild enhancement after contrast administration. Bilateral pleural thickening is observed, along with significant effusion in both pleural cavities and the interlobar fissures.

(A, B) The pathological findings were consistent with mesothelioma, most likely of the malignant type. The immunohistochemical results were as follows: CR (+), D2-40 (+), WT-1 (-), CK5/6 (+), CK7 (+), CK20 (-), TTF-1 (-), NapsinA (-), CEA (-), P40 (-), Ki-67 (approximately 10%)

Table 1
Laboratory tests *

Item	Result	Reference Range
May 12, 2024**		
NT-proBNP (pg/mL)	41.91	0-900
Blood biochemistry test		
Total protein (g/L)	62.1	65.0–85.0
Albumin (g/L)	38.0	40.0–55.0
Creatine kinase (U/L)	33.3	50.0-310.0
Glucose (mmol/L)	6.86	3.9–6.1
Chloride (mmol/L)	101.5	99.0-110.0
Coagulation related indicators		
APTT (s)	42.0	24.0–39.0
Immunoglobulin and complement		
Immunoglobulin M (g/L)	0.27	0.3–2.2
Tumor marker		
CYFRA21-1 (ng/mL)	5.8	0.0-3.3
TSGF (U/mL)	72.4	0.0–64.0
Blood Gas Analysis		
PaO_2 (mmHg)	77.2	80–100
$PaCO_2$ (mmHg)	48.2	35–45
PaO_2/FiO_2 (mmHg)	369.4	>400
May 16, 2024		
Chest fluid examination		
Pleural Fluid Protein (g/L)	39.2	/ #
Pleural Fluid Glucose (mmol/L)	6.16	/ #

*NT-proBNP: N-terminal pro-B-type Natriuretic Peptide; APTT: Activated Partial Thromboplastin Time; CYFRA21-1: Cytokeratin 19 Fragment; TSGF: Tumor Specific Growth Factor; PaO_2: Partial pressure of arterial oxygen; $PaCO_2$: Partial pressure of arterial carbon dioxide; PaO_2/FiO_2: Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen

Item	Result	Reference Range
May 12, 2024**		
Pleural Fluid Chloride (mmol/L)	102.3	/ #
Color of pleural effusion	light yellow	light yellow
Transparency	slight turbidity	translucent
Sediment	None	None
Rivalta test	(+)	(-)
White blood cell (10^6/L)	170	leakage < 100, exudate > 500
Mononuclear cell ratio (%)	35	/ ##
Multinucleated cell ratio (%)	65	/ ##
Pleural effusion culture	sterile	sterile
Blood Gas Analysis		
PaO_2 (mmHg)	83.5	80–100
$PaCO_2$ (mmHg)	57.9	35–45
PaO_2/FiO_2 (mmHg)	253.0	>400

*NT-proBNP: N-terminal pro-B-type Natriuretic Peptide; APTT: Activated Partial Thromboplastin Time; CYFRA21-1: Cytokeratin 19 Fragment; TSGF: Tumor Specific Growth Factor; PaO_2: Partial pressure of arterial oxygen; $PaCO_2$: Partial pressure of arterial carbon dioxide; PaO_2/FiO_2: Ratio of Arterial Oxygen Partial Pressure to Fraction of Inspired Oxygen

**No abnormalities were reported in other tests not listed above such as complete blood count with C-reactive protein, erythrocyte sedimentation rate, and rheumatism/rheumatoid related testing after admission.

#There is no unified reference range. Its clinical significance depends on the comparison with serum levels to differentiate exudative from transudative effusions.

##There is no unified reference range. Its clinical significance depends on the nature of the pleural effusion and the disease process (i.e., chronic disease vs. acute inflammation).

Discussion

This case report highlights the diagnostic challenges of MPM. As a malignant tumor with poor prognosis, it remains very rare, with a low incidence rate of approximately 1.5 per million people, and

predominantly affects men (3). In China, around 2000 new cases and 1600 deaths occur annually, with a 2.5% annual increase (3). The 5-year survival rate below 10%, with the median overall survival of only 9–12 months (4). The patient, a 58-year-old male cotton mill worker with asbestos exposure, experienced recurrent pleural effusions for five years, undergoing multiple hospitalizations and thoracenteses without a definitive diagnosis until thoracoscopic biopsy and immunohistochemical analysis confirmed MPM in May 2024. This prolonged diagnostic delay underscores MPM's insidious onset and nonspecific presentation, which often lead to late-stage diagnosis, missed surgical opportunities. For patients eligible for surgical resection, surgical is the preferred treatment strategy, typically supplemented with radiotherapy and/or chemotherapy. Patients with unresectable tumors are usually treated with chemotherapy and/or radiotherapy (5). Nevertheless, standardized diagnostic and therapeutic protocols for such cases remain undefined. This case underscores the pressing need to enhance clinical awareness and establish consensus.

Asbestos exposure, the primary risk factor for MPM (6), induces the infiltration of fibers into normal mesothelial cells, macrophages aggregation, and continuous release of inflammatory cytokines, which drives the transformation of normal mesothelial cells into malignant mesothelioma cells (7). Although most MPM cases are linked to occupational or environmental asbestos exposure, some patients lack a clear history. This may be due to underreported indirect exposure in industries such as construction, utilities, transportation, and the military, which are ubiquitous in daily life. This patient's occupational asbestos exposure likely contributed to his disease, emphasizing the need for thorough exposure histories in clinical evaluations.

In clinical, there is a lack of specific manifestations for MPM. Pleural effusion, chest tightness, shortness of breath, and dyspnea could be observed in MPM patients. As reported from 2219 MPM patients in China from 1980 to 2004(8), the common symptoms are chest pain, cough, dyspnea, and pleural effusion in turn. But the above symptoms are not significantly specific, which makes it difficult to distinguish them from other chest disease. In the diagnostic process of MPM, imaging examinations play a critical role, and provide valuable references for the discovery, development, and treatment of patient. Study from Guan Jun Li et al. (9) suggests that, the reduction in the volume of the affected chest and thickening of the circular pleura are helpful for the diagnosis of MPM. The study by Hu Hao et al. (10) suggests that, the CT manifestation from most cases show extensive circular pleura thickening, involving the mediastinal pleura, with mediastinal fixation, presenting as a "frozen chest cavity". In this case, the CT findings include bilateral pleural thickening and incomplete expansion of the lower lobes of both lungs, which are roughly consistent with the CT findings reported in the literature. In addition, Positron Emission Tomography/Computed Tomography (PET/CT) enhances diagnostic accuracy in differentiating malignant from benign pleural disease, with a reported (11) sensitivity and specificity of 88.2% and 92.9%, respectively, for diagnosing MPM.

Although CT, PET/CT, and B-ultrasound imaging examinations are helpful for screening and evaluating MPM, the final diagnosis relies on histopathological and immunohistochemical analysis. At present,

thoracoscopy is the primary method for acquiring effective pathological tissue specimens due to its rapidity, minimal invasiveness, high diagnostic yield (over 90% in MPM), and low complication rate (12).

Reviewing the diagnosis process of this case, the pleural fluid met Light's criteria for an exudate (pleural fluid total protein/serum total protein ratio>0.5). Moreover, the centrifugal smear and ThinPrep Cytologic Test (TCT) revealed numerous morphologically abnormal mesothelial cells, which provided critical evidence for the subsequent diagnosis. Exudative pleural effusions are commonly attributed to tuberculous pleurisy, malignant tumors, or autoimmune diseases (13). Based on the patient's medical history and test results after admission, tuberculous pleurisy and autoimmune diseases were preliminarily excluded. Finally, histopathological and immunohistochemical analysis confirmed a diagnosis of MPM.

The diagnostic delay in this case likely stemmed from an insufficient understanding of MPM among clinicians due to its extremely low incidence, inaccurate pathological sampling leading to false-negative results, and non-specific clinical manifestations combined with a lack of specific diagnostic methods. To improve outcomes, clinicians should improve the diagnosis and treatment of MPM by reviewing literature and enhancing their knowledge of this disease. In addition, a multidisciplinary discussion involving thoracic surgeons, rheumatologists, and pathologists is also necessary. Multi-point biopsy via thoracoscopy, supplemented by immunohistochemical analysis, should be performed promptly and repeated if necessary. Patient education is critical to enhance compliance with diagnostic and treatment plans.

In conclusion, this case underscores the need for heightened clinical suspicion of MPM in patients with recurrent pleural effusions and asbestos exposure. Timely thoracoscopy and immunohistochemical analysis are essential to reduce diagnostic delays and improve management, despite MPM's poor prognosis and limited treatment options.

Declarations

Ethics and consent to participate: Informed consent has been obtained, applying for exemption from ethical review.

Consent to publication: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials: The data generated in the present study may be requested from the corresponding author.

A Conflict-of-Interest Statement.: The authors declare that they have no competing interests.

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An Author Contribution statement: Ruo-Nan Yan organized the clinical data, created figures, and drafted the manuscript. Xue-Qing Yu and Shu-Guang Yang contributed to plan of the diagnosis and treatment. Yuan-Yuan Wang provided professional guidance for bronchoscopy operations and image interpretation. Dan-Yang Zang and Xiang-Yan Guo participated in the collection, sorting, and preliminary analysis of clinical data. All authors contributed to manuscript revision and have read and approved the submitted version.

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Figures

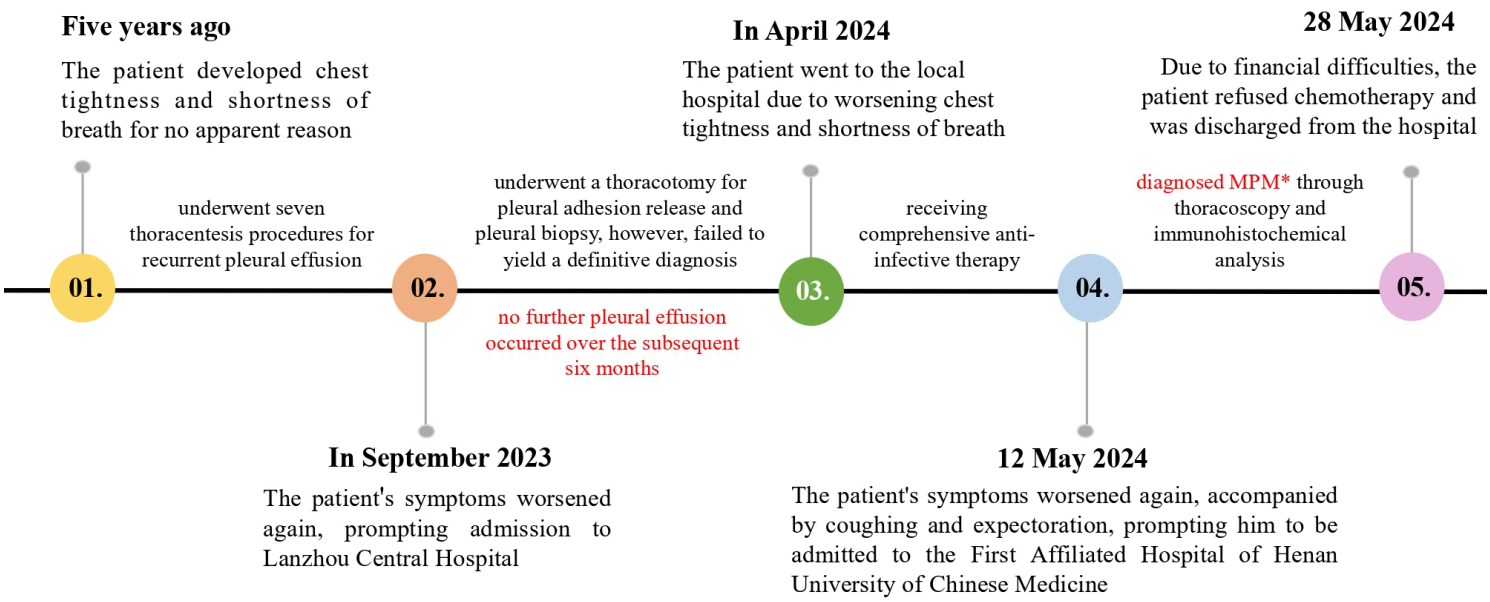


Figure 1

Timeline of the Patient's Clinical Course

MPM: Malignant pleural mesothelioma. On May 24, 2024, the patient was diagnosed with MPM at The First Affiliated Hospital of Henan University of CM, based on pathological and immunohistochemical analysis.

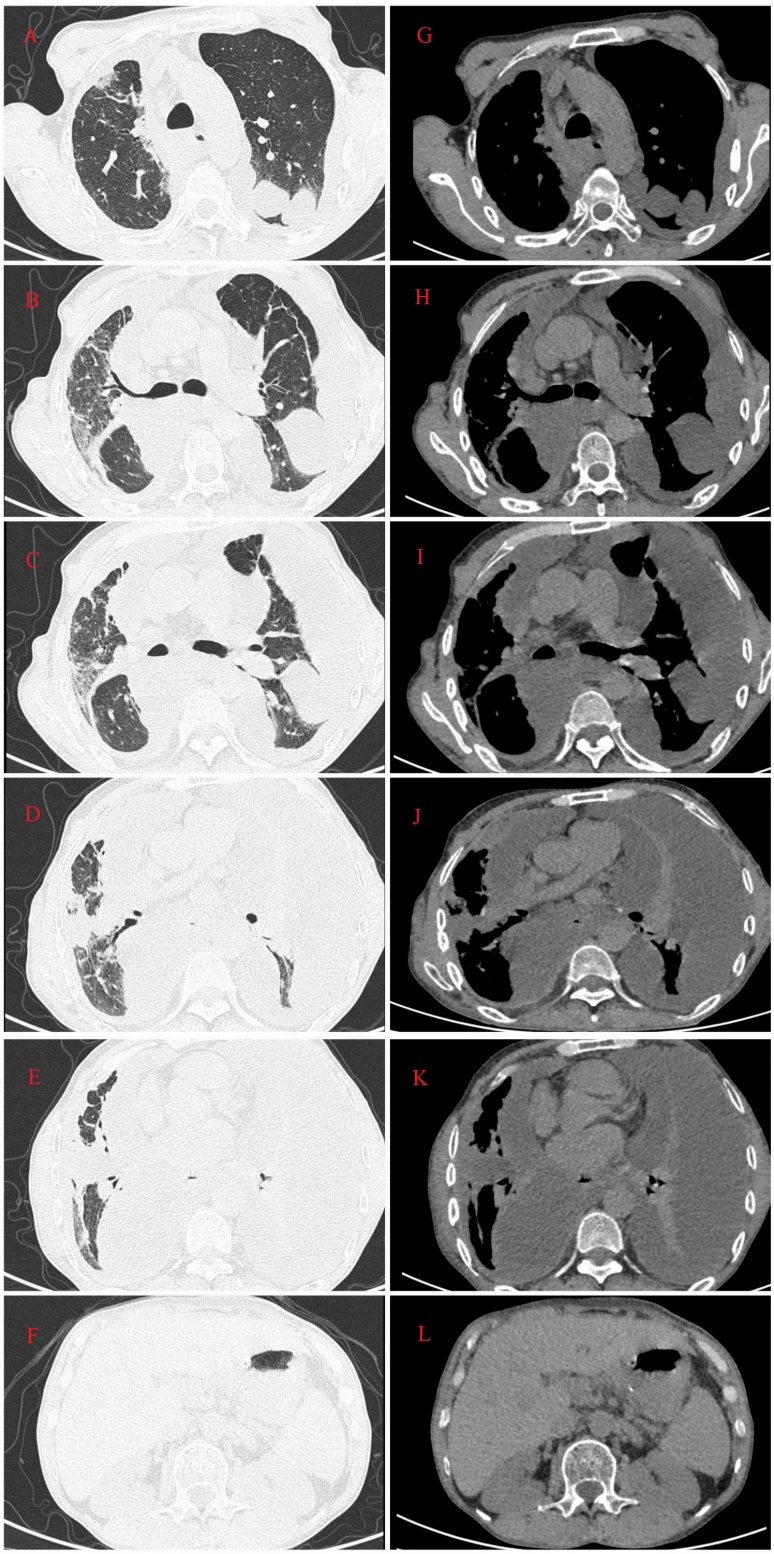


Figure 2

Lung CT images (May 15, 2024)

(A-F) Lung window; (G-L) Mediastinal window.

Multiple patchy opacities are seen in the right lung, with scattered small nodules present in the left lung. The right upper hilum is enlarged and accompanied by a mass, which demonstrates mild enhancement after contrast administration. Bilateral pleural thickening is observed, along with significant effusion in both pleural cavities and the interlobar fissures.

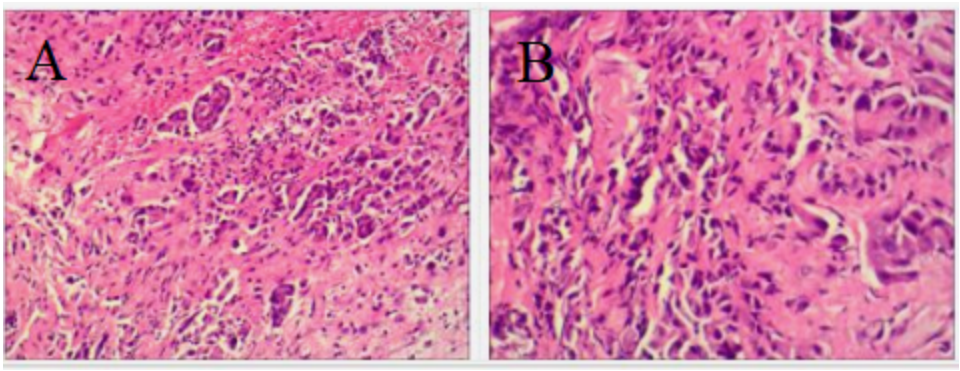


Figure 3

Pleural pathological tissue biopsy

(A, B) The pathological findings were consistent with mesothelioma, most likely of the malignant type. The immunohistochemical results were as follows: CR (+), D2-40 (+), WT-1 (-), CK5/6 (+), CK7 (+), CK20 (-), TTF-1 (-), NapsinA (-), CEA (-), P40 (-), Ki-67 (approximately 10%).

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