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Pleural Mesothelioma: A Case Report Study

Antonia Mourtzikou[1*], Marilena Stamouli[2], Christina Seitopoulou[3] and Maria Kimouli[4]

Abstract

Introduction: Malignant mesothelioma is the most common primary malignancy of the pleura. Its diagnosis is based on imaging techniques as well as on the evaluation of laboratory findings.
Aim: The aim of this study was to investigate a suspected case of pleural mesothelioma.
Case presentation: A 67-year-old male patient presented with pleural effusion and was referred for further evaluation due to anemia that did not improve following iron supplementation. The patient had no family history of thalassemia. He was afebrile but reported fatigue, weight loss, dry cough, and dyspnea during the previous month. His medical history revealed occupational exposure to asbestos.
Materials and Methods: A comprehensive laboratory investigation was performed, including hematological, biochemical, and immunological analyses, coagulation and hemostasis tests, autoantibody screening, molecular testing for SARS-CoV-2, Legionella spp., and Streptococcus pneumoniae, as well as blood cultures.
Results: Biochemical analysis revealed markedly elevated values:
SGOT: 41,300 U/L
SGPT: 23,400 U/L
LDH: 51,720 U/L
CRP: 286.3 mg/L
Hematological findings included:
Hematocrit: 30.6 %
Hemoglobin: 9.6 g/dL
White blood cells: 16,400 /μL
Coagulation and hemostasis parameters were also elevated:
D-Dimers: 33.80 mg/L
Fibrinogen: 585 mg/dL
Blood cultures were sterile (negative).
Cytological examination of pleural fluid demonstrated findings consistent with mesothelioma based on morphological characteristics and positive immunocytochemical staining for vimentin, calretinin, and podoplanin, while staining was negative for WT1, p53, CK5-6, CDX-2, TAG-72, GATA-3, S100, and TTF-1.
Discussion: Asbestos exposure represents the main carcinogenic factor involved in the pathogenesis of malignant mesothelioma. Early diagnosis is challenging because the disease is often asymptomatic in its initial stages, resulting in diagnosis at an advanced stage. The diagnostic process relies on imaging techniques such as CT, MRI, and PET-CT, as well as laboratory, cytological, and histopathological evaluation of biopsy specimens. Currently, there is no curative treatment for mesothelioma; however, advances in surgical techniques, improved chemotherapy regimens, and novel therapeutic agents have contributed to improved overall survival and quality of life for affected patients.
Conclusion: The present case highlights the strong association between occupational asbestos exposure and the development of malignant pleural mesothelioma. The prohibition of the use and commercialization of all types of asbestos in Greece since 2005, in accordance with the relevant European Union directive, may contribute to a reduction in the disease burden in the future.
Keywords: malignant pleural mesothelioma; asbestos exposure; pleural effusion; biomarkers; chemotherapy; radiotherapy; surgery.

*Correspondence:
Antonia Mourtzikou
Laboratory of Molecular Diagnostics, GHNP “Agios Panteleimon”, Greece,
Email: antoniamour@med.uoa.gr

1. Laboratory of Molecular Diagnostics, GHNP “Agios Panteleimon”, Greece
2. Laboratory of Biochemistry, Naval and Veterans Hospital of Athens “NNA”, Greece
3. Biopathology Laboratory, Primary Health Center of Nikea Piraeus, Greece
4. Microbiology Laboratory, GHNP “Agios Panteleimon”, GreeceLaboratory of Molecular Diagnostics, GHNP “Agios Panteleimon”, Greece

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Introduction

Malignant mesothelioma is a rare and highly aggressive malignancy arising from the mesothelial cells lining the serosal cavities, most commonly the pleura, but also the peritoneum, pericardium, and tunica vaginalis testis. Pleural mesothelioma accounts for approximately 70–80% of all cases and represents the most frequent primary malignancy of the pleura. Despite advances in diagnostic techniques and treatment strategies, the prognosis remains poor, with a median survival typically ranging between 12 and 18 months after diagnosis [1-3].

The primary etiological factor associated with malignant mesothelioma is occupational or environmental exposure to asbestos fibers. The carcinogenicity of asbestos is well established, and inhaled fibers can persist in the pleura for decades, inducing chronic inflammation, oxidative stress, and genetic damage that contribute to tumor development. The latency period between initial exposure and disease manifestation is particularly long, typically ranging from 20 to 50 years [3, 4]. Other risk factors have also been identified, including ionizing radiation exposure, certain chemical carcinogens, and genetic susceptibility, particularly germline mutations affecting tumor suppressor genes such as BAP1 and TP53 [1, 5-9].

Globally, the incidence of mesothelioma varies widely depending on historical asbestos consumption and occupational exposure patterns [2].

Industrialized countries experienced a peak in incidence during the late 20th century due to widespread asbestos use in construction, shipbuilding, and manufacturing industries. In Europe, the annual incidence is estimated at approximately 1–1.25 cases per 100,000 population, with a strong predominance among men older than 50 years (figure 1) [4, 10, 11Although many countries have implemented asbestos bans, the disease burden is expected to persist for decades because of the prolonged latency period [5, 12].

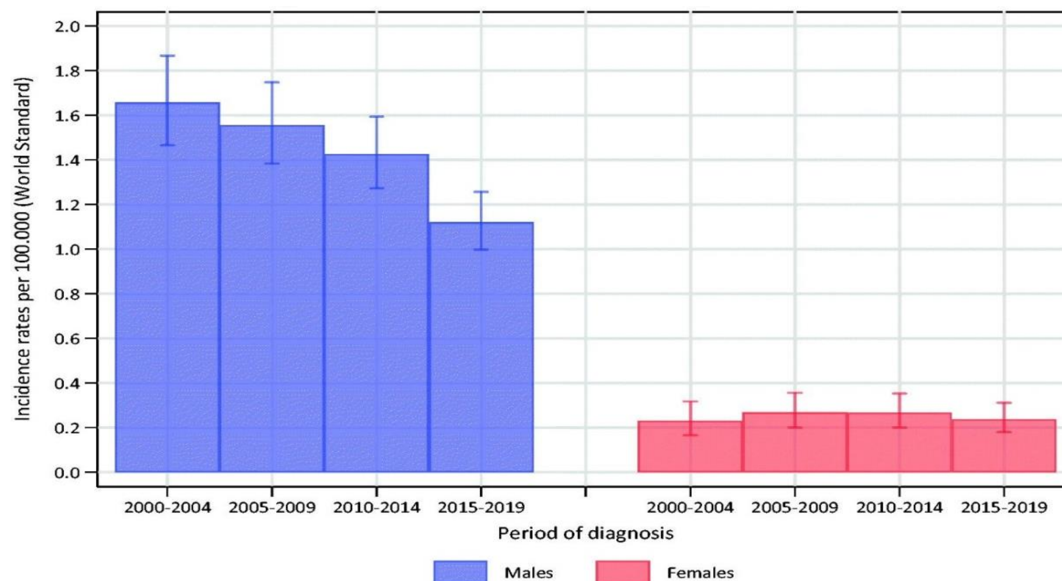

Figure 1: Age-standardised incidence rates of malignant mesothelioma among males and females. [11].

In Greece, geographical differences in mesothelioma incidence have been documented and are closely related to historical exposure patterns. The highest incidence rates are observed in the region of Epirus (~30%), whereas the lowest rates are reported in Thessaly (~10%). In the remaining regions of the country, the incidence rates range approximately between 15% and 20%. In Greece, an increase in the number of mesothelioma cases was recorded during the period from 1994 to 2003. Localized environmental exposure to asbestos, such as that described in the Metsovo region of north-western Greece, has also been associated with a markedly increased

incidence of malignant pleural mesothelioma [13]. Specifically, mortality rates of 0.38 per 100,000 population have been recorded in Epirus, compared with 0.025 per 100,000 in Thessaly, highlighting substantial regional variation [14].

One of the most well-known examples of environmentally related mesothelioma worldwide has been reported in the village of Metsovo, located in north-western Greece. In this area, a remarkably high incidence of pleural mesothelioma and pleural plaques was observed among residents, which was attributed to environmental exposure to tremolite asbestos contained in a traditional whitewash material known as "luto," widely used in local houses until the 1980s [15-17]. Studies have shown that this environmental exposure resulted in a markedly increased risk of mesothelioma among inhabitants, even in the absence of occupational exposure [13, 18].

Following the discontinuation of the use of this asbestos-containing material, a gradual reduction in the incidence of mesothelioma in the region was observed, supporting the causal relationship between environmental asbestos exposure and disease development [17].

More broadly, the number of mesothelioma cases recorded in Greece increased significantly during the late twentieth century, reflecting the long latency period between asbestos exposure and disease manifestation. Epidemiological data indicate that mesothelioma mortality increased substantially between the early 1980s and early 2000s, rising from fewer than 10 deaths in the period 1983–1985 to more than 50 deaths in the period 2001–2003 [19, 20].

The use and commercialization of asbestos were officially banned in Greece in 2005 following the implementation of European Union directives. Although this measure is expected to reduce future incidence rates, the long latency period of mesothelioma suggests that new cases will likely continue to occur for several decades [1, 4, 14, 20-22].

Health effects of asbestos exposure

The harmful effects of asbestos have been recognized since the 1920s, when workers employed in environments with asbestos dust were reported to develop characteristic symptoms associated with lung disease. Continuous exposure to asbestos fibers allows these particles to enter the human body primarily through the respiratory and digestive systems, leading to various health problems. Absorption through the skin does not occur; however, asbestos fibers may penetrate the skin and become locally deposited beneath it [1].

The development of asbestos-related disease is influenced by several factors in addition to exposure itself, including [2]:

• the type of asbestos fiber. Blue and brown asbestos are considered more hazardous than white asbestos
• the age of the individual at the time of first exposure
• the number of fibers inhaled
• the frequency and duration of exposure episodes
• smoking.

Several other diseases are associated with asbestos exposure:

Asbestosis is a degenerative pulmonary disease often referred to as "dust disease." When asbestos fibers are inhaled, a proportion of them bypass the natural defense mechanisms of the respiratory tract and reach the pulmonary alveoli. As a result, the normally elastic and soft lung tissue gradually becomes stiff and fibrotic. Patients progressively develop dyspnea and gradual destruction of lung tissue, which may lead to permanent disability and respiratory failure requiring specialized medical management [23, 24].

Lung cancer is another major disease associated with asbestos exposure. Asbestos is considered one of the most common causes of lung cancer among non-smokers. Individuals exposed to asbestos fibers in occupational settings have approximately a five-fold higher risk of developing lung cancer compared with the general population. Among smokers exposed to asbestos, the risk of lung cancer may increase up to eighty-fold [4, 23].

Pleural plaques represent a benign condition that is characteristic of asbestos exposure and typically does not cause impairment of respiratory function. Pleural plaques are usually bilateral, consist of hyalinized fibrous tissue, and are located in the parietal pleura. Over time, they frequently undergo calcification [25, 26].

Other diseases that occur more frequently among individuals exposed to asbestos include gastrointestinal malignancies, such as cancers of the esophagus, stomach, and colon, while evidence also suggests a possible association with pancreatic cancer in occupationally exposed populations [1, 27-29]. Evidence from multiple studies indicates an increased relative risk (RR) for: esophageal cancer (mRR 1.17), stomach cancer (mRR 1.14) and colorectal cancer (mRR 1.16) [27].

The occurrence of asbestos-related diseases varies

depending on both the type of occupational environment in which exposure occurs and the intensity of exposure itself. Increased risks have been identified among workers in mining, shipbuilding and ship repair, asbestos product manufacturing, insulation work, construction activities, ceramic production, railway maintenance, and brake repair industries [30].

Workers involved in demolition activities, as well as firefighters, are also at increased risk of asbestos exposure. It should be noted that both asbestosis and pleural mesothelioma are recognized as occupational diseases under the relevant regulatory framework.

The present study aims to describe the laboratory and diagnostic investigation of a patient with suspected pleural mesothelioma, emphasizing the role of clinical evaluation, imaging, and immunocytochemical markers in establishing the diagnosis.

Objective

The aim of this study is the laboratory investigation of a case with suspected pleural mesothelioma. The diagnostic evaluation was performed through imaging examinations as well as through the assessment of laboratory findings.

Case Presentation

A 67-year-old male patient of Greek origin was admitted with pleural effusion and anemia that did not improve after iron supplementation. During the month prior to admission, the patient reported fatigue, weight loss, persistent dry cough, and progressive dyspnea. His medical history revealed occupational exposure to asbestos.

The patient underwent extensive laboratory evaluation including hematological, biochemical, immunological, and coagulation tests. Molecular assays for SARS-CoV-2, Legionella spp., and Streptococcus pneumoniae were also performed, along with blood cultures.

Laboratory findings revealed markedly elevated markers of cellular damage and systemic inflammation:

- SGOT: 41,300 U/L
- SGPT: 23,400 U/L
- LDH: 51,720 U/L
- CRP: 286.3 mg/L

Hematological findings included:

- Hematocrit: 30.6 %
- Hemoglobin: 9.6 g/dL
- White blood cells: 16,400 /μL

Coagulation markers were also elevated:

- D-Dimers: 33.80 mg/L
- Fibrinogen: 585 mg/Dl

Molecular assays for SARS-CoV-2, Legionella spp., and Streptococcus pneumonia were negative.
Blood cultures were sterile (negative).

Cytological examination of pleural fluid revealed positive immunostaining for vimentin, calretinin, and podoplanin, while staining for WT1, p53, CK5-6, CDX-2, TAG72, GATA-3, S100, and TTF-1 was negative.

Vimentin is an intermediate filament protein expressed in mesenchymal cells and frequently detected in mesothelial tumors. Calretinin is a calcium-binding protein widely used as a sensitive immunohistochemical marker for mesothelioma. Podoplanin (D2-40) is a transmembrane glycoprotein involved in lymphatic endothelial differentiation and is strongly expressed in mesothelioma cells. The combined expression of these markers strongly supports the diagnosis of malignant mesothelioma [31].

Discussion

The clinical and laboratory findings observed in the present case are consistent with those reported in the literature for patients with malignant pleural mesothelioma. Several studies have shown that the disease often presents with nonspecific symptoms such as dyspnea, persistent cough, chest discomfort, and systemic manifestations including fatigue and weight loss, which frequently delay early diagnosis [1]. Pleural effusion represents one of the most common initial manifestations of malignant pleural mesothelioma and is often the clinical finding that leads to further diagnostic evaluation, with cytological examination of pleural fluid frequently constituting the first available diagnostic specimen [32]. In addition, a history of occupational asbestos exposure, as observed in our patient, has been reported in the majority of cases and remains the most well-established etiological factor associated with the development of malignant mesothelioma [1].
From a laboratory perspective, elevated inflammatory markers and biochemical indicators of tissue injury are commonly observed in patients with advanced malignant disease. Increased levels of LDH and CRP, similar to those detected in our patient, have been associated with tumor progression and systemic inflammatory response. In malignant pleural mesothelioma, elevated CRP levels have been reported as an independent prognostic factor associated with poorer overall

survival [33], while inflammation-related biomarkers such as CRP and CRP-derived indices have also been shown to predict clinical outcomes in affected patients [34]. CRP is widely recognized as a marker of systemic inflammation, whereas LDH reflects cellular damage and increased tumor metabolic activity, both of which may correlate with disease severity and tumor burden. Furthermore, hematological abnormalities such as anemia and leukocytosis are frequently reported in patients with malignancies and may reflect chronic inflammation or tumor-related metabolic disturbances [1, 35]. The markedly elevated coagulation markers in this case, including D-dimers and fibrinogen, are also consistent with previous reports describing a hypercoagulable state in patients with cancer, which is believed to result from tumor-induced activation of the coagulation cascade [36-39].

Importantly, the immunocytochemical profile observed in the pleural fluid cytology of our patient further supports the diagnosis and aligns with current diagnostic recommendations reported in the literature [40]. The combined expression of mesothelial markers such as calretinin, vimentin, and podoplanin (D2-40) is widely used to confirm mesothelial origin, while the absence of epithelial and organ-specific markers such as TTF-1, CDX-2, and GATA-3 helps differentiate malignant mesothelioma from metastatic carcinomas involving the pleura [41]. This panel-based immunohistochemical approach is considered essential for establishing an accurate diagnosis, particularly in cases where cytological morphology alone may not be sufficient.

Malignant pleural mesothelioma (MPM) is a rare but highly aggressive tumor characterized by diffuse infiltration of the pleural surfaces. Approximately 70% of cases arise in the pleura, while the remaining cases originate from the peritoneum, pericardium, or tunica vaginalis testis [2, 3].

The pathogenesis of mesothelioma is closely linked to asbestos exposure. Once inhaled, asbestos fibers penetrate the distal airways and migrate to the pleura, where they induce chronic inflammation, DNA damage, and persistent cellular injury. These processes ultimately lead to malignant transformation of mesothelial cells through mechanisms involving oxidative stress, cytokine release, and genomic instability [5].

One of the major clinical challenges in mesothelioma is delayed diagnosis. Early stages of the disease are frequently asymptomatic or present with nonspecific symptoms such as dyspnea, chest pain, cough, and fatigue. As a result, most patients are diagnosed at advanced stages when therapeutic options are limited and prognosis is poor [1].

Diagnostic evaluation typically involves imaging studies such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) which can reveal pleural thickening, nodular lesions, and pleural effusion [3]. However, definitive diagnosis requires cytological or histopathological confirmation.

Immunohistochemistry plays a crucial role in distinguishing mesothelioma from metastatic adenocarcinoma and other pleural malignancies. Panels including calretinin, podoplanin (D2-40), and vimentin are commonly used markers supporting mesothelial origin, whereas markers such as TTF-1, CEA, and CDX-2 help exclude metastatic carcinomas from lung or gastrointestinal primaries. Studies have demonstrated high sensitivity and specificity of calretinin and podoplanin in differentiating mesothelioma from metastatic adenocarcinoma [31, 42, 43].

Therapeutic management of malignant pleural mesothelioma remains challenging. Standard treatment strategies include multimodal approaches involving surgery, chemotherapy, and radiotherapy. Platinum-based chemotherapy combined with pemetrexed has historically been considered the standard systemic treatment for unresectable disease [3, 44].

More recently, immunotherapy has emerged as a promising therapeutic option. Immune checkpoint inhibitors targeting PD-1 and CTLA-4 pathways have demonstrated improved survival outcomes in selected patients with advanced disease. In addition, ongoing research is exploring novel therapeutic targets and molecular pathways involved in mesothelioma pathogenesis [5].

Despite these advances, overall prognosis remains poor, highlighting the need for improved early diagnostic methods and more effective therapeutic strategies [21].

Conclusion

This case report highlights the strong association between occupational asbestos exposure and the development of malignant pleural mesothelioma. The prolonged latency period between exposure and disease onset underscores the importance of obtaining a detailed occupational history when evaluating patients presenting with pleural effusion and respiratory symptoms.

The present case also demonstrates the crucial role of cytological examination and immunocytochemical markers in confirming the diagnosis. The combined expression of calretinin, podoplanin, and vimentin, along with the absence of markers associated with metastatic carcinomas, provided strong diagnostic evidence for malignant mesothelioma.

Although regulatory measures banning asbestos use have been implemented in many countries, including Greece, the long latency period of the disease means that new cases will likely continue to emerge for decades. Continued research into early diagnostic biomarkers, improved treatment strategies, and long-term surveillance of exposed populations remains essential for reducing the global burden of mesothelioma.

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