Malignant Pleural Mesothelioma Presenting With a Giant Posterior Mediastinal Mass

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A 74-year-old man with a history of oxygen-dependent chronic obstructive pulmonary disease, hypertension, tobacco use disorder, recurrent left pleural effusion, and latent tuberculosis was admitted at an outside hospital for evaluation of dyspnea.

The patient's history was unique in that he had developed recurrent left pleural effusions of unclear etiology, all of which had been treated with multiple thoracentesis procedures. Computed tomography (CT) scans of the chest with intravenous contrast revealed a 24.3-cm posterior mediastinal mass that encased the distal esophagus and thoracic aorta, as well as a recurrent left pleural effusion (Figures 1 and 2). He was then transferred to our institution for thoracic surgery evaluation.

Endobronchial ultrasound-guided fine-needle aspiration was performed, and a drainage catheter was placed in the left pleural space. Biopsy results showed mesothelial differentiation but did not allow for definitive diagnosis. Pleural fluid study results were consistent with an exudative process but were otherwise negative. The patient was discharged and told to follow up.

Four months later, the patient again presented to the emergency department (ED) with worsening dyspnea, productive cough, and increased drainage from his pleural catheter. He reported that he had not followed up as an outpatient and had not been on any therapy for his mass in the meantime. In addition to his worsening dyspnea, he also reported progressive dysphagia to solid foods with episodes of regurgitation, as well as fatigue and weight loss. He denied any recent illnesses, fever, chills, or night sweats. Findings of a review of systems were otherwise negative.

History

The patient had been a smoker for nearly 30 years prior to quitting 4 years prior. He had no known environmental exposures and had worked as a nurse before retiring. He had no history of recent travel. He reported having 1 or 2 alcoholic beverages a week, and he denied recreational drug use. His family history was

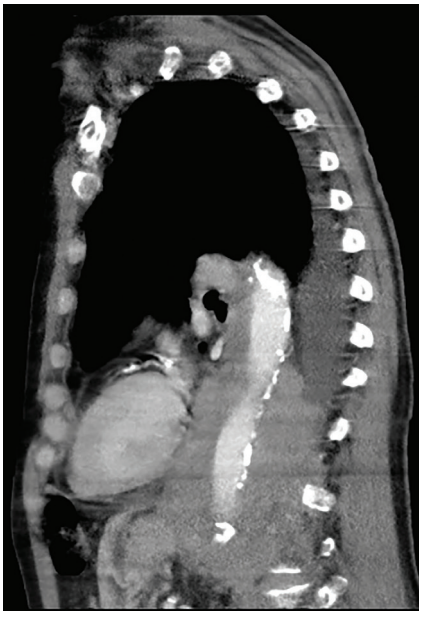

Figure 1. CT scan of the chest, sagittal view, showing a mediastinal mass directly posterior to the left ventricle extending to the thoracic wall.

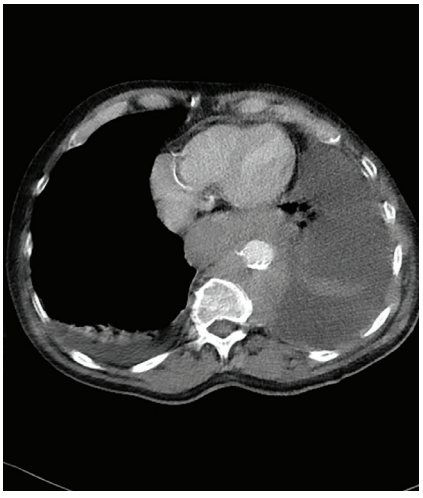

Figure 2. CT scan of the chest, axial view, showing a homogenous mass encasing the descending aorta, and a large pleural effusion in the left lung.

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significant for a malignant neoplasm of the brain in his father but was otherwise noncontributory. His home medications included enalapril, prednisone, and torsemide, as well as fluticasone propionate and salmeterol inhalation powder and albuterol sulfate inhalation powder. He denied taking any over-the-counter medications.

Physical examination

At presentation in the ED, the patient was afebrile, with a blood pressure of 141/78 mm Hg, a heart rate of 118 beats/min, and a respiratory rate of 22 breaths/min. He appeared cachectic. The patient was in mild respiratory distress, using his accessory muscles and speaking in 4- to 5-word sentences. He required 5 L/min of supplemental oxygen, which was an increase from the 3 L/min he typically used at home.

Cardiovascular examination revealed normal heart sounds and regular rhythm but tachycardia. Respiratory examination findings were notable for diminished air entry bilaterally with mild wheezing. His abdomen was soft, nontender, and nondistended. He had bilateral pitting edema of his lower extremities to his shins. The patient was otherwise alert and oriented to person, place, and time. No obvious lymphadenopathy, organomegaly, rash, or joint effusion was present.

Diagnostic tests and management

Laboratory test results at presentation were largely unremarkable: Results of a complete blood cell count were within normal limits, and results of a comprehensive metabolic panel revealed a marginally elevated bicarbonate level of 33 mEq/L but were otherwise unremarkable. The serum total protein level was 6.2 g/dL [6.3-8.2 g/dL], and the serum lactate dehydrogenase (LDH) level was 520 U/L [313-618 U/L]. The brain-type natriuretic peptide level was measured at 68 pg/mL [0-100 pg/mL]. A chest radiograph showed a left pleural effusion and left basilar atelectasis. A transthoracic echocardiogram revealed normal ventricular size and function, with a normal ejection fraction of 55% to 60%.

A CT scan of the chest without contrast was repeated and revealed growth of the known mediastinal mass, which now measured nearly 7.4 × 10.7 × 24 cm and encased the descending thoracic aorta and displaced the heart anteriorly with esophageal distention proximal to the mass (Figure 3). Additionally, a newly growing right pleural effusion was observed along with the patient's known left pleural effusion (Figure 4).

The patient was admitted for further management. A right-sided thoracentesis was performed. Pleural fluid was observed to be cloudy and serosanguinous. Fluid studies revealed an elevated white blood cell count of 474 CFU/mm (normal WBC 0-10 CFU/mm), with 76% lymphocytes, 16% monocytes, and 4% neutrophils. Analysis of the pleural fluid based on Light's criteria led to the conclusion that this was a transudative non-malignant process. Bacterial and acid-fast bacilli cultures showed no growth. Cytology test results were negative for malignancy.

Video-assisted thoracoscopic biopsy was performed for improved diagnostic yield. Specimens were sent for analysis, and a new pleural catheter was placed in his right hemithorax to aid with drainage of the effusion and alleviate his symptoms. The patient's dyspnea improved gradually, and his oxygen requirements improved to 4 L/min, which was his baseline. Immunohistochemical staining results of the tissue sample ultimately returned positive for cytokeratin AE1/AE3, calretinin, and podoplanin (D2-40), finding that confirmed a pathologic diagnosis of malignant mesothelioma (Figures 5-8).

The patient was referred to oncology specialist for treatment, and palliative chemotherapy with a carboplatin-pemetrexed-bevacizumab regimen was initiated. Radiation therapy was not recommended, since the radiation field was too large. Moreover, the mass was not a candidate for resection due to its large size. The patient was offered but declined placement of an esophageal stent to prevent further progressive dysphagia. He was sent home with outpatient follow up for palliative chemotherapy. He continued to follow up with oncology but declined chemotherapy. He was hospitalized for increasing dyspnea and worsening dysphagia. Four months following his formal diagnosis he suffered a cardiac arrest and unfortunately passed away.

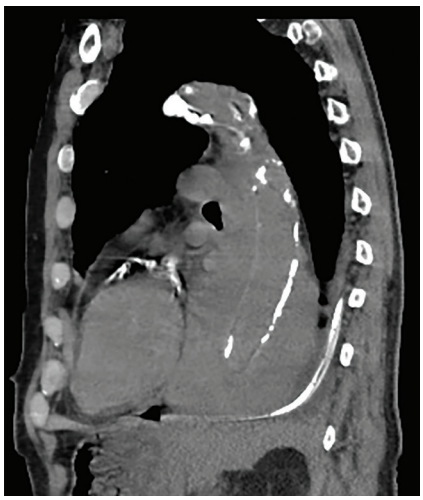

Figure 3. CT of the chest, sagittal view, showing that the mass has increased in size compared with the earlier CT shown in Figure 1 and is now pushing the heart against the anterior chest wall (image courtesy of Terence Cudahy, MD).

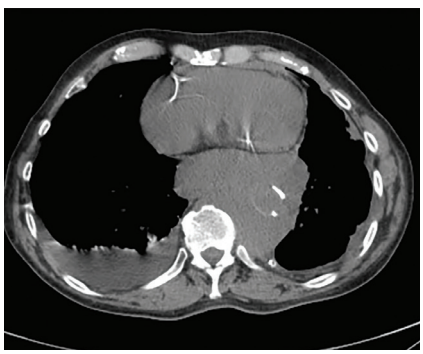

Figure 4. CT scan of the chest, axial view, showing that the posterior mediastinal mass has grown compared with the earlier CT shown in Figure 2. The right lung base shows a small pleural effusion. Calcifications are visible in the descending aorta.

Discussion

Malignant mesothelioma is a rare

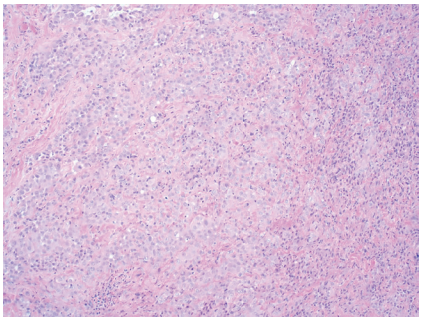

Figure 5. Results of hematoxylin and eosin staining showing nests and cords of large malignant mesothelial cells with abundant pale amphophilic cytoplasm infiltrating through soft tissue—so-called epithelioid malignant mesothelioma. Magnification 100x (image courtesy of Terence Cudahy, MD).

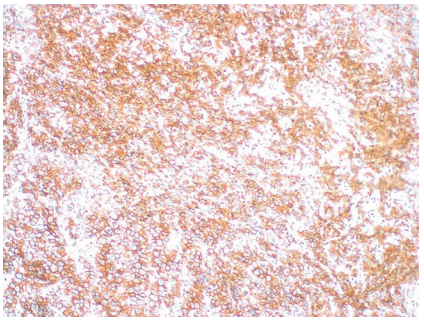

Figure 6. Intense membrane-specific immunohistochemical staining results for podoplanin (D2-40), characteristically seen in epithelioid malignant mesothelioma. Magnification 100x (image courtesy of Terence Cudahy, MD).

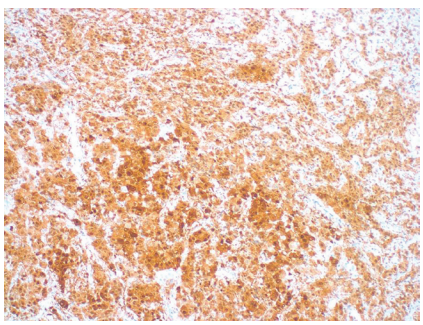

Figure 7. Strong and diffusely positive nuclear and cytoplasmic immunohistochemical staining results for calretinin, establishing mesothelial origin for the tumor. Magnification 100x (image courtesy of Terence Cudahy, MD).

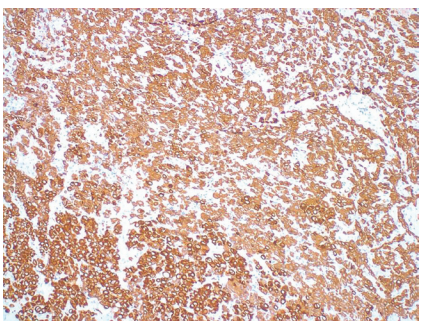

Figure 8. Strong and diffusely positive cytoplasmic staining results for broad-spectrum cytokeratin AE1/AE3, as would be expected in epithelioid malignant mesothelioma. Magnification 100x. (image courtesy of Terence Cudahy, MD).

and aggressive cancer that affects the mesothelial layer of the pleura and that is frequently linked to asbestos exposure.[1] There was an increase from 2,479 deaths in 1999 to 2,597 in 2015[2]. Incidence rate per 100,000 was in 0.8 in 2017 compared with 52.9 per 100,000 for total lung cancers[3,4] Malignant mesothelioma typically starts in the lung and can present as a lung mass or nodule in the pleural lining, but it also can occur in the peritoneum and tunica vaginalis.[1] This disease has a long latency period of up to 40 years, with a peak incidence around the fifth and sixth decades.5 Most mesothelioma cases have a reported history of asbestos exposure, but the disease can occur without known exposure approximately 20% of the time.[1] Other potential etiologies include chest radiation exposure or contact with asbestos workers who may have fibers on clothing items.[6,7]

The clinical presentation is often nonspecific, and mesothelioma can mimic other respiratory diseases.[7] Pleural effusions are a common presenting sign of mesothelioma and tend to be unilateral, although 5% of patients have bilateral pleural effusions, as in our patient's case 5. Local invasion into the diaphragm, lung parenchyma, pericardium, and chest wall are common. Pleural fluid cytology examination is one way in which pleural effusions can be assessed. In a retrospective chart review of 153 cases, pleural cytology had a sensitivity of 85.7%, for lung adenocarcinoma and only 45.5 % for mesothelioma.[8]

In this case, this patient presented with a rapidly growing posterior mediastinal mass. A typical differential diagnosis for posterior mediastinal masses includes malignant and benign neurogenic tumors, metastasis, thoracic spinal lesions, congenital cysts, vascular and esophageal lesions, and other conditions. Most commonly, neurogenic tumors comprise 60% of posterior masses and include nerve sheath tumors, ganglioneuromas, and paragangliomas.[9] Other malignant causes presenting in this compartment include lymphoma, esophageal tumors, and lipoma/lipsarcoma.[10]

Our patient's pleural effusions and smoking history also allowed for primary lung malignancies to be considered, but these are typically not located in the posterior mediastinum and usually present within the lung parenchyma. The patient had no known asbestos exposure. Certainly, his mediastinal mass could have been so large that it may have obscured the view of a pleural lesion on CT scans. Regardless, the histological diagnosis of malignant mesothelioma was surprising. The most useful markers of malignant mesothelioma include cytokeratin AE1/AE3 antibodies, which are positive in almost all mesotheliomas, and calretinin and podoplanin (D2-40), which help to distinguish epithelioid mesotheliomas from their more aggressive sarcomatoid counterparts.[11] Positive calretinin results have the best sensitivity for mesothelioma at 95% and a specificity of 87%.[12]

Most patients with mediastinal pleural mesothelioma are diagnosed with already advanced disease and face a poor prognosis, with a one year survival of 41.7 % and 5 year survival of 10.7% for both genders regardless of treatment, gender, or staging.[13] Multimodal therapy with surgery, radiation, and chemotherapy is recommended if possible, but often treatment is palliative, especially in later stages.[7]

If mesothelioma is detected early, treatment with surgery and radiation could be curative.5 However, this is rarely the case, since many patients present with advanced disease.[5] Our patient's mass showed significant growth in the span of just 4 months. Because of potentially rapid growth, it is imperative to make this diagnosis early, while the mass is still amenable to bulk-reducing chemoradiation and surgery that could extend survival.

This presentation of malignant mesothelioma as a posterior mediastinal mass with bilateral pleural effusions without evidence of primary lung involvement was atypical. As a result, the patient remained undiagnosed for several months, during which time the tumor rapidly progressed. This patient's case illustrates the importance of considering mesothelioma in the differential diagnosis of posterior mediastinal masses. Understanding the unique ways that mesothelioma can present could lead to earlier diagnosis and potentially improved patient outcomes.

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