



Rare Lung, Pleura, and Airway Disorders



Malignant Pleural Mesothelioma: An Overview

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Malignant Pleural Mesothelioma Introduction

- Malignant pleural mesothelioma (MPM), is a rare cancer originating from the parietal pleura:
 - 0.1-0.6 cases/10 millions in China
 - 20 cases/million in Germany
 - 8 cases/million in Japan
 - 10 cases/million in USA
 - Affects elderly patients, F>M
 - Incidence increasing and expected to peak in 2020
- Diagnosed at locally advanced or metastatic stages in most patients.
- **Risk Factors:**
 - Occupational asbestos exposure
 - Simian virus 40 (SV40), erionite, prior radiation, zeolite, fiberglass, and other chemicals
 - Genetic predisposition (autosomal dominant, genetic susceptibility)
 - Collapsotherapy (induction of pneumothorax to treat tuberculosis)



Malignant Pleural Mesothelioma

EPIDEMIOLOGY

- Mesothelioma is an insidious neoplasm because of its long latency period—up to 40 years in some series
- Peak incidence occurs in the 5th and 6th decades of life
- Majority of asbestos fibers are either amphibole or serpentine
- The serpentine fibers make up most of the type seen in the US and are less carcinogenic than the amphibole type.
- Found in brake linings, ship building, cement, and ceiling and pool tiles



Malignant Pleural Mesothelioma PATHOGENESIS

- **Clinical manifestations:**
 - Chest pain, dyspnea, cough, fever, night sweats, and weight loss
- **Pathogenesis:**
 1. Asbestos is inhaled into the lungs
 2. Forms oxidized iron bodies, doesn't get swallowed by the macrophages, causing a reactive hyperplasia of multinucleated macrophages
 3. Uncontrolled proliferation resulting in mutation of mesothelial cells and cancerization
 4. Natural killer (NK) cells activity is inhibited by asbestos

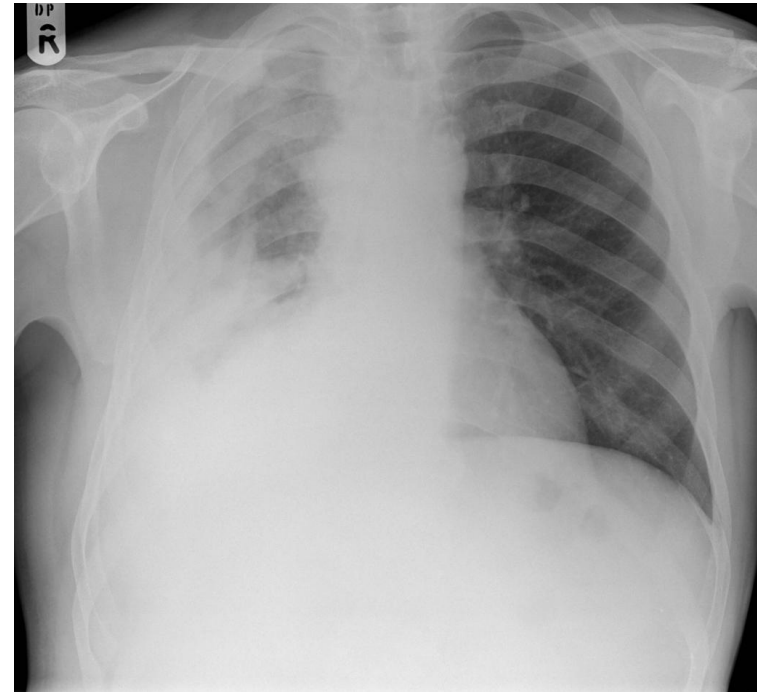


Malignant Pleural Mesothelioma CXR

Value of Chest X-Ray:

- Pleural effusion
- Pleural thickening/mass
- Unable to assess MPM

Courtesy of Dr Ian Bickle, Radiopaedia.org, rID: 30112



Circumferential pleural thickening in the
right thoracic cavity, with volume loss

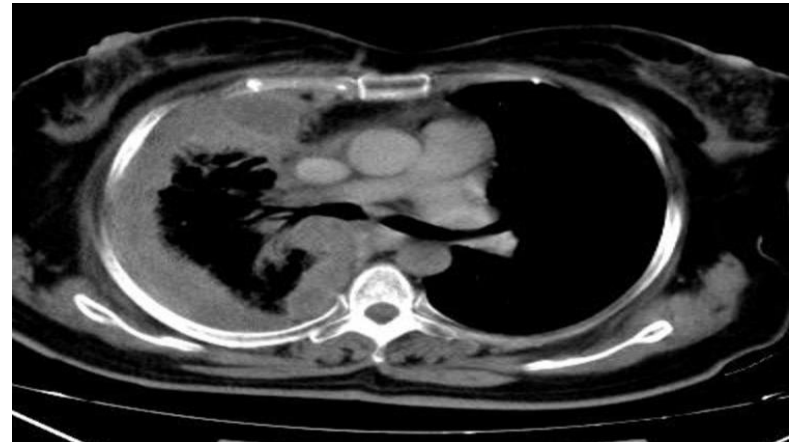


Malignant Pleural Mesothelioma CT Chest

Value of CT scans:

- Pleural thickening, tumors, effusion, plaques
- Assessment of MPM

Courtesy of Dr Ahmed Abdrabou, Radiopaedia.org, rID: 22607



Circumferential nodular right pleural thickening involving the fissures and associated with volume loss



Malignant Pleural Mesothelioma

Pathology of MPM

Malignant Pleural Mesothelioma:

- Epithelial: 50-70%, good prognosis
- Sarcomatoid: 7-20%, poor prognosis,
- Biphasic: 20-35%, intermediate prognosis,

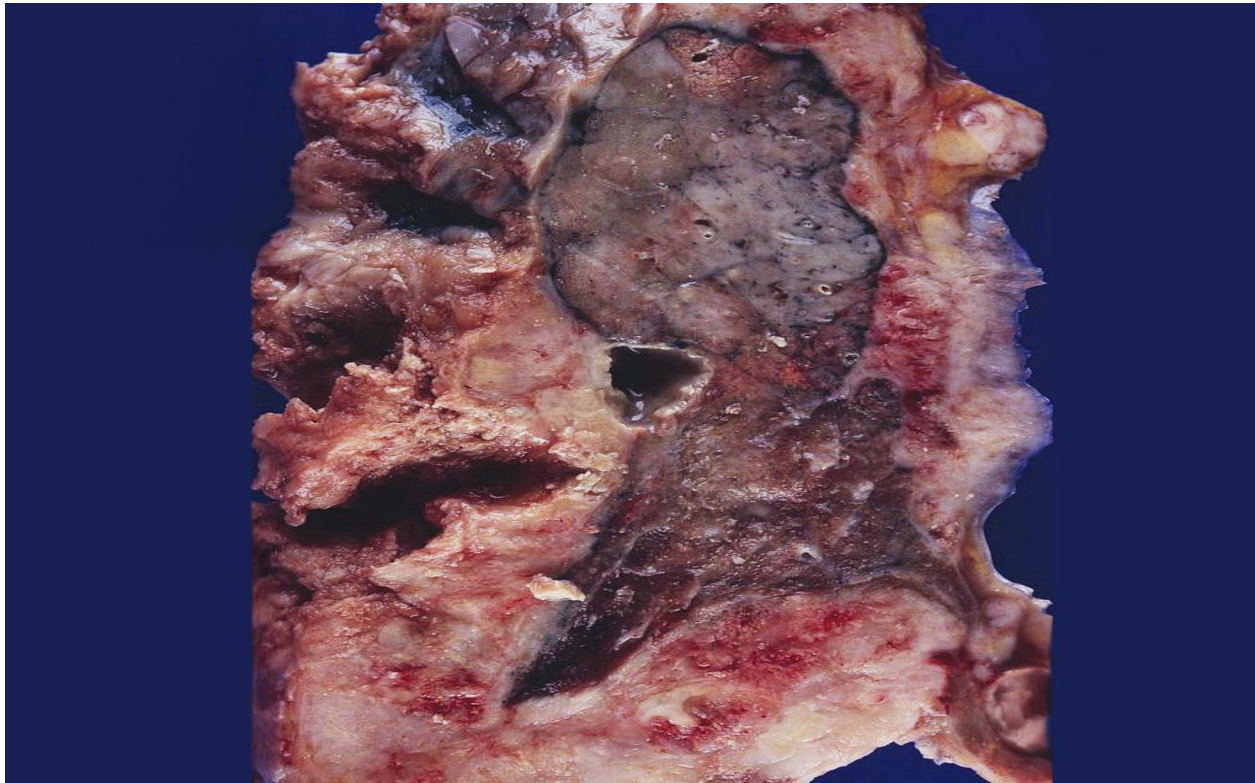
Benign mesothelioma:

- Benign multicystic mesothelioma: large grape-like cystic clusters, usually peritoneal, risk factors: Female and history of endometriosis.
- Well-differential papillary mesothelioma: usually asymptomatic and peritoneal. Mostly cured by surgery.



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Malignant Pleural Mesothelioma Pathology

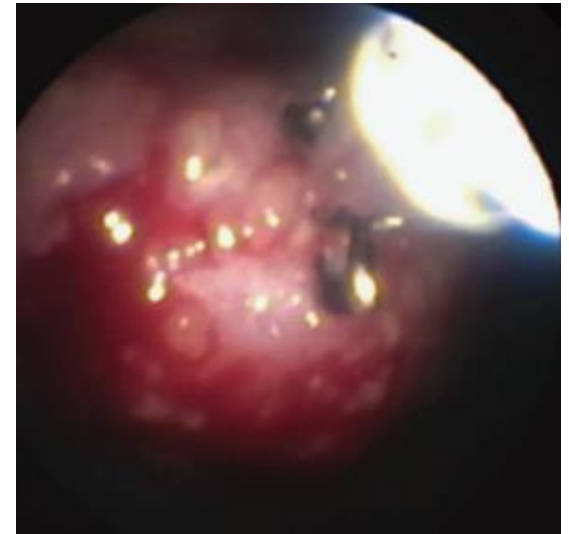


Mesothelioma encasing the lung



Malignant Pleural Mesothelioma Diagnostic Methods

- Pleural fluid cytology: 26% diagnostic yield
- Close pleural biopsy: 21% diagnostic yield
- Pleural fluid cytology + Close pleural biopsy: 39% diagnostic yield
- Medical thoracoscopy: 98% diagnostic yield



Forceps biopsy of the parietal
pleura during medical thoracoscopy



Malignant Pleural Mesothelioma Diagnostic Methods

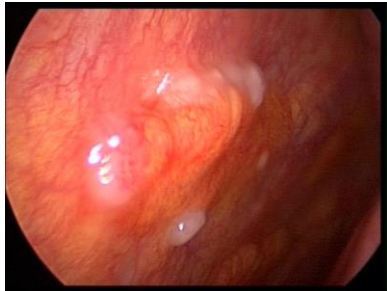
- **US Guided thoracentesis** : First test in MPM presenting with a pleural effusion. low yield overall
- **Thoracoscopy with multiple pleural biopsies**, ideally from several locations in the ipsilateral hemithorax. Very high yield
- Nodular pleural thickening without a pleural effusion: CT guided core biopsy of pleural-based masses can be used

Open pleural biopsy can also be considered for these patients, and for those without an effusion or a patent pleural space to allow for safe thoracoscopy

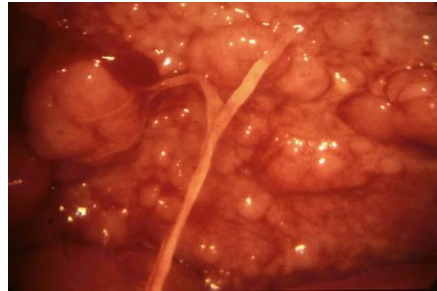


Malignant Pleural Mesothelioma Diagnostic Methods

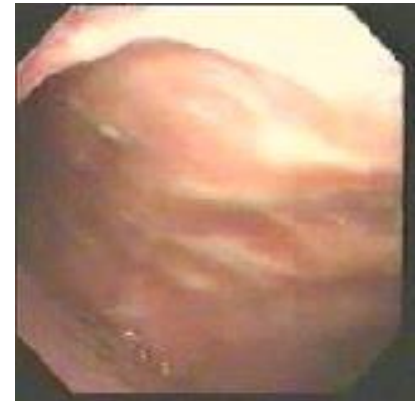
Thoracoscopy



Early nodular mesothelioma



Extensive nodular mesothelioma



Mesothelioma pachypleuritis



Malignant Pleural Mesothelioma

IMMUNO-HISTOCHEMISTRY

- **Positive markers:** Calretinin, keratins 5/6, Wilms tumor protein 1 (WT1), and podoplanin.
- **Negative markers** (positive in adenocarcinoma) :Carcinoembryonic antigen (CEA), epithelial cell adhesion molecule (EPCAM),blood group 8, and Claudin 4, napsin A and thyroid transcription factor 1 (TTF-1).



Malignant Pleural Mesothelioma Staging

- Used to guide treatment and to predict survival.
- Many patients with malignant mesothelioma are locally advanced or metastatic at the time of diagnosis.
- Patients may be upstaged during surgery
- PET/CT scan to evaluate the disease extension may be performed before surgery.



Malignant pleural mesothelioma TNM staging AJCC 2017

Primary tumor (T)			
T category	T criteria		
TX	Primary tumor cannot be assessed		
T0	No evidence of primary tumor		
T1	Tumor limited to the ipsilateral parietal pleura with or without involvement of: <ul style="list-style-type: none"> Visceral pleura Mediastinal pleura Diaphragmatic pleura 		
T2	Tumor involving each of the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features: <ul style="list-style-type: none"> Involvement of diaphragmatic muscle Extension of tumor from visceral pleura into the underlying pulmonary parenchyma 		
T3	Describes locally advanced but potentially resectable tumor. Tumor involving all the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features: <ul style="list-style-type: none"> Involvement of the endothoracic fascia Extension into the mediastinal fat Solitary, completely resectable focus of tumor extending into the soft tissues of the chest wall Nontransmural involvement of the pericardium 		
T4	Describes locally advanced technically unresectable tumor. Tumor involving all the ipsilateral pleural surfaces (parietal, mediastinal, diaphragmatic, and visceral pleura) with at least one of the following features: <ul style="list-style-type: none"> Diffuse extension or multifocal masses of tumor in the chest wall, with or without associated rib destruction Direct transdiaphragmatic extension of tumor to the peritoneum Direct extension of tumor to the contralateral pleura Direct extension of tumor to mediastinal organs Direct extension of tumor into the spine Tumor extending through to the internal surface of the pericardium with or without a pericardial effusion, or tumor involving the myocardium 		
Regional lymph nodes (N)			
N category	N criteria		
NX	Regional lymph nodes cannot be assessed		
N0	No regional lymph node metastases		
N1	Metastases in the ipsilateral bronchopulmonary, hilar, or mediastinal (including the internal mammary, peridiaphragmatic, pericardial fat pad, or intercostal) lymph nodes		
N2	Metastases in the contralateral mediastinal, ipsilateral, or contralateral supraclavicular lymph nodes		
Distant metastasis (M)			
M category	M criteria		
M0	No distant metastasis		
M1	Distant metastasis present		
Prognostic stage groups			
When T is...	And N is...	And M is...	Then the stage group is...
T1	N0	M0	IA
T2 or T3	N0	M0	IB
T1	N1	M0	II
T2	N1	M0	II
T3	N1	M0	IIIA
T1-3	N2	M0	IIIB
T4	Any N	M0	IIIB
Any T	Any N	M1	IV



Malignant Pleural Mesothelioma STAGING

- **Initial test:** CT scan of the chest and upper abdomen with IV contrast
- If abdominal metastasis is suspected : abdominal ±pelvis CT scan, with IV and oral contrast
- MRI IV contrast may be used for invasion of the tumor into the diaphragm, chest wall and mediastinum
- FDG PET/CT can be performed in patients with stage 1 to 3 with epithelial histology to evaluate for N2 involvement. Degree of FDG uptake can have prognostic implications



Malignant Pleural Mesothelioma STAGING

- MPM can metastasizes to mediastinal lymph nodes.

For patients being considered for surgical cytoreduction, a mediastinoscopy and/or EBUS/EUS may be considered if nodes are visible on imaging



Malignant Pleural Mesothelioma CHEMOTHERAPY

- Chemotherapy improves survival and QoL in treated patients
- Selected patients with a poor performance status may be offered a single-agent Chemotherapy, or palliative care alone
- For patients who are not candidates for surgery, the first-line treatment could be chemotherapy with pemetrexed and platinum + VEGF inhibitor with bevacizumab



Malignant Pleural Mesothelioma SURGERY

- Used for early stage disease and in patients with good functional status
- For early stage disease maximal surgical cytoreduction may be considered
- No RCTs comparing surgery for early stage MPM to chemotherapy are available
- **Following surgical resection**, adjuvant chemotherapy and/or radiation therapy is usually offered to decrease the likelihood of local recurrence. Some patients are offered neoadjuvant chemotherapy.
- Maximal surgical cytoreduction involves either extrapleural pneumonectomy or lung-sparing options (pleurectomy/decortication)



Malignant Pleural Mesothelioma

PLEURAL EFFUSIONS

- Tunneled pleural catheters (TPCs) may be avoided in patients who are candidates for maximal surgical cytoreduction, because of the risk of tumor implantation into the chest wall
- TPCs/ pleurodesis/VATS decortication may be offered in symptomatic patients with effusions with poor functional status where maximal cytoreduction is not feasible for palliation



Malignant Pleural Mesothelioma

RADIATION THERAPY

- Radiation therapy can be utilized to palliate symptoms
- It may be offered to patients with localized asymptomatic recurrence
- Prophylactic irradiation of intervention tracts (TPCs/biopsies etc.) is not usually recommended



Malignant Pleural Mesothelioma

PALLIATIVE CARE

- Recommended early on by all major pulmonary societies
- Depression should be recognized and treated
- Goal is to maintain a good quality of life



Malignant Pleural Mesothelioma PROGNOSIS

- Overall survival is 9 to 17 months after diagnosis
- Local invasion and respiratory failure are among the causes of death
- Sarcomatoid and biphasic histologic subtypes have worse outcomes compared with epithelioid mesothelioma
- Advanced age and poor performance status are other poor predictors of outcome



Malignant Pleural Mesothelioma Knowledge Assessment

Question 1: A 68 year old male who worked in the ship building industry for 30 years presents to your office with progressive shortness of breath , weight loss and malaise. He is hemodynamically stable with an O2 saturation of 93% on room air. A CXR shows a pleural based mass and a moderate size right sided pleural effusion . Based on the presentation , MPM is suspected . What is the next step to establish the diagnosis?



Malignant Pleural Mesothelioma Knowledge Assessment

Answer 1 : Ultrasound-guided thoracentesis can be the first diagnostic test and pleural fluid should be sent for cytologic examination for initial assessment for possible mesothelioma . The diagnostic yield is low

Thoracoscopic pleural biopsy is the gold standard diagnostic test.



Malignant Pleural Mesothelioma Knowledge Assessment

Question 2:

A patient with MPM was deemed a candidate for surgical resection. Waiting for his surgery, the pleural fluid reaccumulated within a few days and he became dyspneic.

What would be the next step in the management of the recurrent pleural effusion?



Malignant Pleural Mesothelioma Knowledge Assessment

Answer 2:

Thoracentesis should be the best next step giving that the patient is symptomatic.

TPCs are not usually recommended for patients who are candidates for surgical cytoreduction due to risk of tumor seeding into the chest wall .

TPCs may be useful in patients who are not candidates for surgical resection and for palliation of symptoms.



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