

Mesothelioma

Clinical Background

Mesothelioma is a rare malignancy involving the serous lining of body cavities (pleura, peritoneum, pericardium or tunica vaginalis testis).

Epidemiology

- Incidence – 1/100,000
- Age – peaks in 40s-50s
- Sex – M>F
- Occurrence – rising in males ≥ 75 years; however, it is not increasing in males and females < 75 years (coincides with OSHA restrictions of permissible limits of asbestos exposure)
 - Maximum lifetime risk for the development of mesothelioma falls in the 1925-1929 birth cohort

Risk factors

- Asbestos exposure (amphiboles more carcinogenic than chrysotile fibers)
 - 80% of mesothelioma cases occur in patients with history of asbestos exposure
 - At-risk occupations include shipbuilding, construction, fireproofing, automobile brakes and clutches, ceiling tiles and boilers (especially in construction prior to 1970)
- Genetics
 - Chromosome deletions (1p, 3p, 9p, 6q)

Pathophysiology

- 3 types of malignant pleural mesothelioma
 - Epithelial – 50%
 - Sarcomatous – 15%
 - Biphasic (or mixed) – 25%
- May be mistaken for adenocarcinoma; histologically heterogeneous tumors
 - Histology affects survival
- Long latency period (> 20 years) between asbestos exposure and development of mesothelioma
- Asbestos fibers are mutagenic and carcinogenic to several cells
 - Commonly found in excised tumors
- Peritoneal mesothelioma
 - Cystic – no association with asbestos
 - Well-differentiated papillary
 - Malignant – no association with asbestos

Clinical Presentation

- Pleural
 - Dyspnea, nonpleuritic chest pain, pleural effusion, cough, fatigue
- Peritoneal
 - Abdominal pain, ascites, anorexia, bloating
- Pericardial
 - Chest pain, constrictive pericarditis
- Disease process is usually advanced at time of presentation

Diagnosis

- Indications for testing – high suspicion including abnormal chest x-ray (pleural effusion, pleural plaques) and history of asbestos exposure
- Laboratory testing
 - Histology – special stains for tissue specimens
 - Body cavity fluid cytology – may be negative
 - Not all patients with mesothelioma develop effusions
 - Pleural biopsy – CT guided or thorascopic biopsy
 - Open thoracotomy – last resort
 - Serum testing is not useful in diagnosis
 - Immunohistochemistry
 - Pancytokeratin (AE1/AE3), CK-7, CK-20
 - Typically positive for pancytokeratin and CK-7; may or may not be positive for CK-20 in epithelioid mesothelioma
 - Mesothelial markers – CK5/6, WT-1, calretinin, mesothelin, HBME-1, thrombomodulin, D2-40
 - Tendency to stain higher in epithelioid tumors
 - Sarcomatoid mesothelioma
 - Main differential is adenocarcinoma
 - 2/3 positive for calretinin; usually positive for keratin
 - Typically negative stains include CEA, BG8, moc-31 (ERA), E-Cadherin, Ber-Ep4, TTF-1, CD15
- Imaging studies
 - CT/MRI for initial evaluation of abnormal chest x-ray

Differential Diagnosis

- Pleural
 - Tuberculosis
 - Adenocarcinoma
 - Metastatic malignancy
 - Other malignancy – lymphoma, sarcoma
 - Pneumonia
 - Solitary fibrous tumor
- Peritoneal
 - Ovarian cancer with metastatic disease
 - Tuberculosis
 - Lymphomatosis
 - Peritoneal carcinomatosis
 - Endometriosis

Monitoring

- Soluble mesothelial-related peptides (Mesomark)
 - Useful for monitoring epithelial or biphasic mesothelioma
 - Requires serial measurement
 - Not useful as a diagnostic test

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
Cytology, Body Cavity Fluid 8209701 Method: Routine Cytopathologic Evaluation	Aid in the diagnosis of mesothelioma		
Cytology, Pulmonary 8209702 Method: Routine Cytopathologic Evaluation	Aid in the diagnosis of mesothelioma		
Immunohistochemistry Stain Offering arup005 Method: Immunohistochemistry	For fixed tissue samples, consultative services as well as immunohistochemical staining for AE1/AE3 (pan cytokeratin), Ber-Ep4, calretinin, CEA, CK 5/6, CK-7, CK-20, E-cadherin, EMA, ERA (moc-31), keratin 903 (HMW), WT-1 (monoclonal), calretinin, TTF-1, leu M1 (CD15), D2-40 are available		
Soluble Mesothelin Related Peptides (MESOMARK®) 0081284 Method: Enzyme-Linked Immunosorbent Assay	Monitor mesothelioma	Not a diagnostic test Humanitarian use device which requires IRB approval for use	Requires serial measurements

Additional Information

Interpretation of most stains is only available in conjunction with a consultation. Stains can be performed and returned for client pathologists to interpret unless otherwise noted.

Guidelines

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General References

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