

CURRENT CONCEPTS

Malignant Mesothelioma

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DURING the two decades since the association of asbestos and mesothelioma became established, substantial progress has been made in the understanding of the biology of this previously rare neoplasm. The causative role of asbestos exposure has been extensively investigated, and populations at increased risk have been identified.¹ Observation of the natural history of mesothelioma reveals that in contrast to patients with the other sarcomas, who generally die of hematogenously disseminated metastases, patients with mesothelioma succumb to complications of their primary lesions.² With more appropriate treatment regimens designed specifically for mesotheliomas, series in single institutions have established that mesotheliomas respond to available treatment and that substantial palliation of symptoms with a small number of long-term, disease-free survivors results. This report reviews the epidemiology, natural history, and pathology of mesothelioma, with emphasis on current management and ongoing clinical trials.

EPIDEMIOLOGY

Asbestos is a silicate mineral fiber found in a variety of industrial products, including insulation, roofing and ceiling tiles, and brake linings, and in various small appliances. Asbestos presents a substantial risk to health, however, only when crushed crystals are aerosolized and inhaled.¹ Not only are people who work directly with asbestos at risk, but a substantial "bystander" risk has also been documented. Mesothelioma has developed in engineers, construction workers, and even secretaries employed in asbestos mines and mills or in shipyards where asbestos is used. An increased risk has been documented in persons residing in areas surrounding asbestos mines and mills and in family members of asbestos workers (who are presumably exposed to asbestos on hair and clothes brought into the home).¹

A threshold below which exposure to asbestos is safe or above which exposure to asbestos is dangerous has not been demonstrated.¹ Many patients have reported only a few months of incidental exposure.

The percentage of mesothelioma patients exposed to asbestos ranges from 10 per cent in a series from the mid-western United States,² where no substantial asbestos-using industry exists, to 70 per cent in New England,³ England,⁴ and South Africa, where shipyards or asbestos mines are located. Asbestos may not

be the only causative factor eventually implicated in mesothelioma, since only 7.2 per cent of asbestos workers have the disease¹ and approximately half the reported patients have no documented asbestos exposure. Peritoneal primary lesions are common in patients reporting heavy exposure,^{1,4} whereas pleural primary lesions predominate in the much larger number of transiently exposed patients; the overall ratio of pleural to peritoneal primary mesothelioma is about 3:1.² Reflecting this heavier exposure, asbestosis (calcified pleural plaques and interstitial fibrosis) can be detected in half the patients with peritoneal primary lesions, but only 20 per cent of patients with pleural primary lesions.⁴

CLINICAL PRESENTATION AND DIAGNOSIS

Two thirds of patients with mesothelioma are between the ages of 40 and 70 years.⁴ Exposure to asbestos can seldom be demonstrated in children with mesothelioma; however, patients between 20 and 40 years of age frequently have a parent employed in an asbestos industry.^{1,2} Ninety-five per cent of patients with mesothelioma will first note the insidious onset of pain or shortness of breath.^{3,4} The pain is non-pleuritic, aching, and frequently referred to the upper abdomen or shoulder, occasionally prompting an incorrect diagnosis of cardiac, orthopedic, or gallbladder disease.⁴ Fascinating but rare presentations have included intermittent hypoglycemia and hypertrophic pulmonary osteoarthropathy,^{4,5} both of which are more commonly associated with the benign variant of mesothelioma.^{1,4}

Except for signs of dullness at the site of the lesion and occasional finger clubbing, initial physical examination is generally negative.^{3,4} Patients appear well, and many have been initially reassured and sent home. A delay of four to six months frequently occurs between onset of symptoms and accurate diagnosis.⁴ A chest film when the patient first seeks medical attention, however, almost invariably reveals a unilateral pleural effusion.^{3,4} Thoracentesis yields an exudate that may be hemorrhagic.^{3,4,5} Pleural-fluid hyaluronic acid levels above 0.8 mg per milliliter are reported to establish the diagnosis of mesothelioma.¹ However, the majority of patients with mesothelioma have intermediate hyaluronic acid levels, also frequently seen in metastatic carcinoma. Neither pleural-fluid cytology nor needle biopsy consistently yields a definitive diagnosis of mesothelioma and, more frequently, they prompt a misleading diagnosis of adenocarcinoma.^{3,4} Bronchoscopy and sputum cytology are useful only to rule out a bronchogenic primary lesion. Thoracotomy is generally required to obtain an adequate specimen for histologic examination.^{3,4,5} A small portion of the biopsy specimen should be placed in glutaraldehyde (or formaldehyde) for electron microscopy if later indicated in any patient with a clinical presentation consistent with mesothelioma. Computerized axial tomography has recently proved promising in documenting the extent of disease.

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