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Malignant Mesothelioma in Young Adults

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Ten cases of malignant mesothelioma presenting in patients 40 years old or younger at diagnosis were reviewed. Seven cases had a documented history of asbestos exposure of which five were household exposures. The median age at first exposure to asbestos was 10 years and the median duration of exposure was 120 months. The median latency period (time between initial asbestos exposure and diagnosis of malignant mesothelioma) was 19 years. The median interval from initial symptoms to definitive diagnosis was 5.5 months. The case history of each patient is presented. A significant delay in diagnosis in this age group compared with an age-unrestricted series is noted. The significance of nonoccupational exposure to asbestos is emphasized as a probable causative factor in the development of malignant mesothelioma. In addition, a possible genetic predisposition is briefly discussed. *Cancer* 65:1449–1455, 1990.

THE INCIDENCE of malignant mesothelioma, once an uncommon neoplasm, is increasing.[1] After the landmark epidemiologic study by Wagner *et al.*,[2] its association with asbestos exposure has been well documented.[3–6] There have been additional data to implicate nonoccupational risk factors,[7–13] as well as other etiologic agents such as zeolites,[14,15] radiation,[16,17] chronic serosal irritation,[18] and other agents.[19]

The majority of patients presenting with malignant mesothelioma are older than 40 years at diagnosis.[11,20,21] There are a few reports of childhood presentations with only 49 cases in the literature summarized by Brenner *et al.*[22] in 1981 and several subsequent case reports.[23,24] A comprehensive review of patients with presentations in the third and fourth decades of life has not been published.

We report our experience with malignant mesothelioma in ten adults presenting at age 40 years or younger and prospectively evaluated in the Department of Neoplastic Diseases, Mount Sinai Medical Center, New York, from 1974 through 1987.

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Materials and Methods

Departmental and hospital records were examined for all patients seen by one of us (A.P.C.) with a diagnosis of malignant mesothelioma of the pleura or peritoneum between the years 1974 and 1987. The charts of all patients diagnosed before reaching 41 years of age were reviewed in detail. Particular attention was directed toward exposure history with emphasis on asbestos; age at first exposure and duration of exposure, if applicable; latency period (time from first exposure to diagnosis), if applicable; duration and type of symptoms; extent of prediagnostic evaluation; method of definitive diagnosis; histopathologic subtype; treatment modalities; and, survival from diagnosis.

Results

One hundred eighty-one patients with malignant mesothelioma were seen during the 13-year period, 1974 through 1987. Nine patients including one younger than 40 years were seen in consultation only without any follow-up available. Age distribution of the remaining 172 cases is depicted in Figure 1. Ten patients (Table 1) were age 40 years or younger at diagnosis of mesothelioma. There were six cases of pleural and four cases of peritoneal mesothelioma. Six of the ten patients were women. Median age at diagnosis was 33.5 years (range, 24–40 years) for all patients; 34.5 years for pleural mesothelioma (range, 24–40 years); 30.0 years for peritoneal mesothelioma (range, 26–39 years). Women comprised four of the six cases of pleural mesothelioma and two of the four cases

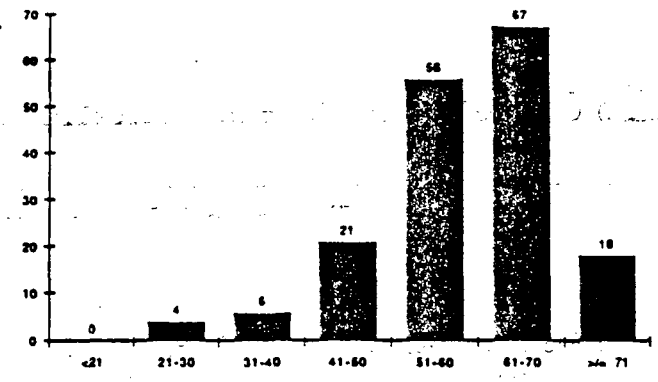

FIG. 1. Age distribution of 172 patients with malignant mesothelioma at Mount Sinai Medical Center, New York (1974–1987).

of peritoneal mesothelioma. Distribution of cell types included the following: biphasic (four), epithelial (three), and fibrosarcomatous (three).

Seven of the ten patients admitted a history of asbestos exposure whereas three (Cases 4, 7, and 8) had no such exposure documented (Table 2). Household exposure to asbestos was prominent in this age group and was present in five cases.

Case 1, an only child, was likely exposed to asbestos from age 11 to 21 years through her father who delivered the product while working for a construction firm. At the time of diagnosis, both of her parents were alive and well. Case 2, an only child, was probably exposed initially at age 6 years and for the next 4 years through his father who worked at a glass factory which also produced an asbestos product. Case 3, one of three sisters, has already been reported.[25] She was exposed to asbestos beginning at birth through her father who worked as a shipyard pipe insulator. Throughout her childhood she lived approximately 6 kilometers from the shipyard. This case is also noteworthy in that the patient's mother was diagnosed with malignant mesothelioma of the pleura at age 50 years and her father with adenocarcinoma of the lung at age 71. Her sisters had no evidence of cancer at the time of her evaluation and treatment.

Case 5 was exposed at age 6 years to asbestos dust through her brother-in-law who worked in an asbestos plant and frequently spent time after work at the patient's home in his dusty work clothing. In addition, she lived within 2 kilometers of a factory using asbestos in manufacturing for fourteen years. Case 6, one of seven children, was 10 years old when exposed to asbestos over a 12-month period through his father's dusty work clothing. His older sister died of "lung cancer" 18 years after the same exposure. Unfortunately, pathology slides of the sister could not be obtained to verify this diagnosis. There is, of course, a possibility that this also may have been a mesothelioma. Overall, five of the seven cases probably were exposed to asbestos nonoccupationally. Cases 9 and 10 each had occupational exposure to asbestos. Case 9 worked for 5 weeks at age 20 in a warehouse handling asbestos. Case 10 had worked as a school teacher for 14 years in a building later cited for asbestos.

The median age at first exposure to asbestos was 10 years for all patients (range, birth–25 years). The median duration of exposure was 120 months (range, 1.25–216 months). Case 7 denied asbestos exposure. She admitted exposure to fiberglass dust throughout childhood because her father would return home from work in clothing covered with fiberglass fibers.

The median latency period (time between probable initial asbestos exposure and diagnosis of malignant mesothelioma) was 19 years for all seven patients with asbestos exposure by history (range, 13–34 years); 13.5 years for peritoneal and 30.0 years for pleural mesothelioma.

The median interval from onset of symptoms to definitive diagnosis was 5.5 months (range, 1–13 months) for all patients; 7.5 months for pleural (range, month to thirteen months) and 4.8 months for peritoneal mesothelioma (range, 1–12 months). The clinical presentation for all patients is depicted in Table 3. Pain (five of six) or dyspnea (three of six) were the most common presenting complaints in patients with pleural mesothelioma, whereas patients with peritoneal mesothelioma had a diverse group of symptoms without a predominant presenting complaint.

The diagnostic workup in each case of malignant mesothelioma varied greatly not only in length but also in number and type of studies performed. A brief summary of each case is presented to highlight frequent delays in diagnosis.

Case Reports

Case 1: Case 1 presented to an orthopedic surgeon with back pain first noted during participation in a sporting event. Analgesics were prescribed for "muscle strain" but symptoms worsened. The patient was hospitalized elsewhere for workup 1 year after initial symptoms when a spine roentgenogram revealed marked scoliosis. A chest roentgenogram was not done at that

TABLE 1. Malignant Mesothelioma Patient Characteristics

Case no.	Age at diagnosis (yr)	Site	Sex	Histopathologic subtype
1	24	Pleural	Female	Biphasic
2	25	Pleural	Male	Epithelial
3	34	Pleural	Female	Biphasic
4	35	Pleural	Female	Fibrosarcomatous
5	36	Pleural	Female	Biphasic
6	40	Pleural	Male	Biphasic
7	26	Peritoneal	Female	Epithelial
8	27	Peritoneal	Male	Epithelial
9	33	Peritoneal	Male	Fibrosarcomatous
10	39	Peritoneal	Female	Fibrosarcomatous

TABLE 2. Asbestos Exposure

Case no.	Asbestos exposure	Method of exposure	Age of first exposure (yr)	Length of exposure (yr)	Time from first exposure to diagnosis (yr)
1	Yes	Household (father)	11	10	13
2	Yes	Household (father)	6	4	19
3	Yes	Household (father)	0	18	34
4	No				
5	Yes	Household (brother-in-law)	6	14	30
6	Yes	Household (father)	10	1	30
7	No				
8	No				
9	Yes	Occupational	20	0.1	13
10	Yes	Occupational	25	14	14

time. Myelography was unremarkable. A computerized tomographic (CT) scan of the abdomen and laparoscopy were done to evaluate a pelvic mass discovered during the hospitalization.

Laparoscopy was unremarkable but the abdominal CT scan revealed a right pleural effusion. A chest roentgenogram confirmed the effusion and suggested pleural thickening (Fig. 2). A CT scan of the thorax (Fig. 3) revealed significant volume loss in the right hemithorax with pleural effusion and pleural thickening. Thoracentesis and bronchoscopy were not diagnostic. Limited thoracotomy with pleural biopsy yielded a diagnosis of malignant mesothelioma. The patient was referred to Mount Sinai Hospital (MSH) where she underwent a right thoracotomy revealing tumor involvement of the entire parietal and portions of the visceral pleura. The extent of disease permitted only a partial decortication. A portion of lung parenchyma analyzed by electron microscopic study for mineral fiber identified tremolite asbestos. The patient was begun on chemotherapy and is alive 15 months after diagnosis.

Case 2: One month of malaise and dyspnea was the chief complaint of Case 2. Upon hospitalization, a chest roentgenogram revealed a right pleural effusion. Thoracentesis yielded class III cytologic results. Bronchoscopy and a percutaneous needle biopsy of the pleura were not diagnostic. The patient was empirically placed on antibiotics and discharged from the hospital with a chest tube in place. Two months later the patient was readmitted for a diagnostic and therapeutic thoracotomy to permit reexpansion of a "trapped lung." An extensive decortication was performed revealing malignant mesothelioma. The patient was then seen at MSH 5 months after symptom onset and began a course of experimental chemotherapy. Disease progression was noted, however, and the patient died 3 months later.

Case 3: Case 3 presented with dyspnea and chest pain. A chest roentgenogram revealed a right pleural effusion and the patient was hospitalized. Thoracentesis was not diagnostic. A limited right thoracotomy with pleural biopsy performed within 1 month of the onset of symptoms yielded the diagnosis. The patient began chemotherapy with doxorubicin, dacarbazine, and cyclophosphamide and exhibited a clinical complete response after 6 months of treatment. She received an additional 2 months of chemotherapy before treatment was stopped. Two months later

TABLE 3. Duration and Character of Initial Symptoms and Length of Survival

Case no.	Symptoms	Duration of symptoms (mo) before diagnosis	Survival (mo) from diagnosis
1	Back pain	12	15+
2	Malaise, dyspnea	3	7
3	Dyspnea, chest pain	1	17
4	Cough, chest pain	13	11
5	Subscapular pain	13	11
6	Dyspnea, chest pain, fever	2	15
7	Infertility	1	226
8	Abdominal pain, ascites	12	48
9	Anorexia, ascites, scapular pain	1.5	3
0	Weight loss, fever, night sweats	8	9

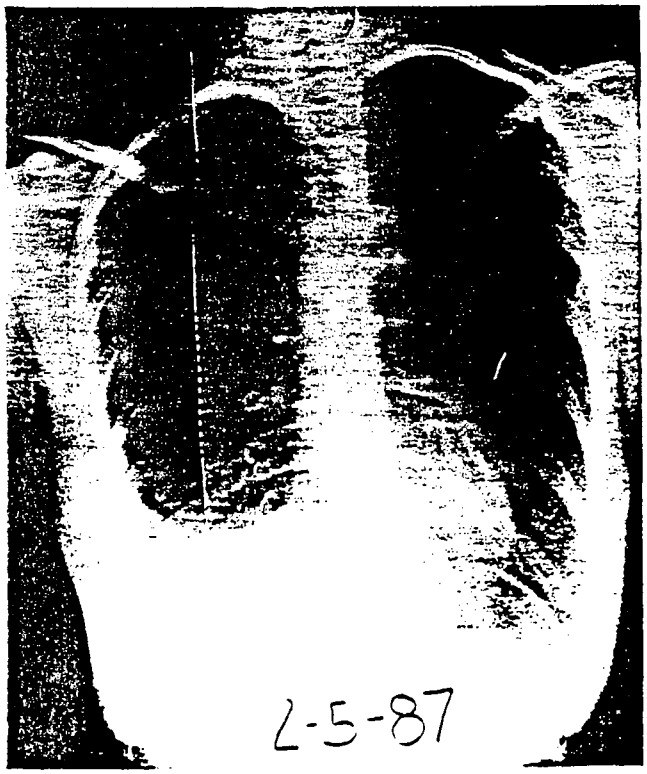

FIG. 2. Chest roentgenogram demonstrating scoliosis and right pleural effusion.

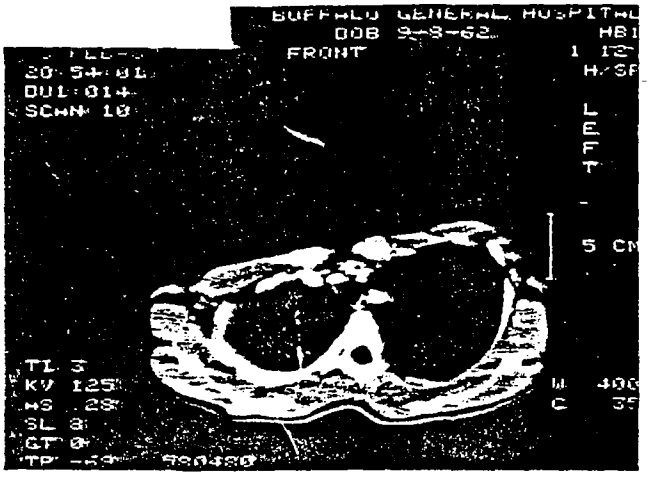

FIG. 3. Computerized tomographic scan of the thorax revealing marked volume loss of the right hemithorax, pleural effusion, and the suggestion of pleural thickening.

she recurred in the initial site of disease and was first seen at MSH. Subsequent treatment with the same chemotherapeutic agents was unsuccessful as were radiation and surgical debulking. The patient died of progressive disease 7 months after recurrence.

Case 4: Case 4 presented elsewhere with a productive cough and chest pain. A lingular lesion was noted on chest roentgenogram. Despite a history of Bacillus Calmette-Guérin (BCG) vaccination as a child, the patient was started on isoniazid and rifampin because of a positive tuberculin skin test. Three months later the lingular lesion had tripled in volume. Thoracotomy was performed with resection of the lingula and a wedge resection of the left lower lobe and adjacent pericardium. Histopathologic diagnosis was reported as malignant mesothelioma or hemangiopericytoma. Six months later the patient developed a pleural friction rub and pleural effusion. A transthoracic percutaneous needle biopsy performed at that time was interpreted as probable malignant mesothelioma. Eleven months after the onset of symptoms, the patient was seen at MSH and underwent a second thoracotomy and pleurectomy confirming the diagnosis of malignant mesothelioma.

Case 5: Case 5 developed right subscapular pain which progressed over 8 weeks to involve the entire right hemithorax. A chest roentgenogram was interpreted as "pleurisy" and steroids were prescribed. The patient's symptoms waxed and waned for 8 months when pain became acutely worse. Spine roentgenograms were unremarkable. A liver/spleen scan and intravenous pyelogram were done to rule out subdiaphragmatic etiologies and both studies were normal. The following month a repeat chest roentgenogram showed a right pleural based mass. Two months later, a thoracotomy and pleural biopsy yielded a diagnosis of malignant mesothelioma. Fourteen months after initial symptoms the patient was referred to MSH where she was treated with chemotherapy and radiotherapy with progression of disease until her death 11 months later.

Case 6: Case 6 presented with fever, dyspnea, and right pleuritic chest pain of 2 months duration. A chest roentgenogram demonstrated a pleural effusion and diffuse pleural thickening. Thoracentesis was not diagnostic. A pleural biopsy was "suspicious for mesothelioma." One month later a right thoracotomy with decortication confirmed the diagnosis. Four months after the onset of symptoms the patient was referred to MSH where he was treated with chemotherapy and radiotherapy until progression of disease resulted in his death 1 year later.

Case 7: Case 7 presented elsewhere for evaluation of infertility. She had a history of familial granular cell myoblastoma, which also affected her mother and brother, resected from her left shoulder 6 years previously and a second resection for local recurrence 2 years before presentation. A bimanual pelvic examination revealed multiple masses. Culdoscopy was unremarkable. One month later, a laparotomy with biopsy yielded the diagnosis of malignant mesothelioma.

Case 8: Over a 12-month period Case 8 developed increasing abdominal girth. Three months before presentation the patient developed right upper quadrant pain exacerbated by fatty foods. Sudden, severe abdominal pain prompted his presentation elsewhere. An abdominal roentgenogram suggested ascites which was confirmed by abdominal sonography. A paracentesis was not diagnostic as were upper gastrointestinal series, barium enema, and computerized abdominal tomogram. Results of a bone marrow aspirate and biopsy were unremarkable. An exploratory laparotomy with partial omentectomy was performed 3 weeks after presentation yielding the diagnosis of malignant mesothelioma. Fourteen months after symptom onset and, 1 month after diagnosis, the patient was seen at MSH and began chemotherapy. He developed progressive disease and died 48 months from the time of diagnosis.

Case 9: A 4-week period of anorexia, right scapular pain, and increasing abdominal girth led Case 9 to his family physician. A barium enema and upper gastrointestinal series were normal. Upon hospitalization elsewhere for further evaluation an abdominal ultrasound revealed ascites and an anterior abdominal mass. Paracentesis was not diagnostic. A liver/spleen scan was normal. An abdominal arteriogram revealed omental neovascularization "consistent with a primary omental tumor." Eleven days after admission an exploratory laparotomy with omental biopsy yielded the diagnosis. The patient was seen at MSH 1 month after diagnosis and began chemotherapy. His disease progressed rapidly and he died 2 months later.

Case 10: Case 10 developed weight loss, night sweats, and anemia over an 8-month period. Chest roentgenogram and mammography were normal. A bone marrow evaluation was remarkable only for mild plasmacytosis. A urinalysis revealed microscopic hematuria. This led to an intravenous pyelogram which demonstrated a pelvic mass. Computerized tomography of the pelvis revealed that it was 10 cm in diameter; it was gallium-avid on scan. Exploratory laparotomy performed within 1 month of presentation revealed a poorly differentiated neoplasm initially interpreted as malignant fibrous histiocytoma. Reevaluation of the slides at another institution 1 month later suggested a diagnosis of malignant mesothelioma which was subsequently confirmed at MSH. The patient was treated elsewhere with chemotherapy and radiotherapy but rapidly progressed. Upon referral to MSH 14 months after initial symptoms, she failed to respond to surgical debulking and chemotherapy and died 3 months later.

Summary of Cases

In summary, all cases of pleural mesothelioma had chest roentgenograms. Thoracentesis was performed in four cases but was not diagnostic, as was bronchoscopy in the two cases in which it was performed. Three cases underwent percutaneous pleural biopsy but in only one was the specimen suggestive of mesothelioma. No patient underwent thoracoscopy. All six cases of pleural mesothelioma ultimately required thoracotomy for diagnosis.

A wide variety of diagnostic studies were performed before laparotomy for diagnosis in peritoneal mesothelioma. In no instance was the diagnosis made without laparotomy.

Nine of ten patients have died (Table 3). Median survival from diagnosis was 13.0 months (range, 3–226 months). Case 1 is alive with residual disease 13 months after a thoracotomy and debulking procedure followed by chemotherapy and radiotherapy. Case 7 died of another cancer and is unique. Her treatment has been reported[26] but is summarized and updated here.

She was treated in 1969 with 60 mg of intraperitoneal thiotepa and abdominal strip radiotherapy at 1000 cGy per strip over a 12-week period. Procarbazine was given orally (50–100 mg per day) over a 5-month period, the first month overlapping with radiotherapy. A repeat laparotomy in August 1970 revealed persistent, unresectable mesothelioma in the cul-de-sac and right lower quadrant of the abdomen. An additional 3000 cGy of whole abdominal radiotherapy was administered over 2 months. Because of an increase in the size of masses in the posterior vaginal fornix and right lower abdominal quadrant in May 1971, doxorubicin (30 mg/m^2/day for 3 days) and bleomycin (20 mg/m^2/day for 4 days) were administered intravenously in combination for two courses followed by one course of doxorubicin alone. Local progression was noted in October 1971 and the patient was treated with methyl-CCNU (100–125 mg/m^2/day once every 6 to 8 weeks) until June 1972.

No progression of disease was evident for the next 13 years. She then developed a Clark's level IV melanoma of the left leg which was excised. Computerized abdominal tomography suggested a renal cyst but no evidence of mesothelioma. One year later a renal sonogram revealed that the right kidney mass was solid. This led to a partial nephrectomy for renal oncocytoma. Regional nodal metastases of malignant melanoma developed 3 months later. After multiple surgical resections that disease was controlled, but in 1987 (18 years after diagnosis of mesothelioma) she developed adenocarcinoma of the bladder which was rapidly fatal. This tumor was compared with the patient's mesothelioma slides and independent histologic types were confirmed.

Discussion

Mesothelioma in young adults is uncommon. Hochberg[27] noted 12.4% of 192 cases presenting at an age younger than 30 years. Elmes and Simpson[11] found only five cases younger than 40 years in a series of 327 patients (1.5%), whereas McDonald *et al.*[28] reported 22 of 165 cases (13.3%) and Brenner and associates[29] noted 20 of 123 cases (16.3%). In a review of 5778 death certificates in Great Britain listing mesothelioma as a cause of death, Jones and Thomas[30] reported 298 cases (5.2%) between the ages of 15 and 44 years at the time of death. In our series, ten of 172 cases (5.8%) were 40 years old or younger at diagnosis. The largest percentage of patients present in the sixth and seventh decades. This finding is consistent with other reports.[20,28]

The sex distribution in our series revealed a male:female ratio of 0.7:1.0. This contrasts to the male predominance in other published series of mesothelioma not age restricted in which the male:female ratio ranged from 1.8:1.0 to 5.0:1.0.[11,21,29,31] In our current updated group of 172 patients with malignant mesothelioma seen at MSH the male:female ratio is 4.0:1.0.[32] A study by McDonald *et al.*[28] has shown a male:female ratio of 0.8:1.0 for 22 patients diagnosed in the third and fourth decades of life. Additionally, Archer and Rom[33] have shown an equal sex incidence in patients younger than 45 years of age but a male predominance in older age groups.

Surprisingly, a comprehensive review of childhood mesothelioma[22] demonstrated a male:female ratio of 1.6:1.0 on a total of 49 cases approximating that seen in age unrestricted series. The difference in sex ratio rather than reflecting a difference in susceptibility to malignant mesothelioma, probably is related to different degrees of occupational exposure to asbestos.[7–13]

Although most series report a predominance of pleural over peritoneal mesothelioma,[11,21,28,31] including the review by Brenner *et al.* of childhood disease,[22] and some have suggested that peritoneal disease is associated with a more "intense" asbestos exposure history[9,11,21] our small series presents an almost equal distribution. In this regard, it may not be fortuitous that both patients with "occupational" exposure (Cases 9 and 10) presented with peritoneal disease. The intensity of exposure, however, is purely subjective and the question of whether intensity of exposure is a significant risk factor remains unanswered.[34]

Case 7 recalled household fiberglass exposure through her father for several years during childhood. In addition to asbestos exposure, peritoneal mesothelioma has been reported as a sequela of therapeutic radiation[16,35,36] thorotrast,[17] pneumoperitoneum,[37] and recurrent peritonitis.[18] To our knowledge, fiberglass has not been shown to

be a risk factor for malignant mesothelioma, although McDonald *et al.*[28] did notice that nine of 19 patients with malignant mesothelioma who did not report definite or probable asbestos exposure had been exposed to copper, nickel, rubber, or fiberglass. In a subsequent study they noted that a history of fiberglass exposure was more frequently found in cases of mesothelioma than in controls.[38] The latter study failed to show a statistically significant increase in fiberglass exposure when allowance for coincidental asbestos exposure was made. Unfortunately, we have no quantitative data detailing intensity of exposure. Of interest is the report by Hueper[39] implicating polyurethane as an inducer of experimental mesothelioma. Polymer resins are often used to cover fiberglass insulation.

The chest roentgenogram in peritoneal mesothelioma is often abnormal. Elmes and Simpson[11] showed that 13 of 27 cases demonstrated pleural plaques and/or parenchymal lesions consistent with asbestos exposure. None of our cases demonstrated these findings on chest roentgenograms or on computerized axial tomography of the chest.

The distribution of histopathologic subtypes is remarkable for the small number of epithelial tumors. This has previously been noted in children[19,22] and varies from the epithelial predominance in age-unrestricted series.[21,40]

We have previously reported that the median interval from initial symptom to diagnosis for a series of 69 patients was 2 months but 25% of patients had symptoms for greater than 6 months before diagnosis.[21] The longer symptomatic period before diagnosis in our current series probably reflects the fact that cancer and, in particular mesothelioma, is generally not considered high in the list of differential diagnostic possibilities in this age group. Another factor might be the possibility that young patients may delay seeking professional medical advice for a longer time period after initial symptoms. Clinical investigations may therefore be not only misdirected but also delayed. The diagnosis of mesothelioma is difficult and requires a high index of suspicion. An appropriate medical history with emphasis on exposure(s) is crucial. Adequate tissue must be available for diagnostic studies that include not only light microscopy[41] but also special stains[20,39] and, on occasion, electron microscopic study.[42] For these reasons, it is not unexpected that our series of cases required thoracotomy or laparotomy in all cases for definitive diagnosis. It is also not unusual that slides required review at several institutions before a definitive diagnosis of malignant mesothelioma.

The median survival of our series is in the range of most larger series. The single long-term survivor (Case 7) had progressed despite a combination of surgery, radiotherapy, and both intraperitoneal and systemic chemotherapy until a new investigational chemotherapeutic agent was used.

Few animal or human studies to date have addressed the question of whether young age at first exposure to asbestos predisposes to development of mesothelioma at a shorter latent period. Wagner[43] inoculated rats intrapleurally with asbestos fibers at either 2 or 10 months of age. Nineteen of 48 animals (39.6%) developed mesothelioma when injected at 2 months, whereas 17 of 90 (18.9%) developed mesothelioma when inoculated at 10 months.

Peto *et al.*[44] examined the influence of age at first exposure and duration of exposure to asbestos with respect to the cumulative probability of dying of malignant mesothelioma by age 80 years in 17800 asbestos workers. The youngest age group evaluated was 15 to 24 years of age at first exposure. The risk of death secondary to mesothelioma was independent of age at first exposure but clearly a function of duration of time since initial exposure.

The high incidence of likely household exposure to asbestos which occurred in five of ten cases reported here is remarkable. All of our household exposures with one exception (Case 5) were father to child. There is no way of quantifying exposure retrospectively. It has been shown that asbestos dusts can remain airborne for days before settling; epidemiologic evidence supports the concept that asbestos may promote the development of mesothelioma after only short-duration occupational exposure.[45] Similar evidence in household exposures is not available.

Host susceptibility to asbestos or other, as yet unappreciated, carcinogens may be important.[46] The finding of tremolite in Case 1 is interesting. The association of malignant pleural mesothelioma and tremolite asbestos in Greece has recently been reported.[47] Martensson *et al.*[48] reported two pairs of siblings that developed mesothelioma after asbestos exposure. One set of "identical" twins were exposed during the same time period and with the same intensity of exposure from ages 16 to 23. Within months of each other at age 42 they both developed pleural mesothelioma. Karyotypes were not reported, however. Nonrandom deletion of a segment of the short arm of chromosome 3 has recently been cited[49] as a common chromosomal abnormality in malignant mesothelioma and such studies, as well as HLA subtyping, would be useful to determine if karyotypic changes are induced by asbestos exposure or if they represent increased susceptibility to asbestos associated illnesses.

The possibility exists that in the first four decades of life mesothelioma is more common than ordinarily believed. A detailed occupational and nonoccupational history may help in suspecting this diagnosis as well as uncovering additional risk factors unrecognized previously.

The diagnosis must be considered whenever pleural or peritoneal disease of unknown etiology presents.

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