

Evaluation of Malignant Mesothelioma Patients: A Ten Years' Experience

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Abstract

We reviewed malignant pleural mesothelioma (MPM) cases diagnosed at our hospital between 1993 and 2002 with respect to age, sex, histologic type, diagnostic method, stage, and history of occupational and environmental asbestos exposure. Of 106 patients aged between 31 and 83 years (mean age 54.75 years), 28 patients (26%) were females and 78 (74%) were males. Ninety-one patients (84%) had asbestos exposure, which was found to be occupational in 14 patients (13%), environmental in 41 patients (39%) and both occupational and environmental in 36 (34%). In 15 patients (14%) no asbestos exposure was reported. Fifty-two patients (49%) were afflicted with the epithelial, 18 (17%) with the mixed, and one patient (1%) with the sarcomatous subtype of MPM. In 35 patients (33%) the histologic subtype was not clear. Diagnosis was confirmed by biopsy alone

in 43 patients (42%), by cytology alone in 5 patients (5%), by open lung biopsy in 53 (50%), by transthoracic needle aspiration biopsy in 3(2%), by skin biopsy in one patient (1%) and by mediastinotomy in one patient (1%). The majority (76%) of the patients were advanced cases at presentation. Distribution of 106 patients according to tumor stages I,II,III and IV were 9%, 15%, 54%, and 22% respectively. Pleural effusion was present in 75 patients (71%). Environmental asbestos exposure rather than occupational exposure was found to be (73% vs. 47%) a major determinant in the etiology of MPM in this group of Turkish patients.

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Introduction

Mesothelioma is a neoplasm which can originate from the mesothelial surfaces of the pleural and peritoneal cavities, the pericardium, or the tunica vaginalis. These neoplasms can be either benign or malignant. A total of 80% of all cases are pleural in origin. Malignant pleural mesothelioma (MPM) is a disease of the pleura that is locally aggressive and persistent but generally does not metastasize until late in its course. If left untreated the median survival of this aggressive tumor is 4 to 12 months (1-5). It is a rare disease and its etiology may be associated with asbestos exposure (1,6). Other possible etiologic factors include radiation exposure and, other fibers such as zeolite with physical properties similar to asbestos which amply exist in some rural areas of Turkey. Pleural thickening, genetic predisposition and a re-

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cently described simian virus 40 have also been reported to be associated with MPM (7-9). This virus was not detected in MPM samples from Turkey (10). MPM incidence appears to be increasing despite regulations on asbestos use. In the US, the total projected number of male mesothelioma cases in 2003-2004 is approximately 71 000 (4).

In this study we present a review of MPM cases diagnosed in our hospital between 1993 and 2002.

Materials and Methods

We reviewed 106 consecutive mesothelioma patients diagnosed between 1993 and 2002 at Sureyyapasa Center for Chest Diseases and Thoracic Surgery in Istanbul, a major tertiary referral chest hospital for patients covered by the state social security health insurance. These MPM cases were evaluated retrospectively with respect to age, sex, clinical presentation, histopathologic subtype, diagnostic method, performance status, stage and history of occupational and/or environmental asbestos exposure. We used the TNM staging system of the International Union Against Cancer (UICC) and the American Joint Committee on Cancer (12).

Results

Of 106 patients aged between 31 and 83-years (mean age: 54.75-years), 28 patients (26%) were females and 78 (74%) were males. Exposure to asbestos was reported in 91 patients (84%). This exposure, was found to be due to occupational hazards in 50 (47%) and to environmental hazards in 77 (73%) of the patients. In the remaining 15 patients (14%), no known asbestos exposure was defined. Sources of asbestos exposure, geographic residences and occupation of the cases are summarized in Tables 1, 2 and 3. Thirty six patients reporting both environmental and occupational exposure were all males with a significantly younger ($p < 0.003$) mean age compared to the rest of the patients with sole environmental or occupational exposure, or no known exposure (48.1 ± 8.4 years vs 55.6 ± 11.4 years).

As patients sought medical attention quite late, mean duration of presenting symptoms was 9.5 months. Chest pain, weight loss and dyspnea were the most common presenting symptoms. In 75 patients (71%) pleural effusion was present. According to UICC staging system, 10 patients (9%) were evaluated as stage I, 16 patients (15%) as stage II, 57 patients

No of patients (%)	Environmental	Occupational
14 (13%)	-	+
41 (39%)	+	-
36 (34%)*	+	+
15 (14%)	-	-
*all males		

Occupation	N:50	%
Welding	8	16
Mining	7	14
Break manufacturing	6	12
Electrical insulating	4	8
Marble work	4	8
Boiler manufacturing	3	6
Construction worker	3	6
Ship mechanic	3	6
Glass industry	2	4
Railway worker	2	4
Shipyards industry	2	4
Tire manufacturing	2	4
Fireman	1	2
Insulating other than electrical	1	2
Packaging	1	2
Petroleum mining	1	2

Province	N:77	%
Kütahya	13	17
Elazığ	10	13
Sivas	7	9
Tokat	7	9
Diyarbakır	6	7
Eskişehir	5	6
Bingöl	4	5
Çankırı	4	5
Nevşehir	4	5
Tunceli	4	5
Afyon	3	4
Balıkesir	3	4
Gümüşhane	3	4
Kastamonu	2	3
Kocaeli	2	3

(54%) as stage III and 23 patients (22%) as stage IV at presentation. Diagnosis was confirmed by open lung biopsy in 53 cases (50%). Cytology alone was diagnostic in only 5 patients (5%). Diagnosis was confirmed by pleural biopsy in 43 patients (41%). Methods used to confirm the diagnosis are given in Table 4.

Method	N: 106	%
Open lung biopsy	53	50
Pleural cytology	5	5
Pleural biopsy	43	41
TFNA biopsy	3	2
Mediastinotomy	1	1
Skin biopsy	1	1

*TFNA: Transthoracic Fine Needle Aspiration

Histologic subtypes	N	%
Epithelial	52	49
Mixed	18	17
Sarcomatous	1	1
Unknown	33	33

Seventy one patients (67%) had a histopathologic subtype diagnosis. The remaining 35 patients (33%) had insufficient evidence for typing the tumor (Table 5).

Discussion

The causal relationship of asbestos and zeolite with diffuse MPM has been shown in various studies. In some studies the frequency of such a positive relationship was reported to be as high as 85%. However, no definite relationship was found between the progression of the disease and the duration or density of the exposure (3,13). While the leading cause of MPM is asbestos exposure, there is evidence that simian virus 40 plays a role as a cocarcinogene (7-9). MPM has also been reported among family members of asbestos workers and in young adults as a consequence of environmental exposure. Baris et al. showed a high prevalence of asbestos related diseases in a large scale epidemiologic study conducted in some rural areas of Anatolia where people are exposed to asbestos environmentally (14). In our study, 91 patients (84%) reported asbestos exposure, which was either occupational and/or environmental. Thirty-six patients (34%) reported both environmental and occupational exposure.

Considering the important impact of workplace exposure, MPM is seen more frequently in men than in women and is considered as a disease of men who are 50 to 70 years in age (11). This age distribution reflects a long period of latency. In Turkey, although there are plenty of asbestos related industries such as the cement industry, the insulation/isolation industry, car break manufacturing plants, the main source of asbestos exposure seems to be environmental rather than occupational (73% vs 47%) in this series). In fifteen patients

(14%) no known asbestos exposure was defined. Of 106 patients in our series, 77 patients (73%) were found to be living in endemic areas of Anatolia such as Kutahya, Elazig, Sivas and Tokat provinces (Table 3). These patients comprised nearly half of the environmentally exposed cases. The inhabitants of endemic regions are constantly exposed to asbestos in their daily lives since white soil containing asbestos is used as an insulating material in their houses and is used even as baby powder. Thus these people start inhaling asbestos fibers from early lifetime on (14,15).

MPM related to workplace exposure is seen more commonly in men. In our study too, MPM was found to be three times more common in men compared to women (74% vs 26%). Women in this series reported environmental exposure or no known exposure. Metintas et al indicated that the risk of MPM in environmental exposure were nine times greater in women in comparison to world background incidence rates as they spend more time indoors (16). While the median age at presentation has been reported to be at least 60 years in many reports, the mean age of our patients was 54.7 years. Mean age was even lower in those reporting both environmental and occupational exposure compared to the rest of the patients (those reporting environmental or occupational exposure or no known exposure) (48.1 vs 55.6 years). This relatively younger age can be explained by the earlier lifetime exposure to asbestos and a possible shorter latency with combined exposure patterns.

Our patients seemingly sought medical attention quite late, since only one quarter of the patients were in stage I or II at presentation and the mean duration of presenting symptoms was 9.5 months.

Mostly it is the onset of signs and symptoms associated with pleural effusion or non pleuritic chest pain which induces the patients to seek medical attention. Frequency of a positive pleural fluid cytology is quite low in the literature. Percutaneous pleural biopsy has a diagnostic efficacy in only 20 to 30% of the patients. Larger tissue samples are usually required for other advanced techniques, namely, for immunocytochemistry and electron microscopy. For obtaining adequate tissue samples newer techniques such as thoracoscopy and pleuroscopy have been proposed and used successfully (17,18). Boutin et al showed thoracoscopy as a 95% accurate technique competing with open thoracotomy (17,18). In our series, 75 patients (71%) had pleural effusion and pleural biopsy was diagnostic in 43 patients (41%). The diagnosis was made by cytology alone in 5 patients (5%), due to the fact that for technical reasons, no thoracoscopic procedure was performed at our center during this period. For adequate tissue sampling, either thoracotomy or mediastinotomy were performed in 54 patients (52%). In 3 patients who were reluctant to undergo a surgical intervention, the diagnosis was confirmed by CT-guided transt-

horacic fine needle aspiration biopsy. In one pleural biopsy proven mesothelioma case, the diagnosis was reconfirmed by skin biopsy of the ipsilateral skin nodules which had developed after having a 34 months disease-free post chemotherapy survival.

Diagnosis of MPM is not easy because reactive mesothelial cells seen with pleural needle biopsy specimens and cells seen in pleura fluid cytologic studies can be difficult to distinguish from subpleural adenocarcinoma or small cell carcinoma, both of which are tumors with very different treatment options. This is a real challenge even for experienced pathologists. Today, immunohistochemical markers such as calretinin, WT-1, and cytokeratin 5/6 have become established as diagnostic markers and a soluble form of mesothelin has been reported as a serum marker for early cases of mesothelioma (19). Three histologic subtypes of mesothelioma are usually defined: epithelial, sarcomatous, and mixed (epithelial/sarcomatous). Most mesotheliomas are of the epithelial subtype and these have been associated with a better prognosis either with or without treatment (20). In our series of 106 patients, an epithelial subtype was confirmed in 52 patients (49%), a mixed type in 18 patients (17%) and a sarcomatous type in one patient (1%). In 35 cases of our series (33%) the histopathologic subtype was not clearly established. These patients were all pathologically, clinically and radiologically confirmed mesothelioma cases.

In this study, we focused on the clinicopathological presentation of the MPM cases we encountered within the last decade, rather than the treatment outcomes and prognosis. Further studies are needed to elucidate the treatment and prognostic issues in this population. We conclude that the etiology of MPM cases in Turkey can be attributed to environmental asbestos exposure in more than half of the cases. Significantly younger age of the patients with a combined exposure pattern reflects a shorter latency period of this disease in this group. Thus, priority should be given to primary prevention of early environmental asbestos exposure by the local health authorities and, to eliminate combined exposure, also to offer guidance in job selection to people living in potentially asbestos inhaling areas.

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