Malignant Pleural Mesothelioma: Evaluation of Clinical, Radiological and Histological Features in 136 Cases#

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SUMMARY

Malignant pleural mesothelioma (MPM) is a rare but fatal neoplasm which frequently results from exposure to asbestos. In this study, 136 cases with MPM were retrospectively assessed for their clinical, radiological, histological and laboratory findings. In addition, the comparison of cases coming from the regions where contact with asbestos was determined previously and those coming from the regions except for these ones was carried out. Of the cases, 59 were female and 77 were male, and male/female ratio was found to be 1.3/1. The mean age was 53.7 in women, 51.8 in men, being 52.6 in all cases. Dyspnea (26.4%), chest pain (20.5%) and cough (6.6%) were determined to be the most frequent onset symptoms. Ipsilateral pleural effusion (78.1%), diffuse pleural thickening (76.3%), volume loss (56.3%), involvement of interlobar fissure (54.5%) and were most common CT findings where as pleural effusion (75.4%) and pleural thickening (46.3%) were most common standard radiographic findings. Among laboratory findings thrombocytosis was seen in 37%, and sedimentation was found to be remarkably higher in the majority of patients especially in patients under 50 years. The diagnosis was established by percutaneous needle biopsy in 111 patients (81.6%), by cytological examination of pleural effusion in 16 (11.7%), by histopathological examination of pleural tissue specimen and rulling out benign asbestos pleurisy during follow up in 5 (3.6%), by VATS in 3 (2.2%) and by cervical lymph node biopsy in 1 (0.7%). The histological subtypes of MPM were determined in 57 cases, as epithelial in 70%, as mixed in 24.5% and as sarcomatous in 5.2%. The mean survival was found to be 12 months for epithelial, 9 months for mixed and 7 months for sarcomatous subtype. Furthermore when compared with previous studies, an increase in the number of cases was evident especially those from Ergani. Although 57% of the cases were from where they had previously direct exposure to asbestos, it was identified that 43% of the cases were from settlement areas where direct exposure to asbestos was not determined. We conclude that MPM should be considered when exudative pleural effusion is detected in a patient who had exposed to asbestos, is over 50 years' old, and presents with dyspnea and weight loss, and that further investigations should be carried out to determine other possible ethiological factors in MPM cases without a history of asbestos or erionite exposure.

Key Words: *Asbestos, malignant pleural mesothelioma.*

ÖZET

Malign Plevral Mezotelyoma: 136 Olgunun Klinik Radyolojik ve Histolojik Değerlendirilmesi

Malign plevral mezotelyoma (MPM) nadir görülen ancak fatal olan bir tümör olup sıklıkla asbest maruziyeti sonucu oluşur. Bu çalışmada 136 MPM vakası retrospektif olarak klinik, radyolojik, histolojik ve laboratuvar verileri yönünden değerlendirildi. Ayrıca önceden asbestle temasın saptandığı bölgelerden gelen olgular ile bu yerleşim birimleri dışından gelen olguların karşılaştırılması yapıldı. Olguların 59'u kadın, 77'si erkek olup E/K oranı 1.3/1 olarak saptandı. Kadınlarda 53.7, er-

keklerde 51.8 olan yaş ortalaması tüm olgularda 52.6 olarak hesaplandı. Başlangıç semptomları olarak en fazla dispne (%26.4), göğüs ağrısı (%20.5) ve öksürük (%6.6) tespit edilmiştir. Bilgisayarlı toraks tomografisi (BTT) bulguları içinde ipsilateral plevral effüzyon %78.1, diffüz plevral kalınlaşma (DPK) %76.3, volüm kaybı %56.3 ve interlober fissür tutulumu %54.5, standart akciğer radyografisinde ise plevral sıvı %75.4 ve plevral kalınlaşma (PK) %46.3 oranında en fazla sıklıkla saptanan görünümlerdi. Laboratuvar bulguları arasında trombositoz %37 olguda görülürken sedimentasyon özellikle 50 yaş altındaki hastalarda daha fazla oranda yüksek olarak bulundu. Yüzonbir hastada (%81.6) perkütan iğne biyopsisi, 16 hastada (%11.7) plevral efüzyonun sitolojik incelenmesi, 5 hastada (%3.6) plevral dokunun histopatolojik incelemesi yanında takipte selim asbest plörezisinin ekarte edilmesi, 3 hastada (%2.2) VATS ve 1 vakada (%0.7) servikal lenf bezi biyopsisi ile teşhise gidildiği saptandı. Subgrup tayini 57 olguda yapılmış ve epitelyal tip %70, mikst tip %24.5 ve sarkomatöz tip %5.2 oranında belirlenmiştir. Olgularımızda ortalama sürvey epitelyal tipte 12, mikst tipte 9 ve sarkomatöz tipte ise 7 ay olarak bulunmuştur. Ayrıca önceki çalışmalarla kıyaslandığında özellikle Ergani yerleşim bölgesinden gelen olguların sayısında belirgin bir artış saptanmıştır. Olguların yaşadıkları bölgeler araştırıldığında %57'sinin önceden asbestle temasın tespit edildiği, %43'ünün ise önceden böyle bir temasın saptanmadığı bölgelerden geldikleri belirlenmiştir. Sonuçta özellikle 50 yaş üzeri olup asbestle temasın saptandığı bölgelerden dispne, zayıflama gibi şikayetlerle başvuran olgularda eksudatif vasıfta plevral efüzyon saptandığında ayırıcı teşhiste MPM'nin de düşünülmesi gerektiği, asbest veya erionit temasının saptanmadığı olgularda diğer muhtemel etyolojik faktörleri ortaya çıkarmak için ileri çalışmalar yapılması gerektiği kanaatine vardık.

Anahtar Kelimeler: *Asbest, malign plevral mezotelyoma.*

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Asbestos which is composed of fibrous silicates has been widely used in various industrial areas being most frequent in cement production, for the last century (1-4). Diameter and length of its fibers, exposure dosage and time, and the ability of the body to degrade it effects its pathogenic specialities.

The association between asbestos exposure and the development of MPM is well recognised (3,5-10). There are many asbestos deposits in some rural parts of central and eastern Anatolia (11). Our region is one of the place in Turkey that has the high incidence of malignant mesothelioma. Direct contact with asbestos of patients was defined in some borough of Diyarbakır (Çermik, Çüngüş, Ergani), Elazığ (Maden) and Şanlıurfa (Siverek) by Yazıcıoğlu et al. These investigators had also detected that serpantine and amphibole (tremolite) asbestos, as well as talc, all of which have no economic value, were also present in above mentioned places (4,12). The type of asbestos found in most of this region is either tremolite or chrysolite asbestos. The material containing asbestos is quarried from the mountains by the male population both for local use and for sale elsewhere. It is used as a whitewash for the walls and floors of the houses. The application is usually done by women who grind the material to a powder and suspend it in water. The process is repeated each year. Consequently householders are repeatedly exposed from an early age, and this exposure can be described as both environmental and occupational but not industrial (4).

MPM is one of the major health problems facing Turkey today (11). This tumor is uncommon and a primary tumor originates from the mesothelial cells located in anatomic spaces (1,13-17). Its incidence is 1.2-2/million per year. It is 300 times greater in asbestos workers than the general population (5). A little exposure for a short period of time is sometimes a considerable risk for mesothelioma (1,6). There are three distinct histologic patterns of malignant mesothelioma: epithelial, sarcomatous and mixed (6,13,18,19). It is sometimes hard to differentiate this tumor from metastatic adenocarcinomas, pleural plaques, benign inflammatory fibrosis of the pleura, localised mesothelioma and reactive mesothelial hyperplasia (1,6,13). In this condition, histochemical studies are helpful (16,18).

Closed pleural needle biopsy (CPNB) is valuable diagnostic procedure which has a low risk of complication (20). Video-assisted thoracoscopy

(VATS) should be applied when cytologic and histopathologic examination are insufficient for diagnosis (1,21). There is no standard therapy method for this disease (17). Chemotherapy, radiotherapy or surgery has no valuable effect on survival when applied alone (22,23). The median survival of patients with MPM is approximately 12 months (3,8,13,16,24). Respiratory insufficiency and pneumonia are the most frequent reasons of mortality (23).

In this study concerning a large number of mesothelioma cases, we aimed to detect the symptoms and patients' features, to determine histologic, radiographic, laboratory findings, and places where these cases come from, especially where enviromental asbestos exposure have not been reported to exist.

MATERIALS and METHODS

Clinical, radiographic, and histologic findings and survival in 144 patients with MPM who were examined at the Dicle University hospital between 1990 and 1996, were studied retrospectively. Eight cases were excluded from the study because the tissue consisted of badly crushed needle biopsy specimens that were thought to be inadequate for diagnosis.

Clinical information, included age, sex, birthplace, implantation metastases, history of occupational and environmental exposure to mineral fibers or chemicals, duration and character of symptoms, and clinical findings at presentation, were extracted from the patient records. Thrombocytes count and erythrocyte sedimentation rate were examined.

Findings of standard chest radiography which is supplied during hospitalisation were compared to those of CT (If present). The diagnostic methods were evaluated. Pleural biopsies were obtained by a Ramel needle. The pathologic diagnosis was made on the basis of ordinary tissue sections stained with hematoxylin and eosin. In some cases, different immunohistochemical stains were used to determine histologic subtypes.

VATS was applied when cytological examination of the pleural effusion or histopathological examination of the pleural biopsy specimen was insufficient for diagnosis. The contribution of other invasive or non-invasive methods to diagnosis was also evaluated.

All cases were investigated for asbestos exposure. Asbestos exposure was noted as positive for who lived or had lived in places where direct asbestos exposure were known to exist. This exposure was investigated by asking if the asbestos containing soil, which is known as white wash among public, was used, and by showing a sample of this soil to who hadn't been aware of it. The cases who were from where asbestos exposure were not known were grouped as "asbestos non-exposed cases". Asbestos exposure was especially investigated in this group. Cases who are from where enviromental asbestos exposure haven't been detected previously and who experienced asbestos containg soil, were investigated in detail and classified. Subgroup determination was carried out, if possible.

Bronchoscopy was performed if adenocarcinoma and MPM discrimination couldn't be sufficient during histopathological examination. The survival of followed cases was also examined. Subgroups, clinical features and laboratory findings which may effect the survival were investigated in detail.

The results were evaluated by student's t test.

RESULTS

Of the 136 patients, 77 (56.6%) were men and 59 (43.4%) were women. The ages of the women ranged from 21 to 74 years (mean, 53.7 years). The ages of the men ranged from 25 to 76 (mean, 51.8 years). The male-females ratios were 1.3/1. The mean ages were 52.6 for all patients. The tumor was right-sided in 80 patients (58.8%), left-sided in 48 patients (35.2%), and bilateral in 8 (5.8%). Encapsulated effusion was detected in 5 of the cases with effusion.

Shortness of breath (26.4%), chest pain (20.5%), and cough (6.6%) were the most common presenting symptoms. Signs compatible with pleural effusion were detected in the majority of cases (95 percent). Volume loss of the affected hemithorax and tenderness on the chest wall were detected 55% and 31.6%, respectively.

Furthermore clubbing (7.5%) and peripheric lymphadenopaty (5.1%) were noted as interesting findings.

The characteristic of pleural effusion had been recorded in 127, being serous in 77 (60.6%), serosanguineous in 35 (27.5%) and hemorrhagic in 15 (11.8%). The mean interval between the onset of symptoms and the diagnosis was found to be 141 days.

Methods of diagnosis of 136 patients are reviewed in Table 1.

As can be seen above, histopathological examination had revealed only mesothelioma in 5 cases. These case were accepted as MPM because increase in the pleural effusion and development of pleural mass were detected during follow up these cases who are considered to have benign asbestos pleurisy or MPM. Cytological examination had been carried out in all patients who have pleural effusion. The diagnosis was established by cytologic examination in 16 of them whose pleural biopsy specimen were insufficient, but subgroup determination couldn't be possible. Because of nondiagnostic or indeterminate results of samples taken by closed pleural biopsies, the diagnosis was established by VATS in three patients. The diagnosis was established by cervical lymph node biopsy in 1 case.

We detected implantation metastases at the entrance of the biopsy needle on thoracic wall in 1 case 5 months after thoracentesis, in 5 cases 4 months after closed thoracal drainage, in 4 cases 7 months after CPNB and 1 case 3 months after VATS.

As laboratory findings, thrombocytosis was present in 37% of cases. Erythrocyte sedimentation rate was increased in 100% of men and in 94% of women both of who were younger than 50 years. In patients older than 50 years, these ratios were 76% for men and 70% for women.

Total 132 cytologic examination were carried out in all cases. Cytologic examination was dignostic in 15.9% of cases while inflammation process were reported in 51.5%.

Total 198 CPNB were performed to our cases. The results are shown in Table 2.

Our cases per year are shown in Table 3.

The most common findings detected in the standard chest radiography performed during hospitalisation were pleural effusion (75.7%), pleural thickening (46.3%), and volume loss of the hemithorax (34.5%). Involvement of interlobar fissure and mediastinal pleura were found to be 10.1% and 22%, retrospectively.

The CT examination of the thorax was performed on 55 patients. The most common CT findings were ipsilateral pleural effusion (78.1%), diffuse pleural thickening (DPT) (76.3%), volume loss at affected hemithorax (56.3%), interlobar fissure involvement (54.5%), and mediastinal pleural involvement (52.7%). Furthermore, penetration of the lung parenchyma was detected to be 9%.

We detected at the end of evaluation that 7.3% of cases had no pleural effusion and 3.6% had no significant pleural thickening.

Table 1. Diagnostic methods applied to 136 patients with MPM.

Diagnostic method	No of patients	%
Percutenous pleural biopsy	111	81.6
Cytology of pleural fluid	16	11.7
Reported as just mesothelioma by		
Histopatological examination	5	3.6
VATS	3	2.2
Servical lymph node biopsy	1	0.7
Total	136	100

Table 2. Results of pleural biopsies of our cases (198 procedures).

Results	No of biopsies	%
MPM	111	56
Mesothelioma	5	2.5
Chronic pleuritis	27	13.6
Insufficient specimen	16	8
Fibrinous pleuritis	13	6.5
Fibromuscular adipous tissue	13	6.5
Malignant cells (no type detection)	12	6
Tuberculosis	1	0.5
Total	198	100

Table 3. Our cases per year.

Year	No of cases	%
1990	11	8
1991	17	12.5
1992	18	13.2
1993	28	20.5
1994	30	22
1995	24	17.6
1996 (Until May)	8	5.8
Total	136	100

Twentythree cases had been subjected to bronchoscopy. Four cases had findings of chronic bronchitis and 1 had endobronchial tumor. Another one showed narrowing of the lumen due to external pressure.

With the use of defined criteria and ordinary tissue stains, the 57 cases were classified into the following histologic subtypes: purely epithelial, 40 cases (70%); mixed, 14 cases (24.5%); and sarcomatous, 3 cases (5.2%).

57% of our cases were detected to come from where environmental asbestos exposure was known to exist while 43% were from where no such an exposure was previously known to exist. Distribution of the cases who are from where enviromental asbestos exposure was known to exist, is as follows: 24 cases (22.4%) were from Ergani, 13 cases (12.1%) from Siverek; 11 cases (10.2%) from Çermik; 10 cases (9.3%) from Maden and 3 cases (2.8%) from Çüngüş. Cases who are from Ergani constitutes the 33.9% of total. These and the cases who are probably from where asbestos containg soil is used although asbestostos exposure had not been reported previously, are shown in Table 4.

Table 4. Regional distribution of all cases according to asbestos exposure.

Region	n= 136	%
Known asbestos exposure	78	57
No asbestos exposure	46	34
Probably asbestos exposure	12	9

Cases from regions where asbestos exposure probably exists, were detected to come from Egil and Dicle districts of Diyarbakır, Arıcak district of Elazıg, Genc and cenral districts of Bingol, and Adıyaman province.

Therapeautic approaches could be detected in 109 cases: 13 had surgical treatment (10 cases were subjected to decortication and 3 to extrapleural pneumonectomy while 96 had been treated by only pleurodesis. Mean survival was found to be 10 months in 104 who could been followed up.

DISCUSSION

Male/female ratio of our cases were 1.3/1. Adams et al. had reported male cases to be 77% and female case to be 23% of total (13). This ratio had been reported to be 2.15/1 by Brenner et al. and 4/1 by Sridhar et al (9,14). Males were more effected in those studies because the exposure is mainly occupational and male workers were mainly effected. The reason why women were found to suffer from MPM more then men in this study when compared to previous studies, may be that they are much more exposed to asbestos in processing soil, and afterwards. Women take part in digging, transport and processing (for use in plastering and white-washing) of asbestos containg soil more than men. Furthermore, because of the socioal status of the region, they spend more time in houses than men

thus being longer and more exposed to asbestos which is used as a plastering and white-washing material. Since only a few men who are ocuupied in digging and transport of the asbestos containg soil, are exposed during these processes, others are exposed during their stay at houses rather than during those processes. Women repeat white-washing of their houses with asbestos containg soil every year, thus exposing themselves continuosly to this hazardous material.

On the basis of the data our cases were investigated and documented according to where they are from. In contrast Çermik which was the first places where most of the cases from in previous studies, is now the third.

We detected that nearly 43% of our cases were from where direct asbestos exposure was not known previously. The cities of Batman, Mardin, and Şanlıurfa constitute the majority of these patients. It was reported by Balcı et al. that 12 cases (75%) out of 16 were coming from where direct asbestos exposure was not known previously, 1 case was from city of Siirt and 2 were from city of Batman (25). In this small series only 2 cases were from Ergani constituting 12.5% of total, and 16.6% of the cases who were from where direct exposure to asbestos has already been known. In our series we detected these ratios 22.4% and 39.3% respectively. Asbestos containg soil is thougt to be (probably) used in many villages of Egil and Dicle districts of Diyarbakır, of Arıcak district of Elazıg (like Simselmkis), of Genc and central districts of Bingol, and of central district of Adıyaman. That's why we think that regions -especially the ones mentioned above- where enviromental asbestos exposure had not been detected previously should be investigated especially for asbestos and asbestiform minerals in order to find the etiology of the disease.

In our cases the mean symptomatic time before the diagnosis was detected to be 141 days (7 days-18 months). Brenner et al. had reported this time to be 90 day (14).

We detected thrombocytosis in 37% of our cases. Adams et al. had reported thrombocytosis as the poor prognosis sign (6), whereas Manzini et al. had reported this finding to be 56% (26). We found mean survival 20% less in cases with thrombocytosis than it was in cases with normal thrombocyte count. Erythrocyte sedimentation rate in all male patients less than 50 years of age was detected to be high.

11.7% of our cases has been diagnosed only cytological studies. MPM cases diagnosed by cytological examination are 11.7% of total. Manzini et al. had reported 4% cytological and 96% histopathological diagnosis (26). For MPM accuracy of cytological examination is reported be 0-64% but generally is low (21). An interesting point is the report of inflammatory process in 51.5%. If MPM is suspected by clinical and radiological findings, and cytological examination of pleural fluid reveals inflammatory process and if clinical findings are not compatible with infection, other diagnostic procedures should be performed.

Because MPM has various microscopic appearances and most pathologists encounter few cases in a lifetime, the diagnosis is considered difficult (13). The diagnosis of MPM by light microscopy is difficult so immunohistochemical examination is needed for most of the cases (13,24). Another problem for diagnosis is that differentiation, cell type and structural properties differ from one to the other. That's why lots of biopsy specimen are needed (21). The diagnosis is made by microscopic examination of tissue. The value of CPNB is variable. Diagnostic value were reported to be 40-60% by experts (1). Gelder et al. reported the diagnostic accuracy to be 68% by using Abrams needle biopsy (19). As shown in Table 1, the diagnosis established by histopathological examination of the needle biopsy specimen at our cases was 81.6%. One case had been reported to be tuberculosis and was given antituberculous regimen. Since he had no use of that regimen CPNB was repeated 2 months later and MPM was diagnosed. In 34.6% of cases, however some insufficient results had been reported such as chronic pleuritis or fibrinous pleuritis. An interesting point was that only mesothelioma had been reported in 2.5% of the cases and that malignant cells had been detected in 6%. In summary the define

diagnosis of MPM could be established in 56% of cases by CPNB without any other more invasive procedures such as VATS or thoracoscopy.

It is important to note that thoracentesis, needle biopsy, tube thoracostomy for drainage, thoracoscopy, and thoracotomy for diagnosis in MPM are complicated by implantation metastases in the needle tract, the biopsy site, or the surgical incision in nearly one-third of patients and in this situation mean interval between the procedure and the time when nodules become significant had been reported to be 6 (1-13) months (16,21). Adams et al. had showed the spread of the tumor to the biopsy site in 1 case out of 52 who were subjected to biopsy (13). We detected implantation metastases in 11 of our cases. None of these cases had prophylactic radiotherapy after the procedure. That's why we think that radiotherapy should be applied to chest wall after these kind of procedures.

Pleural effusion could not be detected in 7.3% of our cases. Manzini et al. had reported absence of pleural effusion as 19% (26). That's why MPM should be also considered in elder patients who had been exposed to asbestos, if pleural thickening or mass was detected though effusion is absent.

With bronchoscopy, 1 case was showed endobronchial tumor while another one was showed narrowing of the lumen due to external pressure. Medial enlargement of the tumor is the main cause of bronchial obstruction (13). We think that bronchoscopy is valuable to differentiate MPM from pulmonary adenocarcinoma especially in whom the diagnosis could not been established by closed pleural biopsy, although it has no diagnostic value if MPM had not caused an endobronchial lesion.

Though CT is superior to standard chest radiographs in the evaluation of the extension of the lesions, there is not any patognomonic CT findings for MPM (27). The earliest CT findings of MPM are atelectasia and pleural thickening together with involvement of interlobar fissures (6,28). Involvement of interlobar fissures were reported to be as 86% by Selçuk et al., and as 66.7% by Bilici et al. (11,29). We found it to be 54.5%. The tumor generally spreads locally and rarely penetrates into lung parenchyma (29). We detected parenchymal penetration in 9% of our cases.

Involvement of the mediastinal pleura and the interlobar fissure are detected by CT rather than standard chest radiography (11). We determined that lots of lesions, especially involvement of interlobar fissure and the mediastinum, are hidden especially in cases who have massive pleural effusion. For example we detected involvement of interlobar fissure in 54.2% of our cases by CT and in 10.1% by standard graph. Adams et al. had reported that pleural thickening was invisible because pleural effusion (13). Diffuse pleural thickening was found to be 46.3% by standard chest radiography and to be 76.3% by CT in our cases.

Pleural effusions is sometimes the only findings without significant mass or thickening (16). Leung et al. had reported pleural effusion to be 7.6% as the only finding of neoplastic pleural involvement (27). We diagnosed MPM at a rate of 3.6% without significant pleural thickening. That's why MPM should not be definitely excluded in older patients especially who had exposed to asbestos and had had pleural effusion without pleural thickening or mass.

Subtypes had been previously reported as follows: Epithelial 25-81%, mixed 0-66% and sarcomatous 4-32% (19). Subtypes detected in our cases are compatible with this figures. It had been reported that the bigger tissue specimen from the tumor, the higher chance of detection of mixed type (1,20). In a study mixed type had been found to be 36% in little biopsy specimens whereas it had been detected to be 63% in cases who had been subjected to thoracotomy or thoracoscopy (19). Two cases who were considered to have epithelial type by CPNB, were subjected to VATS for definitive diagnosis and for staging and both of them found to have epithelial type MPM. VATS can be suggested in order to obtain larger tissue specimen if surgical treatment is considered.

The major spread of this tumor is by local invasion. Distant hematogenous metastases are rare

and usually appear at late stages of the disease (14). Adams et al. had reported abdominal metastasis in 3, brain metastasis in 2, and brachial plexus, chest wall, vertebrae, axilla and inguinal involvement each in 1 in out of 92. Furthermore by autopsy they found a brain metastasis which has not been realised before, in a sarcomatous mesothelioma case (13). We could not see regular examination for metastasis detection in advanced stage cases. But we detected hepatic metastasis in sarcomatous type MPM cases and peritoneal mesothelioma with MPM in other two. A secondary malignant tumor (metachronous tumor) may be present with MPM. For example Sridhar et al. had detected secondary tumors independent from MPM such as cancer of urinary bladder, colon cancer, low grade lymphoma. This condition is present in men rather than women (30). We detected a benign neurinoma in a male patient in our group.

Treatment is generally unsatisfactory, and long-term survival is generally not attained (1,8,14,26,31). The most common cause of death are respiratory failure and pneumonia. Furthermore intestinal obstruction due to direct diaphragmatic spread is present in 1/3 of patients. Death may also result from complications due to pericardial and myocardial involvement (23). The median survival of patients with MPM is approximately 12 months (3,8,13,14,16,24). But some clinical and pathological findings such as epithelial type, female sex, being younger than 60, dyspnea as the single symptom, unilateral involvement of the left side are associated with better prognosis although they are present in a short time. Miller et al. had reported that there may be some surprising events although the mean survival is 6 months and that 1 of their cases is still alive for 5 years with persistent pleural effusion 8. Therapeautic approaches could be detected in 109 cases: 13 had surgical treatment (10 cases were subjected to decortication and 3 to extrapleural pneumonectomy while 96 had been treated by only pleurodesis. We could follow-up of 104 cases and detected mean survival to be 10 months (12 months for epithelial type, 9 months for mixed and 7 months for sarcomatous type). There was no significant difference in the mean survivals of surgically treated cases and of cases who had been subjected to pleurodesis (10.7 months in surgery group versus 9.6 in pleurodesis group). ($p > 0.05$). We could follow a female patient who has epithelial type MPM and subjected to pleurodesis with tetracycline, for only 3 years but she did not come for control after then. Another female patient with MPM had peritoneal mesothelioma after followed up 4 years without any treatment but she died 5 months after. Fifteen patients were being followed until May-1996 and the mean follow up is 6 months.

We concluded that:

1. Standard chest radiography is very important found the detection of the disease, but CT especially plays an important role in detection of parenchymal and pleural changes due to asbestos exposure, and follow up (progress) of these lesions. Furthermore CT is valuable in staging and determining the appropriate therapy.

2. The pleural biopsy is the most useful diagnostic tool for the tissue diagnosis of MPM. VATS can be performed if diagnosis cannot be established by CPNB. CPNB should be the first to be considered in the diagnostic process because VATS is more expensive and invasive, requires general anaesthesia and may cause complications due to anaesthesia. But if surgery is considered, VATS should be applied for staging.

3. Ratio of the cases who are from regions where enviromental asbestos exposure had not been known to exist, is 43% and it is constituted in part by cases who defines usage of probably asbestos containing soil. These regions should be investigated for asbestos and asbestiform minerals.

4. Treatment of mesothelioma has proved disappoinsting, regardless of the modality used. Further investigations are needed to determine new chemotherapeutic agents in order to improve the poor prognosis and to increase the effectiveness of chemotherapy, and to explain the resistance of tumor cells to the agents.

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