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Analysis of patients with malignant and paramalignant pleural effusion.

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Abstract

Introduction: While the malignant cells in the fluid are available in malignant pleural effusions (MPE), in paramalignant pleural effusions (PMPE), the malignant cells do not exist. We aimed to compare the results of patients with MPE and PMPE.
Materials and methods: 134 patients (MPE: 106 PMPE: 28) were analysed retrospectively. Patients were divided into 2 groups as MPE, and PMPE. Results were analysed. P<0.05 was considered significant.
Results: 65 of the patients with MPE were malignant mesothelioma (MM), while 41 of them were pleural metastasis. 28 of patients were PMPE. Male gender, right localization and exudative feature were found to be significant for patients with MPE. On the other hand, pleural effusion having exudative feature was significant for patients with PMPE. MM, chondrosarcoma, lung and liver cancer were found to be more effective in the formation MPE. Mortality was higher in patients with MPE (n=4). Tube thoracostomy was found as primary treatment method in treatment of patients with MPE.
Conclusion: MPE and PMPE are caused by underlying malignant diseases. The mortality rate is higher in patients with pleural metastatic. Tube thoracostomy and pleurodesis are the primary treatment methods.

Keywords: Malignant, Paramalignant, Effusion.

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Introduction

Pleural effusion is a clinical finding which develops due to lung, pleura or a systemic disease. All pleural membrane pathologies except primary pleural mesotheliomaare caused by an abnormality of pleural membrane maintenance or its dynamic balance [1]. Pleural effusions are divided into two groups as benign and malignant pleural effusions. Malignant pleural effusions (MPE) can occur in all types of cancer. The most common causes are lung cancer, breast cancer, lymphoma and gastrointestinal cancer [2-4]. Although malignant cells are found in pleural effusions in MPE, malignant cells in effusion are not available in some cancer patients. Such effusions are called as paramalign pleural effusions (PMPE) [5]. In addition, pleural effusions are divided into two as transudative and exudative according to their biochemical properties. MPE's have exudative properties [6].

Symptoms depend on the amount of liquid accumulated in the pleural space. Fluid accumulation up to 300 ml does not usually cause symptoms. If this amount is exceeded, shortness of breath and chest pain occur. Additionally, when the amount of fluid exceeds 1000 ml, displacement in mediastinal shift and severe symptoms occur [7]. Diagnosis can be made by anamnesis, chest radiography, ultrasonography and computed tomography [8].

Observation, thoracentesis, chest tube drainage, video-assisted thoracoscopic surgery (VATS) and thoracotomy are the main treatment methods [9].

In this study, our aim is to compare the results of the patients with malignant or paramalignant pleural effusions treated with surgery in accordance with the related literature.

Materials and Methods

The files of 134 patients hospitalized with a diagnosis of pleural effusion and treated surgically between 2004-2014 were analysed retrospectively. Patients not treated with surgical procedures were excluded from the study.

Patients were divided into 2 groups as malignant (MPE) and paramalignant (MPE) pleural effusions. The presence of malignant cells being positive for patients with MPE and being negative for patients with PMPE were taken as a criterion. In addition, patients were classified as patients underwent tube thoracostomy, patients underwent VATS, and patients underwent thoracotomy. The procedure effective in grouping and producing produce results was taken into consideration. Tube thoracostomies performed before VATS or thoracotomy was excluded.

The patients' age, sex, symptoms, vital signs, laboratory findings (leukocyte (WBC), hemoglobin (HB), hematocrit (HTC), sedimentation, total protein (TP), albumin (ALB), transudate, exudate) comorbid disease, disease location (the

place where surgical procedures were performed was taken into account in patients with bilateral effusions), diagnostic procedures, surgical procedures, complications, length of stay, mortality and morbidity were examined. The significance of gender, localization, type of concomitant diseases, and treatment methods in patients with MPE and PMPE were evaluated.

Statistical analysis

Data were analyzed by Statistical Package for the Social Sciences (SPSS 21, Chicago, IL, USA). The numerical and categorical data were expressed as mean ± standard deviation and percentage, respectively. Kolmogorov-Smirnov and Shapiro-Wilk tests were used as tests of normality for continuous variables. Mann-Whitney U test was used for determining the relationship between two groups. Non-parametric binominal test was used for comparison of two groups rates. P<0.05 was considered significant.

Results

Between January 2004 and December 2014, it was found that a total of 345 patients with pleural effusion underwent surgical intervention. Additionally, the rate of MPE and PMPE patients underwent surgical intervention was found to be 2.57 (39%). 106 patients (79%) were MPE, whereas 28 (21%) were PMPE.

65 of the patients with malignant pleural effusion (61%) were malignant mesothelioma (epithelial types: 38, sarcomatoid types: 12, mixed: 12), while 41 (39%) had the pleural metastasis.

In patients with malignant pleural effusion (n=106), the mean age was 54.13 ± 4.71. Seventy one (67%) were male and 35 (33%) were female. In 63 patients (59%), effusion was on the right, while in 43 patients (41%), it was on the left. 99 of the effusions were exudative (93%), whereas 7 (7%) were transudative. Male gender (p=0.0001<0.05), right localization (p=0.0091<0.05) were found to be significant in patients with MPE (Table 1).

Table 1. *Distribution of patients with pleural effusion.*

Effusion	Male	Female	P*	Right	Left	P*
MPE	71	35	<0.001	63	43	0.0091
PMPE	18	10	0.0615	16	12	0.4229

PMPE: Paramalignant pleural Effusion; MPE: Malignant pleural Effusion; P*-Non-parametric Binominal test

The mean age of the patients with paramalignant pleural effusion (n=28) was 54.53 ± 5.62. Eighteen (64%) were male and 10 (36%) were female. Effusion was on the right in 16 patients (57%), while it was on the left in 12 patients (43%). All of the effusion was exudative. In patients with PMPE, Male gender (p=0.0615>0.05) and localization (p=0.4229>0.05) were not found to be significant in patients with PMPE (Table 1).

Comorbid malignancies in patients with MPE were malignant mesothelioma (n=65, 100%), lung ca (n=11, 78.58%), breast ca (n: 10, 55.56%), liver ca (n=6, 85.71%), chondrosarcoma (n=4, 100%), osteosarcoma (n=3, 100%), larynx ca (n=2, 40%), pancreas ca (n=2, 28.57%), surrenal ca (n=2, 28.57%), and colon ca (n=1, 100%) (Table 2).

Comorbid malignancies in PMPE were breast ca (n=8, 44.44%), pancreatic ca (n=5, 71.43%), surrenal ca (n=5, 71.43%), lung ca (n=3, 21.42%), prostate ca (n=3, 100%), larynx ca (n=3, 21.42%), and liver ca (n=1, 14.29%) (Table 2).

Table 2. *Distribution of malignant and paramalignant pleural effusion.*

Concomitant malignancy	Total	PMPE N (%)	MPE N (%)	P*
Malignant mesothelioma	65	-	65 (100)	0.001
Lung cancer	14	3 (21.42)	11(78.58)	0.0081
Breast cancer	18	8 (44.44)	10 (55.56)	0.7385
Laryngeal cancer	5	3 (60)	2 (40)	1
Chondrosarcoma	4	-	4 (100)	0.0339
Osteosarcoma	3	-	3 (100)	0.1025
Pancreatic cancer	7	5 (71.43)	2 (28.57)	0.285
Adrenal cancer	7	5 (71.43)	2 (28.57)	0.285
Liver cancer	7	1 (14.29)	6 (85.71)	0.2416
Colon cancer	1	-	1 (100)	1
Prostate cancer	3	3 (100)	-	0.1025

PMPE: Paramalignant Pleural Effusion, **MPE:** Malignant Pleural Effusion, **P*:** Non-parametric Binominal test, **N:** Number

The most common comorbid malignancies in patients with MPE were malignant mesothelioma, lung ca, breast ca and liver ca, whereas the most commonly encountered comorbid malignancies in patients with PMPE were breast, pancreatic, surrenal, and lung ca. Moreover, mesothelioma, lung cancer and chondrosarcoma were found to be significantly effective in MPE development (respectively, P=0.001-0.0081-0.0339<0.05) (Table 2).

In laboratory studies of patients, decrease in the number of WBC was found to be significant in patients with MPE (p=0.001<0.05), but reduction in the level of HTC and total protein were found to be significant in patients with PMPE (respectively, p=0.001-0.001<0.05) (Table 3).

The most common symptoms of patients were shortness of breath, chest pain and cough. Other symptoms were fatigue, fever, nausea, vomiting and palpitation. While the first diagnostic method used in patients was chest radiography, computed chest tomography and ultrasonography were the other methods.

Table 3. *Laboratory findings of patients with pleural effusion.*

Parameters	MPE(106)	PMPE(28)	P*
Leukocyte (10^3/mcgL) (mean ± SD)	4966 ± 19.1	5325 ± 22.1	0.001
Hemoglobin(g/dL) (mean ± SD)	10.08 ± 12.1	9.5 ± 10.8	0.8181
Hematocrit (%) (mean ± SD)	32.52 ± 3.5	29.57 ± 3.1	0.001
ESR(mm/h)(mean ± SD)	43.55 ± 15	46.25 ± 13	0.3861
Total protein (g/dL) (mean ± SD)	5.85 ± 0.18	5.6 ± 0.25	0.001
Albumin (g/dL) (mean ± SD)	2.95 ± 0.17	2.9 ± 0.14	0.1545

PMPE: Paramalignant Pleural Effusion; MPE: Malignant Pleural Effusion; ESR: Erythrocyte Sedimentation Rate; P*: Mann-Whitney U test

In the treatment of patients, a total of 88 (66%) underwent tube thoracostomy under local anesthesia, and under general anesthesia, eleven (8%) underwent thoracotomy, 35 (26%) underwent VATS. 73 (69%) of the patients with MPE underwent tube thoracostomy, 11 (10%) underwent thoracotomy and 22 (21%) had VATS. On the other hand, 15 (54%) of the patients with PMPE underwent tube thoracostomy, and 13 (46%) had VATS. In the treatment of patients with MPE, tube thoracostomy (under local anesthesia) was found to be much more effective than thoracotomy or VATS (under general anesthesia) (P=0.001<0.05) (Table 4).

Table 4. *Treatments of patients with malignant and paramalignant.*

Effusion	Local anesth.	General anesth**	P*
MPE	73	33	<0.001
PMPE	15	13	0.7894

PMPE: Paramalignant Pleural Effusion; MPE: Malignant Pleural Effusion; P*: Non-parametric Binominal test; Anesth: Anesthesia

General anesth**: Thoracotomy (MPE: 11, PMPE: 0) or VATS (MPE: 22, PMPE: 13)

Thoracotomy indications in patients with MPE were expansion defect in 3 (3%) patients and empyema in 8 (8%) patients. VATS indications in patients with MPE were expansion defect in 2 (2%) patients and loculated fluid collection in 20 (19%) patients. It was seen that enucleation of empyema and decortication were applied through thoracotomy, and drainage of loculated collections, partial decortication and abrasion were applied by VATS.

Video-assisted thoracoscopic surgery indications for patients with PMPE were the presence of loculated collections in 5 (18%) patients, for both diagnosis and treatment in 8 (29%) patients.

The most common problems of patients were expansion defects, prolonged air leak and atelectasis. Mortality rate of our study was 2.98% (n=4). Two patients with MPE (50%) died due to lung cancer, 1 (25%) died because of larynx and 1 (25%) died due to surrenal cancer. The average length of stay for patients was 7 ± 4 days.

Discussion

Pleural effusion is the accumulation of fluid between parietal and visceral pleural due to the imbalance between pleural fluid formation and reabsorption. Although it is seen equally in both genders, gender distribution may vary depending on the etiological factors. It was reported that 2/3 of malignant pleural effusions related to breast ca and gynecologic causes were more common in females, and effusions related to mm and pancreatitis were more common in males [2]. In our study, the number of male patients with pleural effusion was higher, and male gender was found to be significant especially in patients with MPE.

Mihmanlı et al. [10] reported that effusions concomitant of malignant disease are more common in males over 50. In our study, the mean age of the patients was consistent with the literature.

Pleural effusions are divided into two groups as transudates and exudates. Pleural fluids being exudative or transudative vary depending on the underlying disease [11]. In our study, exudates were dominant in patients with both MPE and PMPE.

It was reported that the most common causes of malignant pleural effusions were lung cancer, malignant mesothelioma and breast cancer. The most common causes for females were breast, gynecologic, and lung cancer. On the other hand, for males, the most common causes were lung, lymphoma, and gastrointestinal cancer [1]. The most common cause of MPE for our patients was malignant mesothelioma, and the most common reason of PMPE was breast cancer. The reason why malignant mesothelioma was higher might be that the incidence of asbestos exposure was common in our region.

Pleural effusion develops only in 60% of patients with pleural metastasis. It has been reported that the reasons why malignant pleural effusions develop are tumor embolisms to visceral pleura, direct invasion from cancerous tissue, hematogenous metastasis to the parietal pleura, lymphatic blockage due to mediastinal lymph node invasion. In such cases, treatment is planned according to etiology, prognosis and condition of the patient [2,3,12]. In our study, pleural metastasis rate was 39%. Furthermore; lung cancer and chondrosarcoma were found to be significantly effective in MPE development.

Malignant mesothelioma is a common primary pleural tumor seen especially in males in 5 and 7 decades. It is divided into 3 as epithelial, sarcomatoid and mixed. The most common type is epithelial, while the least one is sarkomatiod. It often causes one-sided pleural effusion and thickening. Diagnosis is made by biopsy of the pleura. In treatment, surgery, radiotherapy and chemotherapy may be used separately or in combination [13,14]. In our study, there is pleural effusion in all patients with malignant mesothelioma and malignant mesothelioma was found to be significantly effective in MPE.

The most common symptom in pleural effusion is dyspnea. Cough is slight and nonproductive. Chest pain may be sharp or blunt type. Pain increases with deep inspiration. Weight loss, fever, and hemoptysis may be encountered [7,11]. The most common symptoms in our patients were shortness of breath, chest pain and coughing.

In diagnosis, chest X-ray is the first imaging method for the evaluation of pleura. Ultrasonography is superior radiological methods in determining the location of the liquid. Computed tomography is usually used in displaying the parenchyma with pleural effusion, and in the evaluation of nodular mass or structure [8].

In the treatment of pleural effusion, thoracentesis, tube thoracostomy, the removal of adhesions by thoracoscopy or thoracotomy, decortication and open drainage methods are used [9]. In patients with malignant pleural effusions, it was found that surgical interventions with local anesthesia were more significant than surgeries with general anesthesia.

The presence of malignant cells in pleural fluid indicates the existence of poor prognosis, and the average survival of 4-6 months [2,12]. The rate of mortality in our study was 2.98% [n=4]. All of the patients were MPE patients with pleural metastasis.

Conclusion

Pleural effusion is a group of disease which may occur due to many reasons, can be recognized, and planned and managed according to the underlying disease. The data obtained from the effusion may vary according to the region where the underlying disease exists. Although tube thoracostomy is the primary treatment method, diagnostic and therapeutic thoracotomy and VATS may be preferable.

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