Original Article

Clinico-epidemiological profile and short-term outcomes of patients with metastatic malignant pleural effusion in Baghdad, Iraq

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Objectives: To describe the epidemiological profile of metastatic malignant pleural effusion (MPE) in patients admitted to the surgical wards at a tertiary hospital in Baghdad, Iraq.

Methodology: The study was single-center, cross-sectional, and comprised 90 successive patients who were hospitalized with MPE.

Results: Out of 90 patients, 60% were females and the age group 46 – 55 years formed the highest percentage (33.3%). We found that 97.8% had pre-existing malignancy, mainly breast cancer and 85.5% suffered non-specific generalized symptoms related to the primary malignancy. All the cases presented with shortness of breath, cough, and chest pain, and only 3.3% were asymptomatic. Pleurodesis was done in 84 patients and in the majority of them (86.7%) bleomycin was used. The majority of the pleural fluid aspirates were exudate according to Light criteria. 40% patients improved during hospitalization. Better improvement was observed among unilateral, and small MPE. Less than one-third of the cases had recurrent effusion, which was mostly in those with bilateral and secondary MPE. The survival rate was relatively good (82%). Around 6% cases were referred to oncologists.

Conclusion: Although the therapeutic approaches of MPE were mostly palliative not curative, a substantial improvement in outcome after the management of MPE was noted. Parameters that predict favorable short-term outcomes are unilateral and small pleural effusions.

Keywords: Outcomes, malignant, pleural effusion, pleurodesis.

INTRODUCTION

Pleural effusion (PE), is a very common pathological condition in which, there is an accumulation of fluid in the pleural space.[1] Annually, it is estimated that around 1.5 million patients have PE in the USA, with the majority due to congestive cardiac failure, pneumonia, and malignancies. Metastatic malignant PE (MPE) is related to very high death rates, with a life expectancy of 3-12 months, and is a common finding in metastatic tumors and progresses in 15% of patients with malignancy.[2]

Detection of malignant cells in the pleural aspirate or tissue suggests the presence of a disseminated tumor and is associated with a reduced life span. Around 50,000 in the UK and 150,000 in the USA are diagnosed with MPE yearly, with hospitalization costs exceeding five billion dollars.[3] Nevertheless; clinical or epidemiological studies on metastatic PE among Iraqis are scarce. The objective of this study was to describe the epidemiological profile of metastatic MPE in patients admitted to inpatient wards at a tertiary hospital, in Baghdad, Iraq.

METHODOLOGY

This was a single-center; cross-sectional studythat comprised 90 successive patients who were hospitalized with MPE, at Al-Imamian Al-Kadhimiyain Medical City during the first half of the year 2022. The diagnosis of PE is confirmed by ultrasound, chest X-Rays, or computed tomography (CT). Those with PE that lacked any evidence of malignancy during the initial and subsequent analyses and pleural effusion caused by any causes other than malignancies were excluded from the study.

The Ethical Committee of Al-Nahrain University approved the study protocol (Document number BMS 346/016 on 11 Dec 2022). All patients gave informed consent and entire study protocol was completed according to the principles of the Helsinki Declaration.

The number of PEs was counted by size by division of the hemithorax on CT into four quadrants by the midclavicular line into small (< 25%), moderate (25 – 50%), and large (> 50%). In suspicious cases, the small PE was designed when it was around 3cm in size and the medium > 3 – 10 cm. In cases where the pulmonary atelectasis was bounded by parenchymal fluid, this was calculated in the overall size of the PE.[4] In unconfirmed

cases (whether unilateral or bilateral); the size of the largest accumulation was considered. The PEs was not the main cause for inclusion in this study. In such instances, the diagnostic approach rests on the best medical regimen and the decision of the doctor.

The data were collected from the medical records of patients included age, gender, preexisting malignancy, the clinical presentation of either non-specific generalized symptoms related to the primary malignancy itself including fever, anorexia, weight loss, cachexia, malaise, or specific (cough, shortness of breath, and chest pain), site (right or left), diagnostic technique (cytology) or imaging (chest x-ray and CT scan), treatment modalities (pleural aspiration, chest tube, and pleurodesis), and outcomes.

Thoracocentesis that was done by standard approach and a panel of cardiovascular surgeons confirmed the diagnosis of PE and identified its causes according to international guidelines.[5] The MPE was categorized as such if neoplastic cells were identified upon pleural fluid cytology or biopsy. Those who have a negative initial cytology (exudate pleural aspirate with absent malignant cells) with high suspicion of malignancy submitted for further workup for malignancy screening investigations and only those who later revealed positive results were included. While those with benign etiologies of pleural fluid accumulation were identified using specific clinical criteria.[6]

Statistical Analysis: The data were collected and transferred to Microsoft Excel Worksheet to calculate the descriptive results.

RESULTS

Out of 90 patients, 54 (60%) were females with an age ranging from 29 to 75 years. Out of the 90 cases, 88 (97.8%) had pre-existing malignancy, mainly breast cancer (34.4%). All presented with shortness of breath.

The majority of the cases showed medium to large effusion, mainly on right side and pleurodesis was done in majority with bleomycin (Table 1).Cytological analysis of pleural aspirate revealed the presence of malignant cells (Table 2).

Of the total cases of the MPE in this study, 40% (equal

Table 1: Sociodemographic features of patients.

Variable		**Frequency**	**(%)**
Gender	Male	36	40%
	Female	54	60%
Age group (years)	25 – 35	12	13.3%
	36 – 45	12	13.3%
	46 – 55	30	33.3%
	56 – 65	18	20%
	66 – 75	18	20%
	Origin of malignant pleural effusion		
	Metastatic MPE of unknown Primary	2	2.3%
Metastatic MPE Secondary to	Breast	31	34.4%
	Bronchogenic	12	13.3 %
	Stomach	6	6.7%
	Colon	6	6.7%
	Uterus	6	6.7%
	Ovaries	6	6.7%
	Lymphoma	6	6.7%
	Small bowel	6	6.7%
	Renal cell carcinoma	4	4.4%

	Brain and spinal cord	3	3.4%
	Bony extremities	2	2.2%
Frequency of General clinical presentation			
Clinical Presentation	Generalized symptoms	77	(85.5%)
	Shortness of breath	90	(100%)
	Cough	42	(46.6%)
	Chest pain	36	(40%)
	Asymptomatic	3	(3.3%)
Imaging technique	Chest X-ray	84	(93.3%)
	Chest CT scan	90	(100%)
	Abdomen CT scan	65	(72.2%)
	Chest and abdomen CT scan	40	(44.3%)
	Other sites CT scan	7	(7.7%)
Size of MPE	Small	20	(22.2%)
	Medium	34	(37.8%)
	Large	36	(40%)
Cytology of pleural aspirate	Malignant cells on initial tests	60	(66.7%)
	Initially, no malignant cells with later positive results	30	(33.3%)
Site of involvement	Right	36	(40%)
	Left	18	(20%)
	Bilateral	36	(40%)
Frequency of treatment modalities			
Treatment	Aspiration	90	(100%)
	Chest tube	90	(100%)
	Pleurodesis with bleomycin	78	(86.7%)
	Pleurodesis with talc	6	(6.7%)
Days of admission, mean (range)		14	(10 – 27)

number of both sexes) improved during their in-hospital. Better improvement was observed among unilateral, and small MPE. Less than one-third developed recurrent PE, which was mostly among those with bilateral and the total 90 cases were referred to oncologists secondary MPE. The survival rate was relatively good among the MPE patients (82%) (Table 3).

DISCUSSION

In the current study, the ratio of female to male subjects (1.5:1) and the mean age of 63 years contrary to demographic features reported by other researchers in several studies.[7] Warnishern et al, found that males were more affected than females.[8] Zamboni et al, reported that males were 47% and females were 53% with a median age of 60 years,[9] which was similar to findings of current study.

Discordant with an earlier study,[10] breast carcinoma (34.4%) and bronchogenic carcinoma (12%) were the most frequent primary malignancies in our series. Breast cancer displayed the highest portion of the entire 90 cases, which is concordant with findings of a study involving 725 patients suspected of MPE.[11] The

difference between the two percentages could be due to the differences in the sample size of the two studies.

The clinical manifestations of MPE can range from asymptomatic to acute distressing dyspnea. We found that 85.5% cases presented with generalized non-specific symptoms that could be related to any cancer. All the studied patients suffered shortness of breath followed by cough, and chest pain, and a very small percentage was asymptomatic (3.3%). American Thoracic Society also reported a comparable finding.[12] The most imperative initial diagnostic tool for PE is standard chest radiography.[13] Chest CT scan has a superior diagnostic ability and was performed for 84 patients (93.3).

Vigilant consideration of the expected survival and quality of life is desirable when determining the optimal therapeutic modality.[10] Therapeutic thoracentesis, chemical pleurodesis (with bleomycin or talc), a pleuroperitoneal shunt, an ambulatory or indwelling catheter for pleural drainage, as well as open pleurectomy can effectively reduce dyspnea, nevertheless, not all are free from possible complications.

The technique of pleural aspiration from the pleural space needs a minimum invasive route and is based on the expected survival period. Simple one-time aspiration is a good choice for those with short expected survival life[14] and was performed in this study for all patients. Repeated pleural aspiration can be selected to relieve the symptoms of respiratory distress.[10,15] A long-term pleural indwelling catheter is analogous to talc pleurodesis in those with 6 months of expected life.[16]

Table 2: Cytology findings in a patient with malignant pleural effusion.

Characteristics	%, Count, or Range
Malignant cells on initial tests	66.7%
Malignant cells on repeated tests	33.3%
Lymphocytes % (range)	55% (3 – 110)
Erythrocytes (range)	15 – 25% (1 – 6)
Eosinophils (range)	12 – 24% (10 – 33)
Chemical Analysis	
LDH (range), U/L	25% (LDH more than 1000) 497 (112 – 479)
Protein (range), g/dl	15 – 20%, 4.4 (0.5 – 5.9)
Glucose (range), mg/dl	15 – 20%, 87.0 (72.0 – 440.0)
PH	30% (pH < 7.3)
Amylase IU/L	10% (LDH more than 100)

Table 3: Short-term outcomes of patients with malignant pleural effusion.

Outcome	Frequency (%)	Primary MPE	Secondary MPE	Unilateral MPE	Bilateral MPE	Small MPE	Large MPE
In-hospital days	14 (10–27)	17 (12–35)	21 (10–23)	12 (10–22)	19 (16–28)	11 (10–17)	26 (10–30)
Improvement	36 (40%)	2 (2.2%)	34 (37.8%)	26 (28.9%)	14 (15.6%)	27 (%)	9 (%)
Recurrence	30 (33.3%)	0	30 (33.3%)	11 (12.2%)	19 (21.1%)	4 (%)	26 (%)
Death	18 (20%)	0	18 (20%)	6 (6.7%)	12 (13.3%)	5 (%)	13 (%)
Referral to oncologist	6 (6.7%)	2 (2.2%)	4 (4.4%)	4 (4.4%)	2 (2.2%)	2 (2.2%)	4 (4.4%)

The pleurodesis acts to induce inflammation in the pleura that induces the adhesion of the two pleural layers to avoid fluid re-accumulation.[17] In the present study, bleomycin was used in 86.7% patients, whereas talc was applied only in 6.66% patients.

Felz and Neely reported in 1997 that left-sided PE is an uncommon clinical event compared with right-sided or bilateral PE,[18] which is in agreement with the findings of our study.

The overall cytology sensitivity of PE for ascertaining malignancy is around 55%,[19] however, in our cohort, it reached 66.7%, which is not far from other reports.[11,12,20] However, the sensitivity percentage reached 100% with repeated pleural aspiration. Biochemical analysis of the pleural aspirate is useful in differentiating MPE, which usually expected to be an exudate per Light criteria.[21]

In this study, majority of the pleural fluid aspirates were exudate according to Light criteria, which have an overall accuracy of around 93%.[22] The Light criteria were modified later by the "abbreviated Light criteria".[23] Light criteria can be efficiently applied to classify PE as exudates since they are linked with the higher permeability of pleural walls or the interruption of intrapleural cells, permitting ingredients of high–molecular weight to accumulate inside the pleural space. MPE is a sign of disease with advanced stage, often carrying poor prognosis, with a survival rate ranging from 1 to 12 months according to the underlying malignancy and other risk factors. Still, the study outcomes regarding outcome showed a good rate of improvement (40%), whereas lower rates of recurrence, reference to oncologists, and death.

Despite recent well-tolerated procedures to treat PE via thoracentesis, pleurodesis, or long-term tube drainage, all therapeutic techniques remain palliative. Cardiovascular surgeons should consider the general status of the patient, charge, estimated life survival, local proficiency, and available facilities while selecting appropriate techniques. Patients with an initially large volume of effusion that reaccumulates after examination should be closely monitored.

There are some limitations of this study. First, the cohort was obtained from a single tertiary center and extended over a somewhat long period during which therapeutic modalities had changed. Second, the small sample size and the retrospective study design, although the authors tried their best. Immunocytochemistry is a very useful tool to specify the primary location of MPE in case of occult primary malignancy.

CONCLUSION

In the current retrospective study, although the therapeutic approaches of MPE were mostly palliative not curative, a substantial improvement in outcome after the management of MPE was noted. Parameters that predict favorable short-term outcomes are unilateral and small pleural effusions.

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Conflict of Interest: None declared.
Rec. Date: Feb 16, 2023 Revision Rec. Date: Apr 19, 2023 Accept Date: Apr 28, 2023.

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