RESEARCH ARTICLE

Survival of Mesothelioma in a Palliative Medical Care Unit in Egypt

Noha Ibrahim, Enas Abou-Elela, Dalia Darwish*

Abstract

Background: This study was to evaluate the survival of patients with pleural and intraperitoneal malignant mesothelioma and to investigate the efficacy of chemotherapy (CT) as well as radiotherapy (RTH) and surgery compared to best supportive care (BSC). Materials and Methods: Forty patients with malignant mesothelioma (38 with pleural and 2 with intraperitoneal) were enrolled. Twenty seven patients underwent (CT) chemotherapy of which 2 also received (RTH) and surgery was only for biopsy in 15/40. Combination chemotherapy included cisplatin-gemcitabine, cisplatin-navelbine and cisplatin (or carboplatin) with premetrexed. Thirteen patients received only best supportive care. Results: A total of 12 (30%) patients were male, and 28 (70%) female. Median age was 54.0 years and the male/female ratio was 1/2.33 (P=0.210). Residential exposure played a major role in two regions, Helwan and Shoubra, in 20% and 15%, respectively. Overall mean survival time was 13.9±2.29 months. That for patients who had received best supportive care was 7.57±1.85 months, for chemotherapy was 16.5±3.20 months, and multimodality treatment regimen 27±21.0 months (P=0.028). Kaplan-Meier survival did not significantly vary for sex, residence and the pathological types epithelial, mixed and sarcomatous. The median survival for performance status and treatment modalities was significant (P=0.001 and 0.028). Best supportive care using opioids with a mean dose of 147.1 mg (range 0-1680) of morphine sulphate produced good subjective response and reasonable quality of life but did not affect survival. Conclusions: We conclude that CT prolongs survival compared to BSC in patients with malignant mesothelioma. Moreover, using escalating doses of opioids provides good pain relief and subjective responses.

Keywords: Mesothelioma - survival - quality of life - best supportive care - chemotherapy - radiotherapy

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Introduction

Malignant mesothelioma (MM) is an aggressive tumor arising from the pleural mesothelial cells. It may also arise from other serous membranes such as the peritoneum, pericardium, and tunica vaginalis (Attanoos, 2010). Mesothelioma is a cancer that is linked to environmental exposure of carcinogenic mineral fibers, especially asbestos and erionite (Philip, 2011).

Occupational asbestos exposure starts at the beginning of a worker's career and continues for 8 hours per day, 5 days per week, 46-48 weeks per year. In an asbestos-affected area, however, the environmental exposure starts at birth and continues. The concentration of the fibers varies over long and short periods (O'Reilly et al., 2007).

In Egypt, asbestos has been recognized since a long time, since ancient Egyptians used it in the mummification process. Asbestos exposure in Egypt is generally environmental and is found in certain regions (Helwan, Shoubra and surrounding areas) (Akl et al., 2010; Valerie et al., 2012).

The median survival of patients with unresectable malignant mesothelioma ranges approximately between 6-12 months. Survival is poor because there is no curative treatment (Borasio et al., 2008; Montanaro et al., 2009). Treatment options include surgery, chemotherapy and radiotherapy. Recently multimodality treatment regimens have been reported to prolong survival (Batirel et al., 2008).

In our study, we aimed to investigate the factors affecting the survival of patients with malignant mesothelioma according to clinical, radiological characteristics and treatment modalities in Egypt in a single centre study.

Materials and Methods

This retrospective study included all cases of malignant mesothelioma presenting to the palliative care unit from January 2009 to December 2011. They were diagnosed in the period between June 2005 and July 2011 in Kasr Al Aini center of Radiation Oncology and Nuclear Medicine (NEMROCK), Kasr Al Aini School of Medicine, Cairo University.

*Palliative Medicine Unit, Kasr Al-Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK), Kasr El-Aini School of Medicine, Cairo University *For correspondence: daliaomard@yahoo.com*

Statistical analysis

Data were statistically described in terms of range, mean±standard deviation (±SD), median, frequencies and percentages. Kaplan-Meier survival for different parameters was done. A probability value (P value) <0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2003 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Sciences; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

Results

In our study the total number of cases of malignant mesothelioma in the period from January 2009 to December 2011 presenting to the palliative care unit were 58. Only 40 cases had full medical data and so were the only ones included in the study. Full demographic data of the 40 cases showed that the mean age was 54 years, ranging from 27-80 years, 12 were males (30%) and 28 were females (70%), male/female ratio was 1/2.33 (Table 1).

Distribution of mesothelioma by residence

Out of the 40 cases, 15 (37.5%) cases were reported from Shoubra, followed by 8 (20%) cases from Helwan

Table 1. Demographic Features Patients with Malignant Mesothelioma

Features			No. %
Total number of patients			40 (100)
Age (years)		Mean	54
		Range	27-80
Gender		Male	12 (30)
		Female	28 (70)
Residence and asbestos exposure			
		Shoubra	15 (37.5)
		Kaliobeya	3 (7.5)
		Helwan	8 (20.0)
		Giza (south helwan)	2 (5.0)
		Others	12 (30.0)
Performance Status		1	16 (40.0)
		2	13 (32.5)
		3	11 (27.5)
Symptoms	Pain		23 (57.5)
	Dyspnea		13 (32.5)
	Cough		4 (10.0)
	Smoking history		0 (0)
	Presence of pleural effusion		20 (50.0)
Primary involvment		Pleura	38 (95.0)
		Peritoneum	2 (5.0)
Histopathological Subtype		Epithelial	23 (57.5)
		Sarcomatous	3 (7.5)
		Mixed	4 (10.0)
		Unspecified	10 (25.0)
Stage		1	38 (95.0)
		2	2 (5.0)

Table 2. Collective Radiological and Surgical Data

Item	Parameter	No. %
Radiological immaging	Pleural effusion and thickening	20 (50.0)
	pleural nodule and thickening	16 (40.0)
	Hilar lymph node and pleural mass	2 (5.0)
	Abdominal mass	2 (5.0)
Biopsy technique	Open	15 (37.5)
	C-T guided	20 (40.0)
	FNAC	5 (12.5)

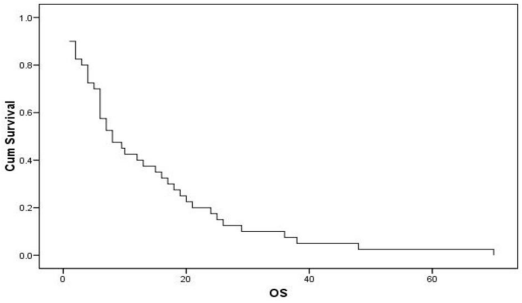

Figure 1. Kaplan-Meier Overall Survival

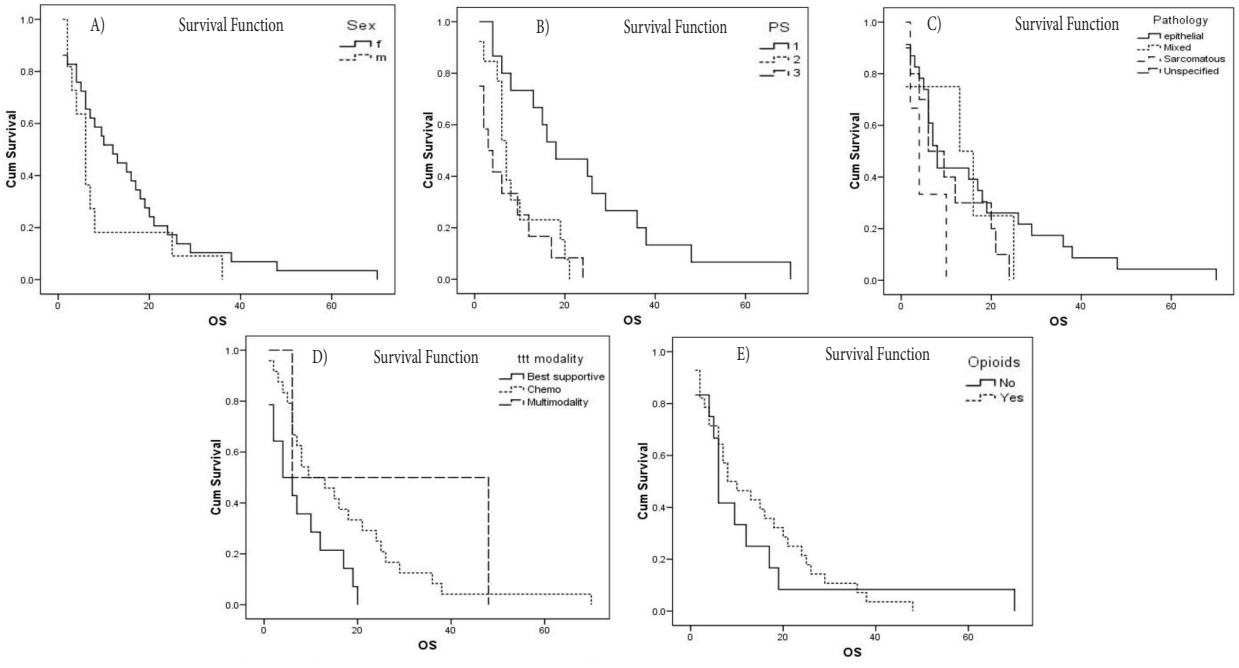

Figure 2. Kaplan-Meier Overall Survival. A) Sex, B) Performance Status, C) Pathology, D) Treatment Modlity and E) Opoids

Table 3. Median and Mean Survival of Patients

Item	No. %	Median survival (months)	Mean survival (months)	p value
Total	40 (100)	8±2.211	13.913±2.296	
Sex				0.21
Male	12 (30)	6±1.064	9.545±3.265	
Female	28 (70)	13±3.139	15.569±2.886	
Performance status				0.001
1	16 (40.0)	18±6.441	23.733±4.752	
2	13 (32.5)	7±0.702	9.007±1.845	
3	11 (27.5)	3±1.732	6.875±2.682	
Histopathology				0.276
Epithelial	23 (57.5)	8±1.189	16.522±3.658	
Sarcomatous	3 (7.5)	4±1.633	5.333±2.404	
Mixed	4 (10.0)	13±7.500	13.750±4.956	
Unspecified	10 (25.0)	6±2.899	10.550±2.648	
Treatment Modality				0.028
Best Supportive Care	13 (32.5)	4±2.494	7.571±1.845	
Chemotherapy	24 (60.0)	9.5±3.919	16.521±3.200	
Multimodality	3 (7.5)	6±2.211	27.000±21.000	
Opioids				0.632
No	12 (30.0)	13.042±5.432	13.042±5.432	
Yes	28 (70.0)	14.286±2.389	14.286±2.389	

and in the neighboring areas of both, 3 (7.5%) cases in Kaliobeya and 2 (5%) cases in Giza. Twelve cases (30%) were from other parts of Cairo (Table 1).

Radiological features The main radiological features in 50% of cases, was pleural thickening and typical finger-like projections and pleural effusion which was usually unilateral and massive; Pleural nodules were revealed in 16 (40%) cases. Two cases (5%) presented with bilateral hilar lymphadenopathy in addition to a large pleural mass. Another 2 cases (5%) presented with abdominal mass (Table 2).

Sampling techniques and histological diagnosis

Open pleural biopsy was done in 15 (37.5%) cases, fine needle aspiration cytology (FNAC) in 12.5% (5 cases), and CT-guided biopsy in 50% (20 cases). Epithelial mesothelioma representeed the most common histopathological subtype, 23 (57.5%) cases, followed by mixed in 4 cases (10%) and sarcomatoid type 3 cases (7.5%). Ten cases (25%) were unspecified.

Role of the palliative treatment

All of the 40 patients were referred to the palliative care unit. The time of referral ranged between 0-17 months with a mean of 8.3 and a median of 5.5 months. The drugs consisted of tramadol, morphine sulphate and fentanyl. The dose of morphine sulphate ranged between 0-1680 mg with a median of 60 and a mean of 147.13. Thoracocentesis was done when required. Bronchodilators, sedatives and oxygen supply were offered with proper instructions and follow up.

Treatment modalities of MM

Regarding the treatment modalities of the 40 cases, all of them were subjective to palliative treatment. Chemotherapy alone was used in 24 (60%) cases, radiotherapy was added to chemotherapy in 3 cases (7.5%) and palliative treatment was the only offered option in 13 cases (32.5%). Surgery was limited to biopsy only.

Median survival of MM patients (Kaplan-Meier)

Overall survival of 40 cases ranged from one month to 70 months; the median survival duration was 8±2.211months. Kaplan-Meier survival analysis for all the studied parameters was done. The median survival for sex was 12±3.139 months for females and 6.0±1.064 months for males. It is statistically insignificant. The median survival for histopathological type was 8±1.189 months for the epithelial type, 13±7.5 months for the mixed type and 4±1.633 months for the sarcomatoid type. These differences were statistically insignificant. The median survival for the treatment modalities was 9.5±3.919 months for chemotherapy alone, 6 months for chemoradiotherapy and 4.0±2.494 months for best supportive care. The difference is statistically significant (P=0.028). Opioids use was not associated with survival benefit (P=0.632). Performance status affected survival significantly (p=0.001) (Table 3. Figure 1 and 2A-1E)

Discussion

In the palliative unit we observed a long term survival among mesothelioma patients receiving opioids. Many of these patients were referred early and did not receive any active treatment which supported that survival depending upon the natural history of the disease.

On analyzing the data we found that most patients were living in areas affected by asbestos. In the study population, the survival was longer in patients receiving opioids but was not statistically significant. Survival increased significantly by performance status and multimodality treatment.

The median survival was 14 and 13 months in patients receiving opioids and non opioids respectively. This was not significant (P=0.632).The median survival for performance status (PS) 1 was 18 months which was significantly higher than PS 2 and 3, 7 and 4 months respectively (P=0.001).This was in accordance with many studies(Ak et al.,2009). As regard the treatment modality, the median survival was significantly higher for chemotherapy and multimodality treatment versus best supportive care, 9.5, 6, and 4 months respectively (p value 0.028) this consisted with the study done by Metinas et al. (2007) which revealed a median survival of 11.3 and 8months respectively (Metinas et al., 2007). Early referral of the patients to the palliative unit and the use of opioids improved the quality of life of patients and produced good subjective response. Residential exposure presented 70% of cases and was highly significant (P=0.0001). This is in accordance with other studies done in Egypt (Gaafar et al., 2005; Akl et al., 2010).

The male to female ratio was 1/2.33 and this was contrary to most of the studies (Abakay et al., 2011). This was due mainly to residency and not occupational exposure. Pathology in our study was not significant contrary to many studies (Christensen et al., 2008; Ak et al., 2009). The mean survival was 16 and 13 months for the epithelial and mixed versus 5months for the sarcomatous. This is explained by the small number of patients and big percent of unspecified pathology 25% which affected the results.

Restriction of asbestos is a main solution of this fatal non curable disease. This should be done through the government. Also the new generations should be encouraged to change the location of their residency. Pain relief through the use of opioids should be encouraged early and be considered as a part of treatment when needed as this provides better quality of life.

Multimodality treatment should be offered to patients with good performance status, epithelial type and early stage. Early referral to the palliative unit was associated with a better quality of life as regard pain relief and improvement of dyspnea irrespective of the treatment modality.

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