RESEARCH ARTICLE

Secondline Chemotherapy Versus Best Supportive Care in Patient with Malignant Pleural Mesothelioma: A Retrospective Study

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Abstract

Introduction: Mesothelioma is a rare neoplasm arising from mesothelial surfaces with the malignant pleural mesothelioma (MPM) as the most common form. Secondline chemotherapy in MPM is still controversial and in this study we evaluated whether it is superior to best supportive care. Materials and Methods: A total of 51 patients with MPM from Acibadem Kayseri Hospital, Kayseri Training and Research Hospital and Erciyes University were analyzed retrospectively. The patients treated with secondline chemotherapies (SLCT) were compared with those treated with best supportive care (BSC) for overall survival. Results: The median overall survival (OS) for firstline chemotherapy→SLCT and firstline chemotherapy→BSC groups were 20.3 and 14.7 months respectively (p=0.079). After firstline chemotherapy the median OS for SLCT and BSC were 5.9 and 4.7 months (p=0.355). Discussion: Although there was a trend for improvement in overall survival in patients treated with secondline chemotherapy, the difference was not statistically significant. Our results do not support the proposal that secondline chemotherapy could be effective in patients with MPM.

Keywords: Mesothelioma - survival - secondline chemotherapy - best supportive care

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Introduction

Mesothelioma is a rare neoplasm arising from mesothelial surfaces such as pleural, peritoneal and pericardial cavities and the tunica vaginalis. It was reported that asbestos exposure, radiation therapy, carbon nanoparticles, viral oncogens, fibrous silicates, growth factors and genetic predisposition may play a role in the development of mesothelioma (Bott et al., 2011; Pass et al., 2011). In some countries, the incidence of MPM was higher compared the other region. Turkey is one of those such countries and the incidence of MPM was higher in Cappadocia, a region in central Anatolian. In this region, MPM are linked to exposure to erionite that it is a mineral fiber.

Of patients with mesothelioma, approximately 80% are pleural origin. The only curative treatment modality is surgery in the treatment of malignant pleural mesothelioma (MPM). Pleurectomy, decortication and extrapleural pneumonectomy are surgical options, but curative surgery could be done in only minority of patients with MPM because the majority of patients with MPM have advanced disease at diagnosis. Therefore, many patients with MPM are candidate for palliative chemotherapy and radiotherapy. The five years overall survival rate in patients with MPM is 7.7% (Seer.cancer.gov/csr/2004_2008/results). The median overall survival was 6-9 months without in patients with advanced MPM (Remon et al., 2012). In MPM, two phase III studies were reported that the median overall survival was 11.4-12.1 months with firstline combination chemotherapy with new generation of multitargated antifolates such as pemetrexed and raltitrexed (Vogelzang et al., 2003; van Meerbeeck et al., 2005). In some countries, the incidence of MPM was higher compared the other region. Turkey is one of those countries and the incidence of MPM was higher in Cappadocia, a region in central Anatolian. In this region, MPM are linked to exposure to erionite that it is a mineral fiber (Gulmez et al., 2004; Pass et al., 2011).

In presented study, we aimed to evaluate the effect of secondline chemotherapy on the survival in patients with MPM.

Materials and Methods

A total of 51 patients with MPM from Acibadem

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Kayseri Hospital, Kayseri Training and Research Hospital and Erciyes University were analyzed retrospectively using hospital records between 2003-2012. All patients had received firstline chemotherapy (only pemetrexed or platinium+pemetrexed combination) and divided into two groups after firstline chemotherapy: the patients receiving secondline chemotherapy (SLCT) or best supportive care (BSC). Of patients 29.4% (n:15) had received secondline chemotherapy and 70.6% (n:36) had received no further chemotherapy after firstline chemotherapy. The factors such as age, sex, stage, smoking, comorbidity (yes or no), histology (epitheloid, sarcomatoid or biphasic), radical surgery (yes or no) were recorded into the Statistical Package for the Social Sciences version 16.0 (SPSS 16.0) from the medical archives retrospectively. Staging was done according to The American Joint Committee on Cancer (AJCC) Cancer Staging Manuel (7th edition). Also the date of secondline chemotherapy time and date of death were recorded in SPSS 16.0. To determine the characteristics of patients, descriptive statistics (mean, frequency analysis and crosstabs) were performed. To evaluate overall survival, Kaplan-Meier statistical methods using log rank test were used. P<0.05 was considered to be statistically significant.

Results

The clinicopathological characteristics of the patients and the differences between the groups are shown in Table 1. The mean ages of the SLCT and BSC groups were 55.9±10.1 and 61.5±7.7 years respectively (p=0.036). There was a significant difference between the groups in terms of comorbidity (p=0.015). In the SLCT group the presence of comorbidity was higher than that in the BSC group. There were no differences in terms of stage, smoking, histology and radical surgery. The usage of pemetrexed or platinum+pemetrexed combination was similar between groups in firstline setting. The median overall survival (OS) were 20.3 and 14.7 months for SLCT and BSC. After firstline chemotherapy (platinum+pemetrexed or single agent pemetrexed) the median OS were for SLCT and BSC were 5.9 and 4.7 months, respectively (p=0.355). The median OS rates were given in Table 2 and OS curves were shown in Figure 1 and 2. There was no differences regarding OS between groups (p=0.079).

Table 1. Properties of Groups

Parameters		SLCT (n:15) n (%)	BSC (n:36) n (%)	P value
Age (mean)		55.9±10.1	61.5±7.7	0.036
Sex	Male	9 (60)	19 (53)	0.637
	Female	6 (40)	17 (47)	
Stage	1	0	1 (3)	0.882
	2	3 (20)	9 (25)	
	3	5 (33)	12 (33)	
	4	6 (40)	12 (33)	
	Unknown	1 (7)	2 (6)	
Smoking	Yes	6 (40)	15 (42)	0.924
	No	6 (40)	16 (44)	
	Unknown	3 (20)	5 (14)	
Comorbidity	Yes	1 (7)	16 (44)	0.015
	No	7 (47)	10 (28)	
	Unknown	7 (47)	10 (28)	
Pathology	Epitheloid	6 (40)	10 (28)	0.589
	Sarcomatoid	0	0	
	Biphasic	1 (7)	3 (8)	
	Unknown	8 (53)	23 (64)	
Radical Surgery	Yes	3 (20)	5 (14)	0.585
	No	12 (80)	31 (86)	
Firstline chemotherapy				
	Pemetrexed	3 (20)	3 (8)	0.239
	Platinum+Pemetrexed	12 (80)	33 (92)	
Secondline chemotherapy				
	Platinum+gemcitabine	4 (26.7)	-	
	Gemcitabine	9 (60.0)	-	
	Platinum+Pemetrexed	1 (6.7)	-	
	Pemetrexed	1 (6.7)	-	

Table 2. The Overall Survival Values for SLCT and BSC Groups

Parameters	Median OS (95%CI)	P value
Firstline Chemotherapy→SLCT	20.3 (16.9-23.6)	0.079
Firstline Chemotherapy→BSC	14.7 (3.9-25.4)	
SLCT	5.9 (0.1-18)	0.355
BSC	4.7 (1.9-7.4)	

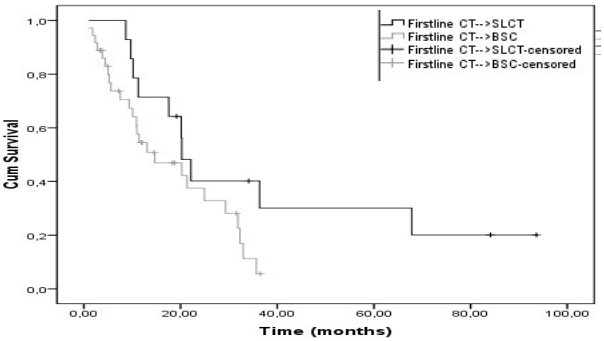

Figure 1. Overall Survival Curves

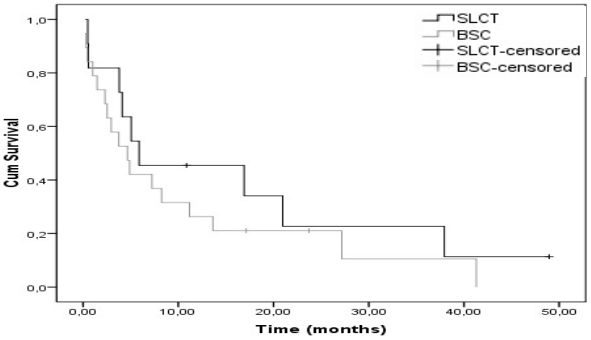

Figure 2. Overall Survival Curves After Firstline Chemotherapy

Discussion

In presented study we evaluated secondline chemotherapy in patients with MPM. We did not find a significant diffence between groups in terms of overall survival.

In MPM, it was known that chemotherapy conferred a survival benefit over best supportive care in firstline setting. Also platinum combination chemotherapy regimen is superior to single agent chemotherapy regimen (Vogelzang et al., 2003; van Meerbeeck et al., 2005). Despite of commonly usage of secondline chemotherapy

in clinical practice, it still remains controversial (Ceresoli et al., 2011). A study reported the survival advantages of secondline chemotherapy over BSC (Manegold et al., 2005). But in the other study compared secondline chemotherapy and BSC, it was not found a significant difference for overall survival (Jassem et al., 2008). In a study evaluated pemetrexed naïve patients with MPM, the median OS were 9.8 months and 8.6 months for pemetrexed and carboplatin (Sorensen et al., 2007). Generally, in most of studies, chemotherapy was able to control symptoms and prolong the time to progression (Agatsuma et al., 2010; Margery et al., 2010; Pasello et al., 2011; Tourkantonis et al., 2011).

According to our results, after firstline chemotherapy, the median OS were 5.9 and 4.7 months for SCLT and BSC, respectively. The median OS was tend to better in SLCT group but the difference was not statistically significant. Both of groups have been received pemetrexed or platinum+pemetrexed combinationin firstline setting. In SLCT group, 86.7% of patients received gemcitabine or platinum+gemcitabine combination regimen as secondline chemotherapy regimen. In BSC group, the mean age and the presence of comorbidity were significantly higher. The age of >65 years is defined a poor prognostic factor at the time of presentation (Curran et al., 1998; Edwards et al., 2000) and the presence of comorbidity is a life-threatening condition. Despite to those negative prognostics in BSC group, the median OS were similar.

The villages of Karain, Tuzkoy and Sarihidir (it was abandoned) were in Cappadocia and >50% of deaths are related to mesothelioma. The patients in this region were mostly treated at Acibadem Kayseri Hospital, Kayseri Training and Research Hospital or Erciyes University in Kayseri state. In patients in those regions, MPM were associated with erionite exposure found in the stones of house and MPM was more frequent in some families (Pass et al., 2011). In our study population, erionite exposure and genetic predisposition may be higher.

In a result, perhaps it is speculated that the effect of SCLT and BSC was similar on survival in patients with MPM with erionite exposure and genetic predisposition. In addition, in our study patients, the overall survival of them was better according to other phase III studies (Vogelzang et al., 2003; van Meerbeeck et al., 2005). The further studies included modern chemotherapeutic agents, antiangiogenic drugs and tyrosine kinase inhibitors are warranted to evaluate the effect of secondline therapy in patients with MPM.

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