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Research Article

A STUDY OF EFFICACY OF PEMETREXED BASED CHEMOTHERAPY IN ADVANCE MALIGNANT PLEURAL MESOTHELIOMA

ANKIT AGARWAL[1], RAMESH PUROHIT[2], AJAY YADAV[3], SHASHANK KOTHARI[2]*, AVI SHAH[1], ASHISH JAKHETIYA[3], RENU MISHRA[1]

[1]Department of Medical Oncology, Geetanjali Medical college, Udaipur, Rajasthan, India, [2]Department of Radiation Oncology, Geetanjali Medical College, Udaipur, Rajasthan, India, [3]Department of Surgical Oncology, Geetanjali Medical College, Udaipur, Rajasthan, India
*Corresponding author: Shashank Kothari; Email: shashankko@gmail.com

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ABSTRACT

Objectives: To study Clinicopathological profile & treatment outcomes of stage IV Malignant pleural mesothelioma (MPM) cases.

Material and methods: The data obtained retrospectively was recorded in preformed proforma. Age, gender, hometown, residence, asbestos usage history, latent period between asbestos exposure and diagnosis, symptoms, histopathological type, stage, karnofsky performance (KPS), treatment regimen, survival were all recorded. Staging was done after histopathological confirmation of diagnosis using thoracic & abdominal Computed tomography, and/or PET CT. Patients were either treated with chemotherapy or immunotherapy.

Results: 124 patients were diagnosed with MPM stage IV. Out of these 124 patients, 23 patients received only Oral metronomic chemotherapy (OMCT) due to poor Performance status (PS), 33 patients lost to follow up, 15 patients were given immunotherapy, and 53 patients were given palliative chemotherapy (pemetrexed plus carboplatin or cisplatin every 21 days until progression or intolerability). The median age at diagnosis was 63 years (41 yrs to 79 yrs). The male: female ratio was 2:1. Patients on palliative chemotherapy had response rate of 55% (29 patients out of 53 patients responded to chemotherapy). Median PFS and median OS for those patients on palliative chemotherapy was 3.9 months and 9.1 months respectively. The patients on OMCT had response rate of 27%, median PFS of 2.7 months and median OS of 6.9 months.

Conclusion: We conclude that Advanced pleural mesothelioma has overall poor survival outcomes. Palliative pemetrexed based chemotherapy has shown better survival benefits in terms of OS & PFS as compared to OMCT alone.

Keywords: Advanced pleural mesothelioma, Pemetrexed based chemotherapy, OMCT

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INTRODUCTION

Malignant mesothelioma (MM) is a rare, aggressive, lethal, and rapidly progressive malignancy of the pleura and peritoneum. Very few randomized trials are conducted on it resulting in scarce data. Joseph Lieutaud, the founder of pathologic anatomy from France was the first to mention possible malignancy of the chest wall (the pleura) in 1767 after finding two cases of pleural tumors while conducting a study on 3000 autopsies. In 1819, René-Théophile-Hyacinthe Laennec, the French physician based on his knowledge on the nature of pleural cells, suggested the origin from the pleura. Peritoneal mesothelioma was first described in 1908 by Miller and Wynn [1,2].

The incidence of mesothelioma has increased in the past two decades but is still considered a rare tumor [1,3]. The disease incidence varies geographically i.e., from <1/1,000,000 in Tunisia and Morocco, to the highest rate in Britain, Australia, and Belgium i.e., 30/1,000,000/year [3]. Currently, the incidence ranges from about 7 to 40/1,000,000 in industrialized Western nations, depending upon the amount of asbestos exposure in the past several decades [4].

The most common complaints of patients with MM are dyspnea (due to effusion) and chest pain. Pain is often expansive and obtuse on the lateral wall of the chest, generally chronic, persistent, and non-pleuritic in character [5].

There is no curative treatment for mesothelioma resulting in a poor survival rate. Recently, a randomized trial has shown some efficacy of immunotherapy in mesothelioma. Mean survival has been reported as about 6–12 months in many patient series treated with chemotherapy. Treatment modalities in use are surgery, chemotherapy, and radiotherapy. In recent years, multimodality treatment regimens have been reported to prolong survival [6].

We aimed to investigate the clinical profile and treatment outcomes of stage 4 malignant pleural mesothelioma (MPM) cases diagnosed at our center.

METHODS

Type of study
Retrospective study.

Sample size
Total 124 patients with MPM (stage 4) from January 2016 to December 2023.

The data obtained were recorded in preformed pro forma. Age, gender, hometown, residence, asbestos usage history, latent period between asbestos exposure and diagnosis, symptoms, symptom duration, diagnosis date, diagnostic method, localization, histopathological type, routine laboratory results, stage, karnofsky performance score, treatment regimen, pleurodesis, treatment response, date of death and survival time of patients were all recorded. Survival time was defined as the time between diagnosis and death, or the end of the study time if the patient was then still alive. The period between the first complaint and diagnosis was defined as symptom duration and that between the first asbestos exposure and diagnosis as the latent period. Diagnostic methods were classified as either closed pleural biopsy with ramel

needle or surgical biopsy. Hematoxylin and eosin staining was used as standard histopathological evaluation. The histological investigation was used on surgical and/or necropsy material and proven MM patients were included. Diagnosis and subtype assessment was carried out with differential immunohistochemical staining in cases where hematoxylin and eosin staining could not be done. Staging was done after histopathological confirmation of diagnosis using thoracic and abdominal computed tomography (CT), and/or positron emission tomography CT. One chest physician and two radiology physicians evaluated radiological data. Because some patients did not consent for thoracoscopy, the Butchart staging system was used, as it is widely applicable [7]. Patients were either treated with chemotherapy or immunotherapy. Some patients were also given palliative radiation for pain management. A modified response evaluation criteria in solid tumors was used to evaluate the treatment response of patients undergoing chemotherapy [8,9]. Baseline values were calculated by taking the total long diameters of measurable lesions, adding them, and comparing them with values post-chemotherapy.

Results were defined and recorded as follows

- Complete response: Disappearance of all target lesions with no evidence of tumor elsewhere
- Partial response (PR): Reduction of at least 30% in the total tumor measurement (sum of six unidimensional measurements, acquired in two positions at three separate levels on transverse cuts of CT scan)
- Progressive disease (PD): Increase of at least 20% in the total tumor measurement
- Stable response: Disease meeting the criteria of neither PR nor PD.

Data analysis

Data were analyzed for response rates, overall survival (OS), and progression-free survival (PFS) using the Kaplan-Meier curves for OS and PFS.

RESULTS

A total of 124 patients were diagnosed with MPM stage 4. Out of these 124 patients, 23 patients received only oral metronomic chemotherapy (OMCT) due to poor performance status (PS). The rest of the 101 patients were advised of palliative chemotherapy/immunotherapy. Out of these, 33 patients lost to follow-up and 68 patients were given treatment (either chemotherapy or immunotherapy depending on logistics). The baseline characteristics of the patients have been detailed in Table 1. The median age at diagnosis was 63 years (range 41 years–79 years). The male: female ratio was 2:1. Patient occupation history was also taken as mesothelioma is associated with asbestos exposure. Out of 68 patients, 15 patients were given immunotherapy, and 53 patients were given palliative chemotherapy (pemetrexed 500mg/m^2 plus carboplatin area under the curve 5 or cisplatin 75mg/m^2 every 21 days until progression or intolerability) as detailed in Table 1. The Median number of chemotherapy cycles received was 4. We report the response rate, median OS and median PFS of those patients who were given intravenous chemotherapy or OMCT.

Patients who were given palliative chemotherapy had a response rate of 55% (29 patients out of 53 patients responded to chemotherapy). Median PFS and median OS for those patients who received palliative chemotherapy were 3.9 months and 9.1 months, respectively. The patients who received OMCT had a response rate of 27%, median PFS of 2.7 months, and median OS of 6.9 months. The incidence of febrile neutropenia among those who received intravenous chemotherapy was 13% and chemotherapy-induced fatigue was 67%.

DISCUSSION

MM related to asbestos exposure is seen frequently in Southern Rajasthan. Patients present with the typical clinical features of dyspnea, weight loss, and chest pain. The etiological relationship of mesothelioma with asbestos was first identified in 1960, and the first studies into the disease in Turkey were undertaken in the early 1970s [10]. MM is a rare tumor in the normal population, only 10–22/100,000 in a year for societies in which asbestos or mineral fiber contact has never been reported [11].

Table 1: Baseline characteristics of the patients

Characteristics	% (n=124)
Age	Median age 63 years
Presenting symptoms	
1. Shortness of breath	30 (37)
2. Chest pain	15 (18)
3. SOB plus chest pain	50 (62)
4. Cough	4 (5)
5. fever	1 (2)
Sex ratio	2:1
Male	67 (83)
Female	33 (41)
Pemetrexed plus cisplatin	66 (35 out of 53 patients)
Pemetrexed plus carboplatin	34 (18 out of 53 patients)
OMCT	23 out of 124 patients
History of asbestos exposure	
Yes	72
No	28
Histology	
Epithelioid	92 (114)
Sarcomatoid	3 (3)
N/A	5 (7)

There are only a few trials from India (all are retrospective) that have reported data on survival outcomes in mesothelioma due to the rarity of this disease. One of the data reported from Tata Memorial Hospital (TMH), Mumbai had shown a median PFS and median OS of 9.7 months and 12.4 months, respectively, with palliative chemotherapy [12]. We could find only one study from India that has reported survival outcomes in stage 4 MPM. Our study has shown survival data, which is inferior to the data reported from TMH, Mumbai. This difference could be due to the difference in baseline characteristics of the study population, such as PS and number of the patients analyzed. Mesothelioma is a rare disease and it needs a properly conducted randomized trial from India to evaluate the role of immunotherapy and chemotherapy especially for advanced/metastatic disease.

CONCLUSION

We conclude that Advanced pleural mesothelioma has overall poor survival outcomes. Palliative pemetrexed based chemotherapy has shown better survival benefits in terms of OS & PFS as compared to OMCT alone. Further larger randomised trials are needed to establish role of immunotherapy and chemotherapy in advanced mesothelioma cases.

REFERENCES

1. Bridda A, Padoan I, Mencarelli R, Frego M. Peritoneal mesothelioma: A review. MedGenMed. 2007;9(2):32.
2. Bianchi C, Bianchi T. Malignant mesothelioma: Global incidence and relationship with asbestos. Ind Health. 2007;45(3):379-387.
3. Boffetta P. Epidemiology of peritoneal mesothelioma: A review. Ann Oncol. 2007;18(6):985-990.
4. De Pangher Manzini V. Malignant peritoneal mesothelioma. Tumori. 2005;91:1-5.
5. Ahmed I, Koulaouzidis A, Iqbal J, Tan WC. Malignant peritoneal mesothelioma as a rare cause of ascites: A case report. J Med Case Rep. 2008;2:121.
6. Teta MJ, Mink PJ, Lane E. US mesothelioma pattern 1973-2002: Indicators of change and insights into background rate. Eu J Cancer Prev. 2008;17:525.
7. Butchart EG, Ashcroft T, Barnsley WC, Holden MP. Pleuropneumonectomy in the management of diffuse malignant mesothelioma of the pleura. Experience with 29 patients. Thorax. 1976;31:15-24.

8. Ceresoli GL, Chiti A, Zucali PA, Cappuzzo F, De Vincenzo F, Cavina R, *et al*. Assessment of tumor response in malignant pleural mesothelioma. Cancer Treat Rev. 2007;33:533-41.
9. Yazicioglu S, Ilçayto R, Balci K, Sayli BS, Yorulmaz B. Pleural calcification, pleural mesotheliomas, and bronchial cancers caused by tremolite dust. Thorax. 1980;35:564-9.
10. Hillerdal G. Mesothelioma: Cases associated with non-occupational and low dose exposures. Occup Environ Med. 1999;56:505-13.
11. Senyiğit A, Bayram H, Babayiğit C, Topçu F, Nazaroğlu H, Bilici A, *et al*. Malignant pleural mesothelioma caused by environmental exposure to asbestos in the Southeast of Turkey: CT findings in 117 patients. Respiration. 2000;67:615-22.
12. Chanana R, Prabhash K, Noronha V, Joshi A, Patil VM, Nakti D. P2-122 Retrospective study to evaluate treatment outcomes of pleural mesothelioma treated in a tertiary care centre in India. Ann Oncol. 2018;29:vii75-6.