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A Case Series of Malignant Myelomatous Pleural Effusion with Detailed Karyotyping

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Authors' contributions

This work was carried out in collaboration among all authors. 'All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Primary myelomatous pleural effusion (PMMPE) is a rare presentation. It is diagnosed based on the presence of plasma cells in pleural fluid along with elevated Monoclonal protein. PMMPE is considered to have poor prognosis with reported survival of 4 to 6 months. This study reports 6 such cases, whose survival was better than earlier reports.

Keywords: Multiple myeloma; pleural effusion; myelomatous pleural effusion; karyotyping.

1. INTRODUCTION

Primary malignant myelomatous pleural effusion (PMMPE) is a pleural effusion in a patient with MM which occurs due to the myelomatous involvement of the pleura or of the surrounding structures which eventually invade into the pleural cavity [1]. Secondary pleural effusion in myeloma could be due to Nephrotic syndrome, Heart failure, Pneumonia and Pulmonary embolism. The diagnosis of myelomatous pleural effusion is established on the basis of presence of plasma cells and monoclonal proteins in the pleural fluid. The presence of myelomatous pleural effusion itself is a poor prognostic indicator and a rare terminal event with a

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reported median survival of 4 months. Effusions due to myeloma are rare (non infectious and non pleural based plasmacytoma related)and has been reported to be present in <1% of all myeloma cases. We present one such series of cases with focus on the prognostic markers, outcome with therapy and survival. One of the review series published so far has 64 cases and since then the search on Pubmed added few other cases [2-4].

2. METHODS

The study was conducted at tertiary care caner hospital from 2014-2019 at the department of Medical oncology. All the case records of myeloma were reviewed in retrospective nature after taking ethics committee clearance. The standard guidelines were followed for the diagnosis and work up. The diagnosis of myeloma was based on the presence of M Protein and the Ig type on SIFE(Serum Immunofixative electrophoresis), UIFE(Urine Immunofixative Electrophoresis) and with presence of plasma cells in bone marrow studies. Among these, patients with pleural effusion were subjected to diagnostic pleural fluid aspiration or pleural biopsy and were labelled as primary myelomatous Pleural Effusion based on "Demonstration of malignant myeloma cells by either cytological examination of the pleural fluid or by pleural biopsy after excluding other secondary causes" between 2012- 2018. The clinical characteristics, treatment received, and the responses were evaluated. Descriptive statistics were used to enumerate the disease and patient characters.

3. RESULTS

During this period after reviewing 286 subjects with myeloma, 6 were found to have PMMPE. All the patients received the standard of treatment as per the institutional protocl. All the patients had multiple poor prognostic factors and none of them (like beta 2-microglobulin, karyotype, Stage of disease, C-reactive protein etc.) singly or collectively predicted the survival in the present series as it is evident from the table. It was observed that most all of the subjects had normal karyotype except for one who has 13q deletion. It is also observed that all the patients had a very good response to treatment and had a better survival ranging from 3.5 years to 5.9 years compared to the reported cases so far.

Table 1. Characteristics and outcomes of the study patients

Characteristics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age/ Gender	55/F	64/M	59/M	67/M	48/F	46/M
Duration of symptoms	3 months	2 months	2.5 months	3.5 months	3 months	2.5months
M band – levels	IgG- 6 gm/dl	IgG- 6 gm/dl	IgG- 6 gm/dl	IgA- 6 gm/dl	IgG- 6 gm/dl	IgG- 6 gm/dl
Plasma cell % in pleural fluids	35%	43%	12%	28%	32%	30%
Karyotyping	Normal	13q Del	Normal	Normal	Normal	Normal
Beta 2 Microglobulin	3.6	8.4	2.1	2.2	3.4	3.8
ISS- stage	III	III	II	II	III	III
Calcium	9.8	10.5	11.2	10.4	9.6	8.9
LDH	680	454	586	1598	140	360
Hb	8.6	10.5	9.8	10.2	11.2	9.4
Creatinine	1.0	1.2	0.9	0.7	1.1	0.6
% Marrow plasma cells	45%	52%	18%	22%	38%	44%
Treatment offered	RVD	RVD	VAD	RVD	Len+Dexa	RVD
Grade III/ IV toxicities	None	None	None	None	None	None
Survival	4.6 Yr	5.2Yr	3.8yr	3.5Yr*	4.4yrs	5.9yr

4. DISCUSSION

Myelomatous pleural effusion is a rare presentation with poor survival of around 4 months. The effusion generally develops as a late complication of the disease but there have been various reports of patients presenting with pleural effusion at the time of diagnosis [3-6]. Left-sided PMMPE is more common than right side involvement and it tends to be associated more with IgA MM, which in turn is associated more with del(13) [1]. The mechanism of disease for MPE is largely unknown. Local invasion from nearby bone lesions and direct infiltration as in a pleural plasmacytoma were believed to be the possible pathways for the development of this condition, most commonly presenting in later stages of disease. Reactive plasma cells may be present in serous effusions secondary to cardiac surgery, tuberculosis, Hodgkins disease and carcinomatosis [7]. However Cytologic analysis of pleural fluid or pleural biopsy is used for confirmation of diagnosis. There is no approved recommendation for the management of MMPE. Treatment is usually initiated when myeloma is diagnosed and drugs like Bortezomib, Lenalidomide along with Dexamethasone or 2nd generation proteasome inhibitors like Carfilzomib remains the front-line treatment for Multiple Myeloma. In practice, pleural involvement with myeloma cells is associated with an aggressive course which is poorly responsive to first or second-line therapies used in conventional myeloma treatment [8-12].

5. CONCLUSION

In contrast to literature, survival in this series is better, despite presenting in advanced stage. After reviewing the literature carefully, timing of development of pleural effusion is probably the most important prognostic factor. Those with effusion at presentation had a higher survival (upto 50 months) [1] when treated with high dose chemotherapy with stem cell rescue (HDC-SR). Though pleural effusion is considered as a poor prognostic indicator but in general R-ISS (revised international staging system) is only used to determine poor prognosis. As most of the patients had normal karyotyping in this series, it did not have any impact on the survival. With the advent of RVd regimen the survivals among these patients have improved. However in patients, who developed effusion in the course of therapy, the prognosis is poor and median survival is only four months despite HDC-SR (irrespective of the initial stage). Therefore, it may be inferred from the series that effusion as presenting feature may not have a negative impact on the cancer outcomes and all these patients have standard survival if treated as per the institutional protocols.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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