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Primary Malignant Myelomatous Pleural Effusion- what we Learned from Past

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Authors' contributions

This work was carried out in collaboration among all authors. Authors PSD and AVSS contributed for the subject management and content writing and accuracy. While with author RS helped in the biostatistics and manuscript complication. All authors read and approved the final manuscript.

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ABSTRACT

Multiple myeloma forms 10% of all haematological malignancies and of these approximately 1-18% has pleural effusion at some point in their life time. The aetiology of primary malignant myelomatous pleural effusion (PMMPE) is quite varied with defined diagnostic criteria. It usually effects the middle aged males with Ig G or IgA as the dominant variant. Besides the prognostic factors used for the multiple myeloma, the morphology of the cells in effusion also matters and have to be focused. With more aggressive chemo regimens and the newer agents the median overall survival improved from 2.4 months to more than 18 months and all the subjects should be aggressively treated, wherever possible. However in patients, who develop 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)

Keywords: Myeloma; effusion; plasma cell.

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1. INTRODUCTION

Multiple myeloma forms 10% of all haematological malignancies and of these approximately 1-18% has pleural effusion at some point in their life time [1,2,3,4,5]. The reasons can be anything from:

- Infection
- Renal failure
- Nephrotic syndrome
- Cardiac failure
- Myeloma per se
- Other rare causes

When it happens at the time of diagnosis it is referred as Primary malignant myelomatous pleural effusion (PMMPE), the reasons include involvement of the pleura or of the surrounding structures which eventually invade into the pleural cavity. The diagnostic criteria should include.

1. Presence of plasma cells in pleural fluid along with
2. Elevated monoclonal protein in pleural fluid, besides the patient meeting the criteria of the myeloma.

While the prognosis was initially thought to be the very poor with median overall survival ranging from 2.4-5 months, recent reports showed that it could range as high as 19 months plus with newer agents [1,2,3,4,5]. By following a more stringent criteria (non infectious and non pleural based plasmacytoma related) only 168 cases reported till August 2018 worldwide as per the literature search [1,2,3,4,5,6]. We thought of doing a systemic study on the response rates of various regimens in this condition and like to present the best option for future studies.

2. REVIEW AND DISCUSSION

We took as many reports of cases presented in literature as possible since 1980 who were diagnosed as Multiple Myeloma based on the presence of M Protein and the Ig type on SIFE, UIFE and with presence of plasma cells in bone marrow studies and also meeting the criteria of pleural effusion as stated above.

Various agents have been used since the first presentation starting from VAD [3], VTD along with radiation [1], Thaladomide with dexamethasone [4], newer drugs such as bortezomib, lenalidomide along with dexamethasone or 2nd generation proteasome inhibitors like carfilzomib.

In practice, pleural involvement with myeloma cells is associated with an aggressive course [1,2,5,6,7,8] as reported by many and few of the reports showing contrary results [3,4].

The median age of the myelomatous pleural effusion was 50 years with male preponderance among the cases presented. The majority of these patients in the India and Asia had immunoglobin (Ig)G Kappa disease, while the MPEs from other regions associated with the presence of an IgA paraprotein (in up to 80% of cases) [9]. Almost 90% of the patents can be classified into either ISS stage III of durie salmon stage III [1,2,3,4,5,6,7,8,9]. The most common presenting features were breathlessness (100%), bone pains (86%), anemia (68%) and others are reported sporadically.

MPE presented predominant 81.8% as a unilateral effusion. Concurrent extramedullary involvement at other site was seen in 45.45% and in up to 14% patients they have concurrent myelomatous ascites.

There is a significant amount of diagnostic dilemma and to address this it is advisable to do a through examination of plueral fluid , and the tests like electrophoresis, flow shall help immensely besides the calcium levels and ADA (later ones have quite a bit of variability) [10,11,12,13,14]. In rare cases, one might have to go for more invasive tests like thoracoscopy.

The management strategies varied significantly different as reported by various authors like in the series of Yanamandra U et al, in which Six of these were managed aggressively, whereas 5 patients opted for palliation. The outcomes were dismal (90.9% mortality), with a median survival of 2.47 months [2]. While authors like Attili et al reported various regimens having responses in excess of 18 months of overall survival [3,4].

The attempts to look for the prognostic markers did not yield different results compared with other myeloma patients. Most of the patients usually have multiple poor prognostic factors and none of them (like beta 2-microglobulin, karyotype, Stage of disease, C-reactive protein etc.), which could accurately predicts the survival [4]. Mangla A et al. reported that morphology of the plasma cells also have a bearing on the prognosis of the patient where plasmablastic differentiation has been shown to be associated with poor prognosis.

Table 1. The characters of patients presenting with effusion vs developing effusion after myeloma diagnosis

	Effusion as presenting feature	Effusion during the course
Median age	5th decade	6th decade
Median stage at first diagnosis	III	II
Predominant Type	IgA	IgG
Median survival after treatment	18 months	4 months
Laterality	Unilateral	Bilateral

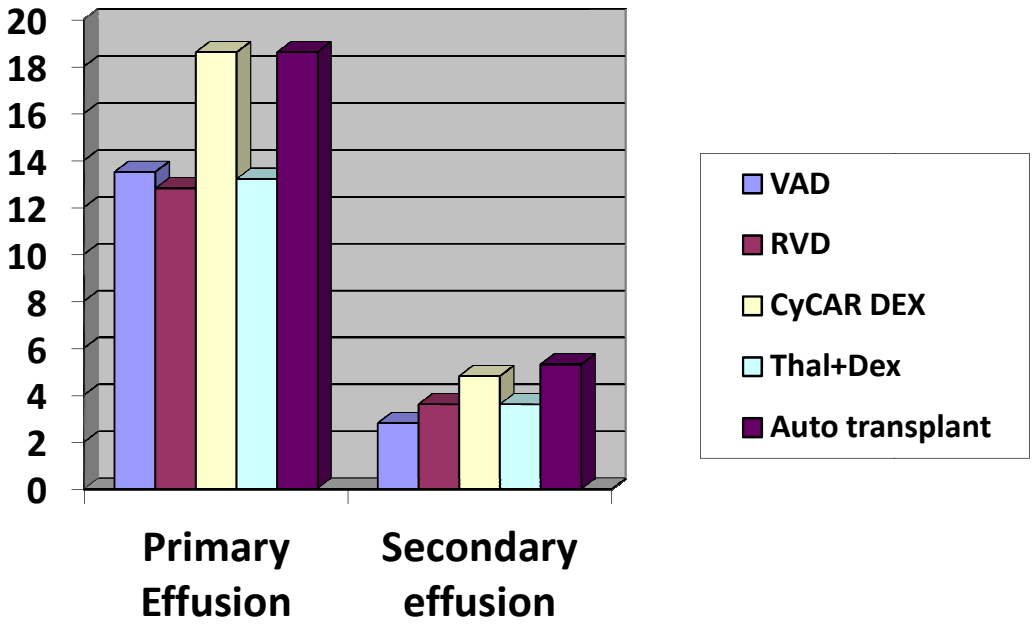

Fig. 1. The survival (in months) of various regimens complied from literature

The salient features of the differences in effusions when presented upfront vs during the later part of disease are enumerated [1-18] in Table 1.

3. CONCLUSION

The etiology of primary malignant myelomatous pleural effusion (PMMPE) is quite varied with defined diagnostic criteria. It usually effects the middle aged males with Ig G or IgA as the dominant variant. Besides the prognostic factors used for the multiple myeloma, the morphology of the cells in effusion also matters and have to be focused. With more aggressive chemo regimens and the newer agents the median overall survival improved from 2.4 months to more than 18 months and all the subjects should be aggressively treated, wherever possible. However in patients, who develop 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)

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CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal."

ETHICAL APPROVAL

"All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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