Case Report

Malignant Myelomatous Pleural Effusion with Good Response to Combination Chemotherapy

VSS Attili, VP Singh, S Sundar, H Mehta, ML Negi, A Gogia, SHK Raju, M Rai

Abstract

Malignant pleural effusion in myeloma is a rare terminal event with 91 cases reported so far. Majority of the patients survive less than 4 months. We are presenting a short series of four such cases, who had a good clinical response to combination chemotherapy. ©

Introduction

Multiple myeloma, a malignant proliferation of plasma cells, primarily affects the bone marrow and skeletal system. Occasional involvement of the extraosseous organ systems is known. Effusions due to myeloma are rare with only 91 cases reported till August 2005 worldwide.[1] Etiology of this rare terminal event is varied and can be due to anything from congestive heart failure, amyloidosis, malignant myelomatous pleural effusion, and secondary to infections or other processes.[2,3] Demonstration of malignant myeloma cells by either cytological examination of the pleural fluid or by pleural biopsy establishes the diagnosis.[4] We are reporting four such cases that were treated with Vincristine, Adriamycin, and Dexamethasone (VAD) for four cycles with or without thalidomide and all the patients survived for more than eight months which was higher compared to the literature.

Case Report

Case records of the patients with myelomatous pleural effusion presenting to the Division of hematology, Sir Sunder Lal Hospital in 2001-2003 were reviewed. The clinical characters, treatment received, and the response were evaluated. Total four patients presented with myelomatous pleural effusion in the period. The diagnosis was confirmed by cytology, measurement of the immunoglobulins in the pleural fluid or both. All the patients had effusion at initial presentation. The clinical characters of the patients are represented in Table 1.

Institute of Medical Sciences, Banaras Hindu University, Varanasi - 221 005, India.
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Discussion

Malignant myelomatous effusion is rarely reported in English literature, with Medline search yielding only 91 cases so far till august 2005. The initial estimate of this entity is 0.8% of all cases of myeloma from the Mayo clinic.[3] The commonest criteria followed in the case series are, demonstration of either malignant cells or raised immunoglobulins in the pleural fluid which is greater than that of the serum, suggesting local production of the monoclonal protein.[4] In all our patients the above criteria was met. In the present series, we did not perform a pleural biopsy as we had enough evidence to suggest that the pleural effusion was malignant myelomatous one as per the above said criteria. Ig G myeloma is more common in our series, similar to the current reported trends; as compared to the previously reported IgA predominance.[5] The pathogenesis of myelomatous effusions is unknown. Out of all the proposed mechanisms, the most attractive and widely accepted one is the one proposed by Kim *et al*.[2] In cases of myelomatous pleural effusion there is direct involvement of either pleura or chest wall which will lead to increased production of immunoglobulins. The osmotic gradient thus created will lead to pleural effusion. The same hypothesis is also supported by our findings, in majority of our cases the levels of IgG are too high which might explain in part the pathogenesis of effusion.

Multiple prognostic factors like β_2 macroglobulin, chromosomal abnormality, serum albumin and labeling index etc. were evaluated to look for the outcome. But as most of the reported cases are either small series or single case reports, none of them were studied uniformly. However, wherever studied almost all cases were in advanced stages, with multiple poor prognostic factors. As presence of effusion itself carries poor prognosis, the role of other prognostic markers in such patients cannot

Table 1 : Clinical characters of the patients

Character	Case 1	Case 2	Case 3	Case 4
Age (years)	66	69	65	63
Sex	M	F	M	M
Duration of symptoms (months)	18	17	22	15
IgG- serum/ pleural fluid (gm/dl)	5.8/6.3	7.2/8.8	9.1/ not done	8.8/9.4
Plasma cells in pleural fluid	Present	Present	Present	Present
Serum ca^{++} (mg/dl)	14.6	13.8	12.8	14.8
Creatinine (mg/dl)	3.8	2.6	2.7	2.8
Hb (gm/dl)	7.0	6.5	7.5	8.0
Skeletal survey	Multiple lytic lesions	Multiple lytic lesions	Multiple lytic lesions	Multiple lytic lesions
Stage	IIIB	IIIB	IIIB	IIIB
Treatment	VAD	VAD+ Thal	VAD+ Thal	VAD
Survival	9 months	12 months	11 months	10 months
Cause of mortality	Infection	Infection	Infection	Unknown (lost to follow up)

be defined. Therefore in the present series all the markers were not performed. Outcome of the treatment in cases of myelomatous pleural effusions is disappointing. Many modalities were used to control this condition, rarely achieving more than a partial response with survival of less than 4 months. The ultimate aim in majority of them is being symptom control.[2]

1. Radiation therapy, used by some authors to the chest in combination with systemic therapy resulted in regression in the amount of effusion but no remission of myeloma.
2. Makino *et al* used intracavitary interferon-α (given at 5 MIU dissolved in 100 ml normal saline alternate days), and the patient's effusion resolved after six treatments. Unfortunately, the patient died of myeloma about two months later, therefore this cannot be considered as standard.
3. The mainstay of therapy as of now is systemic chemotherapy.

Survival- Our experience vs. Literature

In contrast to literature, survival in our patients is definitely higher, though all of them were in advanced stage of their disease. In the review too if we closely observe, 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). 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). Therefore, timing of development of malignant effusion is probably an important prognostic marker. Thalidomide, an angiogenesis inhibitor, is one of the promising agents in the therapy of the refractory myeloma[6] that is approved by FDA. Therefore we thought of exploring this agent following therapy with VAD. Though the literature suggest a poor response to thalidomide in extraosseous myeloma,[7] to our surprise all the patients treated in that way had much superior survival compared to historical case reports. Though the number of patients is too small for any comments, owing to rarity of this condition, addition of thalidomide can be considered as potential therapeutic modality to improve survival in such patients.

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