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Original Research Article

A Prospective Understanding of the Prognostic Markers of Multiple Myeloma Disease

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Abstract

Aim: Understanding the prognostic markers of multiple myeloma disease hoping to incorporate the new therapeutic modalities to convert the disease into curable one.

Materials and methods: A total of 100 patients diagnosed as MM according to the criteria of the Chronic Leukemia-Myeloma Task Force (Committee of Chronic Leukemia-Myeloma Task Force, 1973) admitted to DMCH, Darbhanga, Laheriasarai, Bihar, India were evaluated. In each patient, factors like anemia, urea, serum calcium, percentage of plasma cells, renal insufficiency, infections, performance status, Bence-Jones proteinuria, and para-protein index are evaluated for their prognostic significance.

Results: Out of 100 enrolled patients, 56 were males and 44 were females. Four variables that had the highest correlation with the first component were creatinine, haemoglobin, performance status and paraprotein index.

Conclusion: We found that the combination of clinical performance status, serum creatinine, haemoglobin and paraprotein index allowed us to discriminate three groups of patients with different survivals. It can be a useful complementary tool for classifying patients according to prognostic factors.

Keywords: Creatinine, Paraprotein index, Myeloma, Bence-Jones proteinuria.

Introduction

Multiple myeloma is also known as Kahler disease, myelomatosis, and plasma cell myeloma. It is a malignant neoplastic disease, characterized by uncontrolled proliferation and accumulation of plasma cells in the bone marrow, which is usually connected with production of a monoclonal protein. It is the second most common hematologic malignancy. It involves the proliferation of plasma cells derived by different genetic events contributing to the development, progression, and prognosis of this disease. [1] Patients with multiple myeloma (MM) display a very heterogeneous clinical and biological course, their survival ranging from a few months to more than 5 years. [2-4]

Multiple myeloma accounts for 10% of all malignant hematologic neoplasms.[5]

Traditional prognostic factors in MM measure plasma cell proliferation (plasma cell labeling index, Ki-67), plasma cell mass (clinical stage, plasmacytosis), or the status of the patient (hemoglobin, calcium, creatinine, albumin). The most consistently powerful prognostic marker is β2-microglobulin that in one variable measures a combination of cell proliferation, cell mass, and renal function. Genetic factors are also important prognostic factors, perhaps the most important being the loss of all or part of chromosome 13 (detected either by interphase FISH or conventional cytogenetics), and hypoploidy (detected by conventional cytogenetics) [6]. The problem with some of these factors is that they are not universally available.

Several important prognostic factors identify patients with poor outcomes: serum beta$_2$-microglobulin (β_2M), bone marrow plasma cell labeling index (PCLI), cytogenetics, plasmablastic morphology, lactate dehydrogenase (LDH), and C-reactive protein (CRP). [7, 8] Some factors such as cytogenetics appear to have particular value in patients undergoing stem cell transplantation. [9] Others such as the plasma cell labeling index (PCLI) have yielded consistent results but are not readily available at most centers. Combinations of independent prognostic factors provide more information than any one factor alone. Factors like demographic, clinical and laboratory factors were evaluated for their prognostic significance which can be really helpful universally.

Materials and methods:

A total of 100 patients diagnosed as MM according to the criteria of the Chronic Leukemia-Myeloma Task Force (Committee of Chronic Leukemia-Myeloma Task Force, 1973) admitted to DMCH, Darbhanga, Laheriasarai, Bihar, India

Methodology

In each patient the following clinical and laboratory characteristics documented at diagnosis as well as subsequent details of response to therapy were evaluated for their prognostic significance: anemia, urea, serum calcium, percentage of plasma cells, renal insufficiency, infections, performance status, Bence-Jones proteinuria, and para-protein index. Performance status was assessed by Karnofsky scaling system. Renal impairment was assessed by creatinitine clearance levels. These prognostic factors were based on an earlier study done by J.F. San Miguel et al [10], where all these parameters had significant adverse effects on survival.

Results

Out of 100 enrolled patients, 56 were males and 44 were females. The analysis showed that the four variables that had the highest correlation with the first component were creatinine, haemoglobin, performance status, and paraprotein index.

Table 1:

Factors		No. of cases	Survival in Months	P value
Anemia	≤8.5 g/dl	19	16.8	0.045
	>8.5 g/dl	81	28.5	
Urea	≤40 mg/dl	32	34.1	0.002
	>40 mg/dl	68	19.4	
Serum calcium	≤10 mg/dl	63	25.5	0.018
	>10 mg/dl	37	21.9	
% Plasma cell	≤40%	59	29.2	0.01
	>40%	41	19.2	
	Cr. ≤ 2 mg/dl	73	27.5	0.0001

Renal insufficiency	Cr. > 2 mg/dl	27	14.8	
Infections	Yes	31	18.8	0.048
	No	69	27.3	
Performance status	≤70	64	19.7	0.001
	>70	36	47.4	
Bence-Jones proteinuria	Yes	55	20.7	0.05
	No	45	31.5	
Paraprotein index	≤0.09	39	18.9	0.0028
	>0.09	61	28.0	

Discussion

Traditional prognostic factors in multiple myeloma measure plasma cell proliferation (plasma cell labeling index, Ki-67), plasma cell mass (clinical stage, plasmacytosis), or the status of the patient (hemoglobin, calcium, creatinine, albumin). The most consistently powerful prognostic marker is β2-microglobulin that in one variable measures a combination of cell proliferation, cell mass and renal function. There is an excellent correlation between serum β_2M levels and myeloma tumor burden. [11] Among patients with newly diagnosed myeloma treated with standard-dose chemotherapy, presence of cytogenetic abnormalities has prognostic value. [12] With the use of multiparameter flow cytometry, or by using the slide-based immunofluorescence method (similar to that described for the PCLI), these myeloma cells can be easily detected and quantified in patients with multiple myelom [13].

Studies have shown the prognostic value of lactate dehydrogenase (LDH) in myeloma, but because only a small proportion of patients have increased levels, its usefulness is limited.31 In some patients, high levels of serum LDH have been associated with an aggressive, lymphoma-like presentation of the disease. [14] Most malignant neoplasms depend on angiogenesis to sustain proliferation. [15] To ensure adequate blood supply, tumor cells release various cytokines to induce microvessel proliferation. Induction of tumor angiogenesis leads to increased metastatic potential and has been shown to be of prognostic value in several tumors. [16] Mutations in the *ras* oncogene have been noted in plasma cells of myeloma, more commonly in the advanced phase of the disease. [17]

In this study, we have analyzed prognostic factors based on patients' clinical and laboratory parameters to check their significance as prognostic factors for multiple myeloma. Hansen &Galton (1985) have reviewed the prognostic factors with significance for survival in myelomatosis [3]; of them the only important one that does not appear in our study is serum albumin concentration. Recently, some new parameters, such as thymidine kinase (Simonsson et al., 1985) [18], T-cell subsets (San Miguel et al., 1985) [19], plasma cell morphology (Greipp et al., 1985) [20], plasma cell antigens (Ruiz Arguelles et al., 1984) [21], plasma cell labelling index (Durie et al., 1980) [22] and beta-2-microglobulin (Bataille et al., 1984) [23] have emerged as possible prognostic factors in multiple myeloma.

Conclusion

We found that the combination of clinical performance status, serum creatinine, haemoglobin and paraprotein index allowed us to discriminate three groups of patients with different survivals. It can be a useful complementary tool for classifying patients according to prognostic factors.

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