CASE REPORT

Clinical Spectrum and Prognosis of Multiple Myeloma in Patients Younger than 30 Years : Is it Different from the Elderly ?

R Kapoor, M Bansal, GJ Sastri, MS Sandhu*, M Garg*, SC Sharma+

Abstract

Multiple Myeloma (MM) is a disease of the elderly. The occurrence of MM in patients younger than thirty years is rare. Over the last ten years five patients with MM of less than thirty years of age were evaluated at our centre and which constituted 3.3% of all the MM cases. Three patients had initial extramedullary involvement. All patients responded to the initial planned therapy and were clinically disease free at the time of last follow-up. In the background of clinical and laboratory features, a brief review of literature was carried out and the prognosis of this subgroup has been discussed.

Key Words

Multiple Myeloma, Extramedullary, Tumour

Introduction

Multiple Myeloma (MM) is a malignant disorder of the plasma cells that accounts for about 1% of malignant disorders. MM has a strong correlation with age and the risk increases with age, peaking at about 60-70 years. In the United States, the median age of onset is 68 years for men and 70 years for women. MM is rare in patients less than thirty years of age. Blade et al reported a series of 72 patients with MM younger than 40 and 30 years respectively (1). The frequency of MM in patients younger than 40 and 30 years was 2.2% and 0.3% respectively. We have reviewed 150 Myeloma cases of past ten years who were treated in our center. Of these only 5 patients (3.3%) were less than 30 years age. In this article we are presenting the clinical spectrum of these five patients with a brief review of literature.

Adolescents and very young adults may have an atypical presentation and an indolent course with prolonged survival. However, an aggressive clinical course has also been reported in very few young patients (2). Our case series however, revealed a predictable and perhaps better prognosis for these young patients. The purpose of this study was to see the incidence of young patients presenting with meyeloma at our institution, to study the presenting clinicoradiological and laboratory features of these patients to evaluate the response to treatment and survival in these patients and to compare the above findings with those of elderly patients.

Material and Methods

We analyzed all patients of MM who presented to our center from January 1993 to December 2003. Complete diagnostic work up was carried out for all the patients. Besides the routine hematological investigations, diagnostic work up included serum calcium levels, urine for Bence Jones Protein (BJP), serum electrophoresis

From the Departments of Radiotherapy & Oncology and Radiodiagnosis, PGIMER, Chandigarh, India.
Correspondence to : Dr. Rakesh Kapoor, Consultant, Radiotherapy And Oncology, PGIMER, Chandigarh, India.

and bone marrow examination for plasma cells. Radiological examination included skeleta survey and X-rays of the local site if exteramedullary involvement was present. Diagnosis of MM was done using the Salmon Durie criteria (3). All the patients were offered systemic chemotherapy with a combination of cyclophosphamide, vincristine and prednisolone (COP regimen, six cycles at three weekly intervals). Subsequently, they received maintenance dose of oral Cyclophosphamide Three patients received palliative radiotherapy to the involved bony sites to a dose of 25-35 Gy with 2.5 -3 Gy per fraction.

Results

Of the150 patients of MM who attended the clinic from January 1993 through December 2003, only 5 patients were less than 30 years of age and thus constituted about 3.3% of all cases of MM. The youngest of these was a 13 years old boy. The laboratory data and clinical profile of our patients is given in Table 1 and 2 respectively. The radiological data of these patients is represented in Fig 1 to Fig 3.

All patients had a hemoglobin value of more that 12 g/dl. The serum calcium value was also within normal range in all the patients. The youngest patient, a 13 year old male had 30% plasma cells in marrow. All the patients had involvement of the marrow, making it a major criteria (>30%) in three patients and minor criteria in two (10-30%) patients. All patients showed 'M' band in serum electrophoresis except patient no 4. However, no patient had 'M' band in urine.

All patients presented with a history of localised pain. All the patients had radiological involvement in the form of lytic areas in the bones. (Fig 1 to 3). The mean duration of symptoms was 5.6 months with a range of 4-8 months. Three patients had extramedullary involvement at presentation. Two patients had cervical lympha-denopathy. Another presented with soft tissue mass in the hip (Table 1 and 2). All patients completed the planned course of treatment and were on regular follow up. The mean overall survival in these patients was 41 months with a range of 30-60 months.

Table 1 . Clinical Profile of Patients of MM < 30 Years

Sr No.	Age/Sex	Presenting complaint	Duration of symptoms (MO)	Extramedullary involvement	Chemotherapy regimen	Local RT dose	Total follow-up (MO)	Survival
1	15/F	Neck Swelling	8	Neck nodes	COP(I.V.)-oral cyclophosphamide	35 Gy/15fr	37	Alive
2	13/M	Backache	6	Swelling skull, neck nodes	COP(I.V.)-oral cyclophosphamide	--	42	Alive
3	29/M	Backache	5	None	COP(I.V.)-oral cyclophosphamide	--	30	Alive
4	29/F	Backache	4	None	COP(I.V.)-oral cylophosphamide	35 Gy/15fr	36	Alive
5	25/M	Pain and swelling Rt hip	5	Soft tissue swelling right hip	COP(I.V.)-oral cyclophosphamide	25 Gy/10fr	60	Alive

Table 2. Laboratory Details of Patients of MM Less than 30 Years

Sr. No	Age/Sex	Hb gm%	Cr mg/dl	Ca mg/dl cells(%)	BM plasma protein	Serum. M criteria	Urine M radiography	Salmon Durie	Bone
1	15/F	12.3	1	10.2	10	+	-	2 maj.+ 2 min	Lytic humerus
2	13/M	13.4	0.5	9.1	30	+	-	3 maj.+ 1 min	Lytic skull
3	30/M	12.0	1.2	9.4	82	+	-	3 maj.+ 1 min	Lytic ribs
4	30/F	14	1.0	8.9	38	-	-	1 maj.+ 1 min	Lytic L4 vert.
5	25/M	12	1.2	8.6	40	+	-	3 maj.+ 1 min	Lytic pelvis.

Table 3. Comparison of Multiple Myeloma in Elderly and Young Patients

Clinical and Biochemical Spectrum	Elderly	Young
Presenting Complaints	Bony Pains	Bony pains, lump
Association with viruses(EBV, HIV)	-	+
BJP	Present more often	Present less often
Prognosis	Worse comparatively	Better in comparison
Survival	2-3 years	5-6 years
Hypercalcaemia (>11.5 mg./dl)	25-30%	30-35%
Renal Failure	20-31%	29-32%
Anaemia (<12 g/dl)	62-65%	Less common

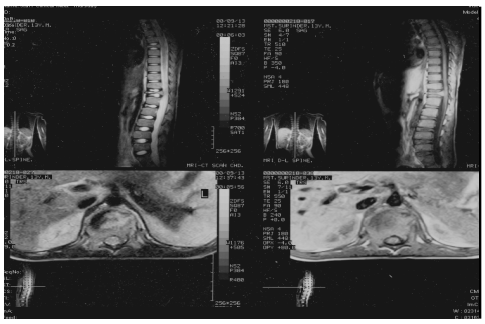

Fig. 1. Post gadolinium enhanced sagittal and axial T2 and T1 weighted MR images of Dorso lumbar spine reveal multiple collapsed non-contiguous dorsal vertebrae with adjacent disc bulge and associated pre-vertebral enhancing soft tissue mass.

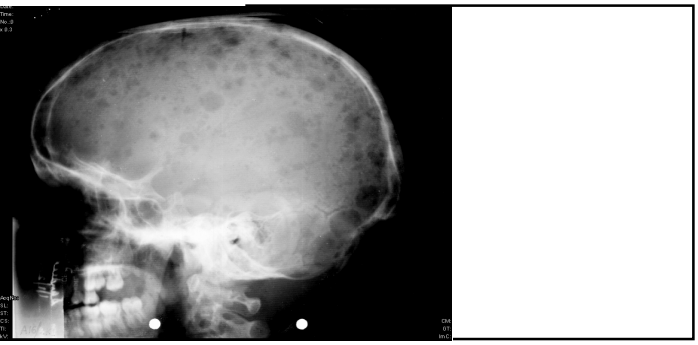

Fig. 2. Plain skiagram of skull-lateral view demonstrates classic, well defined punched out round lytic lesions involving the skull vault.

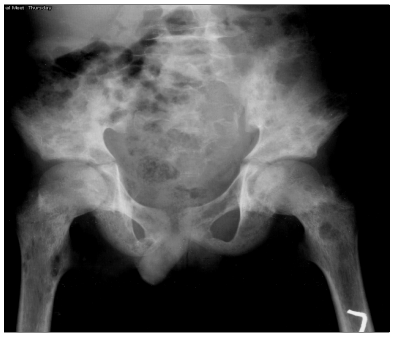

Fig. 3. X-ray pelvis (AP view) showing destructive lytic lesions involving bilateral pelvic bones and also proximal parts of both femur bones.

Discussion

MM is a malignant disorder of monoclonal plasma cells. Besides the serum or urinary M protein, patients also had increased plasma cells in bone marrow, lytic areas in bone and various other clinical and laboratory abnormalities characteristics of this disease. It has been mentioned that approximately 2% of patients with MM are younger than 40 years and it is still rarer in patients younger than 30 years (4). In the study by National Cancer Institute, the frequency of such occurrence was 7/3815(0.18%) (1). Hewell *et al* have reported frequency of 1%(5). These patients were the first well-documented group of young persons with MM. The records of all patients younger than 30 years with MM evaluated at the Mayo Clinic were reviewed and the incidence was found as 0.3% (6). We have reviewed the records of past ten years of our institute and found a frequency of about 3.3%.

MM is unusual in the young patients. The clinical course in adolescents and young individuals is generally indolent and the survival is longer. However the response to chemotherapy is variable (6). Lazarus reported two cases of plasma cell myeloma in young patients (7). One was a case of MM involving the skull and ribs in a 23 year old woman, the other was a solitary myeloma of the tibia in a 21 years old man. Both the cases were diagnosed non-secretory myelomas. However, monoclonal immunoglobulins were demonstrated by immuno-histochemical studies. None of our five subjects showed presence of M band or Bence Jones protein (BJP) in urine. This is consistent with most of the cases reported in literature, which have rarely reported BJP in their subjects. Only the report by Blade *et al.* found BJP in 5 out of 10 patients (1).

Usually renal function impairment is a common phenomenon in Multiple Myeloma. Mayo Clinic analysis revealed renal function impairment (creatinine level > or = 177 micromol/L) and hypercalcaemia (serum calcium value > or = 2.75 mmol/1/1) in 29% and 30% of the 72 patients respectively. In our subjects however, we did not find any evidence of renal impairment, hypercalcemia or any other electrolyte imbalance.

Literature review suggests that there may be an associated extramedullary component in most of these patients. In the review of young myeloma patients by Blade *et al* (1), 14 out of 17 patients had an extramedullary component. Geetha et al from India described two young patients (20 years, 18 years) who presented with extradural cord compression, lytic bone lesions and bone marrow plasmacytosis (8). In our case series three out of five (60%) patients had extra medullary component.

An association of Human Immunodeficiency Virus (HIV) with development of MM in young patients has also been reported. Monoclonal gammopathy, plasmachytoma and MM have been reported in young patients with HIV infection (9). Other viruses such as Epstein-Barr Virus (EBV) have also been implicated in a report. Our patients were not screened for HIV or EBV infections but we suggest that young patients with MM particularly those with extramedullary disease should be screened for HIV and/ or EBV infection.

Treatment of young patients with MM has not been different from that of the elderly patients. In literature, both radiotherapy (RT) and chemotherapy have been used for the management of these patients. It is obvious that RT has to be carefully used in very young subjects. The chemotherapeutic agents that have been used are melphalan, predinosolone, adriamycin and Cyclophosphamide. Our patients were treated with chemotherapy with or without local radiotherapy. While the first patient was given a radiation dose of 35 Gy in 15 fractions over 3 weeks to the local site, the fifth patient received 25 Gy in 10 fractions over 2 weeks locally. The rest of the patients were given systemic chemotherapy alone. We gave a combination of Cyclophosphamide, Vincristine and prednisolone. Blade et al have recommended high dose chemotherapy in patients resistant to conventional dose chemotherapy (10).

The median duration of survival of patients with MM ranges between 2-3 years. In the study from Mayo clinic, the median duration of survival of the patients was 87 months. The survival of the younger patients was considerably longer than that of patients of all ages with MM 5. Thus the occurrence of myeloma in the younger individual does not appear to impart a worse prognosis or survival. All the patients in our study were alive at the time of analysis (mean survival of 41 months) and had shown good clinical response to treatment. However high dose chemotherapy with ABMT may be an effective option in younger patients because of better tolerance to conditioning regimes with good long lasting responses obtained. From our study, we feel that age does seem to have some beneficial effect on the natural history and the course of the disease. It may be cautionary to add that at present as there is limited scientific reasoning for this observation.

References

1. Blade J, Kyle RA, Greipp PR. Presenting features and prognosis in 72 paitents with multiple myeloma who were younger than 40 years. *Br J Haematol* 1996 ; 93 : 345-51.
2. Clough V, Delamore IW, Whittaker JA. Multiple myeloma in a young woman. *Ann Intern Med* 1977 ; 86 : 117-18.
3. Durie BGM, Salmon SE. Multiple myeloma, macroglobulinemia and monoclonal gammopathies. In : Hofbrand AV, Brain MC, Hirsh J. (eds). Recent Advances in Haematology. Churchill-Livingstone, Edinbrugh. 1977, pp. 43.
4. Young JL, Percy CL, Asire AJ. Survillance, epidemiology and end result. Bethesda. MD. US department of Health and Human services. National Cancer Institute Monograph 1981 ; 57.
5. Hewell GM, Alexanian R. Multiple meyeloma in young persons. *Ann Intern Med* 1976 ; 84(4) : 441-43.
6. Blade J, Kyle RA, Greipp PR. Multiple myeloma in patients younger than 30 years. Report of 10 cases and review of the literature. *Arch Intern Med* 1996 ; 156 (13) : 1463-68.
7. Lazarus HM, Kellermeyer RW, Aikawa M, Herzig RH. Multiple myeloma in young men. Clinical course and electron microscopic studies of bone marrow plasma cells. *Cancer* 1980 ; 46(6) : 1397-1400.
8. Geetha N, Jayaprakash M, Rekhanair A, Ramachandran K, Rajan B. Plasma cell neoplasma in the young. *Br J Radiol* 1999 ; 72(862) : 1012-15.
9. Gold JE, Schwann L, Castella A, pike SB, Opfell R, Zalusky R. Malignant plasma cell tumours in Human Immunodeficiency virus infected patients. *Cancer* 1990 ; 66 : 363-368.
10. Ventura G, lucia F, Cauda R, Larocca LM., Multiple myeloma associated with Epstein Barr virus in an AIDS patient. A case report. *Eur J Hematol* 1995 ; 55 : 332-34.