Multiple myeloma in the University Hospital: a retrospective study of biodata, clinical, laboratory and radiological profiles, 1980 — 1987

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Summary

A retrospective study of 37 cases of multiple myeloma admitted from 1980 to 1987 to the University Hospital Kuala Lumpur, Malaysia, was carried out to analyse the biodata, clinical presentation, laboratory and radiological profiles. The cases were selected after they had satisfied preset diagnostic criteria.

The mean age was 60 years. There was no sex or ethnic preponderance. The most common symptom was bone pain. Pallor was detected in 73% of the patients. Haemoglobin was < 120 g/L in 95%, and ESR was > 100 mm/hr in 70% of cases. Bone marrow and trephine biopsies were diagnostically important. Hypercalcaemia occurred in seven cases out of which three were IgA myelomas. Either serum creatinine or blood urea was raised in nearly 50% of cases. The most common heavy chain paraprotein was IgG while Kappa light chain was the commoner light chain type. 86% of cases had osteolytic lesions.

These findings are, in general, similar to those of larger studies on multiple myeloma.

Key words: Multiple myeloma, retrospective study, biodata, clinical, laboratory, radiological.

Introduction

Multiple myeloma is a haematological malignancy with protean manifestations, producing disease in bones, kidneys and other organs. This distinct entity was recognised in the late 1800's and the term "multiple myeloma" was suggested in 1873 as a result of Rustizky's studies on a disease characterised by skeletal fractures and paraprotein in the urine. Paraprotein was discovered earlier by several workers including Bence Jones in 1845.[1]

The purpose of this review is to study the biodata, clinical presentations, haematological, biochemical and radiological profiles of proven cases of multiple myeloma because to date, there

is no published report on such data from Malaysia. Indeed, there is also a dearth of such published retrospective studies in Asia as a whole.

Methods and Materials

The case records of patients diagnosed as multiple myeloma in the University Hospital, Kuala Lumpur from 1980 to 1987 were retrospectively reviewed. A total of 37 cases were selected for study based on preset diagnostic criteria, modified from that used in the Medical Research Council (United Kingdom) trials.[2,3] The cases were deemed to have satisfied these criteria if they had two or more of the following freatures:

1. Marrow plasma cells more than 30% of the total nucleated cells.
2. Definite osteolytic lesions in skeletal x-rays.
3. Paraprotein in the serum and/or urine.

One case that fulfilled the above diagnostic criteria but did not have adequate information for analysis was excluded.

Each case record was carefully reviewed and analysed for the following: 1. biodata (age, sex and ethnic group); 2. haematological profile (haemoglobin, total white cell count, platelet count, erythrocyte sedimentation rate, and bone marrow aspirate and trephine findings), 3. biochemical profile (serum calcium, alkaline phosphatase, urea, serum creatinine, and paraprotein), and 4. radiological findings.

Results

Haematological: The age range was from 42 to 78 and the mean age was 60. No case less than 40 years of age was found. Males and females were effected almost equally. The ethnic and sex distribution is shown in Table 1.

Table 1
Multiple Myeloma in the University Hospital:
Ethnic and Sex Distribution

	Chinese	Malay	Indian	Others
Male	8	3	8	0
Female	9	5	2	2
Total	17 (46)*	8 (22)	10 (27)	2 (5)

* Percentages in parentheses. (The cumulative racial distribution in the adult patient population in the University Hospital from 1980 to 1987, excluding obstetric patients and registered babies, is as follows: Chinese 46%, Malay 25%, Indian 28% and Others 1%).

The symptoms and signs found in our patients are listed in Table 2. Thirty five cases (95%) presented with haemoglobin level of less than 120 g/L (see Table 3). Nine patients had leucopenia

Table 2
Multiple Myeloma in the University Hospital
Symptoms and Signs at Presentation

	No. of Cases	%
SYMPTOMS		
Bone Pain	27	73
Constitutional*	21	57
Urinary +	5	14
Cough	3	8
Breathlessness	2	5
Vomiting	2	5
Pallor	2	5
Bruises	1	3
Epigastric Pain	1	3
Cutis Laxa**	1	3
Gluteal Ulcer	1	3
SIGNS		
Pallor	27	73
Bony Tenderness	18	49
Hepatomegaly	12	32
Respiratory	11	30
Cardiovascular	7	19
Central Nervous System	5	14
Pedal Oedema	4	11
Fracture	4	11
Jaundice	3	8

* e.g. loss of weight, loss of appetite, lethargy.
\+ e.g. haematuria, polyuria, nocturia and frequency.
** referred as cutis laxa and incidental finding of multiple myeloma.

(total white cell count less than $4x10^9/L$). Thrombocytopenia (platelet count less than $150x10^9/L$) was present in 11 cases. Erythrocyte sedimentation rate (ESR) results was available in 33 patients and are shown in Table 3. Twenty three (70%) of the patients had an ESR of $>$ 100 mm/hr.

Thirty three out of 34 cases had a plasma cell percentage of 15% or more in their aspirates (Table 3). Of the three cases in which no bone marrow aspiration results were available, two of thm had trephine biopsies supportive of the diagnosis of multiple myeloma. Seventeen patients had trephine biopsies and in all of these cases, the findings were supportive of multiple myeloma.

Biochemical: Calcium, alkaline phosphatase, blood urea, serum creatinine levels, and paraprotein patterns are shown in Table 4. In instances where serum albumin levels were not done or were done more than a day's interval from that of calcium, the calcium levels were regarded as not available for analysis. All calcium levels were corrected for serum albumin. Out of the seven cases with hypercalcaemia, three cases were IgA myelomas.

Table 3
Multiple Myeloma in the Univeristy Hospital – Haematological findings: Blood Count, Erythrocyte Sedimentation Rate (ESR) and Bone Marrow Aspirate Findings at Presentation

		No. of Cases	%
Haemoglobin (g/L)	<50	3	8
	50–80	11	30
	90–120	21	57
	>120	2	5
	Total	37	100
Total White Cell Count ($x10^9$/L)	<4	9	24
	4–11	26	70
	>11	2	5
	Total	37	100
Platelet Count ($x10^9$/L)	<20	1	3
	20–150	10	33
	160–400	19	63
	Total	30	100
ESR (mm/hr)	<100	10	30
	>100	23	70
	Total	33	100
Plasma Cells in Marrow Aspirate	<15%	1	3
	15–30%	7	21
	>30%	26	76
	Total	34	100

Of the seven cases of raised alkaline phosphatase activity, two had radiological evidence of fractures without hepatomegaly, two cases had hepatomegaly, while two other cases had both fractures and hepatomegaly. The remaining case had no apparent cause for raised alkaline phosphatase. In those two cases with raised alkaline phosphatase activity, and hepatomegaly only, there was concomitant hypercalcaemia as well.

In 12 cases (32%) the serum creatinine and blood urea levels were raised simultaneously.

In only one case was the paraprotein profile entirely unknown. In seven patients (19%), no IgG or IgA paraproteins were detected but the levels of IgG, IgA and IgM were all suppressed. These cases probably comprised 'light-chain', IgD, IgE or other types of myelomas. Since further

Table 4
Multiple Myeloma in the University Hospital:
Calcium, Alkaline Phosphatase, Urea and Serum Creatinine Levels and Paraprotein Pattern

		No. of Cases	%
Calcium (mmol/L)	Not Raised	21	75
	Raised*	7	25
	Total	28	100
Alkaline Phosphatase (iu/L)	Not Raised	24	77
	Raised**	7	23
	Total	31	100
Urea (mmol/L)	Not Raised	18	55
	Raised +	15	45
	Total	33	100
Serum Creatinine (umol/L)	Not Raised	20	56
	Raised ++	16	44
	Total	36	100
Paraprotein Type			
	IgG	20	56
	Kappa	9	45
	Lambda	5	25
	N.A. +++	6	30
	IgA	9	25
	Kappa	5	56
	Lambda	1	11
	N.A.	3	33
	Others ***	7	19
	Kappa	4	57
	Lambda	1	14
	N.A.	2	29

* >2.6 mmol/L
** >135 iu/L
\+ >6.8 mmol/L
++ >130 mmol/L
*** Cases where neither IgG or IgA were detected.
+++ N.A. = not available

chemical analyses were unavailable, this group was not analysed further. Kappa light chains were found in a total of 18 out of 25 patients in which light chains were characterised.

Radiological: Table 5 shows the radiological bony lesions found in this series. A total of 29 (86%) cases showed obsteolytic lesions typical of multiple myeloma.

Table 5
Multiple Myeloma in the University Hospital:
Radiological Findings

Radiological Finding	No. of Cases	%
Osteolytic lesion only	22	65
Osteolytic lesion & generalised osteopenia	7	21
Generalised osteopenia only	4	12
Fracture	9	24
No lesions	1	3

Discussion

In general, the findings were similar to those found in larger series.[4,5,6,7]

There were no cases below the age of 40. Although there have been reported cases of multiple myeloma affecting patients less than 40 years of age, this is relatively uncommon. The peak incidence reported was from 50 to 70 years.[4,8] The mean age of 60 in our series therefore falls within this range. Our study did not show a male or female preponderance but more recent and larger studies showed a slight male preponderance.[4,9] Ethnic Chinese patients made up about 46% of the cases, ethnic Malays about 22%, while ethnic Indians about 27% of the study population. This racial distribution was not found to be significantly different from the racial distribution of our hospital admissions during the period of study.

Bone pain and the following constitutional symptoms, loss of weight, loss of appetite and lethargy were the commonest symptoms, and were seen in 73% and 57% respectively of patients. This was found to be also true in other studies.[4,5,10] Pallor was the most frequent sign (73%) detected in our series. Again, this was in keeping with other reported studies.[4,5] Anaemia was found in the majority of our patients. About 38% of our patients presented with haemoglobin levels of 80g/L or less. In contrast, Kyle[4] has found only 8% of his patients with this level of haemoglobin.

Thrombocytopenia was found in less than 50% of cases as was the case in other series.[4,5] Erythrocyte Sedimentation Rate (ESR) was more than 100 mm/hr in 70% of patients. Kyle found 76% of his cases with ESR more than 50 mm/hr.[4] In all the cases where trephine biopsies were carried out, the results were consistent with multiple myeloma in that there was an invariable diffuse involvement of the marrow with plasma cells. This was also true where bone marrow aspiration showed plasma cells to be less than 15% (one case). In cases of suspected multiple

myeloma where repeated, bone marrow aspirations have failed, diagnosis is possible with trephine biopsies.

Only 25% of our patients had hypercalcaemia, (hypercalcaemia being defined as calcium levels, corrected for serum albumin, of more than 2.6 mmol/l). Reported figures for hypercalcaemia in other series ranged from 30% to 46%.[4,5] Interestingly, three cases with hypercalcaemia were IgA myeloma, which is in keeping with observations that hypercalcaemia occurs more commonly in IgA myelomas.[13]

Serum creatinine level was found to be raised in 44%, while blood urea was raised in 46% of cases. In Kyle's series,[4] 54% and 56% of males and females respectively had raised serum creatinine. Azotaemia was found in 41% of Kapadia's series.[5] Both normal serum creatinine and blood urea levels at presentation are considered to be good prognostic indicators; raised levels indicating poor prognosis.[1,5,7] Thus amongst our patients, if blood urea and serum creatinine levels were used to pronosticate outcome, nearly half of them would seem to have poor prognoses at presentation. Unfortunately, this cannot be substantiated in this study because the final outcome in many patients were unknown as they were lost to follow-up.

Alkaline phosphatase activity is generally not raised in multiple myeloma except in healing fractures[11] and liver involvement. In our series, it was found to be raised in seven cases, six of which had fractures, hepatomegaly or both. The most commonly occuring paraprotein type is IgG, followed by IgA and light-chain myelomas.[4,6,12] Our results were consistent with these findings. IgG myeloma was found in 20 cases while 9 cases of IgA myeloma was detected. Kappa light chains were found to be more common than lambda chains in cases subtyped for light chains. This finding was also reported by Kyle.[4]

Osteolytic lesions alone or in combination with other findings (fractures and osteopenia) seemed to be the commonest radiological finding in our series. This agrees with the results in other series.[4,5] On the other hand, only 9 cases showed radiological evidence of fractures. This contrasted with other series where a combination of lytic lesions, osteopenia and fractures was the commonest radiological finding.[4,5] This discrepancy could have arisen probably from incomplete skeletal surveys with fractures remaining undetected.

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