MULTIPLE MYELOMA AS SEEN AT KENYATTA NATIONAL HOSPITAL (KNH)

(A prospective study of patients seen in KNH from March 1980 to February 1982).

by

DR. C.M. NYIRENDA, LRCPI, LRCSI., DTM&H(Liverpool)

A thesis submitted in part fulfilment for the degree of Master of Medicine in the University of Nairobi

1982.

DECLARATION

This thesis is my original work and has not been presented for a degree in any other University.

Signature ----------

DR. C.M. NYIRENDA

This thesis has been submitted for examination with my approval as a University supervisor.

Signature ----------

Professor THOMAS OGADA, MBChB., MRCP(UK)FRCP(I

11/5/82

DTM&H (LONDON)

CONTENTS

SUMMARY:

Fifteen patients with multiple myeloma seen at KNH during the period March 1980 to February 1982 were studied. The presenting clinical features, laboratory investigations and initial treatment of these patients are discussed. Most clinical and laboratory features of multiple myeloma in Kenyan patients were essentially the same as elsewhere in the world. This study discusses some aspects of multiple myeloma as seen in Kenyans, compared with similar cases elsewhere. Most of the patients presented in their fourth and fifth decades.

In making diagnosis of myelomatosis these major features were used, viz, (i) presence of myeloma cells in the bone marrow aspirate or in a soft-tissue biopsy, (ii) presence of a paraprotein in the blood and/or urine (iii) osteolytic bone destruction on x-ray. Factors associated with a poor prognosis in myelomatosis are raised serum urea above 13mmol/l and Bence-Jones protein above 200mg/oL. Initial treatment of the patients to induce remission was by the use of alkylating agents such as melphan coupled with prednisone and allopurinol on intermittent course.

INTRODUCTION

Myelomatosis (synonyms: multiple myeloma, multiple plasmacytoma, Kahlers disease) is a neoplastic disease of plasma cells which are abnormal and immature and are known as myeloma cells. It is a lymphocytic-plasmacytic neoplasm, and together with heavy chain disease and primary macroglobulinaemia (Waldenstroms disease) belongs to the lymphoproliferative disorders (13).

The disease is characterized by 3 major features, viz.

i) osteolytic bone destruction

ii) presence of neoplastic plasma cells (myeloma cells) in the bone marrow - concentration of 20% or more of nucleated marrow cells (erythroid elements excluded)

iii) presence of paraproteins in serum or urine electrophoresis (1,2,13,14,15,17, 24).

A diagnosis of multiple myeloma (MM) can be made when only 2 of the 3 above features are present (2,13,14,15). Occasionally plasma cells appear in the peripheral blood in large numbers and the disorder may be referred to a plasma cell leukaemia (2,13,14). Rarely plasma cells involve focal or multiple soft tissies and the disorder is termed plasmacytoma (2,13,14).

Multiple myeloma is a major cause of serum immunoglobulin paraproteins. Other malignant diseases producing paraproteins are Waldenstroms macroglobulinaemia, chronic lymphatic leukaemia and lymphomas (excluding Hodgkins disease (25).

On serum electrophoresis the paraproteins migrate as a marrow band, the so - called M band or M component produced by one clone of plasma cells. This local increase in globulins is termed monoclonal gammopathy (27).

Benign M bands (essential paraproteinaemia) occur in people with no evidence of malignant disease (8). In population the incidence of benign paraproteinaemia is 1% in 50 to 59 years of age, 2% in 60 to 69 years of age, and 3% or more over 70 years. This chance finding accounts for only 10% of the patients with paraproteinaemia (2,8,30).

The immunoglobulin consists of two heavy (H) chains and two light (L) chains. Its structure is illustrated in figures 1 and 2 (18, 32). In multiple myeloma the immunoglobulins IgG are more common (50%) IgA less common (25%), IgD quite rare, less than 1% IgE very rare (10,32). The IgG has four types of H chains which are antigenically distinct and designated as a,b,c,d. IgA contains only one antigenic type of H chain designated an alpha (α) H chain as does the IgM which is called an u H chain (32).

Bence-Jones proteins are monoclonal L chain proteins with low molecular weight (22,000). They usually occur in 25% of multiple myeloma. The Bence-Jones protein usually flocculates or coagulates when its solution is heated slowly to between 45° and 60°C., dissolves on boiling and precipitates on cooling below 60°C. In renal damage the Bence-Jones proteins may be obscured by the other proteins in urine. There are two types of L chains known as Kappa and Lambda in a ratio of 2:1. They never occur together in one molecule. (18,32,33). Plasma cell dyscrasia with Bence-Jones proteinuria carries a poor prognosis (18,19,20,21,24).

Multiple myeloma on average takes about 20 years to present and ends with a very short clinical phase. At clinical presentation the average patient with multiple myeloma has about one kilogram of tumour cells (2,4,6,24). The disease has three phases in its development, (2,31).

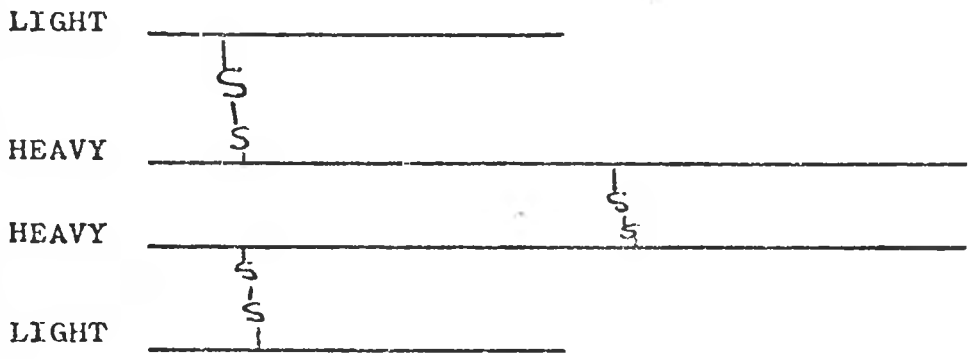
i) the first phase - this is poorly defined with very few available parameters

ii) the second phase - consists of laboratory phase from chance finding of benign paraproteinaemia upto clinical confirmation of MM usually 3-6 years.

iii) the third phase - this the last and shortest is the clinical phase following average presentation with a median survival of 8 months in untreated cases.

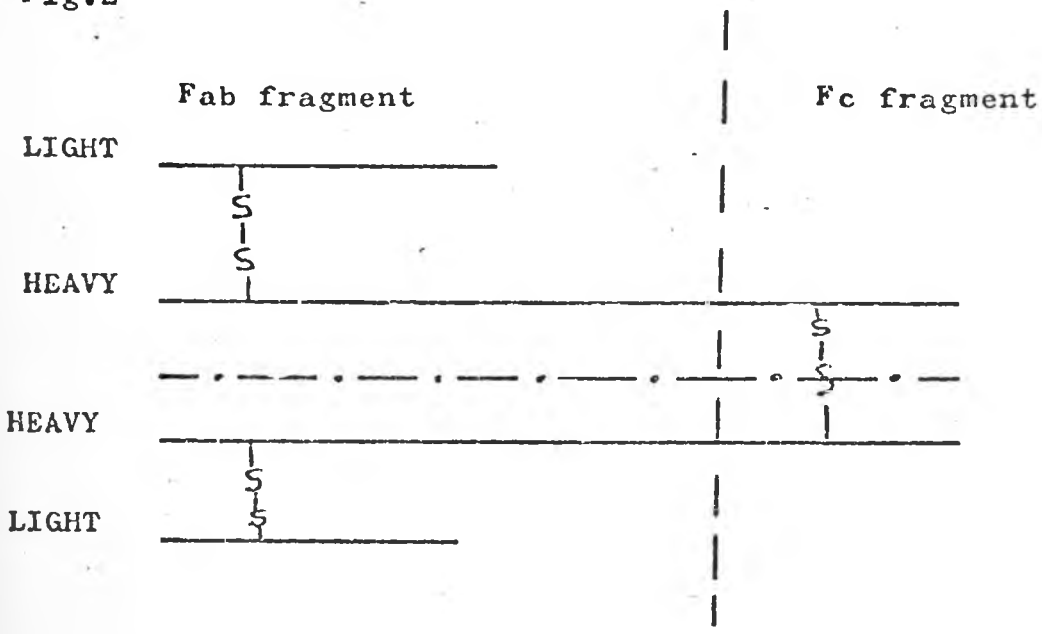
Several studies have been undertaken in indegenous Africans in a number of African countries and have shown that multiple myeloma is not a rare disease (1,16,17,24, 34). These studies have also demonstrated almost similar presenting clinical features in African patients with only few observed differences (1,16,17,24,34).

Fig.1



Light and heavy chains of immunoglobulin molecule

Fig.2



Immunoglobulin molecule split by "papain digestion" into 2 fragments which still have antigenic properties, the antibody fragment Fab and cystalline fragment Fc

AIMS AND OBJECTIVES

1. A prospective study of multiple myeloma as seen at KNH.
2. Determine the clinical extent of the disease at presentation.
3. Determine age, sex and tribal distribution of the disease as seen in KNH.
4. Determine complications of the disease such as hypercalcaemia, anaemia, compression paraplegia, renal failure and infections.

MATERIALS AND METHODS:

A prospective study was undertaken of the patients admitted to KNH from March 1980 to February 1982. They were 15 patients studied with confirmed diagnosis of multiple myeloma.

Complete clinical history and physical examination of each patient were documented on admission.

The following clinical presenting features were used in the study:

i) symptoms of anaemia (fatigue, body weakness palpitation, exertional dyspnoea, leg oedema)
ii) symptoms of bone pain (long bones, clavicle, sternum, pelvis, spine).
iii) fractures (clavicle, femur, humerus, vertebrae)
iv) compression paraplegia
v) bleeding (epistaxis, bleeding from the gums and into the skin)
vi) chest infection (cough, chest pain, haemoptysis)
vii) fever temperature of $38^{o}C$ or more.
viii) hypercalcaemia (anorexia, nausea, polyuria, constipation)
ix) kidney involvement.

The investigations used in the study were as follows:-

1. Haematological tests: full blood count by Coulter Counter method.
   Erythrocyte sedimentation rate (ESR).

: Peripheral blood film for morphology and distribution of cells using Jenner - Giemsa stain.

: Bone marrow aspiration to determine plasma cell concentration and assess iron stores, using May - Grunwald - Giemsa stain and Perl(s Prussian Blue reaction.

Biochemical tests.

Total serum protein - albumin and globulin fractions
serum calcium and phosphate
serum alkaline phosphatase
serum urea
serum uric acid.

Others. (i) skeletal survey to show radiological lytic lesions.

- skull xray - AP and lateral
- chest xray - PA
- Xray of long bones, spine and pelvis.

(ii) Paraproteins. serum electrophoresis
Bence Jones proteinuria.

Results:

Table 1 shows the presenting clinical features.

Bone pain mainly of sternum, clavicle, spine and long bones together with symptoms of anaemia such as fatigue, lassitude, generalized body weakness, exertional breathlessness and leg oedema were the commonest presenting clinical features, each with 73%. Other important presenting features were fever (47%), fractures (40%) compression paraplegia (40%), bleeding (40%), and chest infection (40%). Hypercalcaemia and kidney involvement were 13% and 7% respectively.

Clinical presentation of MM in 15 patients @ KNH

Clinical features	no. of patients affected	% of total
i. anaemia symptoms	11	73
ii. bone pain	11	73
iii. fractures	6	40
iv. compression paraplegia	6	40
v. bleeding	6	40
vi. chest infection	6	40
vii. fever	7	47
viii. hypercalcaemia	2	13
ix. kidney involvement	1	7

Table 2 shows the results of routine investigations.

Most of the patients presented with symptoms of anaemia (73%) namely, generalized body weakness, fatigue, exertional breathlessness, palpitation and in some cases it was sc severe to have resulted in congestive cardiac failure. Normocytic normochromic anaemia occurred in 60% of patients while microcytic hypochromic anaemia only in 13% of the patients. None of the patients had macrocytic anaemia. The erythrocyte sedimentation rate (ESR) was raised in 73% of the patients.

Thrombocytopenia occured in 47% of the patients and roulenax formation in 87%. 53% of the patients had low white blood cell(wbc) count while 47% had normal wbc count. Serum alkaline phosphatase (AP) and serum calcium were elevated in 20% and 13% of patients respectively. Serum BUN and urate were raised only in 7%.

Haematological and biochemical findings in 15 patients with MM at the time presentation.

Parameter	no. of pts	% of total
anaemia (Hb =12g/dl):	11	73
normocytic normochromic	9	60
microcytic hypochromic	2	13
macrocytic	nil	nil
thrombocytopenia	7	47
normal platelet	8	53
ESR (mm/hr) raised	11	73
Rouleaux formation	13	87
Alkaline phosphatase (U/L) elevated	3	20
Calcium (MMOL/L) elevated	2	13
Wbc: low count	8	53
normal count	7	47
BUN (MMOL/L) elevated	1	7
normal	14	93
Urate (UMMOL/L) elevated	1	7
normal	14	93

Table 3 shows the results of specific investigations.

Serum paraproteins were present in 93% of the patients, while Bence-Jones proteinuria occured only in 13%.

Osteolytic skull lesions occured in 87% of the patients, lytic lesions of the pelvis in 20% vertebrae # or wedging in 20%; fracture of the clavicle in 13% clavicle swelling only in 7% and fractures of long bones in 13% of the patients.

Bone marrow aspirate with myeloma cells occured in 93% of the patients while 7% had myeloma cells in soft - tissue tumour biopsy.

Table 3

Radiological, serum electrophoretic and bone marrow aspiration findings in 15 patients with MM at the time of presentation.

Parameter	no. of patients	% of total
Paraproteins	14	93
Bence Jones proteinuria	2	13
Skull lytic lesions	13	87
Pelvic lytic lesions	3	20
Vertebrae # or Wedging	3	20
Clavicle #	2	13
Clavicle swelling only	1	7
Long bones #	2	13
Bone marrow aspirate with myeloma cells	14	93
Tumour biopsy with myeloma cells	1	7

Table 4 shows investigation results used in confirmation of diagnosis of MM in the 15 patients. 87% of the patients had osteolytic lesions on X-ray, 93% of them had myeloma cells in B.M. aspirate, 93% had paraproteins in serum electrophoresis and 7% with extraosseous plasmacytoma.

13 patients had the diagnosis made by 3 major features, 1 patient had only 2 major features, and one patient had plasmacytoma confirmed by soft-tissue biopsy.

Table 4 Diagnostic features in 15 patients with MM

Major features	no. of patients affected	% of total
Osteolytic lesions on X-ray	13	87
Myeloma cells in marrow aspirate	14	93
Paraproteins in serum electrophoresis	14	93
tumour biopsy with myeloma cells	1	7

Fig. 3 and Table 5 show age incidence in decades. The youngest patient was aged 19 years and the oldest patient was 79 years. The youngest patient had plasmacytoma.

The peak age incidence was between 40-50 years.

Table 6 shows a tribal breakdown of the patients as seen at KNH during the study. The Kikuyu patients were 60%, the Luo patients 20%, the Kamba patients 6%, Luhya patients 6% and the Kalenjin 6%.

Eleven patients out of the fifteen patients were male and four patients were female in the study.

Fig. 4 is a photograph of peripheral blood film illustrating marked rouleaux formation.

Fig. 5 is a photograph of bone marrow aspirate showing myeloma cells in clusters.

Fig. 3

Age distribution of 15 patients with MM at the time of presentation.

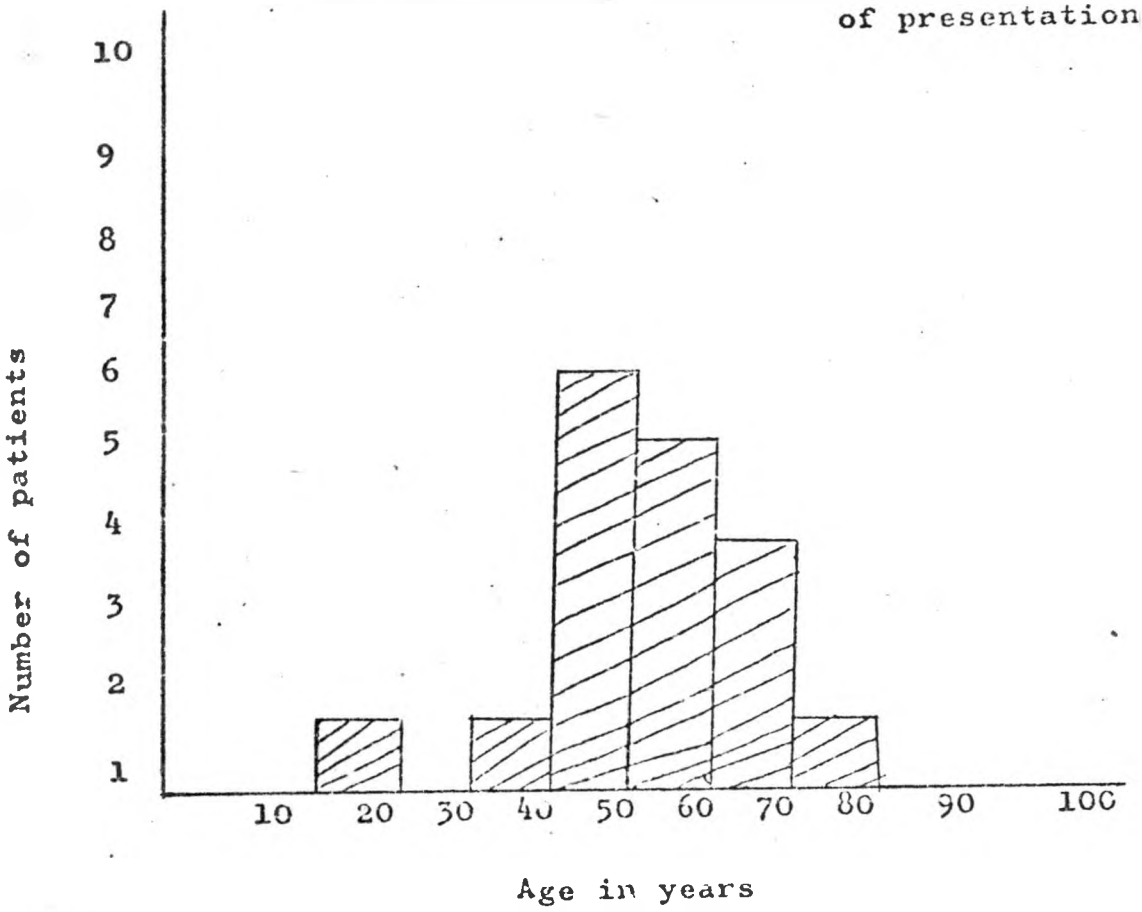


Table 5 Decade age distribution

Decade age group	no. of pts.	% of pts.
11 - 20	1	6
21- 30	-	-
31 - 40	1	6
41 - 50	5	33
51 - 60	4	27
61 - 70	3	20
71 - 80	1	6

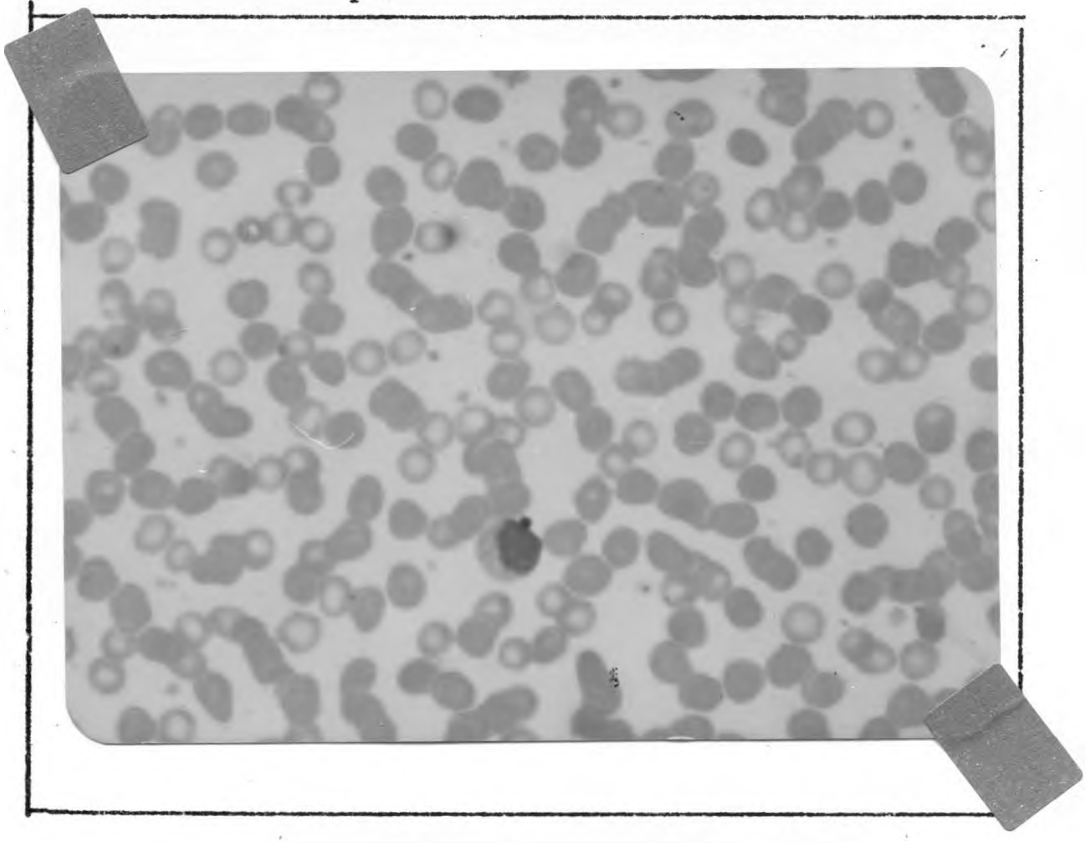
Table 6

Tribe/Sex distribution in 15 patients with MM.

Tribe	Sex			
	Male	Female	total no. of pts.	%
Kikuyu	8	1	9	60
Luo	3	-	3	20
Kamba	-	1	1	6
Luhya	-	1	1	6
Kalenjin	-	1	1	6

Fig 4

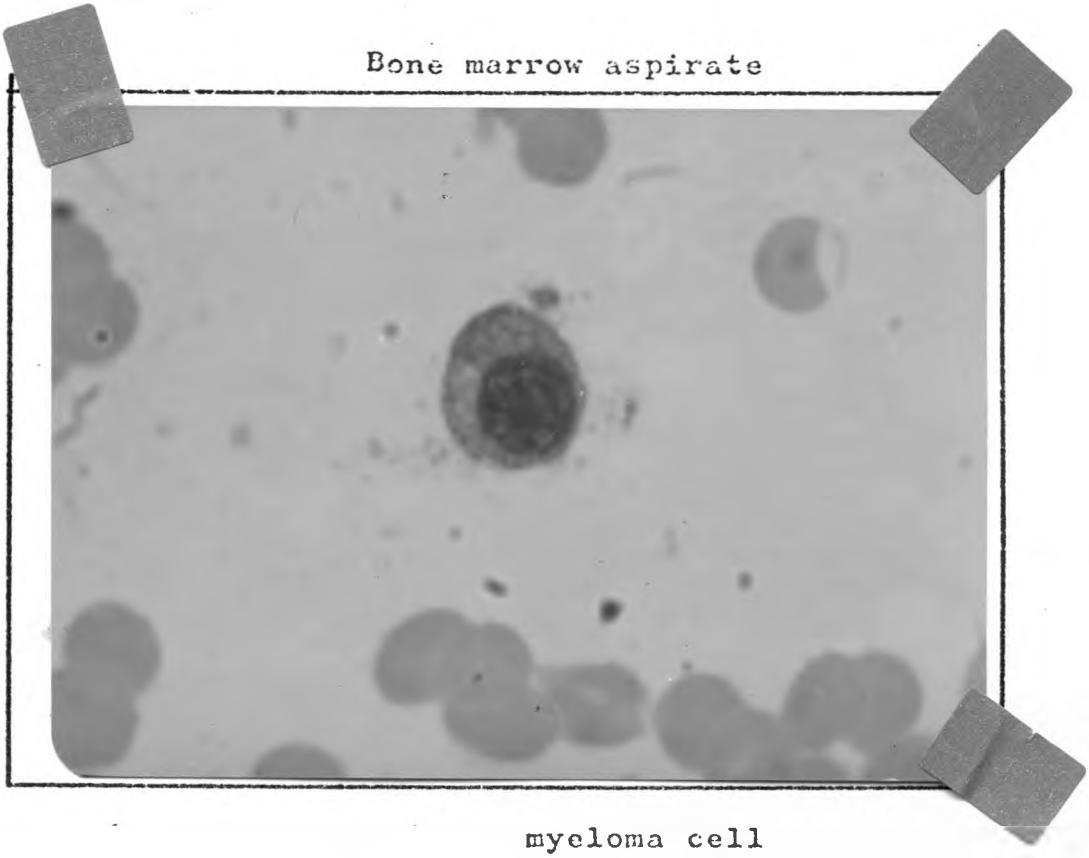
Peripheral blood film



rouleaux formation

Fig 5

Bone marrow aspirate



myeloma cell

DISCUSSION:

This study has shown that multiple myeloma is not uncommon disorder as seen at KNH. This fact is also evident from the other previous studies (1,16,17,24, 34) in which the presenting clinical features are essentially the same with only a few differences noted. The aetiology of multiple myeloma, like most of the malignant disorders of lymphoreticular tissue, is still unknown. Its incidence is aparently on in the increase. This is almost certainly apparent rather than real, and is due to more exact diagnosis, more frequent bone marrow examination and electrophoretic studies of the plasma and urine (1,13,14,24,34).

The peak age incidence in this study was between 40 and 50 years, this being agreeable with the KNH retrospective study (1). This is a decade younger as compared to the Caucasian series (2,13,14,15) where the disease is commonest at the age of 60 years. With high index of suscipicion multiple myeloma should be diagnosed in many adults over 40 years of age presenting with bone pain, anaemia and unexplained infections.

Bonepain was one of the commonest presenting symptom occuring in 73% of the patients (table 7). The KNH restropective study (1) reported 74.2% while in some Caucasian series it is reported 70% (2). Bone pain was most frequent in the axial skeleton and the ribs. It was uncommon in the skull despite its often intensive involvement with multiple punched out osteolytic lesions. Most of the patients had severe diffuse and constant bone pain on admission requiring at times strong analgesics. Bone pain was characteristically aching in character and often aggravated by movement. Tenderness of the bones to palpation or percussion was common.

Anaemia was another outstanding symptom also occuring in 73% of the patient(table 7) Patients with haemoglobin (Hg)$\leq$12g/dl were regarded as being anaemic in the study. This figure is higher than the 15% quoted in some Caucasian series (2,12), 53% of the patients had a haemoglobin of less than 10g/dl which is also higher than the figure of 20.7% quoted in the KNH retrospective study (1).

Normocytic normochromic anaemia occured in 60% while hypochromic microcytic anaemia was detected in 13%. None of the patients had a macrocytic type of anaemia in contrast to 20% of cases in Caucasian (2,5,15). The anaemia was progressive and in later stages was commonly severe.

The pathogenesis of anaemia in MM may be due to several factors such as:-

i) Bone marrow infiltration by myeloma cells which interfere - with haemopoiesis.

ii) Lymphokines released from the myeloma stem cells which suppress erythroblastosis.

iii) hyperiscosity syndrome resulting from presence of abnormal globulins causing haemorrhagic states.

iv) renal component of reduced erythropoietin production in patients with renal insufficiency.

Marked rouleaux formation due to the hyperglobulinaemia was another striking features in the patients' blood films (87%). This feature often suggests diagnosis of MM. The unstained peripheral blood films in these cases showed a bluish tint with a background haze of paraproteins.

Erythrocyte sedimentation rate (ESR) was greatly raised in 73% of the patients (more than 100mm in the first hour by the Westergren method) and was proportional to the serum level of paraprotein. High level of ESR of more 150mm/hour may sometimes render blood grouping and cross matching difficult because of clumping of cell (14). Differential diagnoses of markedly elevated ESR are disseminated TB, leptospirosis, carcinomatosis and connective tissue disorders.

Leukocyte count was low in 53% and was normal in 47% of the cases. Leucopenia is usually common in the later stages of MM and is usual in patients on chemotherapy. A leucoerythrolastic picture with the appearance of immature red cells and granulocytes was absent in all the patients while some Western series quote a figure of 10% (14). None of the patients had a notably increased leukocyte count with a high proportion of plasma cells in the peripheral blood film the so called plasma cells leukaemia quoted by some Caucasian series as 20% (13,14).

Platelets count was low in 47% and was normal in 53%. The platelet and leukocyte counts are important in monitoring the limits of therapy but in themselves have no prognostic value (7).

Fever occured in 47% of cases as compared to 15% in some reported Caucasian series (2). Fever was detected in all those cases with infection.

Chest infections with clinical features of cough, chest pain, haemoptysis, crepitations occured in 40% of the patients (table 7) as compared to 51% reported in KNH retrospective study (1). The figures of 43-50% reported in some Caucasian series agree with this study (5,12,13,26,35). The infections were common because of the immunoparesis.

Bone destruction is one of the major features in MM. This may result into diffuse osteoporosis, osteolytic punched out lesions and pathological fractures of mainly vertebrae, clavicle and ribs.

Typical radiological osteolytic lesions without osteoblastic rim occured in 87% of the patients. This almost agrees with retrospective study (1) which quotes 92.3% while some Western series give the figure of 60%. Usually radiographs of the skull and chest are sufficient to show lytic lesions in most patients.

Pathological fractures were detected in 40% of cases. This figure agrees with the retrospective study (1) as well as some Caucasian reports (2).

Compression paraplegia presented progressively and occured in 40% of the cases. The cause was pathological fractures of the vertebrae. This figure is higher compared to some quoted Caucasian series (23).

Bleeding manifestations occured in 13% and in this series of study they were the first symptoms to bring the patient to the hospital. The bleeding manifestations were in the form of epistaxis, bleeding from the gums and into the skin. One patient presented with frank red blood loss per rectum following recurrent episodes of melaena. Haematuria was not detected. Of the total patients 6% had retinal haemorrhages detected on fundal examination and this was confirmed by an ophthalmologist. The KNH retrospective study did not detect any bleeding feature. Some Caucasian series quote low figures as well.

Pathogenesis of the bleeding may be due to several factors, the most important being,

i) hyperviscosity syndrome due to presence of abnormal globulins.

ii) thrombocytopenia, and in later stages

iii) renal insufficiency with its resultant uraemic toxins.

iv) hypoprothrombinaemia due to liver infiltration.

Bone marrow aspirate showed increase in plasma cells in 93%. They were often found in clumps or sheets and showed nuclear abnormalities, feature which differ from reactive plasmacytosis of the bone marrow which may occur in aplastic anaemia, rheumatoid arthritis, cirrhosis of the liver, Boecks' sarcoid, secondary carcinoma, SLE and chronic inflammation. The plasma cells in these conditions are mature and rarely present in excess of 10%. The three rare findings which are pathognomonic of MM are the distortion of the edge of the cytoplasm by any inclusion trinucleate or binucleate cells with unevenly sized nuclei. The number of plasma cells reflect the amount of immunoglobulin produced. A diagnosis of MM was made if myeloma cells formed 20% or more of the nucleated cells in the marrow (17,24,28).

Paraproteins were detected by means of serum electrophoresis in 93% of the patients. Bence-Jones (BJ) proteinuria occured in 13% of the patients whose serum electrophoresis also revealed an M band. BJ proteinaemia and proteinuria, alone or in combination, are usually of poor prognosis (2,8,13,17,35). BJ proteinuria on its own is not of diagnostic value since it can occur in

malignant lymphomas (Hodgkins disease excluded), Waldenstroms' macroglobulinaemia, chronic lymphotic leukaemia and primary cold - agglutinin disease. Bence Jones myeloma tends to set in early with a rapid progress and is associated with severe bone destruction, hypercalcaemia and amyloidosis. Renal failure is usual.

None of the patients in this series presented with renal failure. The retrospective study (1) reported 43.5% and an even higher incidence of 60-80% is reported in Caucasian series (12,19,20). Urinary tract infection due to immunoparesis was detected in 6%.

Chronic renal failure (CRF) is due to tubular damage from reabsorption of large amounts of Bence-Jones proteins filtered by the glomeruli and proteinaceous casts obstructing and destroying the entire nephrons. This results into the so called "myeloma kidney" associated with proteinuria, nephrotic syndrome and ending in renal failure (14).

Other factors causing CRF are severe hypercalcaemia due to osteoclast - stimulating factor elaborated by plasmacytes and bone dissolution, recurrent pyelonephritis due to immunoparesis and hyperuricaemia due to rapid cellular turnover or cytotoxic therapy. Acute renal failure may however occur in severe dehydration and in massive uricosuria due to chemotherapy.

Renal tubular damage by Bence-Jones proteins may cause specific tubular reabsorption defects termed the adult or secondary Fanconi syndrome (21). Amyloid deposits in the kidney may result into nephrosis and

renal failure and sometimes even into carpal tunnel syndrome, a rare initial symptom.

Multiple myeloma has a variable and unpredictable course. There is some relationship between the course of the disease in the individual and the type of paraprotein. With IgG myeloma immunoparesis is marked, quantity of paraprotein greater, progress of the disease is slow and hypercalcaemia as well as amyloidosis are rare. In IgA myeloma hypercalcaemia and amyloidosis are more common, while Bence Jones proteinuria has a grim prognosis (13).

The single and most valuable guide to prognosis is level of blood urea (11,12). In one series the median survival in patients with blood urea of more than 13mmol/l (80mg/dl) was 2 months compared with 37 months for those with blood urea of less than 6.5mmol/l (40mg/dL (11,12). Early anaemia and thrombocytopaenia also carry a poor outlook. There are reports of survival extending to 20 years in patients receiving no specific treatment. Nevertheless, since the introduction of chemotherapy the median survival has increased from 7 months from the start of treatment to between 24 and 50 months (11,12,22).

Death is mostly due to infection but renal failure is a common cause and other terminal events include haemorrhagic states. Some long surviving patients on melphalan have developed Acute myeloid leukaemia, and it is unknown whether this is due to drug immunosuppression or in some way to disease itself (11,13,15).

In this study 13% of the patient were put on low dosage continuous induction chemotherapy while the remaining 87% were on intermittent therapy. The drugs used were an alkylating agent, (phenylalamine mustard) melphan 0.12mg/kg/day combined with prednisone 0.6mg/kg/day and allopurinol 300mg daily. The intermittent induction chemotherapy is easier to monitor and consists of 6 cases, each course of 5 days duration with a rest period of one week. After inducing remission the patients were discharged to the haematological clinic to be reviewed every 6 weeks. Some of these patients had received irradiation of local points of pain or after emergency decompression for paraplegia.

CONCLUSION:

Multiple myeloma is not a rare disease as seen at KNH. 15 confirmed cases of MM were admitted in this 2 year prospective study 1980 to 1982 as compared to 31 cases admitted in the 4 year retrospective study (1). It has been observed that normally Negroes have about 3 times more plasma cells than Caucasians and a random mutation will occur more frequently resulting into a frequency among Negroes about 3 times greater than in Caucasians (2). In U.K. Hobbs gives an incidence of about 1/500/year in active centres which give a true incidence of the disease in the Caucasian population.

The incidence is apparently on the increase. This is almost certainly apparent rather than real, and is due to more exact diagnosis, more frequent bone marrow aspiration, and electrophoretic studies of plasma coupled with increasing high index of suspicion amongst the physicians when confronted with patients having unexplained infections, bone pain, renal disease and anaemia.

Table7illustrates clinical features in this study as compared with retrospective study (1) and some Caucasian series. Bone pain and anaemia were the outstanding presenting features. Fever was the second common feature while compression paraplegia, chest infection, fractures and bleeding had equal frequency. Hypercalcaemia was not a major feature in this study. Renal failure was not present. Age and tribal distributions are similar to the retrospective study (1).

Table 7

Features in %	Author	KNH retrospective study	Caucasian series
Bone pain	73	74	70
anaemia	73	20	15
fever	47	51	15
compression paraplegia	40	41.9	less common 5%
Chest infection	40	51	43-50
Fractures	40	13	20
Bleeding	40	-	7
Hypercalcaemia	13	10	30
Chronic Renal failure	Nil	9	10

ACKNOWLEDGEMENTS:

My first and sincere thanks must go to Prof. T. Ogada for his encouragement, guidance, patience and constructive criticisms and giving me access to patients in haematological clinic.

I wish to record my gratitude also to Dr. G. Njuguna and Dr. J. M. Mukiibi for reading and interpretting the bone marrow aspirates.

My sincere thanks also go to the following people:-

1. Messrs. C.K. Kanja and D.K. Muchaba in the Department of Medicine for their special help in processing of bone marrow aspirates.
2. All the KNH medical and surgical consultants for giving me access to their patients.
3. Mrs. M. Kamau of Department of Medicine for her typing this manuscript.
4. All those who had assisted me in several ways including the patients for their cooperation.
5. Malawi Government for my sponsorship through European Economic Community funds which have enabled me to undertake this course.
6. Finally and most important to my wife and children, not only for their unfailing moral support and encouragement but also for their patience and perseverance while I have been away from them during my study period.

No.	Patient	anaemia	bonepain	Compression paraplegia	bleeding	chest infection	fever	CCF	
1	DK	-	+	+	-	+	+	-	
2	FM	+	+	-	-	-	-	+	
3	RC	-	+	-	-	-	-	-	
4	JB	+	+	-	+	+	+	-	
5	SG	-	+	+	-	+	+	-	
6	MN	+	-	-	+	-	-	+	
7	EM	+	+	+	+	-	+	-	

Appendix 2

Important Presenting clinical features

No.	Patient	anaemia	bonepain	Compression paraplegia.	bleeding	chest infection	fever	CCF
8	AO	+	+	-	-	+	+	-
9	AOO	-	-	-	-	-	-	-
10	MM	+	+	+	-	-	-	-
11	MeM	+	+	-	-	+	-	+
12	IN	+	-	-	-	+	+	+
13	MuM	-	+	-	-	-	-	-
14	PK	+	+	-	-	-	-	-
15	EK	+	+	+	+	-	-	-

Appendix 3. Important haematological and biochemical data.

No.	Patient's Name.	Hb g/dl	ESR mm/hr	Wbc x10^9/l	Platelets	Rouleaux formation	Ca+ mmol/l	AP u/l	TP G/L	AL G/L	Glob G/L	Urea mmol/l
1	DK	14.0	6	7.5	140,000	+	2.07	155	95	50	45	3.5
2	FM	9.8	62	2.4	90,000	+	3.78	145	67	35	42	5.4
3	RC	12.6	4	7.8	2000,000	+	2.2	106	108	40	68	3.00
4	JB	7.0	120	1.9	41,000	+	2.45	122	140	37	103	3.1
5	SG	15.2	62	6.4	193,000	+	2.25	95	112	43	69	4.2
6	MN	3.8	87	3.1	41,000	+	2.30	54	88	35	53	5.8
7	EW	6.5	65	8.3	190,000	+	2.38	42	116	32	84	8.5
8	AO	10.4	112	2.8	105,000	+	2.25	48	108	42	66	5.8

Key: - Hb - haemoglobin

ESR - erythrocyte sedimentation rate

Wbc - white blood count

Ca - serum calcium

AP - Serum alkaline phosphatase

TP - serum total protein

AL-serum albumin

Glob-serum globuli

Appendix 4

Important haematological and biochemical data

No.	Name of Patient	Hb g/dl	ESR mm/hr	Wbc x10^9/L	Platelets	Rouleaux formation	Ca+ mmol/l	AP U/L	TP U/L	AL G/L	Glob G/L	Urea mmol/l
9	AOO	13.4	12	3.4	280,000	-	2.38	88	94	38	56	3.0
10	MM	11.4	48	8.4	141,000	+	2.49	102	112	40	72	3.5
11	MeM	6.8	65	3.9	120,000	+	2.35	36	98	37	61	6.1
12	IN	8.9	130	7.6	168,000	+	1.76	74	114	28	86	5.9
13	MuM	13.7	84	7.6	168,000	+	2.53	93	73	44	29	3.8
14	PK	10.7	94	2.8	180,000	+	2.3	68	107	38	69	2.6
15	EK	10.4	60	3.9	160,000	+	2.25	133	116	39	77	4.6

Key: Hb - haemoglobin
ESR - erythrocyte sedimentation rate
wbc - white blood count
Ca - serum calcium
AP - serum alkaline phosphatase
TP - serum total protein
AL - Serum albumin
Glob - serum globulin

Major diagnostic features

Patient No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Patient Name	DK	FM	RC	TB	SG	MN	EW	AO	AOO	MM	MeM	IN	MuM	PK	EK
M band	+	+	+		+	+	+	+	1-	+	+				
B.J. Protein	-	+	-	+	-	-	-	-	-	-	-	-	-	-	-
Bone Marrow	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+
Bone lytic lesion	+	+	+	+	+	+	+	+	-	+	+	-	+	+	+
Bone #/collapse	+	-	+	+	+	-	-	-	-	+	+	-	+	-	+

References:

1. Otieno, L.S. and Ogada, T. Multiple myeloma at KNH, E. Afr. Med. J. 54: 574, 1977.

2. Hobbs, J.R. (1978) Myelomatosis. Medicine Quarterly series, Med. Education (International) Ltd. England.

3. Hobbs, J.R. Immunochemical classes of myelomatosis. Brit. J. Haemat 16, 599, 1969.

4. Hobbs, J.R. Growth rates and responses to treatment in human myelomatosis. Brit. J. Haemat. 16: 607, 1969.

5. Rosen, J.B. Multiple Myeloma. A clinical review. Med. Clin. N. America 59, 375, 1975.

6. Hobbs, J.R. Monitoring myelomatosis. Arch Intern. Med. 1975, 135-125-130.

7. Hammack, W.J. Treatment of Multiple Myeloma. Arch. Intern Med. 135: 157, 1975.

8. Ritzmann, S.E. Loukas, D., Sakai, H., Daniel, J.C., Levin, W.C. Idiopathic (asymptomatic) monoclonal gammopathies. Arch. Intern. Med. 135: 95, 1975.

9. Alexanian, R., Salmon, S., Bonnet, J., Chemotherapy of Multiple myeloma. In: Tagnon, H.J., Staquet, M.J., eds. Recent advances in Cancer treatment. New-York: Raven Press 1977: 19-38.

10. Conklin R., and Alexaman R. Clinical classification of plasma cell myeloma Arch. Int. Med. 135, 141, 1975.

11. Medical Research Council (1971) Myelomatosis: Comparison of Melphan and cyclophosphamide therapy Brit. Med. J., 1, 604.

12. Medical Research Council (1973) Report on the first myelomatosis trial Part 1: Analysis of presenting features of progressive significance, Brit. J. Haemat. 24, 123.

13. Snapper, 1 and Khan A. (1971) Myelomatosis. Fundamentals and clinical features, Basel.

14. De Grunchy G.C. and Baice, J.V. Multiple Myeloma Clinical Haematology in Medical practice 1964, Blackwell.

15. Waldenstrom J (1970) Diagnosis and Treatment of Multiple Myeloma, NewYork.

16. Traub, N. Multiple Myeloma at University Teaching Hospital, Lusaka, Med. of Zambia, 11, 148 1977.

17. Iyun, A. and Isaacs-Sodeye A. Multiple Myelomatosis in Ibadan - a comparative study. E. Afr. Med. J. 53: 581, 1976.

18. Stone, M.J. and Frenkel, E.P. Clinical spectrum of light - Chain myeloma: study of 35 patients with special reference to occurence of amyloidosis, Amer. J. Med. 58: 601, 1975.

19. Sanchoz, L.M. and Domz, C.A. Renal patterns in Myeloma, Ann, Intern. Med. 52: 144, 1960.

20. Denfronzo, R.A. Humphrey, R.L. and Wright J.R. Acute Renal Failure in Multiple Myeloma, Medicine (Baltimore) 54: 209, 1975.

21. Maldonado J.E. Velosa J.A. Kyle, R.A., Wagoner, R.D., Holle, K.E. and Salassa, R.M. Fanconi syndrome in adults; Manifestation of a latent form of myeloma. Amer J. Med.58:354. 1975.

22. Bergsagel, D.E. 1972 Plasma cell myeloma. An interpretive review Cancer 30, 1588.

23. Silverstein, A. and Doinger D.E. Neurological complications Multiple Myeloma, Arch Neurol. 9: 534, 1963.

24. Mukiibi, J.M. Karimi, M. and Kyobe J Multiple Myeloma in Kenyan Africans, a prospective study. E. Afr. Med. J. 58, 171, 1981.

25. Hobbs J.R. Paraproteins, benign or malignant? Brit. med. J.3:699 1967.

26. Zinneman H.H. & Wendell, H.H. (1954) Recurrent pneumonia on MM and some observation on immunologic response Ame. Intern. Med. 41, 1152.

27. Griffiths L. & Brews V.A.L. 1953. The electrophoretic pattern in MM. J. Clin. Pathy 6, 187.

28. Bayrd, D. Bone marrow on sternal aspiration in multiple myeloma. Blood 3: 987, 1948.

29. Osserman E.F. (1961) The plasmocytic dyscrasias. Plasma cell myeloma and primary macroglobulin anaemia Ame. J. Med. 31, 671.

30. Williams, R.C. Benlly R.C. and Howe R.B. Studies of benign serum M components Amer. J. Med. Sci. 287. 275 1969.

31. Hobbs J.R. Immunocytoma O'mice and men. Brit. Med. J. 2 :67, 1971.

32. Davies 1.J.T. Multiple Myeloma. Postgraduate Medicine Llyod-Lukes 1972.

33. Hobbs, J.R. The detection of Bence-Jones proteins. Biochem. J. 99: 15, 1966.

34. Waldbaum, B. and Gelfand M. Myelomatosis in the Rhodesian African. Trop. Geogr. Med. 26: 26, 1974.

35. Osserman, E.F. and Fahey, J.L. Plasma cell dyscrasias: Current clinical and biochemical concepts. Combined staff clinic. Amer. J. Med. 44: 256, 1968.