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A review of 74 patients with newly diagnosed multiple myeloma at a tertiary referral hospital in Nairobi, Kenya

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ORIGINAL ARTICLE / *ARTICLE ORIGINAL*

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Une étude de 74 patients chez lesquels un myélome multiple a récemment été diagnostiqué dans un hôpital tertiaire de référence à Nairobi, au Kenya

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Abstract *Introduction*: Multiple myeloma is a neoplastic disorder characterized by clonal proliferation of plasma cells. We aimed to carry out a retrospective audit to describe clinical and laboratory features of patients newly diagnosed with multiple myeloma.
Materials and Methods: Records of all patients initially diagnosed with multiple myeloma at the haematology clinic of Aga Khan University Hospital, Nairobi, from January 1, 1999 to December 31, 2011 were reviewed. Diagnosis of multiple myeloma was based on (1) increased numbers of abnormal, atypical or immature plasma cells in a bone marrow aspirate or trephine, (2) presence of monoclonal protein *or* free light chains in serum or urine and (3) bone lesions consistent with multiple myeloma.
Results: Seventy-four patients were diagnosed with multiple myeloma. The median age at diagnosis was 59 years. Males comprised 53%. The most common presenting complaints were bone pain in 56 (76%), recurrent infections in 11 (16%) and fatigue in 24 (33%) patients. Anaemia (Hb < 10 g/dl) was present at diagnosis in 47% of patients while 25 (34%) presented with hypercalcaemia (serum calcium > 2.6 mmol/l) and 38 patients (52%) had renal failure at diagnosis (serum creatinine > 110μmol/l). A monoclonal band was demonstrated in 56 patients (76%). Nine patients (12%) had light chain myeloma while only 4 patients had non-secretory myeloma. One patient was found to have biclonal myeloma.
Conclusion: The median age of patients at diagnosis is lower than that reported in other populations [59 years versus 66–68 years] and may indicate a younger age of incidence of the pre-malignant monoclonal gammopathy of undetermined significance (MGUS) in African patients.

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Keywords Multiple myeloma · Plasma cell · Monoclonal gammopathy of undetermined significance · MGUS · Monoclonal protein · M protein

Résumé *Introduction* : Le myélome multiple est une néoplasie caractérisée par une prolifération clonale des plasmocytes. Cette étude cherchait à décrire les caractéristiques cliniques et biologiques des nouveaux cas du myélome multiple.
Méthodes : Les dossiers des patients diagnostiqués avec le myélome multiple, du 1er janvier 1999 au 31 décembre 2011 à la clinique d'hématologie de l'Aga Khan University Hospital de Nairobi (AKUH), furent examinés. Le diagnostic était basé sur : 1) excès de plasmocytes anormaux, atypiques ou immatures dans le myélogramme ou dans la biopsie ostéomédullaire ; 2) présence d'une protéine monoclonale *ou* des chaînes légères isolées dans le sérum ou l'urine ; 3) lésions osseuses caractéristiques du myélome multiple.
Résultats : Soixante-quatorze patients étaient diagnostiqués avec le myélome multiple dont 53 % étaient des hommes. L'âge médian au diagnostic était de 59 ans. Les plaintes les plus fréquentes étaient : douleurs osseuses (56 patients, 76 %), infections récurrentes (11 patients, 16 %) et fatigue (24 patients, 33 %). Quarante-sept pour cent des patients avaient une anémie (hémoglobine < 10 g/dl) ; 25 patients (35 %), une hypercalcémie (calcium sérique > 2,6 mmol/l) et 38 patients (52 %), une insuffisance rénale (créatinine sérique > 110 μmol/l). Une bande monoclonale était démontrée chez 56 (76 %) patients. Neuf patients (12 %) avaient le myélome multiple à chaînes légères tandis que seuls quatre patients avaient le myélome non secrétant. Un patient avait le myélome biclonal.
Conclusion : L'âge médian au diagnostic est moins que celui décrit dans les autres populations (59 contre 66–68 ans). Cela suggère que la gammopathie monoclonale prémaligne de signification indéterminée (MGUS) est fréquente à un âge plus jeune chez les Africains.

Mots clés Myélome multiple · Plasmocyte · Gammopathie monoclonale de signification indéterminée · MGUS · Protéine monoclonale · Protéine M

Introduction

Multiple myeloma (MM) is a plasma cell neoplasm that accounts for almost 15% of all haematological malignancies [1]. It is twice as common in African Americans as in white persons and is slightly more common in men than in women. The median age at onset is 66 years [1].

MM evolves from a pre-malignant condition clinically known as monoclonal gammopathy of undetermined significance (MGUS) [2]. The precise mechanisms by which MGUS evolves into MM are unclear [3].

The most common presenting symptoms of MM are fatigue, bone pain and recurrent infections [1]. Anaemia is present in 70% of patients at diagnosis. Hypercalcaemia is found in about one out of four patients. Skeletal abnormalities can be diagnosed by conventional radiography in approximately 80% of patients while a monoclonal [M] protein can be detected by serum protein electrophoresis in 82% of patients. When immunofixation is included, up to 93% of patients will demonstrate an M protein [4,5].

The International Myeloma Working Group criteria for the diagnosis of symptomatic MM demonstrate the importance of end organ damage in addition to laboratory findings in making the diagnosis [2]. The following three criteria must be met:

- presence of a serum or urinary monoclonal protein;
- presence of clonal plasma cells in the bone marrow or a plasmacytoma;
- presence of end organ damage related to the plasma cell dyscrasia which includes: increased calcium concentration, lytic bone lesions, anaemia and renal failure.

Prognostic indicators in MM are scored more commonly using the International Staging System [ISS] which utilizes serum beta 2 microglobulin [B2M] and serum albumin levels to predict disease stage and survival [6,7]. This is shown in Table 1.

Table 1 International Staging System [ISS] scoring system (page 4).

ISS stage	Features
Stage I	B2M < 3.5 mg/l; serum albumin ≥ 3.5 g/dl
Stage II	Neither stage I nor stage II
Stage III	B2M ≥ 5.5 mg/l

Median survival for ISS stage I is estimated at 62 months, ISS stage II at 44 months and 29-month median survival for ISS stage III [7]. Other independent prognostic factors include performance status, lactate dehydrogenase levels, plasma cell labelling index and plasmablastic morphology [6,8,9]. Presence of cytogenetic abnormalities, such as deletion of chromosomes 13 and17, hypodiploidy and demonstration of translocations t(4;14) and t(14;16), have been proposed as potentially useful prognostic markers and future therapeutic targets [3,8]. These are all of limited availability in Kenya as few laboratories have the capacity for molecular testing. The cost is also prohibitive to most of our patients.

Autologous stem cell transplant is considered the gold standard curative option for young patients with MM. Therapy for patients not eligible for stem cell transplants has evolved from melphalan and prednisone combination which results in partial remission in about 50% of patients. Current therapy utilizes the novel agents – thalidomide, bortezomib and lenalidomide with or without conventional chemotherapy [10–12].

Materials and methods

Hospital records of all patients diagnosed of MM at the haematology clinic of Aga Khan University Hospital (AKUH) from January 1, 1999 to December 31, 2011 were reviewed. Diagnosis of MM was based on findings of:

- plasmacytosis equal to or greater than 10% in a bone marrow specimen;
- presence of a monoclonal protein in serum or urine;
- clinical findings of anaemia, bone lesions characteristic of myeloma, hypercalcaemia and renal impairment.

Patients with plasmacytosis due to underlying connective tissue disorders, liver disease, metastatic carcinoma or HIV infection were excluded. Also excluded were patients with monoclonal gammopathy of undetermined significance (MGUS), smoldering MM, solitary plasmacytoma and plasma cell leukemia.

Physical examination, laboratory results and radiology findings dating to within three months of diagnosis were reviewed and recorded. Information was obtained from patients' medical records.

Results

Seventy-four patients were initially diagnosed with MM from January 1, 1999 to December 31, 2011. The patients ranged in age from 30 to 99 years. The median age at

diagnosis was 59 years. Thirty-one patients (53%) were male. This is shown in Fig. 1.

Presenting complaints

The most common presenting complaints were bone pain in 56 (77%) and fatigue in 24 (33%) patients. Recurrent infections, considered a common feature of MM in other studies, were only reported in 11 patients (17%) in this cohort. This is depicted in Fig. 2.

Haematologic and biochemical blood findings

Anaemia, defined as haemoglobin of less than 10 g/dl, was present in 47% of patients. Renal failure, defined by serum creatinine greater than 110 μmol/l, was present in 52% of patients. The patient haematologic and biochemical abnormalities on presentation are shown in Fig. 3.

Monoclonal proteins

A monoclonal band was demonstrated by serum protein electrophoresis in 45 patients (78%). Nine patients (16%) had light chain myeloma. One patient was found to have biclonal myeloma. Four patients had non-secretory myeloma. The demonstration of monoclonal bands is shown in Table 2.

The most common immunoglobulin demonstrated was IgG kappa followed by IgA kappa. Monoclonal proteins by type are depicted in Fig. 4.

Radiographic findings

Skeletal abnormalities were demonstrated in 57 patients (77%). Lytic lesions were the most commonly reported

Table 2 Demonstration of monoclonal bands (page 6).

Serum M protein	78%
Serum + urine M protein	87%
Light chains only	4%
Non-secretory	6%

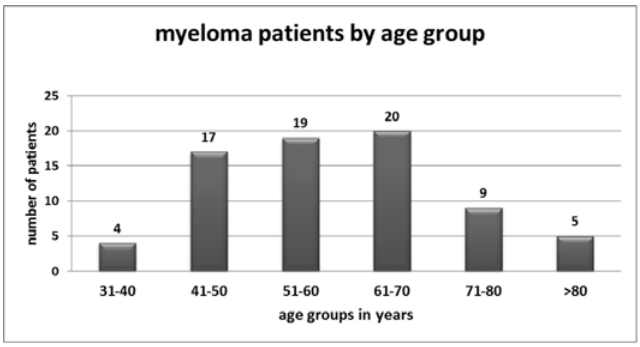

Fig. 1 Patients diagnosed with multiple myeloma defined by age group (page 5)

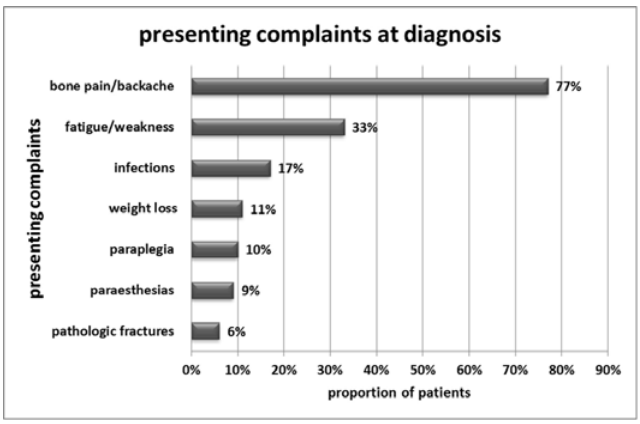

Fig. 2 Patient presenting complaints at time of diagnosis (page 6)

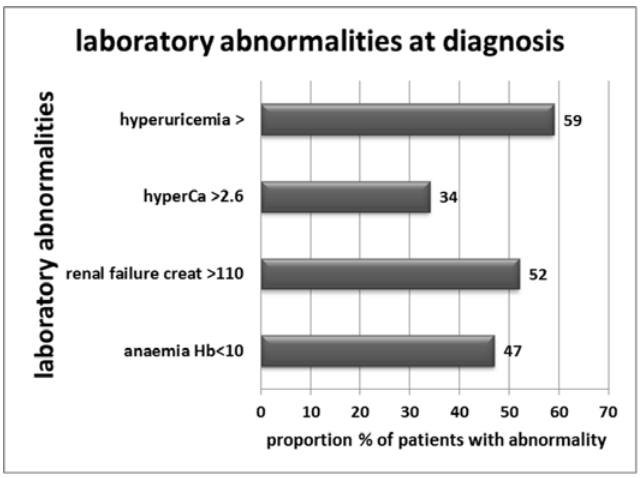

Fig. 3 Patient haematologic and biochemical abnormalities on presentation (page 6)

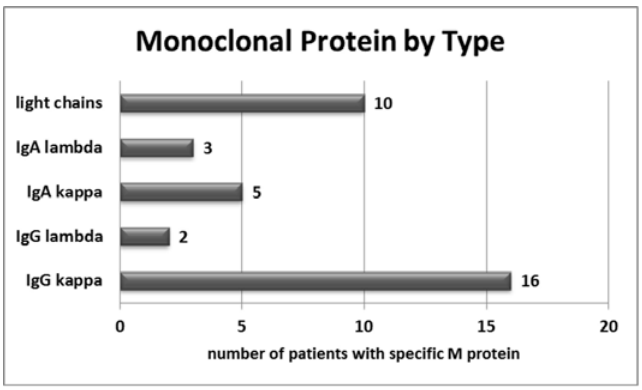

Fig. 4 Monoclonal protein by type (page 6)

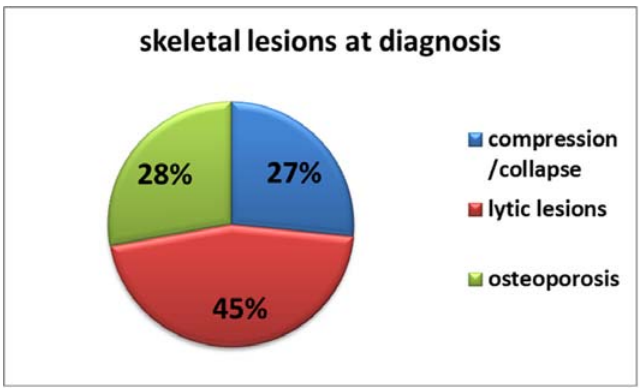

Fig. 5 Skeletal lesions by proportion in patients with multiple myeloma (page 6)

abnormalities on skeletal survey (62%), followed by vertebral collapse/compression (38%) and osteoporosis (36%). The most common sites for radiographic abnormalities were the lumbar spine (50%) and skull (11%). Figure 5 shows skeletal lesions by proportion in patients with MM. Lytic lesions were more common in ribs than in other sites, while compression fractures were most common in the lumbar spine. Pathological fractures not due to compression were reported in 15% of patients.

Bone marrow examination

Bone marrow plasmacytosis was demonstrated via aspirates or trephine biopsies. Plasma cell populations in our patients ranged from 2% to >90% of haematopoietic cells.

Discussion

MM was diagnosed in 74 patients at the haematology clinic of AKUH over a ten-year period from January 1, 1999 to December 31, 2011.

The median age of 59 years at diagnosis is younger than the median age of 66–68 years reported in other studies [1,13]. Our patient population being African in origin might have a younger age of diagnosis of MM than other ethnic groups. This has been proposed to be due to a higher incidence and younger age of development of monoclonal gammopathy of undetermined significance (MGUS) in Africans compared to other ethnic groups [14,15]. MGUS is considered a pre-malignant condition that leads to myeloma and thus it may be deduced that a younger age of development of MGUS leads to younger age of development of myeloma. However, as MGUS screening is not routinely done in Kenya, this fact is yet to be verified in our population. This may also explain why our patients tend to present with overt end organ damage myeloma at a younger age.

Bone pains were the most common presenting complaints present in 76%, followed by fatigue in 33% of patients. A significant proportion of patients (19%) presented with neurologic symptoms such as paraesthesias or paraplegias. This might suggest advanced bony lesions with collapse or compression at the time of diagnosis, perhaps due to delayed presentation of the patient to the haematology clinic, delayed referral to a tertiary institution or delay in diagnosing myeloma.

Renal failure was demonstrated in over half of our patients (58%). Kidney disease in myeloma is often asymptomatic and most commonly results from myeloma kidney (precipitation of monoclonal light chains in distal and collecting tubules). It is of note that kidney disease in African patients is often due to a higher prevalence of diabetes and hypertension with concurrent nephropathy. To what extent this affects the incidence of renal disease in myeloma was not established in our study.

Hypercalcaemia due to lytic bone resorption was present in 33% of our patients, less than half of those who had radiologic evidence of skeletal abnormalities (77%). Hypercalcaemia is also a less described contributor of renal failure in myeloma.

Anaemia was present in 50% of our patients, far less than described in other studies [1]. Anaemia in myeloma results from inadequate production of red blood cells due to either erythropoietin deficiency from accompanying renal failure or pronounced marrow replacement by clonal plasma cells.

Monoclonal proteins were demonstrated by electrophoresis and immunofixation of serum and/or urine, and urine light chain detection. Combinations of serum and urine assays demonstrated M proteins in 94% of patients. Four patients were found to have non-secretory myeloma – defined in our study as the absence of monoclonal proteins by serum or urine electrophoresis. The absence of free light chain assay in our institution at the time of this study might account for these four patients.

One patient was found to have biclonal myeloma with both IgG kappa and IgG lambda monoclonal proteins demonstrated on serum protein electrophoresis. This is a rare finding described in less than 2% of myeloma patients.

This retrospective audit focused on clinical and biochemical findings in patients with MM at diagnosis. Ours is a hospital-based cohort from one referral centre in the country. Prospective studies determining prognostic factors and survival rates in our patient population are lacking and we hope that more publications from other research groups and tertiary institutions in the country will follow.

Declaration This study was carried out in compliance with the laws of Kenya concerning hospital-based retrospective audits.

Conflict of Interest: G. Kiraka, M. Etabale and M. Riyat have no conflict of interest to declare.

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