Myelomatosis: Clinical and laboratory features in Nigerians

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Summary

Background: **The objective was to investigate the factors influencing survival of Nigerians with Myelomatosis.**

Materials and Methods: **The pre-therapy clinical and laboratory features of patients managed at the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, between June 1986 and May 2001 were studied. Diagnosis was based on history of bone pain, marrow plasmacytosis, osteolytic bone lesions, serum biochemical profile, monoclonal (M) band, and/or Bence-Jones proteinuria.**

Results: **Twenty-seven patients (22 males, 5 females) aged 15 to 81 (median, 60) years were managed within the study period. Of the 27, 5 (18.5%) were 40 years or younger while 14(51.8%) were 60 years or older. Multiple myeloma (MM) is the main sub-type seen (81.5%). Majority presented with bone pain, weakness, fatigue and inability to walk. Anaemia, high erythrocyte sedimentation rate and bone marrow plasmacytosis were the significant haematological findings. Serum protein electrophoresis showed M-band in 6 cases of MM, with 3 of them also having Bence-Jones proteinuria. Renal function impairment and hypercalcaemia occurred mainly in those with MM. Multiple osteolytic lesions and pathological fractures were recorded in 44% of those with MM and Solitary Myeloma of Bone. Twelve patients were already dead at the time of analysis, with renal failure being the cause in 8 and anaemia in the rest. The median survival was 1.2 months.**

Conclusions: **We could conclude that the presenting features of Nigerian patients with myelomatosis are not different from reports elsewhere, but high default rate and short survival are particularly noted.**

Keywords: ***Myelomatosis, Clinical features, Survival, Nigerians.***

Résumé

Introduction: L'objectif était d'étudier les facteurs qui influencent la survivie des Nigerians atteints de la myolomatose.

Matériels et Méthodes: Les traits laboratoires et pré-thérapie cliniques des patients soignés au centre hospitalier universitaire d'Obafemi Awolowo, Ile-Ife entre juin 1986 et 2001 ont été étudiés. Le diagnostic était fondé sur l'histoire de la douleur osseuse, des plasmocytes dans les moelle osseuse, lésions ostéolytique osseuses, sérum de profile biochimique, monoclonal (M) groupe et/ou protéinurie Bence-Jones.

Résultats: Vingt sept patients (22 du sexe masculin, 5 du sexe féminin) âgés 15 a 81 (moyen 60) ans ont été soignés au cours de la durée de cette étude. Entre 27,5 (18,5%) nous avions 40 ans ou moins tandis que 14 soit (51,8%) nous avions 60 ans ou âgé de plus de 60. Myélome Multiple (MM) est principalement le sous-type vu (81,5%). La plus grande partie se sont présentées atteintes de la douleur osseuse, faiblesse, la fatigue, incapacité de marcher. Anémie, taux élévé de la sédimentation érythrocyte et la plasmocytes dans les moelles osseuses étaient notamment les résultats hématologiques. Sérum de la protéine électrophorèse avait indiqué M-groupe chez 6 cas de MM, avec 3 d'entre eux également atteints de la proténurie Bence-Jones.

Affiablessement de la fonction rénale, et l'hypercalcémie ont été provoqués surtout chez ceux avec MM. Lésions ostéolytiques multiples et des fractures pathologiques ont été notées chez 44% de ceux avec MM et le myélome solitaire osseux. Douze patients sont déjà morts au moment d'analyse, atteints de l'insuffisance rénale étant la cause attribuable chez 8 et anémie chez d'autres. La survie moyenne était 1, 2 mois.

Conclusions: De ceci nous conclons que les traits accusés des patients nigerians atteints de myélomatose ne sont pas différents des rapports d'ailleurs, mais on avait particulièrement noté le taux élevé de défaut et survie brève.

Introduction

Myelomatosis is a haematological cancer that is more commonly seen in blacks than in the Caucasians[1, 2]. The disease is invariably fatal with a median survival of about 3 years[3]. The disorder is characterized by malignant proliferation of a clone of plasma cells in the bone marrow and excessive secretion of monoclonal (M) immunoglobulin (or paraprotein) in the serum and/or urine[4]. This is associated with a decrease in the normal polyclonal immunoglobulin in the serum (immunoparesis). In the majority of cases, complete immunoglobulin molecule (both heavy and light chains) is synthesized, while in about 15% of cases, only light chains (Bence-Jones proteins) are synthesized[5]. The light chain may be kappa (k) or lambda[1] but never the two together[6]. A minority of cases, described as non-secretory myelomatosis, produces neither M-protein nor light chains[7]. The clinical and laboratory features of myelomatosis are attributable to the effects of the neoplastic plasma cells and the paraproteins. These are anaemia, weakness, bone pain, pathological fractures, hypercalcaemia, renal insufficiency, bleeding diathesis and neurological complications. Myelomatosis has a progressive course with a median survival of six months when no treatment is given and about three years with therapy[8]. Prediction of survival at diagnosis is aimed at identifying adverse prognostic factors. Those presenting with adverse prognostic factors would benefit from aggressive and more toxic therapy than those with favourable prognostic factors that suggest a longer survival.

The purpose of this review is to analyze the presenting features at diagnosis and assess their predictive value on survival in a group of Nigerians with this neoplastic disease.

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which is said to be more prevalent in blacks than in the Caucasians[1].

Materials and methods

Charts of all patients with myelomatosis managed at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, between June 1986 and May 2001 were reviewed. The pre-therapy clinical, laboratory, and radiological features were extracted from the case records. The total number of other haematological malignancies managed within the same study period was also noted.

Diagnosis of the disease was based on history, physical examination, results of bone marrow aspirates and/or biopsies (or other tissue biopsies), skeletal survey, complete blood count (CBC) and erythrocyte sedimentation rate (ESR). Serum biochemical indices, including serum protein electrophoresis, and Bence-Jones proteinuria were also checked. The results of bone marrow/tissue biopsies, skeletal survey and CBC were used in categorizing patients into the various subtypes, such as multiple myeloma (MM), solitary myeloma of bone (SMB), extramedullary myelomatosis (EMM) and plasma cell leukaemia (PCL). Survival of patients was calculated from the date of diagnosis until the date of death. Proportions of patients lost to follow up were noted.

SPSS for windows version 10 was used for all statistical calculations.

Results

Twenty-seven patients (22 males and 5 females, M: F ratio 4.4:1) with myelomatosis were identified out of a total of 483 haematological malignancies managed within the study period, giving an incidence of 5.6% of haematological cancers. Multiple myeloma constituted the major subtype (81.5%), followed by EMM and SMB (7.4%, respectively) and PCL (3.7%) (Table1). The median age at presentation was 60 years with 74% of the patients aged 50 years and above (Fig. 1). The main presenting symptoms (Table 2) were bone pain (53.3%), fatigue (15.6%) and inability to walk (15.6%). Others include mucosal bleeding (8.9%), breathlessness (4.4%) and weight loss (2.2%). Multiple osteolytic lesions, compression wedge fracture of the vertebrae and long bone fractures were confirmed radiologically in 44.4% of cases.

Table 1 Myelomatosis subtypes seen in Ile-Ife, Nigeria.

Myelomatosis subtype	No (%)
Multiple myeloma	22(81.5%)
Extramedullary myelomatosis	2(7.4%)
Solitary myeloma of bone	2(7.4%)
Plasma cell leukaemia	1(3.7%)

Table 2 Symptom at diagnosis

Symptom	No of cases
Bone pain	27(53.3%)
Weakness and fatigue	7(15.6%)
Inability to walk	7(15.6%)
Mucosal bleeding	4(8.9%)
Breathlessness	2(4.4%)
Weight loss	1(2.2%)

Table 3 Mean ± SD of haematological parameters at diagnosis

Parameter	Mean ± sd
PCV (%)	23.6 ± 7.4
WBC (x10^9/L)	7.1 ± 4.1
Platelet (x10^9/L)	155.0 ± 101.8
ESR (mm/hr)	118.3 ± 46.9
Marrow plasma cells (%)	53.8 ± 21.5

Table 4 Mean ± SD of Biochemical parameter at diagnosis

Parameter	Mean ± SD
Creatinine (μmol/L)	339.7± 335.6
Calcium (mmol/L)	2.44 ± 0.40
Albumin (g/L)	29.50 ± 8.12
Globulin (g/L)	54.62 ± 29.51
Urea (mmol/L)	12.50 ± 7.70
Uric acid (mmol/L)	0.39 ± 0.18

Table 5 Some laboratory parameters and survival in myelomatosis

Parameter	Multivariate Beta (β) value	Multivariate p-value	Univariate Beta (β) value	Univariate p-value
Calcium	-0.361	0.308	-0.331	0.211
Creatinine	-0.045	0.897	-0.173	0.418
Albumin	-0.225	0.450	-0.299	0.138
PCV	0.317	0.296	0.102	0.619
ESR	0.020	0.980	-0.460	0.031

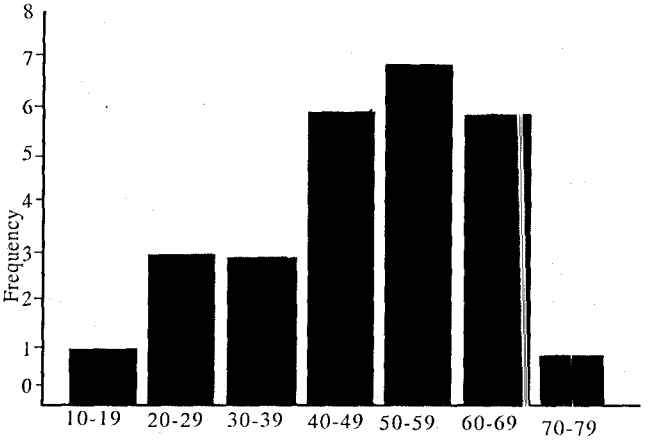

Fig. 1 *Age distribution of Myeloma patients in Ile-Ife, Nigeria*

Haematological indices (Table 3)

A majority of the patients presented with moderate to severe anaemia, with a mean ± standard deviation (mean ± sd) of 23.6 ± 7.4%. Erythrocyte sedimentation rate (ESR) was markedly elevated (>100mm/hr) in 72.7% of cases with a Mean ± SD of 118.3 ± 46.9mm/hr (Westergren). Increased plasma cell (>20%) with abnormal morphology in the bone marrow was seen in 82.6% of cases with a Mean ± SD of 53.1 ± 11.5%. However, patients with extramedullary Myelomatosis presented with essentially normal bone marrow. Thrombocytopaenia (platelet count < 90 x 10^9/L) was recorded in 42.3% (mean ± sd = 155 ± 101.78 x 10^9/L). Leucocytes counts were essentially normal.

Biochemical indices (Table 4)

The serum electrophoretic pattern showed M band in

29.6% of cases, the rest were reported as either non-gamma hyperglobulinaemia or normal appearing pattern. Bence-Jones proteinuria was detected in 25.9% of cases. High peak of abnormal globulin (> 40g/L) was found in 65.4% of cases with a mean ± sd of 54.6 ± 29.0g/L, while marked hypoalbuminaemia (<30.0g/L) was found in 65.4%, with a mean ± sd of 29.50 ± 8.12g/L. It is interesting to note that Bence-Jones proteinuria and raised immunoglobulins were found mainly in cases of Multiple myeloma. Renal function impairment (serum creatinine >200μmol/L) was observed in 40% of cases. High serum urea (>20mmol/L) and uric acid (>15mmol/L) were obtained in 51.9% and 40.9% of cases, respectively. Remarkable serum calcium levels (>3.0mmol/L) were found in only 12.5% of cases. The abnormal renal function and hypercalcaemia were observed mainly in cases of Multiple myeloma.

Therapy and survival

Although 77.8% of the patients received chemotherapy (Cyclophosphamide or Melphalan plus prednisolone combination), this was inadequate in 85.7% of the cases as only 3 patients had up to 6 cycles of drugs before death or voluntary cessation of clinic attendance. The median period of follow-up was 2.75 months. Nine of the patients were seen for up to 6 months and only 3 beyond 1 year. The secondary causes of death were attributed to renal failure (66.7%) and anaemia (25.0%). However cause(s) of death could not be ascertained in one patient that died at home. Analyzing both jointly and separately, the serum calcium, creatinine, albumin, and haematocrit levels, have high coefficient of regression (i.e., beta- [β] values) when regressed with survival. However, the p-values were not statistically significant. Univariate regression of ESR against survival showed significant correlation ($\beta = -0.460$, $P = 0.03$)(Table 5).

Discussion

Myelomatosis has an incidence twofold greater in blacks than in whites and it accounts for about 10% of other haematological malignancies[8]. The incidence in the present study is about 5.6% of other haematological cancers. The male to female ratio was 4.4:1. The male preponderance found in this review is at variance with some other series that reported a ratio of 1:1[9,10]. This difference may be due to the poor economic power of women in our environment, which made it difficult for many of them to come to the hospital.

Multiple myeloma is the most common subtype of myelomatosis. This was the case in this review as it constituted about 81.5% of the cases seen. Others have reported similar proportion[11]. The incidence of myelomatosis increases with age and it is uncommon in persons younger than 40 years[12]. This was the observation in this review, in that less than 15% of our cases were 40 years and below at diagnosis, thus confirming the finding of Nossent et al[13]. Bone pain and weakness due to bone marrow disease were the major presenting symptoms. Reports from other workers[14, 15, 16] were in line with this observation. In addition, 15.6% of our patients also presented with neurological complications that could have resulted from wedge compression fracture of the vertebrae or extradural extension of myeloma tissue from the vertebral body, mucosal bleeding (8.9%) that could result from platelet coating by the M-protein[17], weight loss and breathlessness. Others have also reported these uncommon clinical features[18,19]. Severe anaemia, found in a considerable proportion of our cases (63%) has also been documented in other series[20]. Defective erythropoiesis secondary to insufficient endogenous erythropoietin production[21, 22], massive invasion of bone marrow by myeloma cells, autoimmune haemolysis and high levels of interleukin-6 that can suppress erythropoiesis are important contributory factors.

In a review by Nossent et al[13], infection was found to be the immediate cause of death in 54% of cases. This has been ascribed to granulocytopenia, immunoparesis and suppression of CD4+ cells[23]. Interestingly, none of our patients was confirmed to have died of infection. However more than half of the patients died as a result of renal insufficiency, the second most common cause of death in myelomatosis[23]. This is unlike the reports of Blade et al[24] who reported 12% of death as a result of renal failure. This is not unexpected as more than 40% of our patients with Multiple myeloma had high levels of urea (>20mmol/L), creatinine (>200μmol/L) and uric acid (>15mmol/L). In addition, 6(27.3%) had Bence-Jones proteinuria while 2(9.1%) had hypercalcaemia (calcium >3.0mmol/L). Abnormal values in these laboratory parameters are known predisposing factors to renal failure.

The median survival of 2.75 month obtained in this series is unacceptably low when compared with other series such as those of Blade et al[24] (60 months). The shorter survival of patients in this series is, however, not surprising in view of the unfavourable laboratory and clinical indices at presentation. As at the time of analysis, 12 of the patients were already dead with a median survival of 1.2 months. Only 2 patients survived beyond 1 year, while the longest survivor lived for about 2 years after diagnosis. Another important observation from this study is the high default rate. Only 2 of the patients are still being seen at the time of analysis. Default is a problem in cancer management in Nigeria[25]. This could be traced to the general poverty in the society and very high cost of medical facilities.

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