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Biological Aspects of Multiple Myeloma in Pzaga Teaching Hospital Mahajanga, Western Madagascar

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Abstract:- Multiple myeloma is malignant proliferation of a plasma cell clones in the bone marrow. Incidence increases with age. We aimed to report biological aspects of multiple myeloma diagnosed at PZaGa Teaching Hospital, from 2016 to 2021. A 6-year retrospective, descriptive study was conducted including patient files underwent a bone marrow smears at Haematological laboratory. We included all patients diagnosed with myeloma on bone marrow smears with plasmacytosis more than 10%, associated with one or more CRAB criteria (hypercalcaemia, renal involvement, anaemia, bone lesion). Demographic, biological parameters were assessed. We enrolled 15 cases of multiple myeloma (2.5 cases per year). Mean age was 57.93 years, with sex ratio 1.5. Bone pain was the main clinical reason (80%). Anaemia was found in 66.7% of cases. Plasma cells infiltration range between 30 to 60% was found in 86.60%. Serum protein electrophoresis was performed in only 13.30% of cases (n=2), with a monoclonal peak in IgG. Hypercalcaemia was found in 33.30% of myeloma and 86.70% of patients developed renal failure. Practice of cytologic study of bone marrow smears by assessing plasma cell infiltration is a decisive step to diagnose multiple myeloma in this region of Madagascar.

Keywords:- *Mahajanga; Myelogram, Multiple Myeloma, Plasmacytosis.*

I. INTRODUCTION

Multiple myeloma is a malignant proliferation of a plasma cells clone in the bone marrow **[1].** It combines secretion of a monoclonal immunoglobulin with a secondary immune deficiency. This results in a clinical and/or radiological bone syndrome, as well as visceral manifestations, mainly renal. Typically, clinical manifestations are the result of heterogeneous biological disorders from the early, indolent phase to the terminal phase of multiple myeloma **[2].**

Multiple myeloma incidence increases with age; it affects elderly subjects **[3].** Multiple myeloma accounts for 1 to 2% of cancers and 10% of haematological malignancies **[4]**. It leads to 1% of cancer deaths and around 19% of haematological malignancy deaths in adults **[5]**. In Africa, as in most developing countries, diagnosis is not always easy. Management still needs to be improved, given the lack of technical and financial resources and limited access to appropriate healthcare facilities. In Madagascar, multiple myeloma incidence has yet to be determined due to the lack of a national register of tumour pathologies. A retrospective descriptive and cross-sectional study was carried out on the files of patients who requested bone marrow smears from January 2016 to December 2021 at Androva Teaching Hospital, Mahajanga, Western Madagascar. The aim of the study is to describe biological characteristics of multiple myeloma diagnosed in the haematological laboratory.

II. MATERIALS AND METHODS

All patients who underwent a myelogram during the study period were evaluated. We enrolled patients' records whose myelogram diagnosis was multiple myeloma. This diagnosis was based on the presence of significant bone marrow plasmacytosis (more than 10% of plasma cells) associated with one or more CRAB criteria (hypercalcaemia, renal involvement, anaemia, bone lesion). For each case, we recorded patient's age, gender, and main clinical signs. Biological parameters assessed haemoglobin levels, erythrocyte sedimentation rate (ESR), calcemia, protidemia, creatininemia and serum protein electrophoresis. Bone marrow smears was performed to assess bone marrow plasmacytosis, after 2 different biologists 'readings. Data were collected and treated using Microsoft Excel 2013 and SPSS version 20.0.

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III. RESULTS

Fifteen (15) cases of multiple myeloma among 63 patients were diagnosed during 6 years, so 23.80% of patients underwent bone marrow cytologic study. Multiple myeloma incidence was 2.5 cases/year **(Table 1)**. Mean age was 57.93 (± 8.9) years, with extremes of 43 and 71 years. Sex ratio (male/female) was 1.5. Bone pain was the main reason for requesting a myelogram in 80% of cases. Clinical manifestations were dominated by anaemic syndrome in 66.70% of cases. Anaemia with haemoglobin level less than 7g/l was found in 46.70% of patients, followed by a normal haemoglobin level in 33.30% **(Table 2)**. Anaemia was normocytic, normochromic, and non-regenerative. Erythrocyte rolls were found on 80% of blood smears from patients. Erythrocyte sedimentation rate was extremely high in all patients. All patients had bone marrow plasmacytosis more than 10%, and the infiltration rate was between 30 and 60% in 86.60% of cases **(Table 2)**. These plasma cells showed cytological criteria of malignancy under the light microscope according to the recent IMWG publication [6]. Serum protein electrophoresis was performed in 13.30% of cases (n=2) with a monoclonal peak in IgG gamma globulins.

Table 1: Multiple Myeloma Cases In Haematology Laboratory from 2016 - 2021

Years	Frequency (n=15)	(%)
2016	1	6,66
2017	1	6,66
2018	2	13,33
2019	3	20,00
2020	6	40,00
2021	2	13,33

Table 2: Haematological Parameters in Multiple Myeloma Patients

Parameters	Frequency (n=15)	%
Haemoglobin levels (g/l)		
< 70 g/l	7	46,70
[70-100[g/l	1	6,70
[100 -120[g/l	2	13,30
[120-180] g/l	5	33,30
Bone marrow plasmacytosis (%)		
[10-30]	1	6,70
] 30-60]	13	86,60
> 60 %	1	6,70

IV. DISCUSSION

Fifteen cases of multiple myeloma were identified in 6 years in Mahajanga Teaching Hospital with a rate of 2.5 cases per year. In 2015, Harioly *et al* reported an average frequency of 6.85 cases per year in Antananarivo the capital of Madagascar **[7].** Frequency is higher in Senegal with annual frequency of 12.36 cases in 2017 [8]. Multiple myeloma incidence varies according to selection criteria and population. In the literature, multiple myeloma accounts for 10% of haematological malignancies [9]. It is the most common primary malignant bone disease [10]. Its incidence is 4 cases per 100,000 population per year; it is twice as common in the black population. Genetic predisposition and environmental factors increase the risk of developing multiple myeloma. Our findings do not yet allow us to estimate the incidence of the disease throughout the whole island.

Average age of patients with multiple myeloma in Mahajanga Western Madagascar was 57.93 years, with more men than women affected. For instance, these demographic data confirm Nigerian and Moroccan observations reported in 2015 and 2014 with respective mean age of 58.8 and 59.18 years [11, 12]. It is commonly reported that median age at diagnosis of multiple myeloma is 70 years in western countries, and its incidence increases with age [3] such as the United States, where it is 62 years **[13].** In Malagasy people, age of discovery appears to be earlier; this could be explained by the youth of Malagasy population. Male predominance as well as in our findings was reported in African and European studies. Sex ratio was more than 1 [14]. Bone pain was the most common clinical reason for discovery, accounting for 80% of cases. Same findings were registered in 83.3% of multiple myeloma diagnosed in Antananarivo in 2015 according to Harioly *et al* [7].

Anaemia was found in all the 15 patients at the diagnosis time, with nearly 46.70% having haemoglobin level below 7g/dl. Mohammadi. *et al* reported 38.09% of Algerian patients in 2017 with severe anaemia [15]. Those findings result from delayed diagnosis with patients only diagnosed in advanced stages. Anemia results from bone marrow failure due to infiltration by malignant plasma cells,

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haemodilution due to hyperprotidemia and reduced erythropoietin (EPO) secretion due to renal failure [16].

Bone marrow plasmacytosis for all patients with multiple myeloma in Mahajanga were more than 10%. This is an essential test for assessing bone marrow invasion by normal or pathological plasma cells **(Figure 1).** In our study, 86.60% of patients had a bone marrow plasma count of 30-60%. It is close Moncef *et al* in Morocco and Seynabou *et al* in Senegal reports, in which bone marrow plasmacytosis were respectively 30% and 16.8% [17, 8]. Quantitative and qualitative assessment of bone marrow plasmacytosis is therefore a decisive step in the diagnosis of multiple myeloma [17]. It is combined with examination of the monoclonal component of the proteins [18].

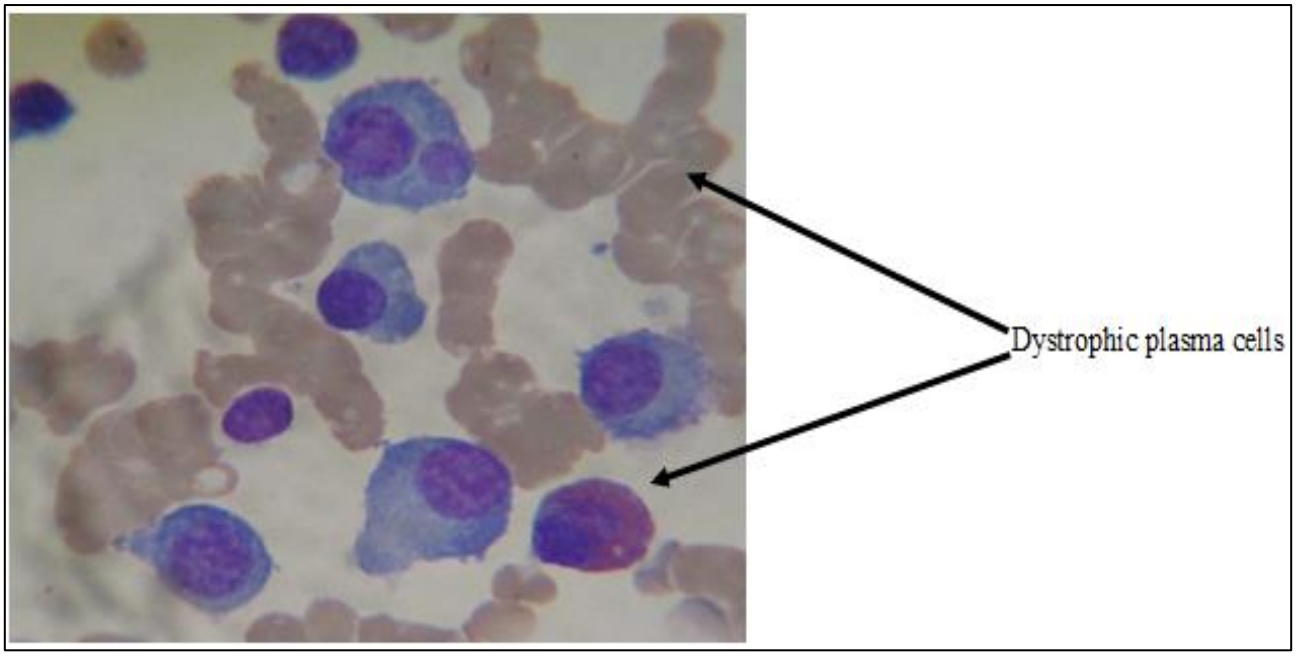

Fig 1: Bone Marrow Infiltration with Dysmorphic Plasma Cells Suggesting Multiple Myeloma.
Source: Medical Analysis Laboratory, PZaga Teaching Hospital Mahajanga, Madagascar

Only 2 out of 15 patients (13.3%) of patients had serum protein electrophoresis. These two cases showed a monoclonal peak in IgG gamma globulins. This biological exam is not yet available in the local Hospital. Patients have to go in the capital to make analysis performed.

Hypercalcaemia was observed in 33.30% of multiple myeloma cases. In 2018, patients with multiple myeloma in Cameroon were reported having elevated calcemia in 31.3% [19]. Several mechanisms could explain the occurrence of hypercalcaemia in multiple myeloma. The main cause is hyperosteoclastosis induced locally by myeloma cells. Reduced glomerular filtration rate, increased tubular calcium resorption and reduced osteoblastic activity also contribute to hypercalcaemia [7].

Therefore, 86.70% of myeloma patients in Mahajanga developed renal failure. Majority of patients (53.30%) had creatinine clearance of 30 to 59 ml/min. In Morocco, renal failure concerned only 32.1% of multiple myeloma patients [20]. Several factors could determine the presence of renal failure in multiple myeloma. Renal impairment is commonly a direct consequence of serum free light chains accumulation and precipitation. Other causes include hypercalcaemia and exposure to drugs and other nephrotoxic substances [21]. The high proportion of renal failure in our study could be explained by the multiple myeloma associated with decoction intake.

Protein levels were elevated in 46.70% of cases. In 2021, El Ghali *et al* reported hyperprotidemia in 50% of cases of multiple myeloma in Morocco [22]. Hyperprotidemia in multiple myeloma is due to monoclonal peak of immunoglobulin.

V. CONCLUSION

Quantitative and qualitative assessment of bone marrow plasmacytosis is a crucial step in multiple myeloma diagnosis. However, it is essential to associate bone marrow examination the results with clinical data and other investigations. This haematological analysis improve medical practice to diagnose haemopathies in different regions of Madagascar.

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