

HEMATOLOGICAL CHANGES IN MULTIPLE MYELOMA

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Abstract: This paper presents the results of some hematological investigations which were done in the laboratory of the Municipal Emergency Hospital, Barlad on a number of 10 patients diagnosed with multiple myeloma. This type of blood cancer, also called plasmocytoma or Kahler's disease, is characterized by a malignant proliferation of the plasmocytes in the bone marrow with serious hematopoietic perturbations, dramatic increase of ESR, bones pain, hypercalcemia, renal affection, etc.

Our results confirm both the grouping of the red cells into scrolls and the presence of the big myeloma plasmocytes, grouped into nests (foci), and sometimes can take unusual shapes (dumb bells). The hemoglobin and hematocyte decrease until 63-65% compared to the normal physiological limit, the number of red cells reaches up to 20-23% from the normal limit, both for men and women, and the ESR amplifies compared to the normal as it follows: up to 12 times for men (65-158 mm/h) and up to 13,2 times for women (33-156 mm/h). The white cells and thrombocytes present some restricted numerical changes compared to the red series.

INTRODUCTION

The multiple myeloma, also called plasmocytoma or Kahler's disease is a neoplastic disease of the blood tissue, characterized by a malign proliferation of the plasmocytes within the bone marrow and a production of an abnormal quantity of immunoglobulins (BUTOIANU and STANICA, 1973). The plasmocytes represent a class of B cells which produce the humoral factors of immunity, that means the antibody.

This type of blood cancer is produced by an unknown cause. It rarely strikes individuals aged under 40; it's more common among those older than 60 years, especially when we talk about individuals exposed to radiations or chemical substances. It is not a contagious disease, not even a hereditary one, even though the first-degree relatives (parents, sisters, brothers) of those patients diagnosed with multiple myeloma present a higher risk to develop neoplasia.

Men are more frequently affected than women are, and the incidence at the black people is double compared to that of the white people. MM is a severe neoplasm which represents about 1% from all the malignant disorders on white people and about 2% on black people, which means an average of 13% from the hematologic cancers at white people and 33% at black people. The life expectancy from the diagnosis is from 3 to 5 years.

The data from the scholarly literature records the fact that the malignant proliferation of the plasmocytes within the multiple myeloma interferes with the normal production of the blood cells, causing anaemia, leukopenia, and even thrombocytopenia. ESR- the red cells sedimentation rate – has high values- most often over 100 mm/h (MUT POPESCU, 2003) and, together with the normochromic anaemia, is an important sign in diagnosing a patient with bone pain.

The main objective of this report is to study the hematological changes collateral to the malignant proliferation of plasmocytes, according to the age and gender of the patients suffering of multiple myeloma. This study was done between 2004-2005, and the surveyed patients were from the Municipal Emergency Hospital in Barlad.

MATERIALS AND METHODS

The investigations were developed on a casuistry composed of a number of 10 patients diagnosed with multiple myeloma (6 women and 4 men), aged between 47 and 70 years. The samples of venous blood were gathered on an anticoagulant (Na₂-EDTA), the morphological examination and the achievement of the haemoleucogram were realized with the help of the hematological analyser called „CELLTAC MEK – 6318K”. Within the comparative study of the cases surveyed, the age and the gender of the patients were correlated with the following hematologic values: the ESR, the strength of hemoglobin (g/dl), hematocyte (%), the number of red cells, (x 10⁶/μl), the number of thrombocytes (x 10³/μl), eosinophils (%), basophils (%), and monocytes (%). The peripheral blood smear and the bone marrow smear were realized according to the classic methods (TANASESCU, 1974; MISAILA nad COMANESCU, 1999), and for colouring it was applied the May-Gründwald Giemsa method (ȚIȚEICA and MARINESCU, 1984). The red cells sedimentation rate was measured through the Westergreen technique (KONDI, 1981). The realization and colouring of these smears were made in Hematology Laboratory from the Municipal Emergency Hospital, Barlad, and the pictures were taken in the Genetics Laboratory of the Biology Department from „A.I.Cuza” University, Iasi, by using a MC 5A microscope.

RESULTS AND DISCUSSIONS

The complexity of the interferences between the malignant proliferation of the plasmocytes within the multiple myeloma and other collateral functional perturbations goes beyond the sphere of the blood tissue, taking the shape of some various complications. The most severe complications dwell on the bone pain, hypercalcemia, renal insufficiency, bone marrow compression. Over 50% of the patients reported these issues of renal pathology, and an average of 80% of the patients with multiple myeloma showed signs of anaemia. Most of the times, this is normochrome and normocytic, as a result of both replacing the hematogenous marrow through the expansion of the tumoral cells, and also due to the hematopoiesis' inhibition by the tumoral factors. Besides that, a moderate hemolysis also contributes to the anaemia. The microscopic examination of the bone marrow smears (fig.1 and fig. 2) has shown the fact that, from a morphological point of view, the aspect of the plasmocytes (myeloma cells) is unstable from a patient to another, remaining relatively constant on the same patient, during the development of the disease. In most of the cases, the big cells with prominent nucleoli are prevalent, while the small cells with characters similar to those of the normal cells are more rare.

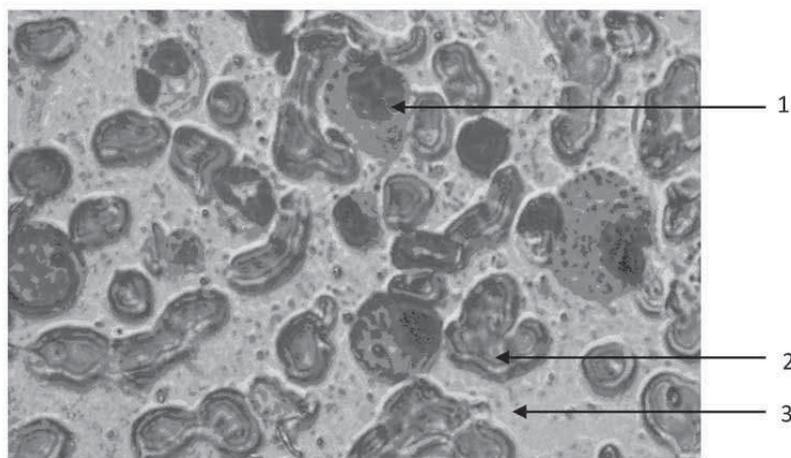


Figure 1: Bone marrow smear (multiple myeloma) – original (20x40)
1 – plasmocytes; 2 – thrombocytes; 3 – red cells grouped in scrolls

On the surface of these smears it could be noticed both the red cells tendency to be grouped in scrolls and the presence of the myeloma plasmocytes. Also the presence of some uncommon shapes of plasmocytes could be seen ((RAILEANU and MOȚOIU, 1974), such as those taking the shape of dumb bells (BERCEANU , 1977). The data from the literature specifies that the appearance and proliferation of the myeloma cells lead to two types of basic perturbations, as it follows: infiltrations of tissues and organs, and protean anomalies. These are directly or indirectly responsible for almost all the other symptoms and signs of the disease. The distribution of these cells can be diffused or insular and this explains the variability of the cytological paintings that can be observed on different bone punctures.

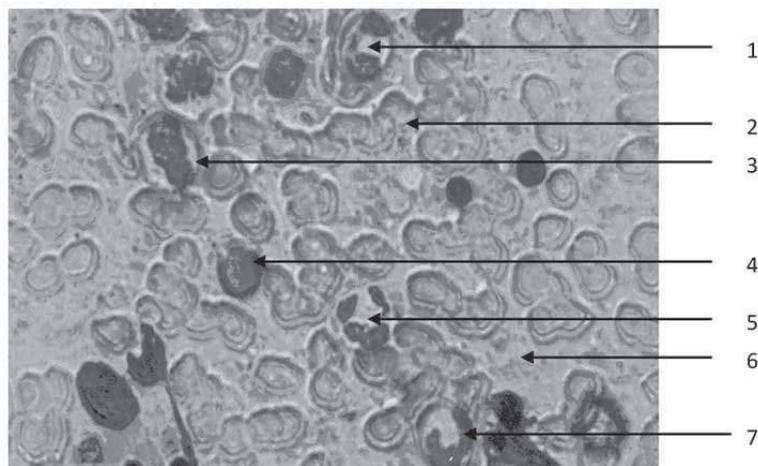


Figure 2: : Bone marrow smear (multiple myeloma) – original (20x40)
 1 – eosinophil; 2 - erythrocytes arranged into scrolls; 3 – basophil;
 4 – lymphocyte; 5 – neutrophil; 6 – blood platelet; 7 – monocyte

Our observation confirm the way of grouping of the red cells, and also the presence of the big myeloma plasmocytes and the aspect of the nucleus which is, obvious, disposed toward to cell periphery. The proliferated plasmocytes present modified morphological features compared to normal plasmocytes, some of them being able to be grouped into nests (foci) or to take various shapes (dumb bells).

It is very important to state precisely that these observations have been made on a heterogeneous casuistry, on patients of both genders, aged between 47 and 70 years and seen in different stages of the disease. As a result, even the degree of irregularity of the studied hematological values from the normal physiologic extreme limit is extremely varied from a patient to another.

Table 1: The distribution of the studied casuistry on genders and ages

Case No	Name's initial letter	Gender	Age (years)
1	C.M.	F	47
2	N.H.	F	50
3	I.O.	B	56
4	S.G.	F	56
5	S.L.	B	57
6	E.R.	B	60
7	N.M.	F	67
8	F.H.	F	69
9	T.O.	F	70
10	N.A.	B	70

The hemoglobin. According to the data from the scholarly literature concerning the normal physiological limits (LOTREANU, 2000) the surveyed patients suffering of multiple myeloma from this report show obvious tendencies to anaemia. For every surveyed individual, the personal values of hemoglobin concentration are constantly situated under the normal physiologic level, representing an average of 64, 4% of the normal physiologic extreme limit in men (fig.3) and 63,3 % in women (fig. 4).

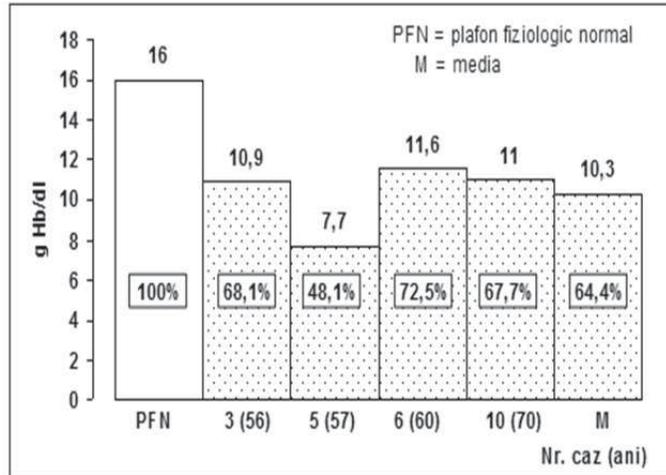


Fig. 3 The variation of the Hb in men with multiple myeloma

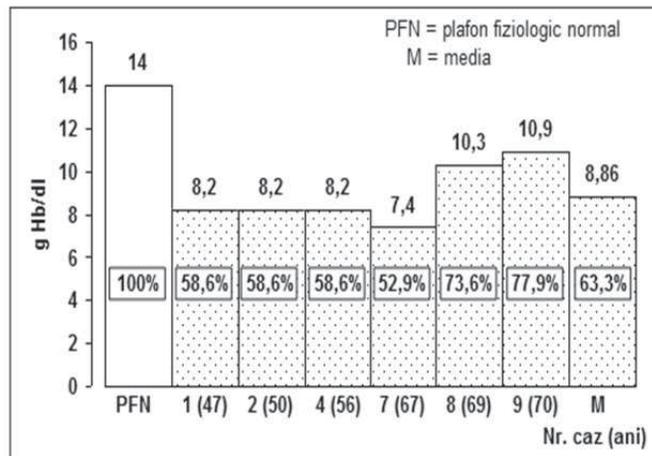


Fig. 4 The variation of Hb in women with multiple myeloma

The Hematocyte. The normal values of the hematocyte present the same tendency to decrease compared to the normal physiological limit, with a more homogeneous distribution between the cases analyzed on men (fig.5) and more irregular on women (fig.6). On average, the values of the hematocyte decrease when we talk about the male patients untill 65,9% of the normal physiologic extreme limit, but when we talk about women, the interindividual variation extends

from 43,6 to 112% of the normal extreme limit. So the average is situated at 82,1% of the normal physiological limit.

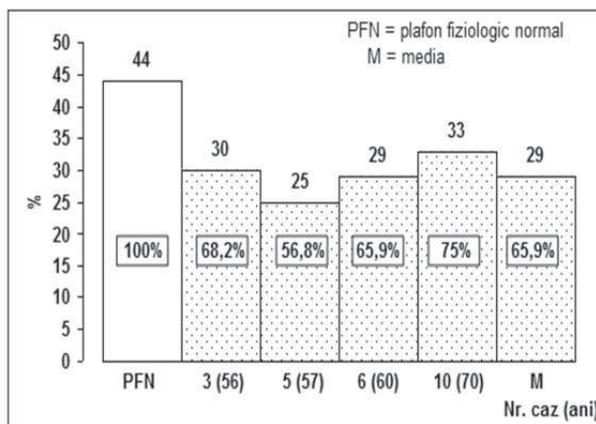


Fig. 5 The Ht variation in men with multiple myeloma

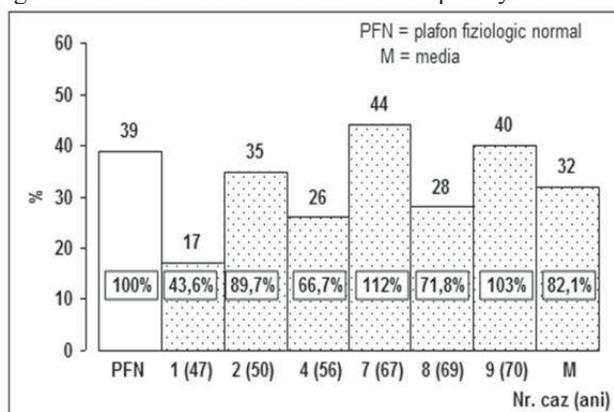


Fig.6 The Ht variation in women with multiple myeloma

The number of red cells. This hematological indicator claims one of the most dramatic levels of insufficiency distinguished on this category of patients. As the data from fig. 7 and fig. 8 have suggested, the number of red cells significantly decreases in all the surveyed patients, reaching to 20,6% of the normal physiological extreme limit in men and 21,6% in women.

Taking account of the much stronger depletion of the red cells number compared to the levels of concentration of hemoglobin, it is easily to understand the fact that anaemia is not hypochromically marked, each of the few left red cells being loaded with normal, even over normal quantities of hemoglobin. The data that we got confirm the fact that the malign proliferation of the plasmocytes in multiple myeloma interferes with the normal production of blood cells, and the reported hemoglobin deficiency is rather a consequence of the erythropoiesis's perturbation than of the hemoglobin synthesis' perturbation.

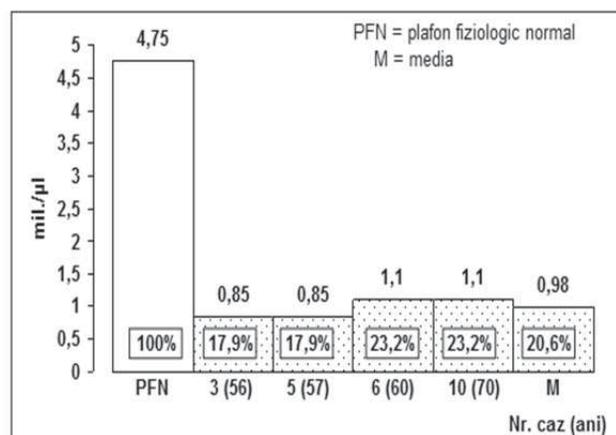


Fig.7 The red cells number variation in men with multiple myeloma

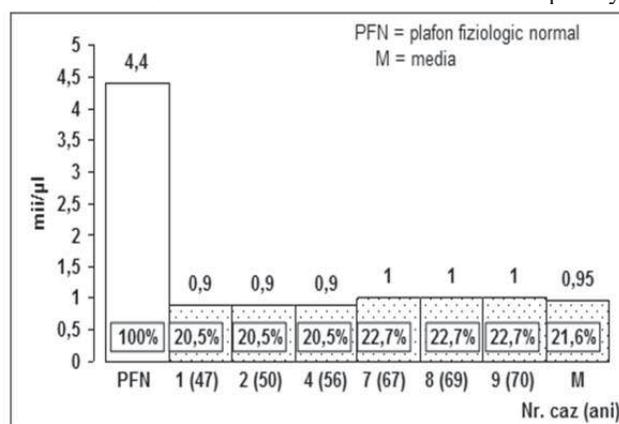


Fig.8 The red cells number variation in women with multiple myeloma

The erythrocyte sedimentation rate. As it results from the studies of other authors, all the patients with multiple myeloma present serious perturbations of the ESR, with values that increase from 5-12 mm/h to more than 100mm/h. Our data (fig.7 and fig.8) certify the extremely pronounced seriousness of the disease in the studied casuistry also through the fact that the values of ESR are amplified, compared to the normal, to 12 times in men (65-158 mm/h) and to 13,2 times in women (33-156 mm/h).

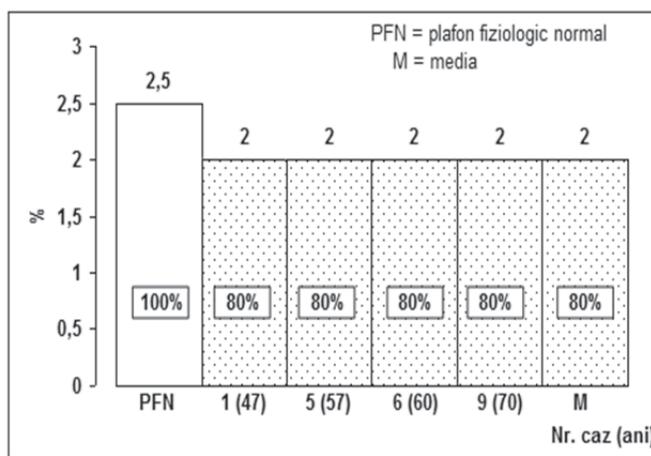


Fig.9 ESR variation in men with multiple myeloma

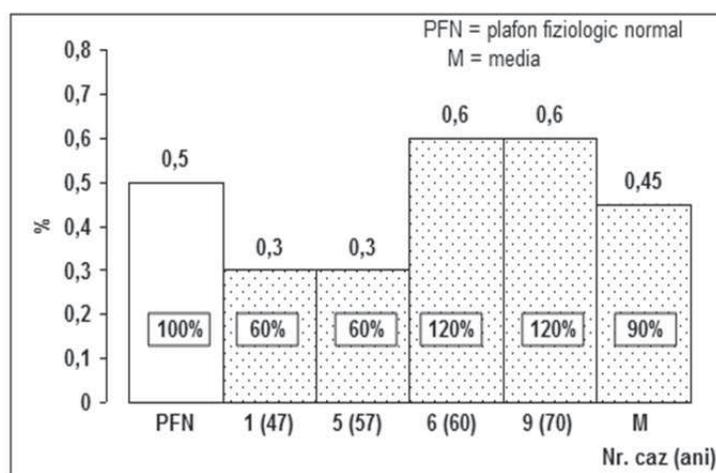


Fig.10 The ESR variation in women with multiple myeloma

Besides the study related to the variation of the hemoglobin concentration, of the hematocrite and of the number of red cells, inclusively the evolution of the ESR values, the investigation on the hematological changes in patients with multiple myeloma have also taken into account the white cells and the thrombocytes.

The white cells. The analysis of the eosinophils number in the cases taken to be studied have emphasized, on the one hand, a small uniformity of the values in the surveyed patients (fid.11), and on the other hand, a light tendency of eosinophilia. The individual values were constantly situated with 20% under the normal physiological extreme limit.

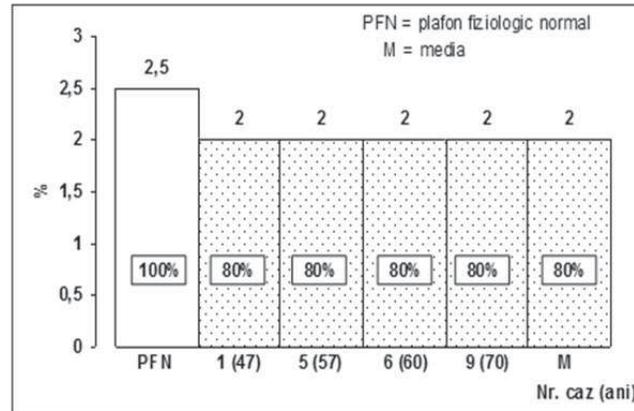


Fig. 11 The variation of the eosinophils percentage in some of the studied cases
 When we refer to the basophils (fig.12) and the monocytes in men (fig. 13), the individual values are distributed both under the normal physiological extreme limit, and over this medium value, so that in the invastigated patients, the average of these individual values remains similar and lightly smaller (-10% on basophils and -17% on monocytes) than the normal physiological limit.
 The number of monocytes in female patients describes a variation different from that of men’s, meaning that at almost all the patients, the individual values are superior in relation to the normal physiological limit, resulting an avergae higher with 25 % compared to this limit. (fig.14).

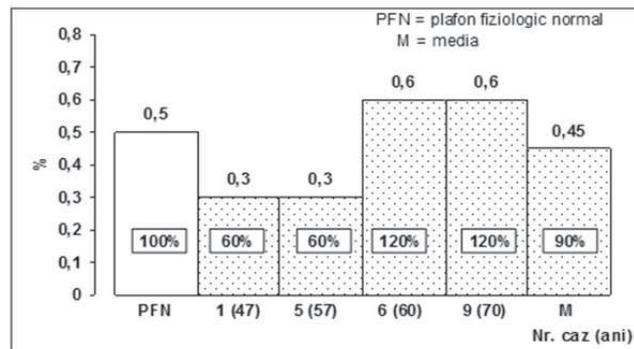


Fig.12 The variation of the basophils percentage in some of the studied cases
The thrombocytes. The analysis of the changes that occurred in the level of the number of blood platelets,in the case of the patients suffering of multiple myeloma, confirms the informations from the scholarly literature related to thrombocytopenia. Indeed , as the data from fig. 15 have shown, the individual values of thrombocytes’ number in the surveyed patients are constantly situated under the normal physiological limit, the medium value representing only 56% of this limit.

CONCLUSIONS

The patients with multiple myeloma from the casuistry of the Municipal Hospital Barlad were between 47 and 70 years old, and related to the genre, the incidence was higher on women than on men;

The homogeneous bone marrow smears have emphasized both the way in which the red cells were grouping into scrolls and that of the proliferated plasmocytes grouping into foci, some of them having uncommon shapes (dumb bells);

The patients have shown real hemoglobin deficiency, the medium values of the Hb concentration being up to 35,6% smaller than those of the normal physiological limits on men and to 36,7% on women;

The hematocryte of the patients suffering from nmyeloma has medium values under the normal physiological limits with 34,1% on men, and 17,9 % on women;

The number of red cells significantly decrease in all the surveyed patients, reaching 20,6% of the normal physiological limit on men and 21,6% on women;

The ESR values are amplified compared to the normal, by 12 times in men (65-158 mm/h) and by 13,2 times in women (33-156mm/h)

The white cells and the blood platelets in patients with multiple myeloma have values which can be compared to or even inferior to the normal physiological extreme limit.

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