Original Article

PLASMA CELL MORPHOLOGY IN MULTIPLE MYELOMA

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ABSTRACT

Objective: To identify the different types of plasma cells in multiple myeloma. To evaluate the survival of patients according to plasma cell morphology.
Method: Cytological aspects of plasma cell were examined according three criteria: the nucleolus, the chromatin and the nuclear-cellular ratio (N/C) of each plasma cell. Each plasma cell was identified by the letter P followed by 3 digits. This identification allowed to classify them as immature plasma cells, intermediate plasma cells and mature plasma cells. The proportions of various plasma cells among patients, were used to determine their group of survival according to the algorithm of morphology of Goasguen
Results: Morphological aspects of plasma cells of 55 cases of multiple myeloma from 2004 to 2010 were analyzed in two laboratories in Kinshasa. The results gave the rate of eight different types of plasma cell, the rate of multiple myeloma of plasmablastic cells, increased levels of aberrant and immature plasma cells. The integration of these aberrant and immature plasma cells in the definitions of survival groups showed that the group of good responders represented 38.2 % of patients. The intermediate group had 32.7%. While the group of poor responders counted 29.1%.
Conclusion: We found a great number of aberrant and immature plasma cells. We reached that the majority of our patients were found in the intermediate group and the group of bad responders. This regrouping explains the aggressive character of the multiple myeloma among our patients

Keywords: Multiple Myeloma - Plasma cell - Morphology - Survival

RESUME

Objectif: Déterminer les différents types de plasmocytes dans le myélome multiple. Evaluer la survie des patients.
Méthodes: Les aspects cytologiques des plasmocytes ont été examinés à la recherche de trois critères : nucléole, chromatine et rapport du noyau au cytoplasme (N/C). Chaque plasmocyte était ainsi identifié par la lettre P suivie de 3 chiffres. Cette identification permettait de classer les plasmocytes en plasmocytes immatures, plasmocytes non mûrs et en plasmocytes mûrs. Les proportions de différents plasmocytes ainsi trouvés chez les patients, ont permis de déterminer leur groupe de survie en fonction de l'algorithme de morphologie de Goasguen.
Résultats: Les aspects morphologiques des plasmocytes de 55 cas de myélome multiple de 2004 à 2010 ont été analysés dans deux laboratoires de Kinshasa. Les résultats obtenus donnaient les taux de huit types plasmocytaires différents, le taux des myélomes à plasmoblastes, l'augmentation des taux des plasmocytes aberrants et des plasmocytes immatures. L'intégration de plasmocytes aberrants et immatures, dans les définitions des groupes de survie, ont montré que le groupe de bons répondeurs représentait 38,2 % des patients. Le groupe intermédiaire à 32,7 %, alors que le groupe de mauvais répondeurs comptait 29,1 %.
Conclusion: Nous avons trouvé un grand nombre de plasmocytes aberrants et immatures. Cela a fait que la plupart de nos malades se sont retrouvés dans le groupe intermédiaire et dans le groupe de mauvais répondeurs. Ce regroupement basé sur la cytologie des plasmocytes pourrait avoir un rapport avec le caractère agressif du myélome multiple chez nos patients.

Mots-clés: Myélome multiple - Plasmocyte - Morphologie - Survie.

INTRODUCTION

The multiple myeloma (MM) is a marrow infiltration by neoplastic plasma cells that secrete a monoclonal immunoglobulin and/or its constituent chains, and substances that alter homeostasis bone cells including RANKL receptor and DKK1 protein. These substances stimulate the overactive osteoclasts and osteolysis diffuse [1-2]. In the literature, the MM comes in second position after the non-Hodgkin lymphoma [3].This was the most frequent hematological malignancies (27.4%) found by our team through the cytological method [4].
Since 1975, the forecast of the disease has been evaluated by the classification of Durie and Salmon, the independent factors of forecasts, the cytogenetics anomalies, and certain serum markers [3, 5]. In addition, it was demonstrated that the prognosis also depended on plasma cell types found according to their degree of maturity [6-12]. The presence of plasmablastic cells at least 2% was regarded as a factor of bad forecast [7-

8]. However, the presence of more mature plasma cells at least 66% was a sign of long-term survival [13].
This disease has a double incidence in the black population in the United States and presents an aggressive character in this population without anyone knowing why. In the countries with primarily black population, some studies were made [4, 14]. We tried through this cytological study to understand if the morphological aspects had an impact on the forecast of the disease among patients treated by prednisone associated with melphalan.

METHODS

Patients and Setting

The study includes 55 patients, referred for diagnostic bone marrow aspiration to 2 laboratories, namely the pathology laboratory of the Kinshasa University Teaching Hospital and the medical laboratory of the Ngaliema Hospital, between 2004-2010. The subjects were all Congolese, of all ages and of both genders. They were referred to us by various Kinshasa Hospitals.

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METHODS

The morphological evaluation was performed on bone marrow smear. Screening 100 consecutive plasma cells to be classified using the algorithm of morphology of Goasguen and Zandeki [15], in prospective multicenter study. We had to ask three consecutive questions before classifying each plasma cell:

1. Nucleoli present? If yes: score1; absent: score 0
2. Blastic chromatin? If yes: score 1; Not: score 0
3. N/C ratio greater or equal to 0.6? If yes: score 1; Less than 0.6: score 0

Applying these three criteria, each plasma cell is identified by the letter P followed by three digits, as advocated by the authors of the algorithm. The survival groups were defined on the basis of the following concepts [15]:
Group 1: group of responders P000 ≥ 66%, with a median survival of 42-61 months for 58.1% of patients.
Group 2: intermediate group P000 <66% and P100 ≥ P110+P111, with a median of 26-32 months for 30.6% of patients.
Group 3: group of non-responders P000 <66% and P100 < P110 + P111, with a median of 10-20 months for 11.3% of patients.
Processing and data analysis were performed using the software Excel 2007 and SPSS 20. Descriptive statistics allowed us to calculate averages, medians and standard deviations.

RESULTS

Cytological characteristics

In total, 5,500 plasma cells were examined in patients with multiple myeloma (n = 55) among them 37 (67.3%) men and 18 (32.7%) women. The distribution of plasma cells according to these three criteria of morphology, enabled us to identify eight types of plasma cells which were in descending order 2645 (48.1%) P000; 1,739 (31.6%) P001; 473 (8.6%) P100; 422 (7.7%) P101; 82 (1.5%) P010; 72 (1.3%) P011; 39 (0.7%) P110 and 28 (0.5%) P111, as shown in table I.

Table1: Plasma cell types. P000, P001, P100 and P101 represent more than 96% of plasma cells

Different types of plasma cells							
Types	P000	P001	P100	P101	P010	P011	P110	P111
Nr	2645	1739	473	422	82	72	39	28
%	48.1	31.6	8.6	7.7	1.5	1.3	0.7	0.5

The identification of plasmablastic cells at least 2% gave eight patients with plasmablastic cells between 2-4%. These cases, defined a group of patients representing 14.5% of all the cases of multiple myeloma.
We grouped multiple myeloma in three categories as shown in table II:
- Plasmablastic group with P111 ≥ 2 % of the plasma cells: 8 cases = 14.5%.
- MM with at least 66% only one type of plasma cells:

MM with P000 38.2 %; MM with P001 at 16.4 %; MM with P101 at 1.8%
- MM with at least 66% 2 types of plasma cells majority: MM with P000 + P001 = 21.8 %; MM with P101+P100 = 5.5% and MM with P000+P010 = 1.8 %.

Table 2: Multiple Myeloma types. Seven types of multiple myeloma, grouped in 3 categories: MM with plasmablastic, MM with only one plasma cell type at least 66% and MM with two plasma cell types at least 66%

Categories	Features	Plasma cell types	Nr	%
I	Plasmablastic group	P111	8	14.5
II	MM with one plasma cell type at least 66%	P000	21	38.2
		P001	9	16.4
		P101	1	1.8
III	MM with 2 plasma cell types at least 66%	P000 + P001	12	21.8
		P101 + P100	3	5.5
		P000 + P010	1	1.8

Survival groups

The group 1 had 21 (38.2%) patients, the intermediate group had 31 (56.4%) patients and the group of non-responders had 3 (5.4%). These survival groups are presented in table

Table 3: Groups of Survival. The increase of aberrant plasma cells affect group 1, whereas the increase of immature plasma cells (with the plasmablastics) inflate group 3

	% of patients per survival groups		
Survival groups with goasguen'formulas	**Group 1**	**Group 2**	**Group 3**
Goasguen'groups	58.1	30.6	11.3
Our groups without P101 integrated	38.2	56.4	5.4
Survival groups with new formulas	**Group 1'**	**Group 2'**	**Group 3'**
Our groups with P101 integrated	38.2	32.7	29.1

When the immature plasma cell P101, which represented 7.7% of plasma cells, was integrated, these new groups of survival gave 18 (32.7%) patients in the middle group 2'; 16 (29.1%) patients in group 3', and group 1' remained the same with 21 (38.2%) patients, as shown in table III. Thus, the formulas of groups became:
-Group 1' remains the same that group 1, P000 ≥ 66%
-Group 2': P000 < 66% and P100 ≥ P110+P111+P101*;
-group 3': P000 < 66% and P100 < P110+P111+P101*.

DISCUSSION

The algorithm of morphology of Goasguen and Zandeki produced eight various plasma cell types which are in Table I. Classified in decreasing frequency order from left to the right, these types were P000, P001, P100 and P101, which together represented 96% of plasma cells. It was found that the whole of plasmablastic cells, proplasma II, proplasma I and mature plasma cells (P111 + P110 + P100 + P000) was only 57.9%, lower than the 93% found by Goasguen [15]. The P001, considered aberrant

plasma cell, represented 31.6% of plasma cells found in our population. The P101 represented 7.7%, whereas the whole of P110 + P011 + P010 + P111 represented less than 4%. Our results differed from those in the literature [15], because we observed a large number of plasma cells considered rare, and called aberrant and immature. It was known that the plasmablastic group was an independent element of bad prognosis [7-8]. It was a factor which defines non-responders regarding at least 2 plasmablastic cells percent of plasma cells. The plasmablastic cell represented 28 (0.5%) of 5500 plasma cells found. The plasmablastic cells at least 2% (variable between 2-4%), were met among 8 (14.5%) patients reached MM. This group of patients represented the plasmablastic group. Our results corroborated those of the literature, which have found this rate of 8-15% of patients [7-8]. The P001 higher than mature plasma cells P000 was encountered in 20 (36.4%) of our patients, which was in fact the rate of MM of high P001, while it was only 10-15% in Angers [16]. It should be noted that in 10 (18.2%) of cases, the P001 only reached at least 66%.

The classification of MM according to plasma cell types enables us to have three categories as table II shows: the MM with plasmablastic cells, the MM with 1 and the MM with 2 types of plasma cells at least 66%. The most frequent MM was the MM with P000, followed by MM with P000 + P001, next the MM with P001, then the MM with P111 and finally the MM with P101 + P100. This unit represented 96.4 % of the MM. The 2 remaining types together amount to only 3.6 %.

Our population had some particularities that the high number of aberrant plasma cells and immature plasma cells were found in 39.3% of cases. By comparing survival groups before and after integration of immature plasma cell, the formulation was modified in groups 2 and 3, as follows: Group 2':P000 < 66% with P100 ≥ 110 + P111 + P101* Group 3': P000 < 66% with P100 < P110 + P111

+ P101* Group 1' remains the same P000 ≥ 66%.

The following results were observed as shown in Table III: Group 1' remained unchanged with 21 (38.2%) patients, group 2' got 18 (32.7%] patients and Group 3' has 16 (29.1 %) patients. These results showed that our group of responders, group 1', was less important than Goasguen [15]. Group 3' of poor prognosis became very important. This showed that the group 1 of responders was affected by the presence of many aberrant plasma cells P001, while group 3 was increased by the presence of immature plasma cells P101 and plasmablastic cells P111.

This could explain the aggressive character known in the MM in the black subject. This feature was mentioned by Koffi in a clinical study, and he attributed it to the delay of diagnosis [14]. We saw that, this aggressive character was related to an increase in the plasma cell immaturity, as, a consequence of the dispersion in the distribution of plasma cell types.

The enlargement of the distribution index of plasma cell types was the logical result of the emergence and growth of aberrant plasma cells and / or immature ones. This increase was a key factor in the decrease in median survival, and therefore an element of poor prognosis. Groups of survival obtained with immature plasma cells P101 showed that multiple myeloma was a severe disease in patients in our series.

CONCLUSION

Despite the small number of patients studied, this work showed that the most frequently encountered plasma cell types were P000, P001, P100 and P101, and represented 96% of plasma cells. This gave high aberrant plasma cells, but also high immature plasma cells.

The vital forecast of the patients affected by MM was function of the morphological characters or features of the present plasma cells among patients.

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