BONE MARROW PLASMA CELL INFILTRATION IN LIGHT-CHAIN AMYLOIDOSIS

L. G. Rodríguez-Lobato¹, N. Tovar¹, M. T. Cibeira¹, L. Magnano², I. Isola¹, L. Rosiñol¹, J. Bladé¹ and C. Fernández de Larrea¹

Department of Haematology (1) and Hematopathology Unit (2). Amyloidosis and Myeloma Unit.

Hospital Clínic. Institut d'Investigacions Biomèdiques August Pi I Sunyer (IDIBAPS). University of Barcelona. Barcelona, Spain.

Introduction

Prognosis of immunoglobulin light-chain (AL) amyloidosis depends mainly on the presence of cardiac involvement and the disease burden. A higher bone marrow plasma cell (BMPC) burden has been suggested as an adverse prognostic factor.

Objectives

The aim of our study was to analyze the correlation between the BMPC infiltration, clinical features and outcomes in patients with AL amyloidosis at Hospital Clínic of Barcelona.

Materials & Methods

- Clinical records of patients with AL amyloidosis (01/2006 to 04/2016) were reviewed.
- Seventy-nine patients (42F/37M; median age at diagnosis 65 years; interquartile range [IQR] 57-72) were the final group.
 - Initial baseline demographics, clinical and laboratory data, treatment and follow-up were collected.
 - Median follow-up for alive patients was 45 months (IQR 24-45 months).

BMPC analysis:

- Optic microscopic revision of May-Grünwald–Giemsa–stained BM smears processed according to standard procedures.
- All 79 patients had BM samples with adequate cellularity and BMPC infiltration was evaluated by senior cytologists.
- A second independent revision was performed. Concordance between the results obtained by both group of cytologists was excellent (R=0.949; $p<0.001$).

Statistical analysis: Baseline characteristics and differences among the subgroups were analyzed by using Student's t-test for continuous variables and χ^2 test for categorical variables, or non-parametric tests when necessary. PFS was defined as survival from diagnosis until relapse or death from any cause. OS was calculated from the date of diagnosis to the date of death from any cause or the date of last follow-up.

Results

- Median BMPC infiltration at diagnosis was 11% (IQR 7-18). 18 patients (23%) presented >20% BMPC infiltration. BMPC infiltration significantly correlated with the serum dFLC (R=0.551; $P<0.001$).
- Patients with >10% BMPCs had more frequent cardiac involvement (86% vs. 63%; $P=0.015$), more stage III or IV of the revised Mayo risk stratification system (61% vs. 29%; $P=0.01$), and a significantly shorter PFS (median of 18 vs. 48 months, $P=0.02$) and OS (median of 33 months vs. not reached; $P=0.046$) (Figure 1 and 2).
- Those patients with lower BMPC infiltration were associated with kidney involvement (86% vs. 48%; $P=0.001$). In the multivariate model, BMPC infiltration >10% retained its independent prognostic value for worse PFS (HR=2.26; 95% CI, 1.048-4.866; $P=0.038$, respectively).
- The use of new drugs (bortezomib or lenalidomide) seemed to overcome the negative prognostic impact of a higher BMPC infiltration (3-year PFS of 47% in $\leq 10\%$ BMPC vs. 35% in >10% BMPC; $P=0.29$ and 3-year OS of 62% in $\leq 10\%$ BMPC vs. 57% in >10% BMPC; $P=0.58$) (Figure 3 and 4).

Characteristics	Low PC ≤10% (N=35)	High PC >10% (N=44)	P
Age, median (IQR)	67 (55-75)	63 (56-71)	0.39
Gender, Male (%)	17 (49)	20 (46)	0.78
Immunological subtype, n (%)			0.46
Light chain			
IgG	18 (51)	16 (36)	
IgA	12 (34)	18 (41)	
IgA	3 (9)	8 (18)	
Light chain isotype, n (%)			0.54
Lambda	29 (83)	34 (77)	
Plasma cell clone			
dFLC (mg/L), median (IQR)	128 (37-469)	450 (161-933)	0.002
CRAB criteria development	0 (0)	1 (2)	1.0
Organ involvement, n (%)			
Heart	22 (63)	38 (86)	0.015
Kidney	30 (86)	21 (48)	0.001
Renal stage, n (%)*			0.001
I	9 (26)	29 (66)	
II	18 (51)	13 (30)	
III	8 (23)	2 (5)	
Number of organs involved, n (%)			
2 or more	23 (66)	39 (89)	0.014
Mayo Risk 2012, n (%)**			
III-IV	8 (29)	23 (61)	0.01

Table 1. Characteristics of the patients regarding BMPC infiltration
*Renal stage is calculated based on eGFR<50 ml / min / 1.73m² and proteinuria >5g / 24h (I-none present; II-either one present; III-both present).
** Available in 66 patients.

Figure 1. PFS regarding BMPC infiltration.

Figure 2. OS regarding BMPC infiltration.

Figure 3. PFS regarding BMPC infiltration in the group of patients who received novel drugs.

Figure 4. OS regarding BMPC infiltration in the group of patients who received novel drugs.

Conclusions

- Higher BMPC infiltration in patients with AL amyloidosis was associated with increased systemic organ damage, particularly cardiac involvement.
- This fact was not related to the development of myeloma features.
- These results suggest that treatment with “novel drugs” (bortezomib and lenalidomide) might overcome the negative prognostic impact of a higher BMPC infiltration.

Contact information

Luis Gerardo Rodríguez-Lobato: Department of Hematology, Hospital Clínic. Villarroel 170, PC: 08036, Barcelona, Spain. e-mail: lgrodriguez@clinic.cat