P-O1 981

Category : HIV-related and non-HIV related malignancies

The Conference on Retroviruses and Opportunistic Infections – Boston, March 3 to March 6, 2014

Monoclonal gammopathy and HIV-1 infection: evolution with highly active antiretroviral therapy

Casanova ML[1], Makinson A[1,2,3], Eymard-Duvernay S[2], Ouedraogo DE[4,5], Badiou S[6], Reynes J[1,2], Tuaillon E[1,4,5].

[1]Department of Infectious Disease, CHRU Montpellier. [2]UMI233-TransVIHMI, Institut de Recherche pour le Développement, Université Montpellier 1. [3]Department of Internal Medicine, Clinique Beau Soleil, Montpellier.
[4]INSERM U1058, Université Montpellier 1. [5]Department of Bacteriology and Virology and Institut de Recherche en Biothérapie, CHRU Montpellier. [6]Department of Biochemistry, CHRU Montpellier.

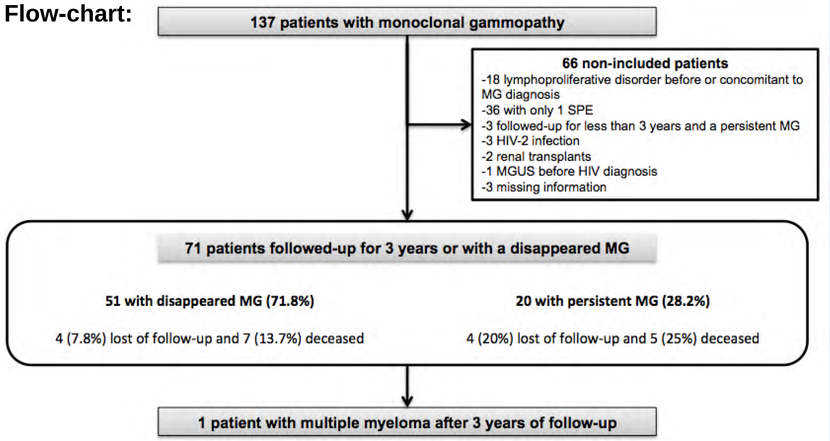
BACKGROUND:

Monoclonal gammopathies (MG) associated with HIV infection are frequent and occur at young age. In this population with a high risk of lymphoproliferative disorders, their evolution remains uncertain, contrary to MG of undetermined significance in the general population which is considered as a pre-malignant state. The aim of this study was to describe the evolution of MG in HIV-infected subjects under highly active antiretroviral therapy (HAART) and the factors associated with MG disappearance.

METHODS:

Retrospective study of HIV-1 infected adults, with a monoclonal protein detected by the serum protein electrophoresis and confirmed by immunofixation between September 1997 and December 2007. Subjects with concomitant or preceding hemopathy, HIV-2 infection or organ-transplant were excluded. All subjects were followed for at least 3 years or possibly less only if MG disappeared. Logistic regression models were used to identify factors associated with disappearance of monoclonal band.

Flow-chart:



Abbreviations: MG, monoclonal gammopathy; SPE, serum protein electrophoresis; MGUS, monoclonal gammopathy of undetermined significance; IQR, interquartile range; OR, odds ratio; CI, confidence interval.

RESULTS:

Seventy-one subjects were included: 65% were male, median age was 41 years, 46% had AIDS, median nadir CD4 count was 237/mm3, 41% had chronic hepatitis B or C infection at MG diagnosis (see table 1). We excluded 66 subjects (see flow-chart) whose characteristics did not differ from the included population. Eighteen subjects were excluded because of a lymphoproliferative disorder: non-Hodgkin lymphoma (n=9), Hodgkin lymphoma (n=5), multiple myeloma (n=1), Castelman disease (n=1), primary effusion lymphoma (n=1) and acute lymphoblastic leukemia (n=1).
After a median follow-up of 7.1 years (IQR 4.5-9.3), 71.8% of the subjects showed spike disappearance. Of the 20 patients with persistent MG, only 5 had virologic success for HIV without HCV active infection at end of follow up. In multivariate analysis, MG disappearance was associated with HIV-virologic success (OR 6.67, CI95% [1.38;32.13], p 0.018), absence of active hepatitis C at end of follow-up (OR 11.16, CI95% [2.20;56.69], p 0.004) and age inferior to 40 years (OR 4.75, CI95% [1.00;22.55], p 0.050) (see table 2). One subject developed a multiple myeloma 3 years after the diagnosis of an IgA kappa MG.

Table 1 : Baseline characteristics of the population

		Population n=71	
		n (%)	median (IQR)
Age (years)			41 (35-51)
Age < 40years		30 (42%)	
Male		48 (68%)	
Risk of HIV transmission	Sexual	41 (58%)	
	Intravenous drug user	23 (32%)	
	Others or not known	7 (10%)	
Time between HIV and MG diagnosis (years)			10 (4-13)
AIDS stage		33 (46%)	
CD4 (/mm^3)			237 (107-447)
CD4 ≥ 350/mm^3		24 (34%)	
Nadir CD4 < 200/mm^3		50 (70%)	
Ratio CD4/CD8			0.3 (0.13-0.43)
HIV viral load < 400 cp/mL		14 (20%)	
Chronic hepatitis B		7 (10%)	
Chronis hepatitis C		22 (31%)	
Type of gammopathy	IgG kappa	26 (37%)	
	IgG lambda	16 (23%)	
	IgM lambda	3 (< 1%)	
	IgA kappa or lambda	3 (< 1%)	
	Biclonale	23 (32%)*	
Type of light chain	Kappa	27 (38%)	
	Lambda	21 (30%)	
	Kappa and lambda	23 (32%)	
Follow-up after MG diagnosis (years)			7.1 (4.5-9.3)
Outcome	Still followed	51 (72%)	
	Lost to follow-up	8 (11%)	
	Dead	12 (17%)	

! * Biclonal gammopathies : IgG kappa and IgG lambda n=21 ; IgG kappa and IgM lambda n=1 ; IgM kappa and IgM lambda n=1

Table 2 : Factors associated with spike disappearance

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Inclusion						
Age < 40 years	2.07	[0.69 ; 6.25]	0.19	4.75	[1.00 ; 22.55]	**0.050**
Female	1.64	[0.51 ; 5.24]	0.41			
AIDS stage	0.47	[0.16 ; 1.34]	0.16	0.62	[0.14 ; 2.67]	0.52
CD4 ≥ 350/mm^3	1.78	[0.56 ; 5.68]	0.33			
Ratio CD4/CD8 ≥ 0.8	3.62	[0.42 ; 31.02]	0.24			
Nadir CD4 < 200/mm^3	1.03	[0.33 ; 3.18]	0.96			
HIV viral load < 400cp/mL	0.98	[0.27 ; 3.56]	0.97			
End of follow-up						
Virologic success*	4.44	[1.47 ; 13.42]	**0.008**	6.67	[1.38 ; 32.13]	**0.018**
CD4 ≥ 350/mm3	3.71	[1.25 ; 11.02]	**0.018**	1.93	[0.43 ; 8.74]	0.39
Ratio CD4/CD8 ≥ 0.8	3.36	[0.87 ; 13.01]	0.079	2.07	[0.32 ; 13.32]	0.45
Absence of chronic hepatitis C	6.13	[1.70 ; 22.18]	**0.006**	11.16	[2.20 ; 56.69]	**0.004**

! * HIV viral load < 400 cp/mL during the last 18 months of follow-up

CONCLUSIONS:

MG associated with HIV infection concerned a young population, seemed to be transient and had a favorable evolution on HAART in most cases. The disappearance of MG was associated with HIV-virologic success, absence of active hepatitis C and younger age. These characteristics underscore the differences in physiopathology between MG associated with HIV infection and MGUS in the general population. Outcomes of HIV-infected subjects with persistent MG despite ART and absence of HCV infection still requires exploration.