Primary Effusion Lymphoma and HIV Infection: 51 Patients From a Single Institution

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Abstract

Background: Primary Effusion Lymphoma (PEL) is a rare B-cell non-Hodgkin lymphoma (NHL) that is almost exclusively observed in HIV-infected patients (pts). It accounts for approximately 4% of all HIV- NHL, with a stable incidence in combined antiretroviral therapy (cART) era. Lymphoma cells are always infected with HHV-8 and in most cases coinfected with EBV. In its classic presentation PEL is characterized by body cavity effusions with or without mass lesions. A variant with extracavitary localisation has more recently been described. We report a large single institution series of 51 pts with PEL in the cART era. Methodology: All consecutive HIV-infected pts with a diagnosis of PEL since 1996 were included in the study. The main objective was to describe the characteristics and the outcome of pts with classic and extracavitary variant. Survival was estimated using Kaplan-Meier method, and was tested using the log-rank test.
Results: 51 pts were included between Jan 1996 and May 2013; 47 male (92%), median age 45 years. At PEL diagnosis, the median duration of HIV infection was 8 years (IQR, 1.4-15.6), 33 pts had prior AIDS and 35 pts received cART for a median of 40 months. The median CD4 cell count was 204 x 106/L (IQR, 90-370), and 25 pts (49%) had undetectable HIV-RNA. An other HHV-8-associated disease was observed in 30 pts (25 Kaposi sarcoma, 17 multicentric Castleman disease). 34 pts presented classic variant and 17 extracavitary variant. No major difference was observed between the 2 groups in terms of demographic, HIV and lymphoma characteristics. In classic PEL, pleural, peritoneal and pericardial involvement were present in 27, 17 and 12 pts, respectively. Extracavitary PEL was exclusively nodal in 6 patients and involved various organs in the others : GI tract (4), spleen (3), CNS (3), BM (2), liver (2), skin (2), testis, bone, sinus and muscle (1 each). 33 tumors were coinfected with EBV. All but 2 pts received chemotherapy, including high dose methotrexate in 13 pts. Complete remission was achieved in 28 pts (56%), without difference between the classic and the extracavitary groups (62% vs 41%). After a median follow-up of 10 years, 34 pts have died (29 with lymphoma), providing a median overall survival (OS) of 10.2 months, without difference between the 2 variant groups (P=0.78). The 5-year Overall Survival rate was 42% [95%CI, 27-55].
Conclusions: Based on a large single institution series of 51 PEL, characteristics of classic and extracavitary variants seems to be very close. Despite cART use, control of HIV infection, and treatment with intensive chemotherapy, similar to that used in HIV-uninfected pts, the prognosis remains poor with a median survival below 1 year. However some pts have long-term survival, and the 5-year OS of 42% compares favorably with earlier series.

BACKGROUND

Primary effusion lymphoma (PEL) is a rare (4%) B-cell non Hodgkin lymphoma, that mostly affects HIV-infected patients.

In this context, lymphoma cells are always infected by HHV-8, and in most cases by EBV.

Two variants are described :

- Classic PEL : body cavity effusions, with or without mass lesions
- Extracavitary PEL : with tumor mass alone without serous cavities involvement.

Very poor prognosis, with a median survival < 6 months.

OBJECTIVE

To describe a large single institution series of 51 pts with PEL in the era of combined antiretroviral therapy (cART).

METHODS

Unicentric, prospective series

Inclusion criteria:

All consecutive HIV-infected patients with PEL diagnosed in the Clinical Immunology Department of Saint-Louis hospital, Paris, France

Study period:

- Recruitment : Jan, 1996– May, 2013
- Follow-up : August, 2013

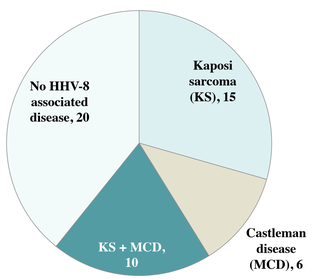
Statistical analysis :

Kaplan Meier method for survival analysis (log rank test)
Comparison between groups: Wilcoxon rank-sum test (continuous variables), Pearson Chi2 or Fisher's exact test (noncontinuous variables)

RESULTS : Demographic and HIV Characteristics

	Total (n=51)	Extracavitary group (n=17)	Classic group (n=34)
Demographic characteristics			
Male, n (%)	47 (92)	16 (94)	31 (91)
Age at diagnosis (years), median (IQR)	45 (39-53)	41 (36-48)	45 (40-54)
Period of diagnosis, n (%) :			
Early cART era (1996-2002)	25 (49)	5 (29)	16 (47)
Late cART era (2003-2013)	26 (51)	12 (71)	18 (53)
HIV characteristics			
HIV duration (years), median (IQR)	8 (1.5-15.7)	10 (8-16)	4 (1-12)
Prior AIDS, n (%)	33 (64.7)	9 (53)	24 (71)
cART at diagnosis, n (%)	35 (68.6)	11 (65)	24 (71)
cART duration (months), median (IQR)	40.1 (18-63.4)	62 (49.3-123)*	30 (12.3-52.6)*
Undetectable HIV-RNA, n (%)	25 (49)	9 (53)	16 (47)
CD4 cell count (x10^6/L), median (IQR)	204 (90-370)	207 (103-377)	185 (90-343)
CD4 nadir (x10^6/L), median (IQR)	99 (45-180)	159 (35-228)	99 (56-145)

HHV-8 associated disease

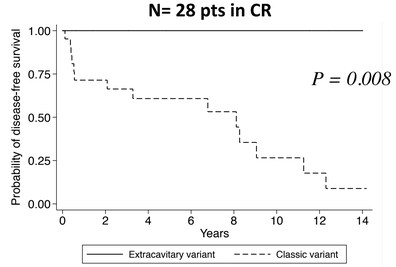


* $P < 0.05$

RESULTS : Response to treatment

	Total (n=51)	Extracavitary group (n=17)	Classic group (n=34)
Complete remission, n (%)	28 (56)	7 (41)	21 (64)
Relapse, n(%)	13 (25.5)	0*	13 (38)*
Time to relapse (months), median (IQR)	25.1 (6.3-97.9)	-	25.1 (6.3-97.9)
5-year disease-free survival (months), % ± sd	69.8 ± 9.0	100	60.8 ± 10.9

Disease-free Survival
N= 28 pts in CR



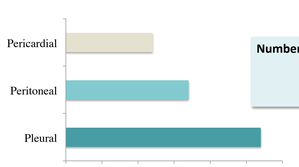
Lymphoma therapy

Chemotherapy regimens :	
CHOP-derived + high dose methotrexate	31
CHOP-derived	14
Autologus stem cell transplantation	3

RESULTS : Lymphoma characteristics

	Total (n=51)	Extracavitary group (n=17)	Classic group (n=34)
Performance status> 2, n (%)	29 (57)	11 (65)	18 (53)
LDH> normal value, n (%)	26 (52)	10 (59)	16 (48.5)
stade IV, n (%)	41 (80)	7 (41)	34 (100)
ICU stay, n (%)	14 (29)	4(23.5)	10 (32)
Tumor cells EBV +, n (%)	33 (65)	10 (59)	23 (70)

Classic PEL localisation



Number of cavities involved :

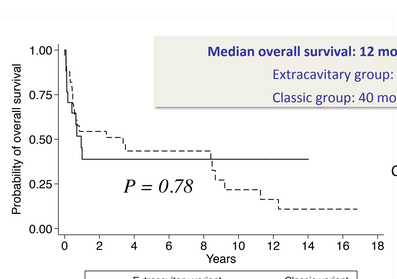
one	22 (44%)
two	24 (47%)
three	5 (9%)

Extracavitary PEL localisation

Nodal	13
GI	3
Neurological	2
Bone marrow	2
Skin	2
Muscle	1
Liver	1
Testis	1
ENT	1

RESULTS : Overall survival

Median follow-up : 10 years (IQR, 4.9-13.1)



Median overall survival: 12 months (95%CI, 5-135)
Extracavitary group: 11 months (95%CI, 2-.)
Classic group: 40 months (95%CI, 5.5-110.5)

5-year overall survival: 42% ± 7.3
Extracavitary group: 38.8% ± 12.2
Classic group: 43.4% ± 8.9

OS > 5 years : n=8

Cause of death (n=34) :

Lymphoma	29
Treatment toxicity	3
AIDS	1
Lung cancer	1

CONCLUSION

- Even if the 5-year OS of 42% compares favorably with earlier series, and long-term survival could be achieved in some patients (n=8),
- The prognosis of PEL remains poor despite control of HIV infection and intensive chemotherapy.
- The 2 variants, classic and extracavitory PEL, had very close characteristics and outcome
- However, relapse seems very rare after obtention of complete remission in extracavitary PEL compared to classic PEL (0% versus 38%, respectively).