



Plasmablastic lymphoma

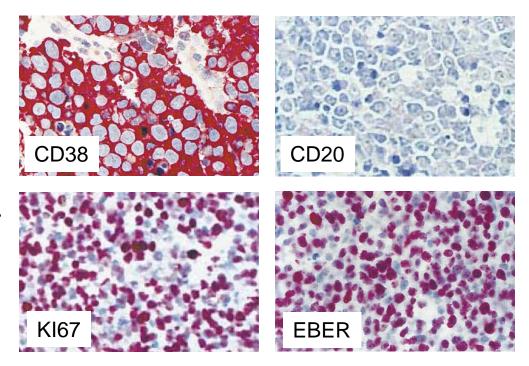
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Plasmablastic Lymphomas of the Oral Cavity: A New Entity Associated With the Human Immunodeficiency Virus Infection

By H.J. Delecluse, I. Anagnostopoulos, F. Dallenbach, M. Hummel, T. Marafioti, U. Schneider, D. Huhn, A. Schmidt-Westhausen, P.A. Reichart, U. Gross, and H. Stein

Patients' characteristics

- N=16
- 14 men
- 15 HIV+
- 11 stage I; 5 stage IV
- 6 chemo; 4 RT; 6 chemo-RT
- 10 died
- 2 alive
- Median OS 6 months



Delecluse et al. Blood 1997

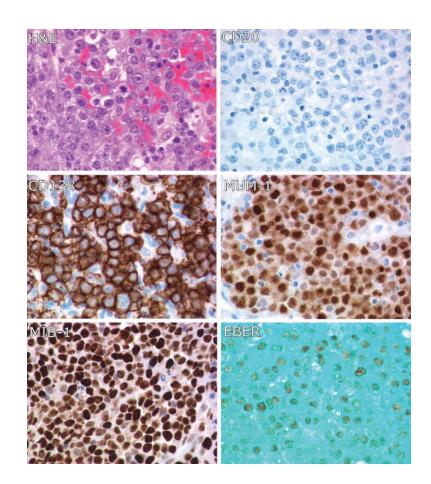
PBL is a real and distinct entity





HIV-associated plasmablastic lymphoma: Lessons learned from 112 published cases

	N		%
Age (n = 112)			
Median (years)	38		
Range (years)	7–65		
Sex $(n = 107)$			
Male	94		88
Female	13		12
CD4 count $(n = 28)$			
Median (cells/mm ³)	178		
Range (cells/mm ³)	10-498		
Duration of HIV infection $(n = 18)$			
Median (years)	5		
Range (years)	0–20		
Ann arbor stage $(n = 85)$			
T		49	58
II		2	2
III		0	0
IV		34	40
Primary lymphoma site $(n = 112)$			
Oral		65	58
Gastrointestinal tract		14	13
Lymph nodes		7	6
Other extranodal nonoral sites ^a		26	23
Therapy $(n = 53)$			
CHOP alone		16	30
Other chemotherapy regimens		13	25
Chemoradiotherapy (including CHOP)		11	21
Other therapies ^b		7	13
No therapy		6	11



Castillo et al. Am J Hematol 2008

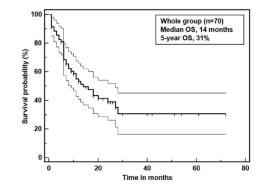
There is PBL outside of the oral cavity

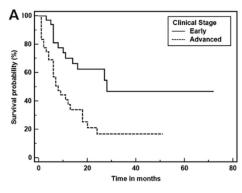


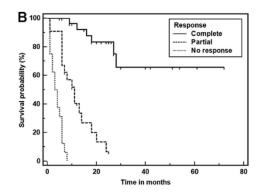


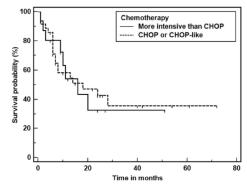
Prognostic Factors in Chemotherapy-Treated Patients with HIV-Associated Plasmablastic Lymphoma

Characteristic	n	Percentage
Age $(n = 70)$		
<40 yrs	28	40%
≥40 yrs	42	60%
$CD4^+$ cell count ($n = 29$)		
$< 200 / \text{mm}^3$	18	62%
$<100/\text{mm}^{3}$	13	45%
$< 50/\text{mm}^3$	11	38%
Clinical stage $(n = 70)$		
Early (1 or 2)	34	49%
Advanced (3 or 4)	36	51%
Chemotherapy $(n = 70)$		
CHOP or CHOP-like	35	50%
More intensive than CHOP	16	23%
Other regimen	19	27%
Response to chemotherapy $(n = 70)$)	
Complete response	32	46%
Partial response	22	31%
No response	16	23%









Castillo et al. Oncologist 2010

Survival is short, regardless of treatment

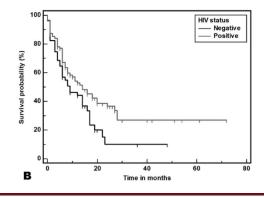




Clinical and pathological differences between human immunodeficiency virus-positive and human immunodeficiency virus-negative patients with plasmablastic lymphoma

Total 157 (69%) 71 (31%) Age $(n=223)$ Older than 60 years 2 (1%) 33 (47%) 60 years or younger 151 (99%) 37 (53%) Mean age (range) 39 (3-65) 58 (1-90) Sex $(n=228)$ Male 128 (82%) 44 (62%) Female 29 (18%) 27 (38%) Stage $(n=174)$ 1 42 (37%) 14 (23%) 11 13 (12%) 10 (16%) III 1 (1%) 9 (15%) IV 57 (50%) 28 (46%) Site of involvement $(n=213)$ Oral 88 (58%) 10 (16%) Extraoral 64 (42%) 51 (84%) Bone marrow $(n=83)$ Involved 17 (30%) 8 (30%) Not involved 39 (70%) 19 (70%) B symptoms $(n=69)$ Present 15 (33%) 13 (54%) Absent 30 (67%) 11 (46%) Therapy $(n=120)$ Chemotherapy 59 (77%) 35 (81%) No chemotherapy 18 (23%) 8 (19%) Response to therapy $(n=78)$ Complete response 23 (55%) 15 (42%) Partial response 11 (26%) 5 (14%) Stable disease 0 (0%) 6 (16%) Progressive disease 8 (19%) 10 (28%)		HIV-positive	HIV-negative
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Partial response 11 (26%) 5 (14%) Stable disease 0 (0%) 6 (16%)	Response to therapy $(n = 78)$, ,	, ,
Partial response 11 (26%) 5 (14%) Stable disease 0 (0%) 6 (16%)		23 (55%)	15 (42%)
Stable disease 0 (0%) 6 (16%)		11 (26%)	5 (14%)
. , ,	•	, ,	, ,
	Progressive disease	8 (19%)	10 (28%)

	HIV-positive	HIV-negative
CD45 expression $(n = 136)$		
Positive	56 (50%)	17 (68%)
Negative	55 (50%)	8 (32%)
CD20 expression $(n = 156)$		
Positive	21 (17%)	0 (0%)
Negative	99 (83%)	36 (100%)
CD79a expression $(n=93)$		
Positive	31 (51%)	12 (37%)
Negative	30 (49%)	20 (63%)
CD4 expression $(n=12)$		
Positive	2 (22%)	1 (33%)
Negative	7 (78%)	2 (67%)
CD56 expression $(n = 38)$		
Positive	14 (67%)	1 (6%)
Negative	7 (33%)	16 (94%)
BCL-2 expression $(n=31)$		
Positive	4 (17%)	2 (25%)
Negative	19 (83%)	6 (75%)
Ki-67 expression $(n=73)$		
80% or higher	39 (75%)	13 (62%)
Lower than 80%	13 (25%)	8 (38%)
EBER expression $(n=142)$		
Positive	83 (82%)	19 (46%)
Negative	18 (18%)	22 (54%)



There is PBL in HIV-negative patients and it might have a worse survival

Castillo et al. Leuk Lymphoma 2010





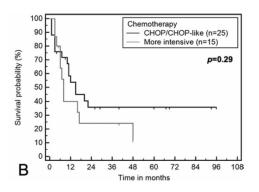
Human Immunodeficiency Virus-Associated Plasmablastic Lymphoma

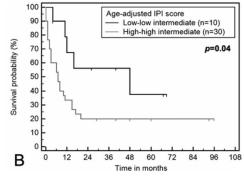
Poor Prognosis in the Era of Highly Active Antiretroviral Therapy

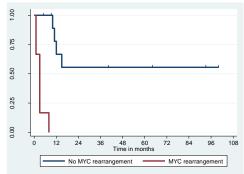
Patients' characteristics

- N=50
- Men 78%
- CD4+ count >200 42%
- HAART 100%
- Stage III/IV 69%
- CHOP 63%
- Other 37%
- MYC rearrangement 41%
- ALK 0%
- HHV8 LANA/PCR 0%

Castillo et al. Cancer 2012





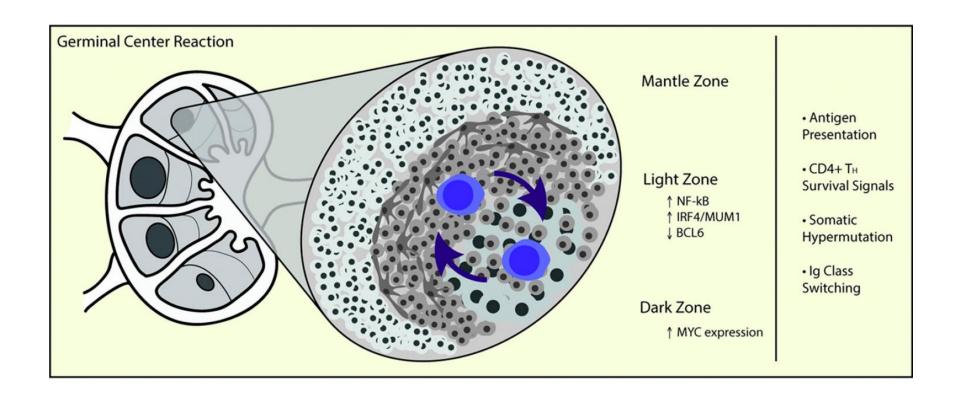


Even with chemotherapy and HAART, PBL patients have a bad outcome





The biology and treatment of plasmablastic lymphoma

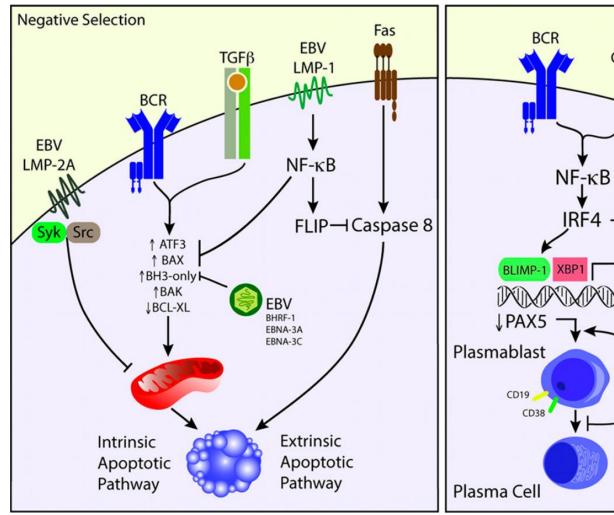


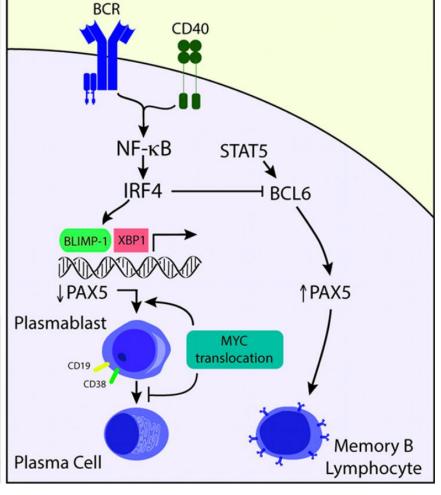
Castillo et al. Blood 2015





The biology and treatment of plasmablastic lymphoma





Castillo et al. Blood 2015

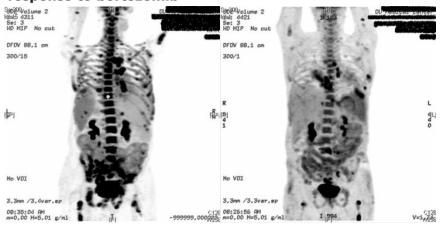




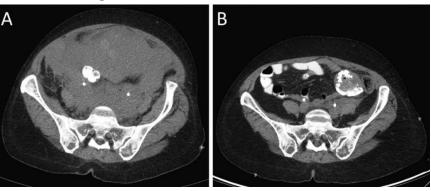
Positive Selection

Reports on bortezomib in PBL

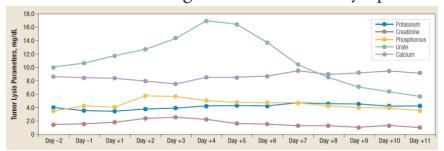
AIDS-related plasmablastic lymphoma with dramatic, early response to bortezomib



Bortezomib in Plasmablastic Lymphoma: A Case Report and Review of the Literature



Bortezomib-Induced Tumor Lysis Syndrome in a Patient With HIV-Negative Plasmablastic Lymphoma



A striking response of plasmablastic lymphoma of the oral cavity to bortezomib:



Bose. Eur J Haematol 2009; Lipstein. Clin Lymphoma Leuk Myeloma 2010; Saba. Onkologie 2013; Hirosawa. Biomarker Res 2015





Bortezomib in combination with infusional dose-adjusted EPOCH for the treatment of plasmablastic lymphoma

Patients

Case 1

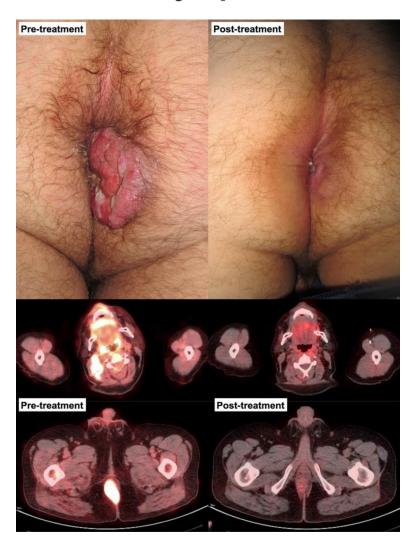
 40M, HIV+, CD4 290, stage IV (rectal and pharyngeal), MYC+ 60%, EBER+, alive at 4 years

Case 2

 36M, HIV+, CD4 34, stage IV (rectal and lung nodules), EBER+, alive at 3 years

Case 3

 66M, HIV-, stage II (nonobstructing colonic mass), MYC+ 15%, alive at 2.5 years



Castillo et al. Br J Haematol 2015





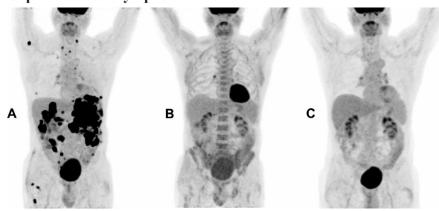
Reports on bortezomib and chemotherapy in PBL

Bortezomib plus CHOP for the treatment of HIV-associated plasmablastic lymphoma: clinical experience in three patients



2 patients alive at 12 and 24 months; 1 patient died at 12 months

Infusional dose-adjusted epoch plus bortezomib for the treatment of plasmablastic lymphoma



Patient alive at 2 years

Fernandez-Alvarez et al. Leuk Lymphoma 2016 Fedele et al. Ann Hematol 2016





The role of transplant in PBL

Case Reports of HIV-Negative Patients with PBL and Their Reported Outcome in Literature

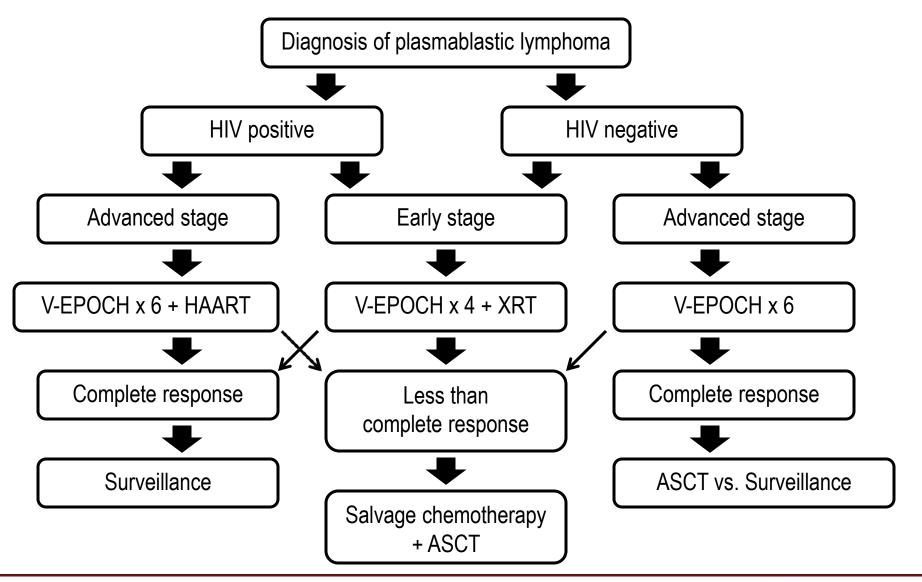
Patient No. [Ref]	Age, yr	Gender (M/F)	Stage	Immune Status	aaIPI	Induction Regimen	Disease Status before AHCT	Conditioning Regimen	Disease Status after AHCT	DFS after AHCT, mo	OS at Last follow-up, mo
1 [18,21]	23	M	IV	Competent	2	HyperCVAD × 2 PD: IVAC × 3	PR2	BEAM	CR	5	12 (died)
2 [18,75]	57	M	IV	Cardiac transplant (cyclosporine)	2	Cyclosporine w/d Cy/MTX PD: ICE × 3	PR2	Chemo-based	PD	PD	6 (died)
3 [18]	63	F	IV	Competent	5	HyperCVAD \times 4	CR1	BEAM	CR	2	13.3 (died)
4 [18]	60	F	IV	Competent	3	HyperCVAD \times 4	PR1	BEAM	CR	14	36.5 (died)
5 [18]	64	M	IIE	Competent	2	R -CHOP \times 6	CR1	BEAM	CR	A-NED	25.3
6 [18]	67	M	IV	Competent	3	$CHOP \times 1$ R- $CHOP \times 5$	CR1	BEAM	CR	A-NED	46.7
7 [60]	36	M	IV	Competent	2	ProMACE/CytaBOM	CR1	BEAM	CR	NR	16.9 (died)
8 [60]	52	F	II	Competent	1	CHOP × 6 PD: MiniBEAM	PR2	Cy-TBI	CR	2.5	17.2 (died)
9 [60]	50	M	II	Competent	0	CHOP: RD MiniBEAM: RD ICE	RD/CR1	BEAM	PD	PD	14 (died)

Al-Malki et al. Biol Blood Marrow Transplant 2014





Recommended treatment algorithm







Key messages

- PBL is a real and distinct entity
- There is PBL outside of the oral cavity
- There is PBL in HIV-negative patients and it might have a worse survival
- Survival is short, regardless of treatment
- Bortezomib in combination with chemotherapy might improve outcomes in PBL
- ASCT in CR1 might improve outcomes in HIVnegative PBL









Plasmablastic lymphoma

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