Management and Outcomes of HIV-Associated Primary Effusion Lymphoma: A Single Center Experience

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Abstract

Primary effusion lymphoma (PEL) is a rare form of lymphoma, primarily seen in individuals who are immunosuppressed. We studied all cases of PEL seen at our institution over a 15-year period and observed that if affected mostly male patients with HIV who were not taking the antiretroviral medication. Newer chemotherapy regimens including the drug bortezomib may be more effective in treating PEL.

Background: Primary effusion lymphoma (PEL) is a rare malignancy usually associated with HIV infection. Management and outcomes are poorly understood. **Methods:** The medical records of all patients diagnosed with HIV-associated PEL at our institution between 1999 and 2014 were reviewed. Patients were followed till death, treatment failure or loss of follow-up. **Results:** Twelve patients with PEL were identified during the 15 year study period; 9 had HIV infection. All 9 were male; median age was 45 years. All presented with local symptoms and were diagnosed with PEL a median of 11 years after HIV diagnosis. Location was pleural (3), pericardial (3), peritoneal (1) and extracavitatory (2). By definition, all had Ann Arbor stage 4 at diagnosis. Median follow-up was 34 months. Two patients had poor performance status and were unable to get chemotherapy. Seven patients had a complete remission (CR) and two died within 1 month of diagnosis. The median CD4 levels at PEL diagnosis in patients with poor versus good outcomes were 54 cells/mm3 (range, 26-82 cells/mm3) and 211 cells/mm3 (range, 73-800 cells/mm3). In contrast, the median lactate dehydrogenase (LDH) levels at PEL diagnosis with poor versus good prognosis were 1074 U/L (range, 703-1445 U/L) and 283 U/L (range, 156-760 U/L). **Conclusions:** Given its rarity, our knowledge of PEL relies solely on case reports and case series. Prompt HAART and chemotherapy may be effective in HIV-associated PEL and good outcomes are possible. LDH and CD4 may be possible prognostic factors in PEL.

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Introduction

Primary effusion lymphoma (PEL) is a relatively rare, but aggressive, non-Hodgkin lymphoma (NHL) characterized by involvement of the body cavities.[1] It occurs primarily in human immunodeficiency virus (HIV)-infected individuals, although it can also occur in other immunocompromised patients (including after organ transplantation and hepatitis virus infection).[2] It is thought that this immunosuppression enables human herpesvirus-8 (HHV-8) (or Kaposi sarcoma-associated herpesvirus), the presence of which defines PEL, to proliferate.[3]

Given its rarity, no prospective trials have ever defined the optimal treatment strategies. Our knowledge has relied solely on the findings from case reports and small case series. The treatment approaches that have been used for PEL include antiretroviral therapy (ART), cytotoxic chemotherapy, radiation therapy, antiviral therapy, and combinations of these.[1,4,5] Most patients will have disease resistant to conventional approaches, with uniformly poor outcomes even with therapy.[6] Even with an initial response to chemotherapy, the remissions have often been short lived. Most data have come from European studies.[1,4,5] In addition, PEL's unique clinical manifestations make the results from trials of other

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Table 1 Demographics, Clinical Features, Management, and Outcomes of HIV-Associated Primary Effusion Lymphoma

Pt. No.	Age (years), Sex, Race	AIDS-Defining Illness	ECOG PS	HIV Duration (years)	CD4 (Cell/mm^3)	Viral Load (copies/mL)	HAART	Symptoms	Site	EBV, EBER	CD30	HBV, HCV	LDH (U/L)	CT Regimen[a]	Bortezomib	Outcome	Follow-Up (mo)
1	44, M, white	None	3	25	26	80,000	No	Dyspnea, back pain	Left pleural	–	–	+, +	1445	None	No	Death	1
2	28, M, black	Anal cancer	0	5	211	260	Yes	Dyspnea	Right pleural	+	+	+, +	347	R-CHOP × 2 cycles, R-EPOCH + bortezomib × 5 cycles	Yes	Good	12
3	57, M, white	None	0-1	26	800	85	Yes	Fatigue, left neck mass	Left neck	+	NA	+, –	760	CHOP × 6 cycles	No	Good	44
4	51, M, white	KS	1	20	192	79	Yes	Ascites	Peritoneal	–	–	+, –	475	CHOP + bortezomib × 6 cycles	Yes	Good	4
5	61, M, Hispanic	KS, PCP, CMV	0	4	133	82	Yes	Right flank pain	Right RP mass	–	NA	+, –	283	EPOCH × 6 cycles + PCN drain	No	Good	34
6	42, M, African-American	KS, anal cancer	0	11	493	0	Yes	Tamponade	Pericardial	–	NA	+, –	156	HyperCVAD + bortezomib + drainage	Yes	Good	100
7	46, M, Hispanic	KS	0	2	214	97	Yes	Chest pain, dyspnea	Pericardial	–	+	+, –	156	CHOP + bortezomib × 6 cycles	Yes	Good	63
8	45, M, white	None	0	14	73	1,100,000	No	Dyspnea	Pericardial	+	+	–, +	212	R-EPOCH × 6	No	Good	46
9	39, M, Hispanic	KS	3	6	82	750,000	No	Dyspnea	Left pleural	–	–	–, –	703	None	No	Death	1

Abbreviations: AIDS = acquired immunodeficiency syndrome; CHOP = cyclophosphamide, hydroxydaunorubicin, Oncovin, prednisone; CMV = cytomegalovirus; CT = chemotherapy; EBER = Epstein-Barr encoding region; EBV = Epstein-Barr virus; ECOG PS = Eastern Cooperative Oncology Group performance status; EPOCH = etoposide, prednisone, Oncovin, cyclophosphamide, hydroxydaunorubicin; HAART = highly active antiretroviral therapy; HBV = hepatitis B virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus; HyperCVAD = hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone; KS = Kaposi sarcoma; LDH = lactate dehydrogenase; NA = not available; PCN = percutaneous nephrostomy drainage; PCP = *Pneumocystis carinii* pneumonia; R = rituximab; RP = retroperitoneal.

[a]All patients received HAART with or without chemotherapy.