

# Human herpesvirus-6 DNAemia in immunosuppressed adult patients with leukemia at risk for mold infection

Roy F. Chemaly, Harrys A. Torres, Ray Hachem, Dimitrios P Kontoyiannis, Amar Safdar, Issam I. Raad

From the Department of Infectious Diseases, Infection Control, and Employee Health, The University of Texas M. D. Anderson Cancer Center, Houston, Tx, USA

Haematologica. 2008 Jan; 93:(1)157-158. DOI: 10.3324/haematol.11638

Supplementary Table 1

**Table 1.** Characteristics of the 11 patients with leukemia and HHV-6 DNAemia.

Case no., Age (yr)	Type of leukemia	Symptoms	Mean no. of HHV-6 copies/mL per patient (range)	No. of positive HHV-6 PCR test/ total no. of HHV-6 PCR tests	Coinfection*	Chemotherapy†	ANC*	ALC*	Antiviral use*	60-day outcome
1. M, 75	AML	Fever, runny nose, nasal congestion, cough, headache	34,319 (11,782-56,856)	2/5 (40%)	None	Clofarabine, ara-C	580	80	Valacyclovir‡	Alive
2. F, 68	CML	Fever, runny nose, cough, dyspnea, vomiting, weakness	2,3263/8 (334-5,569)	3,8 (38%)	None	Hydroxyurea, decitabine	1,250	2,120	Valacyclovir§	Alive
3. F, 51	AML	Fever, cough, dyspnea, hemoptysis, diarrhea, nausea, vomiting, agitation	2,581 (345-4,816)	2/4 (50%)	Fungal pneumonia ( <i>Fusarium sp</i> ), CMV antigenemia	Ara-C, investigational drug	5,020	460	Foscarnet	Died
4. F, 30	AML	Fever, dyspnea, sinus pain, strange dreams, depression, confusion	1,768 (459-4,661)	4/8 (50%)	Polymicrobial sinusitis ( <i>Klebsiella pneumoniae</i> , <i>Candida glabrata</i> )	No	0	740	Valacyclovir‡	Alive
5. F, 58	ALL	None	1,982 **	1/5 (20%)	None	Vincristine, Fluorouracil, doxorubicin, Cy	1,740	220	Valacyclovir‡	Died
6. F, 62	AML	Fever, cough, rash, dyspnea, diarrhea	3,941 (3,072-4,810)	2/4 (50%)	None	Ara-C, investigational drug	0	240	Valacyclovir§	Died
7. F, 52	AML	Dyspnea, chest pain, weakness, confusion	885 **	1/3 (33%)	Polymicrobial pneumonia ( <i>Aspergillus terreus</i> , <i>Aspergillus fumigatus</i> , <i>Aspergillus niger</i> , <i>Mycobacterium abscessus</i> )	None	2,300	350	Foscarnet¶	Died
8. M, 63	AML	Fever, cough, dyspnea, chest pain, weakness, arthralgia, anxiety, depression, diarrhea	371 **	1/3 (33%)	None	Fludarabine, ara-c	<100	<100	Valacyclovir‡	NA
9. M, 39	AML	Fever, cough, dyspnea	27,763 **	1/2 (50%)	Polymicrobial pneumonia (CMV, <i>A. terreus</i> )	Investigational drug	110	240	Ganciclovir	Died
10. F, 54	CLL	Fever, cough, nasal congestion, rash, headache, diarrhea	3,208 **	1/1 (100%)	None	Cy, vincristine, doxorubicin, mtx, ara-c, Rituximab	<200	<200	Valacyclovir‡	Died
11. M, 44	AML	Fever, cough, hemoptysis, rash, headache, myalgias	3,528 **	1/7 (14%)	None	L-asparaginase, ara-c	4,650	50	Valacyclovir‡	Alive

ALC: absolute lymphocyte count; ANC: absolute neutrophil count; ALL: acute lymphoid leukemia; AML: acute myeloid leukemia; Ara-C: cytarabine; AV: antiviral drug; CLL: chronic lymphocytic leukemia; CML: chronic myeloid leukemia; CMV: cytomegalovirus; Cy: cyclophosphamide; HHV-6: human herpesvirus-6; MTX: methotrexate; NA: information not available; PCR, Polymerase chain reaction. \*At onset of HHV-6 DNAemia. † Administered within 1 month. ‡ Patients on prophylactic dose of valacyclovir at onset of HHV-6 DNAemia. §Patient on therapeutic use of valacyclovir against oral Herpes simplex virus infection at onset of HHV-6 DNAemia. || Patients on therapeutic use of either ganciclovir or foscarnet against CMV antigenemia and/or disease at onset of HHV-6 DNAemia. ¶Patient on empiric use of foscarnet at onset of HHV-6 DNAemia. \*\*Only 1 sample was either collected or was positive for HHV-6 DNAemia.

Supplementary Table 2

Table 2. Characteristics of leukemia patients with and without HHV-6 DNAemia.

Characteristic	Patients with HHV-6 DNAemia (n=11)	Patients without HHV-6 DNAemia (n=26)	Univariate P value OR (95% CI)	Multiple logistic regression p value OR (95% CI)
Gender, M/F	4/7	18/8	0.7	
Median age (range), years*	54 (30-75)	56 (10-80)	0.6	
Acute leukemia*	9/11 (82)	17/26 (65)	0.4	
Type of leukemia				
Acute myeloid leukemia	8 (73)	13 (50)	0.2	
Acute lymphoid leukemia	1 (9)	4 (15)	1.0	
Chronic myeloid leukemia	1 (9)	5 (19)	0.6	
Chronic lymphocytic leukemia	1 (9)	1 (4)	0.5	
Other	0 (0)	3 (12)	0.5	
Leukemia in remission*	2 (18)	12 (46)	0.1	
Prior relapse of leukemia*	9 (82)	12 (46)	0.07	0.07
		5.25 (0.79-43.85)	8.60 (0.82-89.89)	
Median time from diagnosis of leukemia* (range), days	438 (138-1,094)	213 (34-3,110)	0.2	
Type of symptoms				
Rash	3 (27)	1 (4) 9.38 (0.68-272.98)	0.06	
Fever	9 (82)	15 (58)	0.2	
CNS symptoms	3 (27)	3 (12)	0.3	
Cough	7 (64)	8 (31) 3.94 (0.73-22.92)	0.08	
Dyspnea	6 (55)	8 (31)	0.2	
Diarrhea	4 (36)	1 (4) 14.29 (1.14-399.15)	0.02	
Clinical syndrome at first positive HHV-6 PCR assay		NA		
Unexplained fever	5 (45)			
Lower respiratory infection†	5 (45)			
Asymptomatic DNAemia	1 (9)			
Median Apache II score (range)*	14 (7-19)	15 (5-26)	0.2	
Blood cell counts*				
Median ANC (range)	1,250 (0-5,020)	600 (0-19,110)	0.7	
Neutropenia (ANC <500/mm <sup>3</sup> )	5 (45)	10/23 (43)	1.0	
Median duration of neutropenia (range), days	8 (3-86)	16 (0-94)	0.9	
Recovery of ANC to ≥500/mm <sup>3</sup>	3/5 (60)	3/8 (38)	0.5	
Median time to recovery of ANC (range), days	9 (5-60)	3 (1-9)	0.1	
Median ALC (range)	240 (50-2,120)	290 (20-950)	0.7	
Lymphopenia (ALC < 200/mm <sup>3</sup> )	4/11 (36)	5/23 (22)	0.4	
Median duration of lymphopenia (range), days	48 (6-140)	26 (0-178)	0.1	
Median n. of HHV-6 PCR tests/patient (range)	4 (1-8)	4 (1-8)	0.4	
Pulmonary infiltrates	8/11 (73)	15/24 (63)	0.7	
Comorbidities *	3 (27)	5 (19)	0.6	
Diabetes mellitus	2 (18)‡	2 (8)	0.5	
Renal insufficiency	2 (18)‡	2 (8)	0.5	
Creatinine level > 1.5 mg/dL*	1 (9)	6/25 (24)	0.3	
History of granulocyte transfusions*	4 (36)	2 (8)	0.05 6.86 (0.80-70.89)	0.05 15.07 (0.98-230.29)
Type of invasive mold infection*				
At risk	0 (0)	6 (23)	0.1	
Possible	6 (55)	13 (50)	0.8	
Probable	3 (27)	3 (12)	0.3	
Proven	2 (18)	4 (15)	1.0	
Infection within 1 month before first HHV-6 test‡	7 (64)	18 (69)	1.0	
Fungal infection	5 (45)	9 (35)	0.7	
Mold infection	5 (45)	5 (19)	0.1	
Bacterial infection	5 (45)	13 (50)	0.8	
Viral infection	4 (36)	0.021 (4) 14.29 (1.14-399.15)	0.1 8.90 (0.37-210.77)	
Coinfection at the time of first HHV-6 test‡				
Fungal coinfection	4 (36)	5 (19)	0.4	
Mold coinfection	3 (27)	4 (15)	0.4	
Bacterial coinfection	1 (9)	4 (15)	1.0	
Viral coinfection	2 (18)	1 (4)	0.2	
Corticosteroids administered within 1 month*	7 (64)			
≥600 mg of prednisone equivalent	3/7 (43)	13 (50)	1.0	
7/13 (54)		1.0		
Prior chemotherapy within 1 month *				
Cytarabine-containing regimen	5/10 (50)	15/24 (63)	0.7	
Fludarabine-containing regimen	1/10 (10)	3/24 (13)	1.0	
Cyclophosphamide-containing regimen	2/10 (20)	2/24 (8)	0.5	
Clofarabine-containing regimen	1/10 (10)	3/24 (13)	1.0	
Antiviral exposure *	11 (100)	23 (88)		
Acyclovir/Valacyclovir	8 (73)	20 (87)	0.3	
Ganciclovir/Valganciclovir	1 (9)	2 (9)	1.0	
Foscarnet	2 (18)	1 (4)	0.2	
Median duration of antiviral usage prior to first sample collected (range), days	29 (6-86)	23 (2-190)	0.6	
60-day mortality rate <sup>§</sup>	6/10 (60)	9/25 (36)	0.2	

Data are number of patients (%) unless otherwise indicated. ALC, absolute lymphocyte count; ANC, absolute neutrophil count; CI, confidence interval; CMV, cytomegalovirus; CNS, central nervous system; HHV-6, human herpesvirus-6; ICU, intensive care unit; NA, not applicable; OR, Odds ratio. \*At the time of first positive PCR assay for patients with HHV-6 DNAemia and the first negative PCR assay among patients without HHV-6 DNAemia. †Lower respiratory infections (pneumonia in 4 patients, pneumonitis in 1), upper respiratory infections (sinusitis in 1). ‡One patient had more than 1 comorbidity. §Some patients had more than 1 coinfection. | For the patients with outcome data available.