P001

Dynamics of CD4 lymphocytes in patients infected by Human Immunodeficiency Virus with non-Hodgkin lymphoma or Kaposi's sarcoma receiving chemotherapy at a National Cancer Reference Center in Mexico

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INTRODUCTION

Immunosuppression has been recognized as risk a factor for cancer. Early in the AIDS epidemic, patients were diagnosed highly wasted with advanced stage of the disease and could not receive standard cancer therapy. However, this situation has changed with the use of Combined Antiretroviral Therapy (cART).

HIV patients with malignancies are a challenge to the health team both diseases need to be treated with potential drug to drug interaction beside primary or secondary prophylaxis for infectious AIDS defining events.

Whether to initiate CT together with cART or to delay the initiation of ART; or adjusted doses of CT is no longer a question. Several studies have shown that shorter survival in HIV patients with cancer is the result of inadequate cancer treatment and not AIDS complications.

There is little information about the association of cART with chemotherapy (CT). The cytotoxic effect of CT on immune recovery may be temporary or long-lasting. The aim of the study is to determine the dynamics of CD4 lymphocytes in patients with HIV and NHL or SK receiving CT.

METHODS

Cohort of HIV patients with KS or NHL treated at the Instituto Nacional de Cancerologia (INCan) from January 2008 to December 2012 with a follow-up greater than or equal to 6 months. Divided in three groups: KS without CT, KS with CT and NHL with CT, all patients received cART.

We analyzed demographic data, coinfections, clinical stage, CT and number of cycles, viral load, CD4 and CD8 lymphocytes (before, during and after CT) (KS patient with no CT CD4 values considered were CD4 cells at diagnosis, 4 to 6 months after initiation of cARt and one year after initiation of cART initiation. We analyzed immune recovery at follow-up, clinical response to CT and outcome. Statistical analysis was done with Stata version 12.

RESULTS

100 cases were reviewed. Twenty nine were excluded, 19 did not have full information for the study, five had virological failure, two abandoned treatment, three for other causes; 71 were included in the analysis: 40 with KS without CT, 13 KS with CT (CT was given accordingly to treating physician) and 18 NHL with CT. All were men. 45 (63%) had less than 200 CD4 at diagnosis. Demographic and baseline characteristics are included in table 1. Patients with KS received a median CT cycles of 6±3 and NHL 6.7±1 (p= 0.847) . At baseline NHL patients had lower CD4 count previous to CT (p = 0.2021) during CT (p = 0.0007) and after CT (0.0033). These lower CD4 and CD8 levels remained throughout CT duration in the NHL group, due to the fact that the scheme used in this type of cancer is more myeloablative than that for KS. The 13 patients with KS treated with CT received Vincristine and Bleomycin. Immune recovery at follow-up did not differ between groups. (Table 2). Only three deaths occurred all in the NHL group.

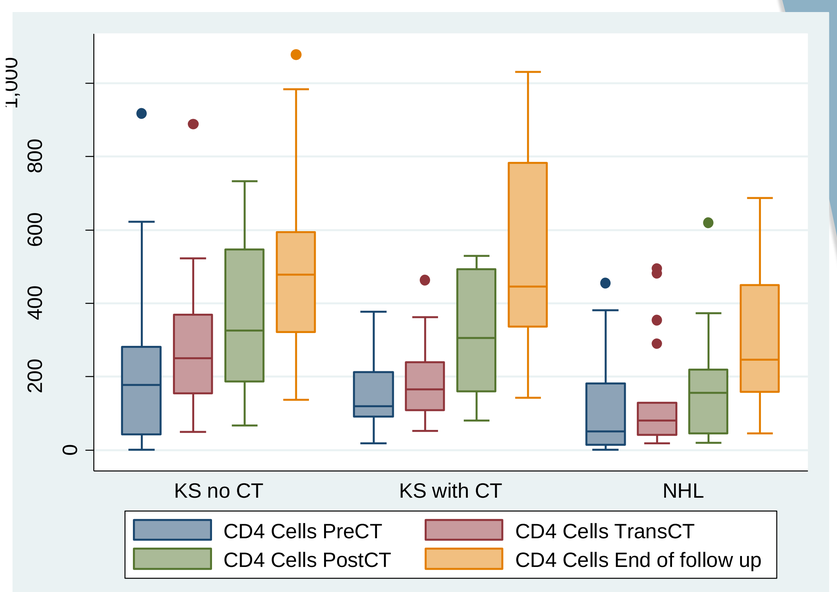

Figure 1. Dynamics of CD4 Lymphocytes before (PreCT), during (TransCT) and after (PostCT) Chemotheraphy and at the end of follow-up.

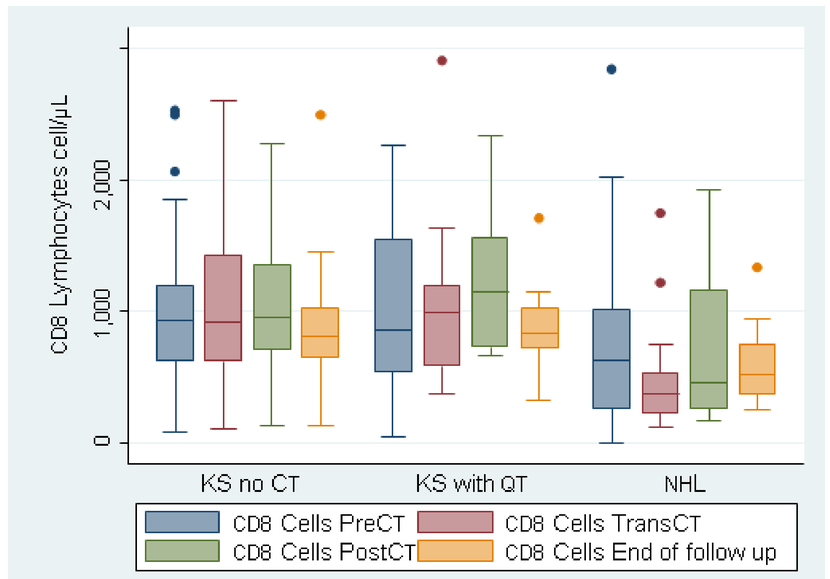

Figure 2. Dynamics of CD8 Lymphocytes before (PreCT), during (TransCT) and after (PostCT) Chemotheraphy and at the end of follow-up.

Variables	KS without CT	KS with CT	NHL	P value
	n= 40	n= 13	n= 18	
Age (median/range)	32.5 (22-53)	33 (19-48)	45 (22-65)	0.0391
Hepatitis B n(%)				0.079
Active infection	3 (7.5)	2 (15.3)	0	
Previous infection	12 (30)	4 (30.7)	3 (16.6)	
Hepatitis C Virus antibodies n(%)	2 (5)	0	2 (11.1)	0.568
Syphilis(%)	14 (35)	1 (7.6)	4 (22.2)	0.381
Opportunistic infection n(%)				0.421
Yes	5 (12.5)	2 (15.3)	5 (27.7)	
No	35 (87.5)	11 (84.6)	13 (72.2)	
ART Regimen n(%)				0.001
NNRTI-based	19 (47.5)	7 (53.8)	16 (88.8)	
PI based	21 (52.5)	6 (46.1)	1 (5.5)	
Other (rescue treatment)	0	0	1 (5.5)	
Response to Chemotheraphy n(%)				
Complete Response	34 (85)	12 (92.3)	12 (66.6)	0.071
Partial Response	6 (15)	1 (7.6)	2 (11.1)	
Stable Disease	0	0	2 (11.1)	
Progression of the disease	0	0	2 (11.1)	
Relapse	0	0	0	
Follow up (mean/SD/interval)	4.2±2 (0.5-7.5)	4.1±2.2 (0.6-7.4)	3.4±1.9 (0.6-6.2)	0.37
CD4 Cell increase >50 cells/year of follow up				0.217
Yes	23 (57.5)	9 (69.2)	7 (38.8)	
No	17 (42.5)	4 (30.7)	11 (61.1)	

ART: Antiretroviral, NNRTI: Non-nucleoside reverse transcriptase inhibitors, PI: Protease inhibitor.

Table 1. Characteristics of the groups, response to chemotheraphy, and immunological response at the end of follow up.

Variables	KS without CT	KS with CT	NHL	P value
	n= 40	n= 13	n= 18	
Baseline studies- Before CT (median/range)				
CD4 T cells (cel/µL)	177 (1-917)	120 (19-377)	51.5 (1-455)	0.2021
CD4 T cells (%)	10 (0-30)	8 (1-17)	7 (0-21)	
CD8 T cells (cel/µL)	931 (76-2524)	856 (47-2253)	629 (1-2840)	0.3075
CD8 T cells (%)	64 (29-80)	58 (34-77)	57.5 (0-83)	
HIV Viral load (copies/mL)	56787 (0-2699914)	38141 (0-412000)	81906 (0-1799295)	0.7574
0-100 cel/µL	13 (32.5)	4 (30.7)	12 (66.6)	0.021
Laboratories during CT (median/range)				
CD4 T cells (cel/µL)	250 (50-888)	165 (52-464)	80.5 (18-494)	0.0007
CD4 T cells (%)	13.5 (4-42)	13 (3-22)	13.5 (3-34)	
CD8 T cells (cel/µL)	916 (104-2598)	989 (375-2902)	371 (120-1744)	0.0001
CD8 T cells (%)	64.5 (25-81)	60 (48-74)	58.5 (25-82)	
Laboratories after CT (median/range)				
CD4 T cells (cel/µL)	325 (67-733)	306 (80-530)	155 (20-619)	0.0033
CD4 T cells (%)	16 (4-44)	15 (4-29)	13 (4-31)	
CD8 T cells (cel/µL)	957 (129-2274)	1151 (655-2329)	450 (160-1921)	0.0175
CD8 T cells (%)	49 (23-72)	54 (42-69)	63 (25-80)	
Laboratories after CT n(%)				0.035
<250	5 (12.5)	2 (15.3)	9 (50)	
251-500	18 (45)	5 (38.4)	6(33.3)	
>500	17 (42.5)	6 (46.1)	3 (16.6)	
Laboratories at end of follow up (median/range)				
CD4 T cells (cel/µL)	478 (137-1078)	446 (143-1031)	247 (46-687)	0.0104
CD4 T cells (%)	24.5 (11-44)	22 (10-33)	19 (6-32)	
CD8 T cells (cel/µL)	808 (129-2491)	830 (323-1707)	514 (246-1330)	0.0143
CD8 T cells (%)	40 (23-63)	39 (28-52)	41 (20-80)	
HIV Viral load (copies/mL)	0 (0-156)	0 (0-0)	0 (0-87)	0.6249

CT: Chemotheraphy

Table 2. Dynamics of viral load, CD4 and CD8 cells during the follow up of patients with HIV and KS or NHL.

CONCLUSION

Immune recovery is transiently hampered by CT, this impact is greater in patients with NHL. Both CD4 and CD8 counts get to levels significantly lower than baseline during CT treatment. In patients with cancer, HIV should be treated as a chronic condition and the same CT regimens should be offered considering potential drug interactions of HIV medications and cancer therapy. Patients should be closely monitored and receive prophylaxis for opportunistic infections.