

MCP-1 AND HIV VIRAL LOAD DYNAMICS IN THE CSF AND PLASMA OF HIV PATIENTS

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BACKGROUND

- Monocyte chemoattractant protein-1 (MCP-1) is a low molecular weight cytokine expressed by a wide variety of cell types including immune, endothelial and neural cells.
- They are associated with the traffic of leukocytes in physiological immunologic surveillance.
- MCP-1 over-expression is related to different neurological illnesses as well as AIDS dementia.
- MCP-1 seems to be a particularly important host immune factor in HIV neuropathogenesis.
- The time course of MCP-1 expression in relation to viral replication has been studied in cell culture and animal models but to date there are no such studies in humans.

OBJECTIVE

To evaluate the time course of MCP-1 expression in CSF and plasma in relation to HIV replication and suppression in humans

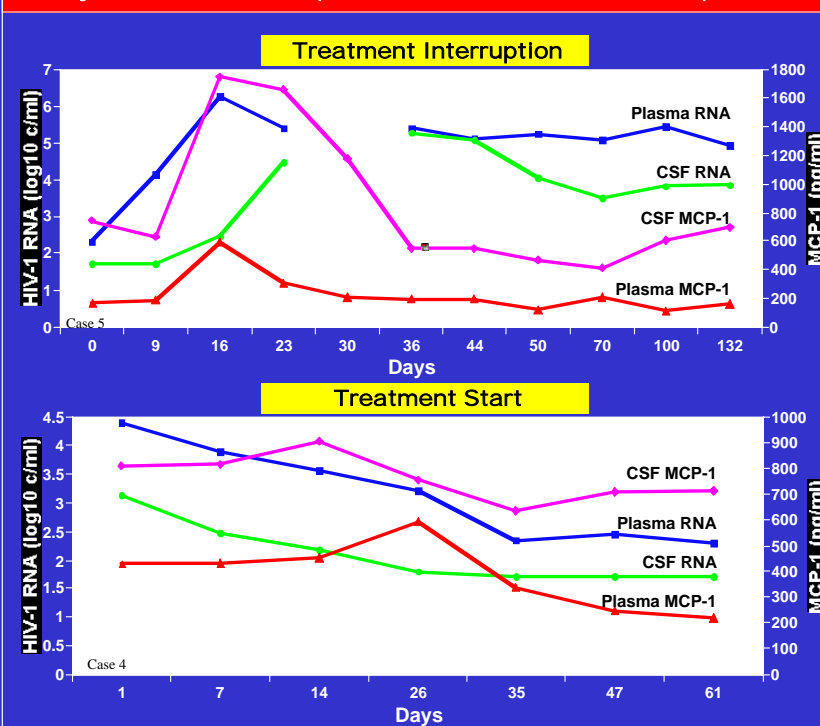
DESIGN & METHODS

- This was a prospective, observational study in serial samples of plasma, and CSF.
- At least 1 pair of plasma-CSF samples was collected prior to interruption, additional samples were to be collected at days 1 to 90 after the interruption.
- MCP-1 levels were quantified in plasma and CSF by ELISA (Quantikine; R&D Systems, Minneapolis). HIV RNA levels (log₁₀ copies/mL) were quantified, in blood and CSF, by RT-PCR.

Timing of HIV RNA (log c/ml) and MCP-1 (pg/ml) changes in plasma and CSF after antiretroviral therapy interruption (TI)

	Onset of Rise		Maximum		End	
	Day	Value	Day	Value	Day	Value
PL RNA	9 (5-22)	2.3 (2.3-4.2)	37 (29-50)	5.4 (4.2-6.3)	44 (42-67)	5.0 (3.7-5.5)
CSF RNA	18 (8-26)	1.7 (1.7-1.9)	47 (40-50)	4.3 (3.3-5.3)	75 (70-79)	3.5 (3.0-5.3)
PL MCP-1	18 (5-29)	176 (150-212)	35 (14-41)	395 (224-575)	41 (27-62)	166 (107-188)
CSF MCP-1	18 (5-29)	634 (366-835)	42 (16-46)	1609 (1162-2879)	43 (26-69)	734 (258-1022)

Dynamics of MCP-1 compared with HIV viral load in CSF and plasma.



Timing of changes in plasma and CSF MCP-1 after ART starting (TS)

	Onset of Rise		Maximum		End	
	Day	Value	Day	Value	Day	Value
PL MCP-1	1 (0-8)	156 (136-262)	4 (1-13)	336 (180-521)	8 (5-27)	132 (124-174)
CSF MCP-1	2 (0.5-6)	495 (265-720)	9 (2-12)	650 (357-790)	30 (6-36)	411 (309-570)

Subject Characteristics

	Treatment Interruption n=6*	Treatment Start n=7*
PL HIV RNA (log ₁₀ c/ml)	2.3 (2.3-2.8)	4.4 (3.4-5.3)
CSF HIV RNA (log ₁₀ c/ml)	1.7 (1.7-1.8)	3.0 (2.8-3.9)
PL MCP-1 (pg/ml)	225 (100-358)	198 (140-417)
CSF MCP-1 (pg/ml)	669 (214-772)	623 (362-663)
Length of Infection, Years	7 (4-13)	8 (4-14)
CD4 Count Nadir	240 (104-357)	280 (130-283)
Age, years	44 (35-60)	35 (35-57)
Male, No. (%)	6 (100%)	7 (100%)
Ethnicity, No. (%)		
White	4 (67%)	5 (71%)
Black	2 (33%)	2 (29%)

*4 subjects were studied both during ART interruption and initiation

CONCLUSIONS

- Changes in plasma viral load occurred first.
- Changes in CSF VL, CSF and plasma MCP-1 occurred almost simultaneously after changes in plasma VL.
- These changes were more evident in the interruption group.
- Peak levels of MCP-1 were higher in CSF than in plasma.
- This pattern of results suggests that in the CNS, HIV replication may be causally linked to local expression of MCP-1.
- We considered the possibility that changes in viral load might directly or indirectly modulate MCP-1 production based on previous studies. Furthermore, we observed changes in MCP-1 prior to, or coincident with changes in CSF viral load, a sequence which is not consistent with the notion that viral load mediates the changes in MCP-1.
- A smaller MCP-1 peak in plasma may represent systemic production of MCP-1 as it is likely that the stimulus for this peak is outside the CNS. But it could also represent a leakage from CSF as MCP-1 is a small protein and acts different from larger proteins as albumin through the BBB.

Acknowledgements

Supported by NIH R01 MH58071 (Dr. Ellis) and the Kobey Fellowship (Dr. Almeida) at the University of California, San Diego