Leptomeningeal Enhancement in the Aging HIV-Positive Population

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Background

- HIV infection is associated with neurologic sequelae that may be related to chronic CNS inflammation despite treatment with antiretroviral therapy (ART).
- Objective biomarkers of CNS involvement with HIV infection are needed to identify patients at risk of neurologic complications.
- Leptomeningeal contrast-enhancing lesions on MRI have been described in:
  - Multiple Sclerosis, a neuro-inflammatory disorder of the brain and spinal cord
  - HTLV-1-associated myelopathy/tropical spastic paraparesis, a retroviral disorder primarily of the spinal cord
  - Pathologic correlates in these diseases correspond to perivascular lymphocytic and mononuclear infiltration of the leptomeninges.
- These lesions have not been described previously in the HIV-positive population.

Aims

- To describe the leptomeningeal enhancements seen in some patients with treated HIV infection.
- To evaluate potential clinical correlates of these enhancements.

Methods

- 61 participants (51 HIV-positive, 10 HIV-negative) were recruited during screening portion of a 5 year longitudinal study of the natural history of neurocognitive impairment in HIV conducted at NIH (clinicaltrials.gov, NCT01875588).
- HIV-positive participants and HIV-negative controls were matched based on age, race, gender, and education
- Brain MRI was completed using an optimized 3D-post-contrast T2-weight fluid-attenuated inversion recovery (FLAIR) technique
- Expert raters evaluated focal gadolinium enhancement in the leptomeningeal compartment.
- Independent sample t-tests were used to compare mean raw scores in HIV-positive participants and HIV-negative controls.

Demographics

Table 1. Demographics

	HIV-positive	HIV-negative
Mean age (years)	50.7	50.4
Male gender (%)	68.7	80
African-American (%)	72.5	60
Diabetes (%)	9.8	0
Chronic Hepatitis C (%)	19.6	0
Mean systolic BP (mmHg)	121.7	121.8
Mean CRP (mg/L)	4.2	2.1

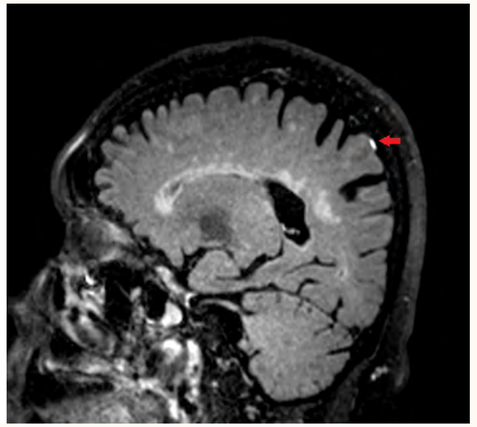
Table 1. HIV-negative participants were recruited from the same communities as HIV-positive participants to minimize demographic differences

Results

Table 2. HIV-positive participants

	+ LME (n= 13)	- LME (n= 38)	p-value
Duration of HIV infection (years)	19.8	17.9	0.48
Nadir CD4 (cells/mm^3)	219.9	177.35	0.47
Current CD4 (cells/mm^3)	595.5	548.1	0.22
Detectable viral load (%)	7.6	0	0.08
ART (%)	100	100	-
Mean age (years)	55.3	49.1	0.03
Male gender (%)	61.2	71.1	0.53
African-American (%)	69.2	73.6	0.76
Diabetes (%)	15.4	7.9	0.44
Chronic Hepatitis C (%)	7.7	26.3	0.22
Mean systolic BP (mmHg)	120.2	126.2	0.15
Mean CRP (mg/L)	3.1	4.6	0.51

Table 2. Leptomeningeal Enhancement on T2 post-contrast FLAIR was associated only with older age of participants.



Sagittal MRI 3D post-contrast FLAIR image of an HIV-positive patient demonstrating a leptomeningeal contrast-enhancement lesion (arrow).

Table 3. HAND Diagnosis

	+ LME (n=13)	- LME (n=28)	p-value
HAND (%)	15.4	25	0.50

Table 3. HAND diagnosis does not correlate with the presence of leptomeningeal enhancement.

Discussion

- Leptomeningeal Enhancement on T2 post-contrast FLAIR is a novel imaging technique.
- The results may represent an imaging biomarker to identify patients at risk of neurologic sequelae, including premature aging.
- Other aging and neurologic biomarkers are needed to correlate our findings in this population.

Limitations

- This is a small sample size of patients and additional enrollment will help clarify the significance of this novel finding.
- Longitudinal results are needed to identify whether the leptomeningeal enhancement is a stable finding.
- These cross-sectional results do not clarify the time of onset of the enhancement, however with longitudinal analyses, we will be able to answer this question better.
- CSF inflammatory biomarkers are needed to identify whether CNS inflammation may account for the leptomeningeal enhancement findings.

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