Higher Levels of CSF NFL in Distal Sensory Polyneuropathy in People with HIV

Mohammadsobhan Sheikh Andalibi[1,2,3], Scott Letendre[3,4], Jerel Adam Fields[2], Jennifer Iudicello[2,3], Bin Tang[3], and Ronald J. Ellis[1,2,3]

1- Department of Neurosciences, University of California San Diego, San Diego, CA 92093, USA
2- Department of Psychiatry, University of California San Diego, San Diego, CA 92093, USA
3- HIV Neurobehavioral Research Program, University of California San Diego, San Diego, CA 92093, USA
4- Division of Infectious Diseases and Global Public Health, Department of Medicine, University of California San Diego, San Diego, CA 92093, USA

Funding Source: This work was supported by the National Institutes of Health (P30MH062512, and 5R25MH081482-03).

Background:

Distal sensory polyneuropathy (DSP) is a chronic and debilitating condition prevalent among individuals with HIV (PWH), persisting despite viral suppression. The etiology of HIV-associated DSP and neuropathic pain (NPP) likely involves inflammatory processes and neurodegeneration, though research on the interplay between DSP and specific biomarkers of these processes remains scarce. This study aimed to investigate the relationship between inflammatory biomarkers in cerebrospinal fluid (CSF) and plasma, and the presence of DSP and NPP in both PWH and people without HIV (PWoH).

Design/Methods:

In this cross-sectional analysis, 158 participants were enrolled, comprising 102 PWH and 56 PWoH. DSP was identified by at least two of the following criteria: symmetrical, bilateral reduction in distal vibratory and sharp sensation, and loss of ankle reflexes. Symptoms of DSP included NPP, sensory loss, and paresthesia. Biomarker assessments included CSF neurofilament light (NFL) chain levels, and plasma and CSF concentrations of interleukin-6, IP-10, MCP-1, soluble CD14, and soluble TNF receptor-II. Logistic regression was employed to assess the association between DSP and these biomarkers, adjusting for confounders such as age, gender, ethnicity, HIV serostatus, and cardiovascular disease risk, known to influence NPP, neurodegeneration, and inflammation.

Results:

The cohort had a mean age of 44.7±12.9 years. A higher male predominance was noted among PWH (89.1% vs. 58.2%, $p<0.001$), who also exhibited a greater incidence of DSP and related symptoms (ps<0.05). Other demographic variables showed no significant differences. Among PWH, 84.8% achieved viral suppression, with a median CD4+ T-cell count of 694/μL (IQR 494–933). Elevated CSF NFL levels were significantly associated with NPP (OR [95% CI]: 2.09

[1.02–4.30] per unit change in log10-transformed NFL). However, separate analyses of PWH and PWoH revealed no significant associations between DSP signs and symptoms and the plasma and CSF biomarkers measured.

Conclusions:

The study identified an association between elevated CSF NFL, a marker of axonal damage, and NPP, suggesting that future research should explore neuroregenerative treatments for alleviating NPP. No significant associations were observed between inflammatory biomarkers and DSP. Larger-scale studies are warranted to further elucidate the role of inflammatory biomarkers in the pathogenesis of HIV-associated DSP.