Cerebrospinal fluid chitotriosidase-1 as a candidate biomarker for the progression of HTLV-1-associated myelopathy/tropical spastic paraparesis (HAM/TSP)

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Background:
HAM/TSP is an inflammatory neurodegenerative disease that affects motor, urinary, intestinal and sensory functions. Typically, HAM/TSP is slowly progressive but it may vary from limited motor disability after decades (very slow progression) to loss of motor function in few years from disease onset (rapid). Therefore, we aimed to identify prognostic biomarkers for HAM/TSP to support patient management.

Methods:
Proteomic analysis was performed with cerebrospinal fluid (CSF) samples from HTLV-1 asymptomatic carriers (AC) (n=13) and HAM/TSP patients (n=21) with rapid, typical, and very slow progression by quantitative label-free liquid chromatography/tandem mass spectrometry. Enrichment analyses were carried out to identify key biological processes associated with distinct neurological conditions in HTLV-1 infection. Candidate biomarkers were validated by ELISA in paired CSF and serum samples, and samples from HTLV-1-seronegative individuals (n=9) were used as controls.

Results:
CSF analysis identified 602 proteins. Leukocyte/cell activation, immune response processes and neurodegeneration pathways were enriched in rapid progressors. Conversely, HTLV-1 AC and HAM/TSP patients with typical and very slow progression had enriched processes for nervous system development. Differential expression analysis showed that soluble vascular cell adhesion molecule 1 (sVCAM-1), chitotriosidase 1 (CHIT1) and cathepsin C (CTSC) were upregulated in HAM/TSP. However, only CHIT1 was significantly elevated after validation, particularly in HAM/TSP rapid progressors. In contrast, none of these biomarkers were altered in serum. Additionally, CSF CHIT1 levels in HAM/TSP patients positively correlated with phosphorylated neurofilament heavy chain, neopterin, IL-18, CXCL5, CXCL10 and CXCL11 levels, and with the HAM/TSP progression rate defined as points in the IPEC-2 HAM/TSP disability scale per year of disease.

Conclusion:
CSF CHIT1 levels were associated with HAM/TSP rapid progression and correlated with other biomarkers of neuroinflammation and neurodegeneration. Therefore, we propose CHIT1 as a biomarker to identify HAM/TSP patients with worse prognosis.

**Disclosure of Interest Statement:**
Nothing to disclose.