COMPREHENSIVE STUDY OF CSF β_2-MICROGLOBULIN, A MARKER OF CNS IMMUNE ACTIVATION IN HIV

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CSF B_2-MICROGLOBULIN IS A ROBUST MARKER OF INTRATHECAL INFLAMMATION IN INDIVIDUALS WITH HIV IN VARIOUS STAGES OF INFECTION

Background

Despite efficient antiretroviral treatment (ART), with undetectable levels of HIV RNA in blood and cerebrospinal fluid (CSF), some individuals have persistent immune activation systemically and in the central nervous system (CNS). There is an association between neuroinflammation and neuronal injury. Several biomarkers of CSF can be used to grade inflammation, whereof neopterin is well elucidated. β2-microglobulin (β_2M) is less explored in people with HIV (PWH).

Method

Individuals were included from the longitudinal study HIV CSF Study Cohort in Gothenburg. In this retrospective study, with both cross-sectional and longitudinal design, we determined levels of β_2M, neopterin, HIV RNA, albumin ratio, IgG index, CD4+ T cell count, neurofilament light chain protein (NfL) and leukocyte counts (WBC), in blood and CSF in PWH with and without ART. Participants were divided into neuroasymptomatic (NA); NA CSF escape; symptomatic escape; secondary escape; HIV-associated dementia (HAD); opportunistic CNS infections (OI); and elite controllers (EC).

The decline of β_2M and neopterin for each individual during the early phase (first 6 months on ART) was measured by dividing the decrease on a logarithmic scale by the time to the measurement. For evaluation over time paired t-test was used with consecutive interpolated values.

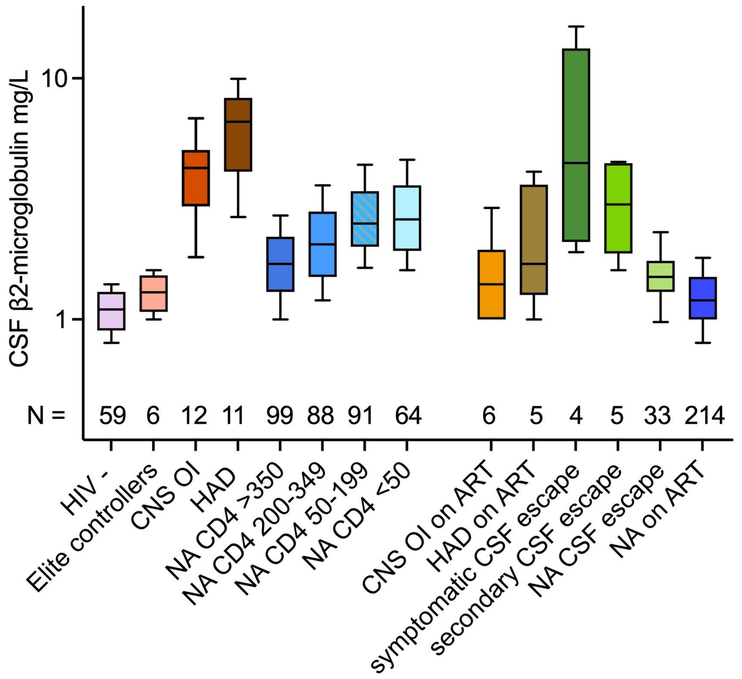


Figure 1. Cerebrospinal fluid (CSF) levels of β_2-microglobulin in participants with HIV-infection and in HIV-negative controls.

Results

638 individuals were included: NA (N = 556); NA CSF escape (N = 33); symptomatic escape (N = 4); secondary escape (N = 5); HAD (N = 16); OI (N = 18); and EC (N = 6). The highest levels of CSF β_2M were found in those with symptomatic escape and in untreated patients with HAD (Figure 1).

In the untreated NA group 91% (310/342) had elevated levels of CSF β_2M. In this group CSF β_2M correlated with age, HIV RNA levels (blood and CSF), $CD4^+$ T cell count, albumin ratio, IgG index, CSF and serum neopterin, CSF NfL and WBC.

Results, cont

Of 112 longitudinally followed NA participants (before and after ART initiation), elevated levels of CSF β_2M and CSF neopterin were found in 90% and 96%, respectively. After ART initiation, CSF β_2M decreased with 9% and CSF neopterin with 16% per month ($p < 0.0001$) (Figure 2), during the first 6 months. After 6 months on ART, 68% of the individuals still had elevated CSF β_2M and 80% had elevated CSF neopterin levels. These percentages had decreased to 42%/44% and 32%/25% respectively, at the 3-year- and the 5-year measuring points.

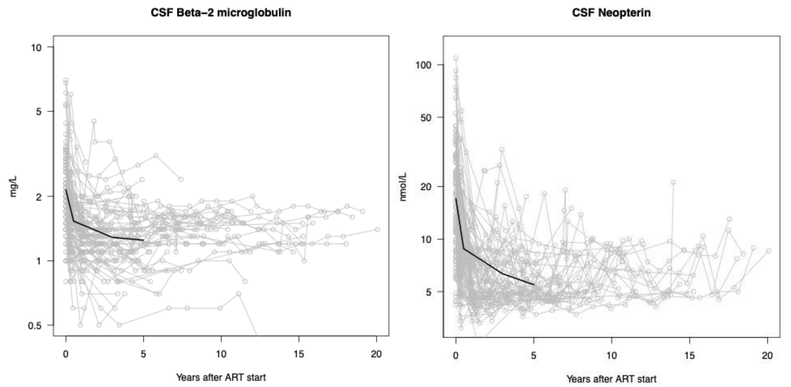


Figure 2. CSF levels of β_2-microglobulin and neopterin measured over time following ART initiation in neuroasymptomatic PWH.

Conclusions

After ART initiation the initial decline rate of CSF β_2M levels is slower than the decline rate of CSF neopterin in NA. The following decrease of CSF inflammation, however, is similar for both markers over time. Given that CSF β_2M is more easily accessible than neopterin and produced through a different pathway, CSF β2M could be a complementary tool in evaluating PWH for CSF inflammation.

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