Research Article

Aspartoacylase Deficiency in the White Matter of Human Immunodeficiency Virus Encephalitis: Novel Mechanism in Axonal Damage

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Aspartoacylase/aminoacylase II (ASPA/ACY II) is mainly synthesized in oligodendrocytes to contribute in myelin synthesis. Although axonal damage is seen in the brain with human immunodeficiency virus encephalitis (HIVE), ASPA contribution in the pathology is not known. Immunostaining study showed that ASPA protein is reduced in the white matter of patients with HIVE compared to the control. Western blot study further confirmed ASPA deficiency in the HIVE brain compared to the control. This paper suggests that HIVE condition affects ASPA to contribute in myelin loss/axonal damage seen in the disease.

1. Introduction

Human aspartoacylase/aminoacylase II (ASPA/ACY II; EC no. 3.5.1.15) gene contains five introns and six exons [1, 2]. Normal level of its substrate, N-acetylaspartic acid (NAA/NA-Asp) is important for the maintenance of healthy neurons. Altered levels of the NAA contribute in disease pathophysiology by inducing oxidative stress and by suppressing potential antioxidants [3–6]. Abnormal level of this pathway contributes in various diseases including Canavan disease [1–4], type 2 diabetes [7], and Parkinson’s disease [8]. Aspartoacylase is mainly synthesized in oligodendrocytes to contribute in myelin synthesis [1, 2].

Human immunodeficiency virus encephalitis (HIVE) is a demyelinating disease of the central nervous system, caused by the lethal virus [9–11]. Approximately 2.7 million new HIV-1 infections and 2.0 million deaths due to AIDS were reported in 2008 [12, 13]. In North America, the epidemic is expanding in the population among men who have sex with men [14, 15]. Brain regions affected in the disease include basal ganglia and deep white matter [16, 17], and these brain regions are also affected in the brain with Canavan disease [1, 2], therefore studying aspartoacylase level in the white matter of the patients with HIVE is important. Thus, the present study was aimed to understand ASPA level in the white matter of patients HIVE.

2. Materials and Methods

Six brain samples each from control and HIVE were used. While control brains showed no histologic abnormalities, HIVE brain showed leucoencephalopathy. All the procedures were performed under the regulations of institutional ethical committee and with the Helsinki Declaration of 1975, as revised in 2000 (World Medical Association Declaration of Helsinki 2000). To perform immunostaining, paraffin sections from three each of control and HIVE were used. The slides were then washed in PBS and incubated with antirabbit conjugated Alexa-fluor 488 (Molecular probes, CA). Sections were photographed as described earlier [18]. To confirm the immunofluorescence findings, western blot was performed using three of each control and HIVE
3. Results and Discussion

Immunostaining of the HIVE brain white matter showed reduced level of ASPA compared to the control (Figure 1). These fluorescent cells were colocalized with oligodendrocyte marker (Data not shown). Western blot study also further confirmed the reduced level of ASPA in HIVE brain compared to the control (Figure 2). Density analysis of the bands showed that two-tailed \( P \) value was 0.02.

HIV has been a devastating disease over decades and white matter degeneration is also reported [20, 21], however, ASPA contribution in the white matter degeneration is not known. ASPA is mainly synthesized in oligodendrocytes [1, 2] and a reduced level of ASPA impedes myelination and thus leads to axonal damage [1, 2, 22, 23].

Human immunodeficiency virus infection starts from periphery and subsequently enters the central nervous system but neurological symptoms occur years later. Axonal damage is reported in the brain with HIVE [24, 25]. Monogene alters other genes expression to contribute in disease pathophysiology [2]. HIV is capable of inserting with genomic DNA [26]. This insertion would impede function of other genes. Thus, deficiency of ASPA in the brain of patients with HIVE observed in the present study suggests that HIVE condition affects ASPA to contribute in myelin loss and axonal damage seen in the disease.

In conclusion, HIVE condition affects ASPA to contribute in axonal damage seen in the disease.

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