CHARACTERISTIC BRAIN MRI FEATURES IN HTRA1 MUTATION HETEROZYGOTES

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Background: Mutations in the HTRA1 (high-temperature requirement serine peptidase A1) gene cause a recessive-inherited cerebral small-vessel disease (CSVD) by loss of HTRA1 protease activity. It has been reported that the HTRA1 mutation heterozygotes (Hetero) also have CSVD. The remaining protease activity of HTRA1 may be higher in Hetero than in the HTRA1 mutation homozygotes (Homo). However, brain MRI findings in Hetero have not been fully investigated. We aimed to clarify the characteristic brain MRI features in Hetero by comparing them to those in Homo. Methods: We evaluated 18 MRIs in seven Hetero patients and 21 MRIs in seven Homo patients with a semi-quantitative scale for white matter lesions (WML)(signal score) and atrophy (atrophy score)(Nozaki et al. Neurology 2015). Each value was compared between Hetero and Homo. Results: Although signal score in Hetero was significantly lower than that in Homo (Mean ± SD; 14.7 ± 1.9 vs 23.1 ± 5.1, p < 0.0001), atrophy score was not different between the two groups (Mean ± SD; 5.4 ± 2.2 vs 7.5 ± 5.0, p = 0.18). Atrophy score showed positive correlation with the disease duration in Hetero or Homo (r² = 0.48, p = 0.0014 vs r² = 0.41, p = 0.0041), however signal score showed no correlation. Conclusion: In comparison with Homo patients, Hetero patients show similar atrophy and milder WML. Brain atrophy is correlated with the disease duration in both conditions. The difference in these conditions suggests that the HTRA1 activity might contribute differently to the progression of MRI findings.