Novel locus-specific genetic characteristics in cadasil

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Objective: We evaluated whether specific gene locus are related to clinical phenotypes. Methods: We screened patients with a suspected diagnosis of Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) between 2005 and 2015. Mutational hotspots of the Notch3 gene in exons 2-23 were screened by using Sanger sequencing. We analyzed magnetic resonance imaging (MRI) in those patients. Results: A total of thirty four patients (women, n=21 and mean age, 52±10 years) were included in our study. The majority of the mutations were in exon 3 and exon 11. The most prevalent mutations were R75P mutations (n=5), followed by Y465C (n=4) and R544C (n=4). Patients with those mutations exhibited less frequent anterior temporal (AT) or external capsular (EC) hyperintensities compared to patients with other locus mutations. Hemorrhagic stroke was found to be associated with mutations in exon 3 (R75P), exon 9 (Y465C), exon 11 (R587C) and exon 22 (R1175W variants). Conclusions: In contrast to westernized countries, CADASIL patients in our study frequently had mutations in exon 3 (R75P) and exon 11, and they did not have typical AT or EC hyperintensities. Although the underlying genetic mechanisms remain unclear, we suggest that some CADASIL mutations appear to have locus-specific characteristics.