＜シンポジウム 12―2＞神経疾患の臨床研究を目指したコンソーシアム

Japan Multiple System Atrophy Research Consortium (JAMSAC)

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Multiple system atrophy (MSA) is a sporadic neurodegenerative disorder characterized by various combinations of autonomic dysfunction, cerbellar symptoms, parkinsonism and pyramidal signs. Although molecular mechanisms of MSA remain to be elucidated, genome-wide association studies (GWAS) may provide clues as to the susceptibility genes for MSA. Establishment of the natural history of MSA is essential not only for clarifying the clinical features of MSA, but also for the basis to design the clinical trials.

To clarify the natural history of MSA, and to elucidate the molecular pathogenetic mechanisms of MSA, Japan Multiple System Atrophy Research Consortium (JAMSAC) was established in 2003. Over 20 institutions throughout Japan participated in the consortium. Cross-sectional studies on a large series of Japanese MSA cases and GWAS have been conducted. Furthermore, we also have been collecting and molecularly analyzing the multiplex families with MSA, and the families with MSA and Parkinson disease. Inclusion criteria are patients fulfilling at least possible category of the consensus statement on the diagnosis of MSA (Gilman et al, J Neurol Sci, 1999). Additional criteria based on specific MRI findings of MSA were adjunctively employed. The established rating scales, including UMSARS and Barthel index, were used for evaluation for clinical features.

We evaluated the clinical features of 208 MSA patients (117 men and 91 women). About 70% of MSA patients were MSA-C (characterized by cerebellar ataxia) in the Japanese population, whereas only around 30% of them were MSA-P (characterized by Parkinsonism). Genomic DNA from 6 multiplex families with MSA, 4 families with MSA and Parkinson disease, and 5 MSA inbred families were collected, and molecularly analyzed. GWAS were conducted on 382 MSA patients and 388 normal controls.

The present cross-sectional analysis as well as the previous studies revealed that MSA-C appears more frequent than MSA-P in the Japanese population, which is in a good contrast to those reported in Europe and North America. We are currently planning a longitudinal study to further clarify the detailed natural history of MSA, especially in the progression profiles of MSA. To identify the causative or susceptibility genes for MSA, we are conducting a replication study of GWAS.

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