＜シンポジウム 12―1＞神経疾患の臨床研究を目指したコンソーシアム

Natural History Studies and the EUROSCA Clinical Research Network

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The spinocerebellar ataxias (SCAs) are a heterogeneous group of autosomal dominantly inherited progressive ataxia disorders. The most common SCAs which together account for more than half of all affected families are SCA1, SCA2, SCA3 and SCA6. Each of these "common" SCAs is caused by a translated CAG repeat expansion mutation. At present, there are no effective treatments for these disorders.

It is the aim of the EUROSCA Clinical Project to create a clinical infrastructure that allows to perform interventional therapeutic trials in SCAs. To guarantee access to a sufficient number of SCA patients we created a European SCA registry that now contains entries of about 4000 SCA patients. An essential prerequisite for future trials is the availability of validated assessment methods to measure severity of ataxia. We therefore devised and validated the Scale for the Assessment and Rating of Ataxia (SARA), a clinical rating scale that allows to reliably measure the severity of ataxia. In addition, we evaluated a multi-dimensional SCA functional index (SCAFI) composed of a timed 8 m walk (8MW), the nine hole pegboard test (9HPT), and the PATA rate, a measure of speech performance. Another instrument, the Inventory of Non-Ataxia Symptoms (INAS) allows to quantitatively assess non-ataxia symptom which frequently occur in SCAs.

In 2005, we initiated a longitudinal observational study (natural history study) of 526 patients suffering from SCA1, SCA2, SCA3 or SCA6. An analysis of covariance of the baseline data with SARA score as dependent variable and repeat lenghts of the expanded and normal allele, age at onset and disease duration as independent variables led to multivariate models that explained 60.4% of the SARA score variance in SCA1, 45.4% in SCA2, 46.8% in SCA3 and 33.7% in SCA6. In SCA1, SCA2 and SCA3, SARA was mainly determined by repeat length of the expanded allele, age at onset and disease duration. Two year follow-up data are now available for 415 patients. Among the four genotypes studies, SCA1 had the fastest and SCA6 the slowest progression. Repeat length of the expanded allele was a major determinant of disease progression in SCA1 and SCA2.

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