

Machado-Joseph Disease (MJD/SCA-3) Workshop: Where do we stand?
March 17, 2016, Lisbon, Portugal

Clinical features and the natural history

T. Klockgether, University of Bonn and German Center for Neurodegenerative Diseases (DZNE), Germany

Machado-Joseph disease/spinocerebellar ataxia (MJD/SCA3) is worldwide the most common autosomal dominantly inherited ataxia disorder. MJD/SCA3 is a multisystem disorder characterized by degeneration of spinocerebellar tracts, dentate nucleus, brainstem nuclei, and basal ganglia. In MJD/SCA3 mutation carriers, ataxia usually starts around 35 years with large variability that partly depends on the repeat length. The clinical syndrome is characterized by prominent cerebellar ataxia in combination with supranuclear gaze palsy and peripheral neuropathy. In addition, patients may present with pyramidal signs, basal ganglia symptoms, such as parkinsonism or dystonia, restless legs syndrome, urinary dysfunction, and mild cognitive dysfunction. As part of the EUROSCA study we followed a cohort of 139 MJD/SCA3 patients over a period of 8 years. The severity of ataxia at baseline, as measured by the Scale for the Assessment and Rating of Ataxia (SARA), was determined by repeat length and disease duration. Longer repeats and earlier age of onset were associated with the occurrence of pyramidal signs, whereas higher age was associated with clinical signs of peripheral neuropathy. SARA progression data were best fitted with a linear model. Annual SARA score increase was 1.56 (SE 0.08). We did not identify factors that affected progression of the SARA score. Progression rate in MJD/SCA3 was slower than in SCA1, but faster than in SCA6. Other than the SARA score, the increase of the number of non-ataxia signs reached a plateau.