**Altered CSF levels of monoamines in hereditary spastic paraparesis 10 – a case series**

CLINICAL PHENOTYPES:

**Family A**. The proband (III:1) is a 46-year-old Swedish woman, without previous history of disease, investigated for progressive gait difficulties and lower back pain presenting at age 34. The patient also suffered from mild urinary urgency and lower limb weakness combined with painful cramps. At the age of 40, the patient exhibited a moderate spastic gait with bilateral lower limb hyperreflexia, ankle clonus, proximal leg weakness, bilateral Babinski sign and a mildly impaired vibratory sensation. Initial work-up included magnetic resonance imaging (MRI) of brain and spine, and routine biochemical analysis of blood and cerebrospinal fluid (CSF) rendering normal results. Electrodiagnostic testing demonstrated a mild axonal sensory polyneuropathy (PNP). At the time of CSF collection, the patient received no other medication despite oral contraceptives and a non-steroidal anti-inflammatory drug (NSAID). At present, the patient uses a walking frame and electric wheelchair for mobility.

The proband’s mother (II:1), whose current age is 68, started to receive comments about her gait at the age of 33. Besides hypertension, dyslipidemia, previous knee and hammer toe surgery, she has no history of other disease. Her medication consists of daily doses of metoprolol, simvastatin and vitamin D. In her mid-fifties, she recognized milder problems with stiffness in the legs, falls and gait difficulties. At the age of 55, the patient showed a mild spastic gait with patellar hyperreflexia and bilateral positive Babinski sign. Electrodiagnostic testing demonstrated a mild mixed axonal and demyelinating sensorimotor PNP, including small fiber involvement (C- and Aδ-fibers). Currently, the patient cannot run but requires no walking aid for mobilization.

The proband’s deceased maternal grandmother (I:1), was reported as physically active in her young years including the ability to ski. However, a progressive gait disorder presented close to the age of 60 with subsequent need of wheelchair 10 years later. Furthermore, the patient had complained of impaired sensation and pain in her lower limbs for a longer duration, reportedly preceding the onset of gait difficulties. Within the family, speculations have taken place on whether the patient could have suffered from multiple sclerosis. Unfortunately, her medical notes have not been possible to retrieve why we consider her possibly symptomatic. She died at the age of 90, reportedly due to a cerebral hemorrhage.

**Family B.** The proband (II:1) is a 67-year-old Swedish man, his past medical history consists of hypertension treated with a daily oral dose of candesartan. He presented with a slowly progressive disturbance of gait starting in his mid-twenties. He maintained the ability to run until the age of 46, but thereafter required walking sticks for mobility. At initial evaluation, at the age of 60, the patient reported paresthesia in the lower limbs, painful nightly leg cramps and weakness of the feet. Examination revealed a spastic paraparesis, right-sided ankle clonus and a scissor gait. Initial work-up included electrodiagnostic testing, revealing a moderate axonal sensorimotor PNP with normal sensory small fiber function, and MRI of brain and spine without significant abnormalities. At present, the patient is in need of a walking frame.

The proband’s son (III:I) was first evaluated at the age of 27. He reported difficulties running as a child, intermittent paresthesia and cramps in the lower limbs together with problems walking stairs. Age of onset was not possible to determine. The patient is not receiving any pharmacological treatment. At initial examination, lower limb hyperreflexia, left ankle clonus and increased muscle tone in the proximal lower limbs were evident. Electrodiagnostic testing demonstrated a moderate axonal sensorimotor PNP, including small fiber involvement (Aδ-fibers). At present, the patient walks independently but recognizes mild lower limb weakness after physical exercise and mild urinary urgency.