We describe spinocerebellar ataxia (SCA) with late onset, progressive, sensorimotor polyneuropathy (PNP) in a 56-year-old patient. The involvement of six other family members lead to a genetic analysis which shows a mutation of the membrane metalloendoproteinase (MME) gene. This gene codes for neprilysin (NEP) which is a membrane protein. Several studies have shown the impact of MME gene mutations on the incidence of late-onset axonal sensorimotor PNP. The interest of this clinical case is the description of a new MME gene mutation, responsible for a late-onset, slowly progressive, inherited PNP affecting mainly motor axons.

**Introduction**

SCA is chronic progressive disease that results from neuronal loss or dysfunction in the cerebellum and spinal cord. Different genetic subtypes has been described from SCA1 to SCA42. PNP are sometimes associated with SCA, axonal and/or demyelinating, according to the genetic subtype.

**Purpose**

A 56-year-old woman suffers ataxic gait and lower limbs neuropathic pain. The clinical examination shows pectus carinatum, pes cavus, distal amyotrophy, distal hypotension and areflexia in the lower limbs. Three years later, patient develops hypometric saccades and dysarthria suggesting a cerebellar syndrome. Three sisters, one brother, and two nieces, present a cerebellar syndrome and a PNP over several years. Some have a pectus carinatum. These familial clinical features lead to a genetic study on 28 family members. The results show a mutation of the MME gene in the 7 affected subjects.

**Method**

The diagnosis is performed by several electrophysiological examinations, brain MRI and molecular genetic study of the patient and his family.

**Results**

Electroneuromyography (ENMG) demonstrates a subacute axonal sensorimotor PNP, mostly motor rather than sensitive, progressive over several years. Indeed, the ENMG shows a predominantly 

**Conclusion**

1. The MME gene encodes NEP which is a membrane metalloendoproteinase, one of the most prominent beta-amyloid (Aβ)-degrading enzymes, expressed in the peripheral and central nervous systems. The pathogenesis due to the loss of function of NEP is still unclear. But amyloid deposit is not found on biopsies (2).
2. In this family, the p.C143Y MME mutation transmitted according to the autosomal dominant mode, is responsible for the phenotype of SCA43, associated to late-onset axonal sensorimotor PNP.
3. Two recent studies (3,4) show a late-onset axonal sensorimotor PNP, without central nervous system involvement, in patients with other MME gene mutations. Different MME mutations induce several phenotypes, ranging from AR-CMT2T to SCA43.

**Abstract**

MME GENE MUTATION CAUSING SPINOCEREBELLAR ATAXIA AND AXONAL POLYNEUROPATHY: CLINICAL CASE

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