## NEUROMUSCULAR DISEASES

### *POLG1* MUTATIONS AND CHARCOT-MARIE-TOOTH DISEASE

A 35-year-old man first diagnosed with autosomal recessive Charcot-Marie-Tooth disease type 2 at 22 years of age had an abnormal gait and pes cavus at age 10 years. Molecular analysis of the *POLG1* (polymerase-g-1) gene in muscle biopsy showed 3 heterozygous mutations, in a study at Queen's Hospital, Romford; Newcastle University; and other centers in the UK. At 22 years, he had bilateral distal weakness and wasting of the extremities, clawing of toes, tremor of hands, loss of joint position and vibration sense, and nerve conduction studies consistent with axonal sensorimotor neuropathy. At 35 years, he was unable to walk and had developed a prominent no-no head tremor, upbeat and pendular nystagmus, cerebellar dysarthria and dysphagia, postural and action tremor, dysmetria, distal limb weakness and wasting, absent reflexes, and diminished sensation to all 4 modalities. Other affected family members include a brother and a sister who developed symptoms at 9 years. Muscle histochemistry findings showed denervation and reinnervation, and a mosaic defect of cytochrome c oxidase. Polymerase chain reaction of skeletal muscle DNA revealed multiple deletions of mtDNA. Segregation analysis in the family showed that heterozygous substitutions in the proband *POLG1* gene sequencing were inherited from the mother and father. The affected brother had the same genotype as that of the proband. (Harrower T, Stewart JD, Hudson G et al. *POLG1* mutations manifesting as autosomal recessive axonal Charcot-Marie-Tooth disease. **Arch Neurol** Jan 2008;65:133-136). (Respond: Patrick F Chinnery PhD, FRCP, Mitochondrial Research Group, The Medical School, Newcastle University, Room M41014, Framlington Place, Newcastle upon Tyne NE2 4HH, England; E-mail: p.f.chinnery@ncl.ac.uk).

COMMENT. *POLG1* mutations cause deletions and depletions of mtDNA , leading to a respiratory chain defect with organ dysfunction and the clinical phenotype of CMT. This case report and family are unusual since all 3 siblings had signs of peripheral neuropathy only, without signs of multisystem mitochondrial disorder. Tremor and ataxia developed late, without the ophthalmoplegia that is characteristic of the mitochondrial phenotype of sensory ataxic neuropathy with dysphagia and ophthalmoplegia (SANDO). The authors recommend that *POLG1* should be sequenced in patients with unexplained CMT, even in the absence of signs of mitochondrial disease.

**Two novel connexin32 mutations cause early onset X-linked CMT** in 2 Norwegian families. (Braathen GJ, et al. **BMC Neurology** 2007;7:19-28).

### NEUROPATHY AND OTHER NEUROLOGICAL DISORDERS IN GAUCHER DISEASE TYPE 1

Neurological manifestations of 31 patients with Gaucher disease type 1 (GD1) were evaluated in a study at Miguel Servet University Hospital, Zaragoza, Spain. Twelve were males and 19 females, mean age 39 years (range 5-77). Age at diagnosis of GD was in early childhood or adolescence in 13