170

MFN2 DELETION FOUNDER MUTATION IN THE UK POPULATION

Aisling Carr,¹ JM Polke,² J Wilson,² T Nanji,² M Laura,¹ AL Pelayo,¹ B Lecky,³ J Vaughan,⁴ J Rankin,⁵ M Sweeny,² MM Reilly¹. ¹MRC Centre for Neuromuscular Diseases, UCL; ²Neurogenetics Unit, NHNN; ³The Walton Centre; ⁴Department of Neurology, Charing Cross Hospital; ⁵Department of Clinical Genetics, Royal Devon and Exeter Hospital

10.1136/jnnp-2014-309236.170

Background Mitofusion 2 (MFN2) mutations are the most common cause of axonal Charcot-Marie-Tooth disease (CMT2). The majority are inherited in an autosomal dominant manner but recessive and semidominant kindreds have been described. We previously reported an exon 7–8 deletion which segregated with disease when present in trans with another pathogenic MFN2 mutation.

Methods Detailed clinical and electrophysiological data on five affected patients and their parents and relatives was collected. MFN2 sequencing, multiplex ligation probe amplification and haplotype analysis was performed.

Results All cases had progressive distal weakness, wasting and sensory loss from infancy or early childhood; optic atrophy was common (4/5); 4/5 were wheelchair dependant by adulthood and 5/5 had electrophysiology consistent with CMT2. All were compound heterozygous for an exon 7–8 deletion in MFN2 with another previously reported pathogenic mutation (Phe216Ser,Thr362Met,Arg707Trp). Carrier parents and relatives were unaffected. All kindreds were of UK ancestry and haplotype analysis suggested that they share a common founder from which the exon 7–8 deletion was inherited.

Conclusion Here we present five patients with severe, early-onset CMT2 compound heterozygous for a deletion of exon 7 and 8 in MFN2 with haplotype analysis confirming this deletion as a founder mutation in the UK population.