CNS phenotype in X-linked Charcot Marie tooth disease

Vinojini Vivekanandam[1], Chandrashekar Hoskote[2], Alexander M. Rossor[1], Mary M. Reilly[1]

[1] MRC Centre for Neuromuscular Diseases, UCL Institute of Neurology, London, UK

[2]Department of Radiology, National Hospital for Neurology and Neurosurgery, London, UK

Correspondence to:

Vinojini Vivekanandam, MRC Centre for Neuromuscular Diseases, UCL Institute of Neurology, London, UK. vinojini.vivekanandam@nhs.net

We read with interest the study by Koutsis et al. reporting an increased prevalence of multiple sclerosis (MS) in their cohort of patients with X-linked Charcot Marie tooth disease (CMTX1) [1]. CMTX1 is a neurological condition with significant disability. The suggestion that CMTX1 may be a risk factor for developing multiple sclerosis will be of significant concern for these patients.

We have a large cohort of patients with CMTX1 (n=133) in our centre. We reviewed the clinical records and MRI brains in our cohort to look for a similar association.

Patients with confirmed *GJB1* mutations were identified from our internal database of individuals with CMT seen in the peripheral neuropathy clinics at the National Hospital for Neurology and Neurosurgery, Queen Square, London, UK. The brain MRI scans of all patients with CMTX1 who underwent imaging (n=26) were reviewed. Of the 26 MRI scans performed, 10 were identified as being abnormal and reviewed with a neuroradiologist. This translates to 7.52% of all CMTX1 patients in our cohort.

Of the 10 abnormal scans, only one patient had T2 white matter lesions (T2WML) resembling those seen in MS – periventricular, and perpendicular to ventricles. This patient at age 61, has accumulated only one new lesion over four years, has not had a clinical attack and as such, does not meet criteria for either radiologically isolated syndrome (RIS) or MS [2,3].

Of the other nine abnormal scans in our cohort, seven patients were characterised as having nonspecific T2 weighted hyperintensities that were not characteristic of MS-like lesions and did not fulfil criteria for RIS [2]; one had diffuse corpus callosum T2 weighted matter changes; and one with isolated volume loss. There was no correlation between the genotype and imaging phenotype.

Four patients had serial imaging which did not demonstrate any new lesions. The clinical indications for performing a brain MRI in our cohort were subtle upper motor neuron signs, which have been reported in CMTX1 patients.

The presence of T2WML in CMTX1 is well described [4]. While these changes appear prevalent in our CMTX1 cohort, no patients had relapsing features or clinical episodes that would fulfil diagnostic criteria for MS. Additionally, diagnostic criteria for RIS require that there is no alternate explanation for the changes seen, and as yet, the spectrum of T2WML in CMTX remains uncharacterised.

In summary, in a larger cohort of patients than that reported by Koutsis et al., we have not identified any cases of MS in patients with CMTX1. With a population prevalence of 1:1000 [1, 2] MS is likely to co-exist in the CMT population, and we have not found an association between CMTX1 and MS in

our cohort. We agree with the Koutsis et al that a limitation of their study was the small sample size and agree with the suggestion that further studies are needed in larger CMTX1 cohorts. Thus, it is premature to suggest that *GJB1* mutations are a possible risk for MS.

References:

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