Background: Mutations in myelin protein zero (MPZ) protein result in a wide spectrum of peripheral neuropathies, from congenital hypomyelinating (CHN and CMT1B) to late onset sensory and motor axonal forms (CMT2J). Rarely, a superimposed inflammatory/disimmune process may worsen the course CMT neuropathies, especially CMT1A.

Objective: Describe a family affected by a MPZ-related neuropathy, with demyelinating and axonal features, in which two members are clearly responsive to immunomodulating treatments

Two years ago a patient (pt. 1, male, 60 yrs old) affected by a distal, demyelinating, sensory-motor polyneuropathy came to our observation. Based on neurophysiologic criteria and CSF examination (markedly increased protein level) a chronic inflammatory polyneuropathy (CIDP) was diagnosed. He was first treated with oral steroids with clinical improvement. A severe psychotic reaction occurred leading to withdrawal of steroids. Monthly IVIG were then prescribed, again with satisfactory results.

More recently, two first cousins (pts. 2 and 3) were evaluated in our Neuromuscular Disease Service for a peripheral neuropathy with axonal and demyelinating features. One of these patients (pt. 2) was clearly responsive to monthly administration of IVIG, started in another hospital. Due to the presence, at neurological examination, of Argyll Robertson pupils and the prominence of axonal features, molecular testing was performed and showed a MPZ Thr124Met mutation in both patients. Then, after a more accurate family anamnesis, it turned out that the pt. 1 was a first cousin of pts. 2 and 3. Molecular testing confirmed the presence of a MPZ Thr124Met mutation also in this case.

At spinal MRI, gadolinium enhancement of lumbar roots was observed, providing radiological evidence of an abnormal blood-nerve barrier and inflammatory damage of the nerves (in all the three patients).

Currently pt. 1 begins to be less responsive to the treatment with IVIG, showing only a subjective improvement of symptoms, without any change at standard outcome measures like the 6 minute walk test, the MRC score and the INCAT scale.

Pt. 2 is still clearly responsive to IVIG therapy, whereas pt. 3 is too mildly affected to be treated.

Inflammatory neuropathy may exacerbate hereditary neuropathy. In particular were described: case of patient with MPZ Arg69His mutation and Ile70Thr mutation all responsive to steroid, five patient with CMT1A and one patient with CMT1X with variable positive response to steroid and immunoglobulin. This is the first report of an MPZ-mediated neuropathy with multiple family members responsive to immunomodulatory treatment.

Conclusion: although unusual, also in CMT2J families a superimposed inflammatory/dysimmune process may be present and be responsive to immunomodulatory treatment. The fact that two family members were responsive to therapy suggests a more complex relationship between CMT2J and CIDP.

References
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