CLINICAL FINDINGS FROM A LARGE SERIES OF CMT2I PATIENTS WITH *MPZ* P70S MUTATION

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Background and Objective

The most common *MPZ* mutation causing CMT2J/I is T124M, and all the others are represented by few cases or single report/families. In the last years we saw almost 30 patients with P70S mutation in *MPZ* all coming from the Lombardy and Emilia-Romagna regions, and our aim was to extensively characterize their clinical and neurophysiological phenotype.

Methods

We collected 26 patients, all from Northern Italy, especially Lodi, Pavia, Bergamo, Cremona, and Piacenza provinces.
We collected data from family and clinical history, neurological evaluation, electrophysiological examination and CMTNS.

Results

Patients	**11 M; 15 F**
Age, mean (SD)	**67 (± 15)**
Age at onset, mean (SD)	**51 (± 9)**
CMTES, mean (SD)	**8 (± 7)**
MRC FDI, mean (SD)	**4 (± 1)**
MRC APB, mean (SD)	**4 (± 1)**
MRC FDF, mean (SD)	**3 (± 3)**
MRC FPF, mean (SD)	**3 (± 2)**
Pinprick impairment	**63%**
Vibration impairment	**68%**
Sense position impairment	**33%**
Ankle reflex absence	**100%**
Ulnar MNCV, mean ± SD (CMAP, mean ± SD)	**52.5 ± 5.6 m/s (12.5 ± 1.9 mV)**

Abbreviations: SD= standard deviation; CMTES= Charcot-Marie-Tooth examination score; MRC= Medical Research Council Scale; FDI= first dorsal interosseous; APB= abductor pollicis brevis; FDF= foot dorsi-flexion; FPF= foot plantar-flexion; MNCV= motor nerve conduction velocity; CMAP= compound muscular action potential.

- Eleven males and 15 females
- Mean age was 67 (± 15) years
- Mean age at onset was 51 (± 9) years with both sensory symptoms and gait difficulties equally complained as onset symptom
- Three asymptomatic patients were <40 years old
- The disease started in the lower limbs with gait abnormalities and then progressed to upper limbs in half of them
- All patients developed wasting and weakness of the distal lower limb muscles, leading to complete foot drop in twelve patients
- Involvement of proximal lower limb muscles was observed in four subjects
- Twelve patients needed foot orthoses and seven needed a cane for walking
- Ankle deep tendon reflexes were absent in all patients
- Sensory impairment involved mainly vibration and pinprick sensation
- Nerve conduction studies showed an axonal neuropathy with marked abnormalities at lower limb motor nerves Motor nerve conduction velocities were normal or slightly reduced in the CMT2 range. Sensory nerves were affected to a lesser extent
- Nerve biopsy from one patient was consistent with a predominantly axonal chronic neuropathy

Conclusions

In conclusion, this is a very large cluster of CMT2I patients that likely share a common founder and that represents a unique model to study the phenotype of this late-onset axonal neuropathy and the potential pathomechanisms of axo-glial interactions.

REFERENCES

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