NATURAL HISTORY OF CHARCOT–MARIE-TOOTH: A 10-YEAR FOLLOW-UP

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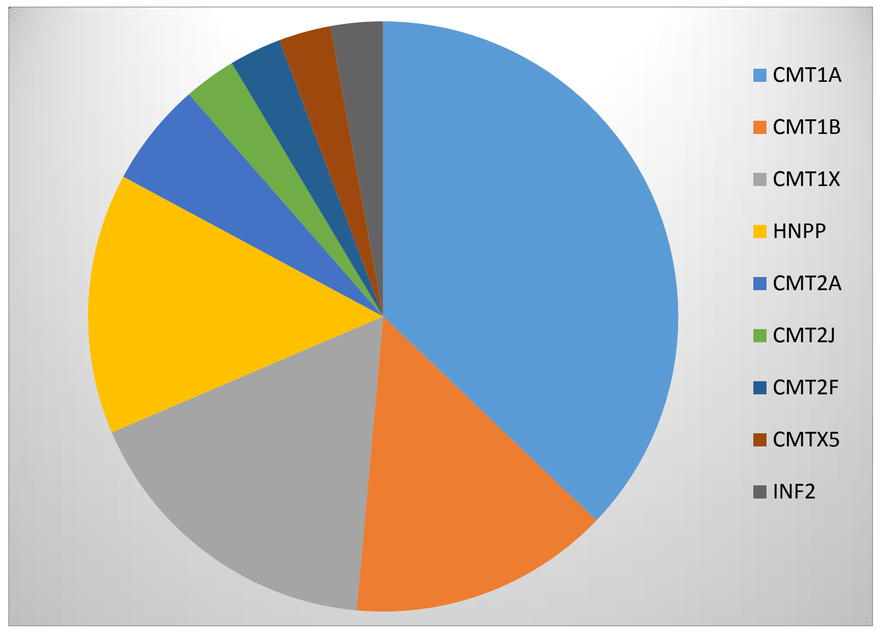
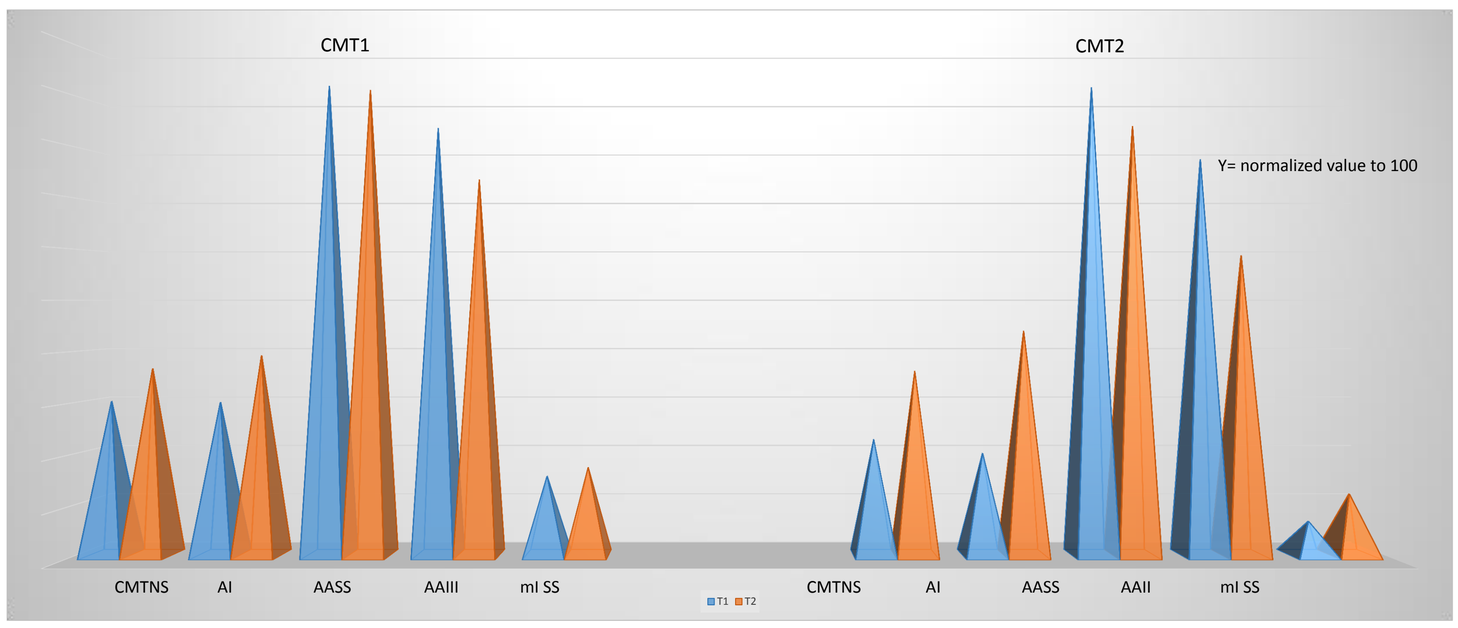
BACKGROUND: Charcot-Marie-Tooth disease (CMT) is the most common inherited neurological disease, however the natural history of CMT remains poorly defined.
We decide to evaluated the long term clinical burden in our CMT patients with the genotype-phenotype correlation with a particular focus on the disease progression.

METHODS: We retrospectively evaluated 36 patients affected by CMT neuropathy with an average clinical follow-up of 10 years (7-12 years). The clinical evaluation included the quantification of both muscular weakness, through the MRC score and sensory impairment with the Modified INCAT Sensory Sum Score. Disability was evaluated with the CMT Neuropathy Score and the Ambulation Index.
Our cohort of patients included patients affected by CMT1A (14), HNPP (5), CMT1B (5), CMT1X (6), CMT2J (1) , HSPB1 (1), MFN2 mutation (2), 1 patient affected by CMTX5 and 1 patient with intermediate form due to INF2 mutation.



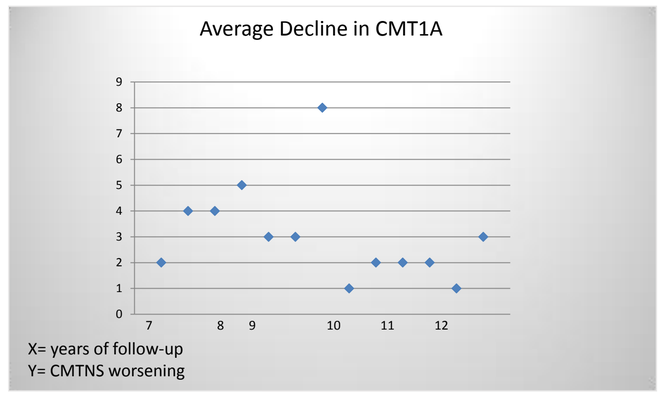
RESULTS: The mean age of first visit was 43 years ± 14,7 and the mean duration of disease was 20,7 years ± 14. There was a slow worsening in almost all patients. Worsening in CMTNS, greater than 3 points, was evident in half patients affected by CMT1A (6 pt, mean f-u 7,8 years), in almost all patients affected by CMT1X (5 pt, mean f-u 9,2 years) and only in 1 of the patients affected by HNPP and CMT1B (10 years of f-u in both of them). The most evident deterioration was in the patient affected by CMT2J (increase in CMTNS of 10 point and in Ambulation index of 3 point in 7 years of f-u, first visit was performed at the age of 44), in one affected by CMT1A (increase in CMTNS of 9 point and in Ambulation index of 3 point in 9 years of f-u, age 47 years-old) and in a female affected by CMT1X (increase in CMTNS of 9 point and in Ambulation Index of one point in 10 years of f-u-). Ambulation index increased at least one point in 15 patients, 75% of CMT2 and 41% of CMT1; clinical comparison of axonal and demyelinating form shows greater worsening in axonal form, despite of younger age (44 years versus 55 years) and lower CMTNS (8,2 versus 10,5) compared to demyelinating patients.(Fig. 1 e 2) Worsening of strength in the lower limbs is present in most patients, whereas sensory impairment appears to have a slower decline.(Fig 3)

CONCLUSION: Overall, all patients affected by CMT showed a tendency to clinical worsening over a long time follow-up. Patients affected by CMT1X showed highest degree of worsening. On the other side, HNPP cases appeared to be the least severely affected and had the slower progression. Interestingly, a large variability of worsening may be observed in CMT1A patients (Fig. 4). Motor more than sensory worsening characterizes our population of patients.



Average Decline

	CMTNS	AMB. INDEX	MRCSS AASS	MRCSS AAII	ml SS
CMT1A	3	0,77	1,5	7,2	0,7
CMT1B	2	0,2	2,6	7	0,2
CMT1X	3,37	0,5	2,8	6	0,87
HNPP	0,6	0,2	1,6	-0,2	0,2
CMT2	4,8	1,2	7,6	13	1,8



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