Multifocal Motor Neuropathy:

Evolution with Long Term Intravenous Immunoglobulin (IVIg) Treatment

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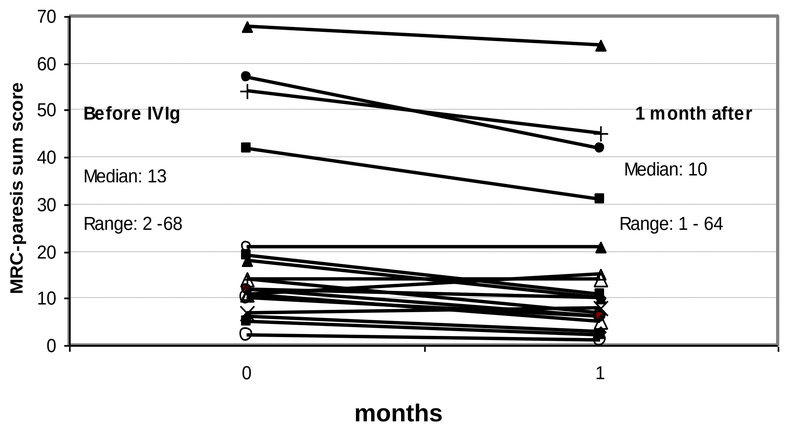
Objectives: To evaluate clinical and electrodiagnostic long term evolution of patients with multifocal motor neuropathy (MMN) on IVIg treatment.

Patients: 18 patients (14 males and 4 females) on repetitive IVIg infusions at regular intervals. Classification: 6 definite, 4 probable, 5 possible and 3 clinical MMN.

Methods: Follow-up, 4.3 (mean, range, 0.3 – 11.8) years. Clinical scores: Subjective functional improvement, Medical Research Council (MRC) rating scale in 40 muscle groups; Guy's Neurological Disability Scale; atrophy score. Electrophysiological studies: Nerve conduction velocities, motor conduction blocks and distal compound muscle action potential (CMAP).

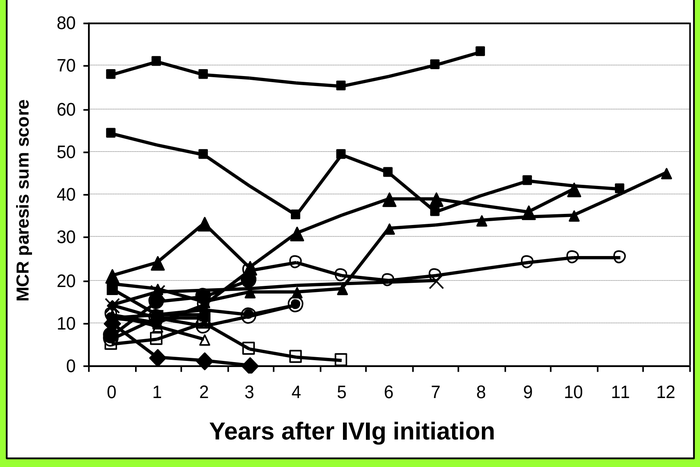
Results: Age at onset of symptoms: 49 (mean, range 28-66) years; delay between onset of symptoms and treatment: 51 (mean, range 2-156) months; mean duration of IVIg therapy: 4.3 years (range, 0.3 – 11.8); atrophy correlated with disease duration (p=0.045) (Mann-Whitney-Test); higher ranking in the diagnostic categorization correlated with longer disease duration (p=0.08) (ANOVA). Dose of IVIg was 7.7 g/kg body weight in the first year of treatment and 4.8 g/kg body weight/year thereafter. Responders: see table. There was no dependence of IVIg treatment response from diagnostic category whether in the short term (1 month) or in the long term (>1 year) (p=0.95) (Chi-Square-Test). In all patients followed-up > 2 years, the distal CMAP amplitudes decreased progressively despite ongoing IVIg therapy and initial transient amplitude increase.

Figure 1. Muscle strength (MRC paresis sum score) during IVIg-treatment (n = 18, 1 month period)



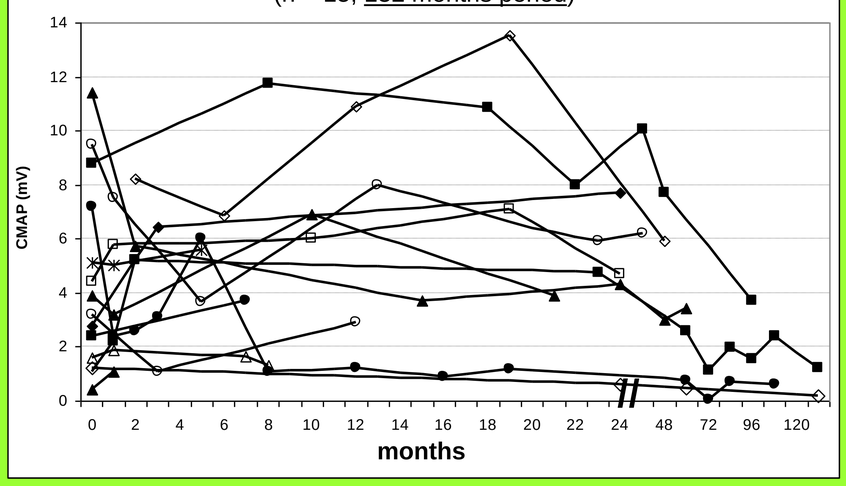
In 14 / 18 patients paresis decreased after the initial course of IVIg.

Figure 2. Muscle strength (MRC paresis sum score) during IVIg-treatment (n = 15, 12 years period)



Beyond one year only 6/15 patients were persistent responders, on the long term, most patients had progressive muscle weakness.

Figure 3. Evolution of distal CMAP during IVIg-treatment (n = 15, 132 months period)



Compund muscle action potential (CMAP) amplitudes monitored in one affected nerve decreased progressively despite ongoing IVIg therapy

Table. Response to IVIg after 1 month and after 1 year depending on diagnostic category

	All	Diagnostic MMN-category			
	(Male/Female)	Definite	Probable	Possible	Clinical
Evaluation at **1 month**					
Number of patients treated	18(14/4)	6 (4/2)	4(3/1)	5(4/1)	3(3/0)
Patients *responding to IVIg*	***14*** (11/3)	5(3/2)	2(2/0)	5(4/1)	2(2/0)
Evaluation at **1 year**					
Number of patients treated	15(11/4)	5 (3/2)	3(2/1)	5 (4/1)	2 (2/0)
Patients *responding to IVIg*	***6*** (4/2)	2(1/1)	1(1/0)	2(1/1)	1(1/0)

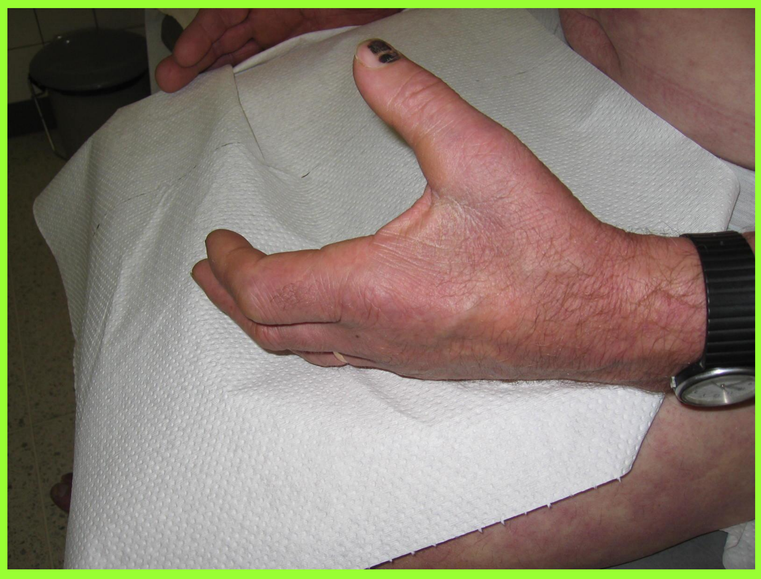


Figure 4: Paresis & atrophy of intrinsic hand musculature (ulnar nerve); disease duration 11 years

Discussion

IVIg was efficacious in 14/18 MMN patients in the short term (1 month) in accordance with previous studies (1). Fading of IVIg efficacy could be observed already in the first year of therapy; after >1 year 9/15 showed deterioration despite ongoing treatment.

Predictive for response were: Long pretreatment disease duration (negativ).

Not predictive: Diagnostic category, presence of motor nerve conduction block.

Long term evaluation of IVIg response is a difficult task. The available clinical measures are not optimal for the follow-up of a slowly progressive weakness & atrophy. The sensitivity of applied measures such as MRC rating scale are insufficient since testing of muscle strength depends strongly on the investigator, who often changes over the years. Furthermore, on long term, persistent weakness of an individual muscle may be masked by compensatory movements which may simulate improvement both subjectively as well as on functional scales. For muscle wasting there is no validated and reliable objective measurement.

Atrophy already in the first year and progressive decline of CMAP (distal compound muscle action potential) in the course is in favor of early and **ongoing axonal injury** (despite treatment).

Role of IVIg dose: Our study revealed a progressive muscle weakness over the time; which is in contrast to other studies that showed a more stable course under regular treatment with IVIg (2, 3). One reason might be the IVIg dose used: With 7.7 g/kg body weight in the first year of treatment and 4.8 g/kg body weight/year thereafter, our cumulative dose of IVIg was considerably lower than those used by Van den Berg et al. (22.4 g/kg body weight in the first year and 20.8 g/kg body weight after).

Therapeutic strategies to be evaluated should be 1) less expensive, and 2) more effective regarding axonal loss, since cases with persistent long term improvement or even allowing withdrawal of IVIg are extremely rare.

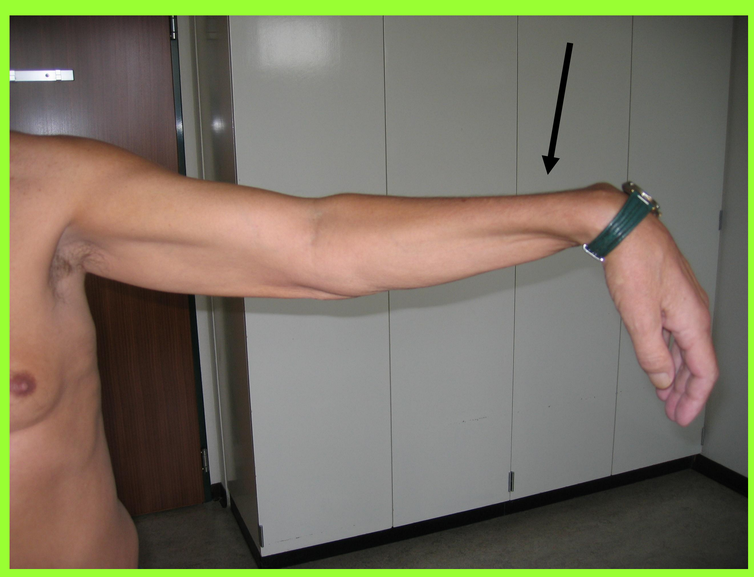


Figure 5: Paresis & atrophy of hand & wrist extensors (arrow) and triceps muscle (radial nerve); disease duration 15 years

1) van Schaik IN, et al. Intravenous immunoglobulin for multifocal motor neuropathy. Cochrane Database Syst Rev 2005:CD004429.

2) Van den Berg-Vos RM, et al. Multifocal motor neuropathy: long-term clinical and electrophysiological assessment of intravenous immunoglobulin maintenance treatment. Brain 2002;125:1875-1886

3) Vucic S, et al. Multifocal motor neuropathy: decrease in conduction blocks and reinnervation with long-term IVIg. Neurology 2004;63:1264-1269.

Berne, 15.11.06