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Long-Term Course of Chronic Inflammatory Demyelinating Polyneuropathy: Clinical and Neurophysiological Outcomes

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Introduction: Chronic inflammatory demyelinating polyneuropathy (CIDP) is the most common chronic immune-mediated polyneuropathy. CIDP is characterized by a long-term progressive or relapsing course of the disease, leading to temporal and permanent disability and requiring maintenance of long-term immunotherapy.

Objective: To assess clinical and paraclinical outcomes in patients with CIDP history of more than 5 years.

Methods: We included 46 adult patients that fulfilled the European Academy of Neurological Societies/Peripheral Nerve Society diagnostic criteria for CIDP 2021 and disease duration of more than 5 years. Treatment response, treatment status, remissions (improved and untreated), treatment changes, and residual symptoms or deficits were assessed. Outcome measures included Medical Research Council (MRC) sum score, the Neurological Impairment Scale (NIS), the Inflammatory Neuropathy Cause and Treatment (INCAT) disability scale, the Inflammatory Rasch-built overall disability scale (I-RODS), CIDP Disease Activity Status (CDAS), Questionnaire Short Form 36 Health Survey (SF-36), chronic acquired polyneuropathy patient-reported index (CAP-PRI). Electrophysiological examination and nerve ultrasound (Ultrasound pattern sum score, Grimm et al, 2015) were performed.

Results: Median follow-up period was 10 [7.0; 13.45], average age 48.1 ± 13.4 years. There were 32 (70%) typical CIDP patients and 14 (30%) CIDP variants (multifocal CIDP). The period from the disease onset to initiation of immunotherapy for typical CIDP was up to a year (60%) and for CIDP variants 5 years (50%). Up to 86% of multifocal CIDP required maintenance treatment after 5 years of the disease. 50% typical CIDP had CDAS 1 (cure: ≥5 years off treatment), 64% multifocal CIDP - CDAS 5 (unstable active disease: abnormal examination with progressive or relapsing course). For CIDP variants NIS motor score ($p=0.002$), INCAT score for arms ($p=0.006$), CAP-PRI score ($p=0.025$) were higher compared to typical CIDP. 80% CIDP patients had neurophysiological signs of a demyelination process, fulfilled the criteria of EAN/PNS 2021. UPSS sum score was 7.7 [2.0; 10.75], but most CIDP patients had nerve enlargement (increased mean cross-sectional area) in proximal ulnar and median nerves segments and brachial plexus.

Conclusions: The typical CIDP is characterized by a favorable long-term course, up to 60% of patients are considered clinically cured or are in stable remission. The progressive unstable course of the disease (64% of patients, $p<0.03$), a more severe neurological deficit with predominant involvement of the hands, and a greater degree of disability are significantly more common in CIDP variants. 80% of patients in the long-term follow-up have neurophysiological and sonographic signs of a chronic demyelinating process, fulfilled the criteria of EAN/PNS 2021.

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Hematological Effects of Intravenous Immunoglobulin Therapy in Patients with Neuromuscular Diseases – A Retrospective Analysis

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Introduction: Administration of intravenous immunoglobulins (IVIGs) is a frequently used treatment in Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN) and myasthenia gravis. IVIGs are generally well-tolerated and adverse reactions seldom prohibit its usage. Recently, an increasing number of cases with IVIG-related hemolysis have been reported. Hemolytic anemia is associated with changes in haptoglobin, lactate dehydrogenase (LDH) and bilirubin combined with a positive direct agglutination test (DAT).

Material and methods: A retrospective analysis of patients hospitalized for IVIG administration for neurological disorders at the department of neurology in an academic and in a general hospital was performed. Data collection period was arbitrarily set between 1 September 2017 and 31 August 2018.

Laboratory data was searched for blood samples of patients taken at hospital admission and at hospi-

tal discharge. Three different brands of IVIG (Privigen, Sandoglobulin and Multigam) were used. Pre-treated patients received a dose of 1.0 g/kg and de novo treated patients a dose of 2.0 g/kg. Duration of administration varied between 2-5 days. Patients were divided in first-time treated versus pre-treated patients.

Statistical analysis was performed using R software (R Core Team). The paired t-test and the Wilcoxon signed rank test were used for normally and non-normally distributed data, respectively.

Furthermore the frequency of "IVIG-associated hemolysis" was calculated and was defined as a decrease of more than 1g/dL in Hb and a positive DAT and at least one of the following findings: 1) increased reticulocyte count 2) increased LDH 3) low haptoglobin 4) unconjugated hyperbilirubinemia or 5) elevated free Hb in plasma.

Results: Forty patients were selected after exclusion based on comorbidities or incomplete datasets. 26 patients had a diagnosis of CIDP, 12 of MMN and 2 of polymyositis. 25 patients were treated with Sandoglobulin, 7 with Privigen and 8 with Multigam.

Treatment with IVIG showed a significant decrease in RBC (-0.31 x10^6/µL, p<0.001), Hb (-0.95 g/dL, p<0.001) and increase in reticulocyte count (+ 0.6/10^3RBC, p=0.01). There was a significant decrease in LDH (-37 U/L, p<0.001), haptoglobin (-0.14 g/L, p=0.001) and increase in unconjugated bilirubin (+0.03 mg/dL, p=0.002). White blood cell and platelet counts dropped significantly after IVIG treatment (-1.9 x10^3/µL, p<0.001 and -33.5 x10^3/µL, p<0.001). There were no significant differences between the first-time treated and pre-treated groups.

DAT was negative in 34 patients, slightly positive or positive in 4 and 2 patients, respectively, prior to IVIG. After IVIG administration DAT was negative in 9 patients, slightly positive or positive in 7 and 24 patients, respectively. 5 out of 40 patients met all the criteria for IVIG associated hemolysis and 3 other patients met the 2 main criteria. Blood groups of the patients meeting all criteria were A+, A-, B+ and AB+.

Discussion: Our data shows significant changes in various hematological parameters in both pre-treated as first-time treated patients. A surprisingly high amount of patients met the criteria for IVIG-related hemolysis. These findings confirm the need for monitoring hematology parameters in all patients treated with IVIG, despite lack of consensus or guidelines.

Parameter	Sub-analysis	Before IVIG	After IVIG	Difference	P-value within groups	P-value between groups
Red blood cell count (x10^6/µL)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
White blood cell count (x10^3/µL)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
Platelet count (x10^3/µL)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
Hemoglobin level (g/dL)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
Reticulocyte count (/10^3 RBC)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
Haptoglobin (g/L)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
Unconjugated bilirubin (mg/dL)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		
Lactate dehydrogenase (U/L)	Total	[illegible]	[illegible]	[illegible]	[illegible]	
	First-time treated			[illegible]		[illegible]
	Pre-treated			[illegible]		