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New insights into atypical forms of chronic inflammatory demyelinating polyneuropathy

Objective — highlighting the clinical peculiarities of atypical chronic inflammatory demyelinating polyneuropathy (CIDP); comparative analysis of nerves conduction studies (NCS) parameters in typical and atypical CIDP; utility of somatosensory evoked potentials to demonstrate the proximal demyelination in pure sensory CIDP with normal NCS parameters; the role of superficial peroneal nerve biopsy in the diagnosis of CIDP.

Methods and subjects. The study included 30 patients with atypical CIDP and 30 patients with typical CIDP. All patients underwent NCS, blood was drawn for biochemical tests, also electrophoresis and serum protein immunofixation. Peroneal nerve biopsy was performed in 9 patients (4 with atypical CIDP and 5 patients with typical CIDP). Overall Neuropathy Limitation Scale questionnaire (ONLS) was used for the assessment of functional disability in all patients.

Results. The mean value ONLS within atypical CIDP was 2.43 ± 0.29 points, lower compared to typical CIDP — 4.17 ± 0.24 points. Monoclonal gammopathies were found in 13 patients, representing 22% of patients with CIDP. Demyelinating criteria most frequently observed in the biopsy material is decreased number of myelinated thick fibers.

Conclusions. NCS is not a gold standard for diagnosis atypical sensory CIDP. According to ONLS scale, atypical CIDP are less disabling compared with typical CIDP. Peroneal nerve biopsy within CIDP is performed only when electrophysiological studies do not elucidate demyelination criteria.

Key words: atypical demyelinating polyneuropathy, biopsy, diagnostic criteria.

Chronic inflammatory demyelinating polyneuropathy (CIDP) have been described for the first time in 1958 by J.H. Austin [1]. Recent epidemiological data show a prevalence of CIDP equal to 2.84 per 100,000 population in the UK [18] and 1.9 per 100,000 population in Japan [9]. In the english study was demonstrated that CIDP predominantly affect male with specific prevalence reaching the maximum 6.7 per 100,000 population aged between 70 and 79 years. The incidence of the disease represents 0.15 per 100,000 population [18]. In a retrospective study involving elder subjects with neuropathy, associated with disability, CIDP ranked second, constituting 14% of all disabling neuropathies in this age group [25]. The same low prevalence is probably erroneous because atypical forms of CIDP are difficult to diagnose, therefore the actual prevalence should be twice as high.

The typical clinical manifestations of CIDP include a motor deficit symmetrically in all limbs, predominantly the proximal portion, associated with a sensory deficiency with the same distribution, with a reduction or abolition of tendon reflexes, duration for at least two months [16].

Sensory impairment prevails over proprioceptive sensitivity (that highlights the involvment of the large nerve fibers type A) which causes numbness and balance disorders ataxia type. Cranial nerves affection (commonly the facial nerve, oculomotor nerve rarely) occurs mainly in the clinical forms of CIDP with relapsing evolution [20]. In practice, clinical picture of CIDP vary greatly from one patient to another, demyelinating lesions occur randomly (but concentrate on proximal and distal segments within peripheral nerves), highlighting the similarity beween CIDP and multiple sclerosis — demyelinating disease of the central nervous system [6].

According to the European Federation of Neurology guideline (EFNS/PNS, revised in 2010) CIDP can

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be classified into two clinical forms: [10] typical CIDP and atypical CIDP.

Atypical forms can be classified according to the clinical manifestations in 4 major groups: pure motor, pure sensory, multifocal and distal symmetrical impairment of upper and lower limbs.

Lewis — Sumner syndrome

In 1982, R.A. Lewis et al. (1982) described five patients with a chronic, acquired, asymmetric sensorimotor demyelinating polyneuropathy which clinically resembled a multiple mononeuropathy syndrome [17]. Electrodiagnostic studies demonstrated multifocal conduction block in motor nerves. CSF protein was normal to mildly elevated. Rajabally Ya in a study conducted in 2009 concluded that the syndrome Lewis — Sumner is characterized by the presence of conduction blocks in median or ulnar nerves in 90 % cases, and demyelination of lower limbs nerves occurs in 40 % of cases [21, 27].

Distal acquired demyelinating symmetric

The term distal acquired demyelinating symmetric (DADS) neuropathy was introduced by J.S. Katz et al. to describe a group of patients with predominantly distal sensory and ataxic demyelinating neuropathy [11, 14]. DADS neuropathies without serum presence of antibodies to myelin associated glycoproteins are considered atypical forms of CIDP [16]. Most of these patients have markedly slowed motor conduction velocities and even more prolonged motor distal latencies. Usually, no conduction blocks are observed on nerves conduction studies (NCS). Sensory impairment, ataxia, and tremor may also be found in patients with DADS as well as a predominant distal impairment [25]. The evolution course usually is more slowly than in typical CIDP.

Sensory chronic inflammatory demyelinating polyneuropathy

Recent epidemiologic data have shown that 35 % of CIDP patients may have only sensory symptoms [2]. Even if these patients have normal strength, most of them have electrodiagnostic abnormalities on motor nerve conduction studies. A particular form of sensory CIDP is chronic immune sensory polyradiculopathy [22]. This entity was first reported by M. Sinnreich et al. (2004) who described 15 patients who had only sensory symptoms for a few years with normal nerve conduction studies. In these patients, somatosensory evoked potentials (SSEP) were delayed, cerebrospinal fluid (CSF) proteins were increased, and lumbar magnetic resonance imaging (MRI) revealed an enlargement of lumbar roots [22].

Electrophysiological criteria are essential for diagnosis of CIDP [26]. The main four parameters that indicate the presence of a demyelinating process are: decreased motor conduction velocity, delayed distal motor latency, delayed latency or disappearance of F waves and presence of conduction blocks. These features, although not unique to CIDP, are suggestive of the diagnosis of CIDP.

Electrodiagnostic criteria of CIDP according to EFNS/PNS Guideline 2010

(1) Definite

At least one of the following:

- Motor distal latency prolongation ≥ 50 % above ULN in two nerves (excluding median neuropathy at the wrist from carpal tunnel syndrome)
- Reduction of motor conduction velocity ≥ 30 % below LLN in two nerves
- Prolongation of F-wave latency ≥ 30 % above ULN in two nerves (≥ 50 % if amplitude of distal negative peak CMAP < 80 % of LLN values)
- Absence of F-waves in two nerves if these nerves have distal negative peak CMAP amplitudes ≥ 20 % of LLN + ≥ 1 other demyelinating parameter in ≥ 1 other nerve
- Partial motor conduction block: ≥ 50 % amplitude reduction of the proximal negative peak CMAP relative to distal, if distal negative peak CMAP ≥ 20 % of LLN, in two nerves, or in one nerve + ≥ 1 other demyelinating parameter in ≥ 1 other nerve
- Abnormal temporal dispersion (> 30 % duration increase between the proximal and distal negative peak CMAP) in ≥ 2 nerves
- Distal CMAP duration (interval between onset of the first negative peak and return to baseline of the last negative peak) increase in ≥ 1 nerve (median ≥ 6.6 ms, ulnar ≥ 6.7 ms, peroneal ≥ 7.6 ms, tibial ≥ 8.8 ms) + ≥ 1 other demyelinating parametera in ≥ 1 other nerve

(2) Probable

- ≥ 30 % amplitude reduction of the proximal negative peak CMAP relative to distal, excluding the posterior tibial nerve, if distal negative peak
- CMAP ≥ 20 % of LLN, in two nerves, or in one nerve + ≥ 1 other demyelinating parameter in ≥ 1 other nerve

(3) Possible

As in (1) but in only one nerve

To apply these criteria, the median, ulnar (stimulated below the elbow), peroneal (stimulated below the fibular head), and tibial nerves on one side are tested. If criteria are not fulfilled, the same nerves are tested at the other side, and/or the ulnar and median nerves are stimulated bilaterally at the axilla and at Erb's point. Motor conduction block is not considered in the ulnar nerve across the elbow and at least 50 % amplitude reduction between Erb's point and the wrist is required for probable conduction block. Temperatures should be maintained to at least 33 °C at the palm and 30 °C at the external malleolus (good practice points).

CMAP, compound muscle action potential; ULN, upper limit of normal values; LLN, lower limit of normal values.

Supportive criteria for CIDP

1. Elevated CSF protein with leukocyte count $< 10/mm^3$ (level A recommendation)

2. MRI showing gadolinium enhancement and/or hypertrophy of the cauda equina, lumbosacral or cervical nerve roots, or the brachial or

lumbosacral plexuses (level C recommendation)

3. Abnormal sensory electrophysiology in at least one nerve (good practice points):

- normal sural with abnormal median (excluding median neuropathy at the wrist from carpal tunnel syndrome) or radial sensory nerve action potential (SNAP) amplitudes; or
- conduction velocity < 80 % of lower limit of normal (< 70 % if SNAP amplitude < 80 % of lower limit of normal); or
- delayed somatosensory evoked potentials without central nervous system disease

4. Objective clinical improvement following immunomodulatory treatment (level A recommendation)

5. Nerve biopsy showing unequivocal evidence of demyelination and/or remyelination by electron microscopy or teased fibre analysis (good practice point)

Characteristic features of monoclonal gammopathies

Monoclonal gammopathies result from an overproduction of a single abnormal clone of a plasma cell or B lymphocyte [24]. It is important to note that many monoclonal gammopathies identified on serum electrophoresis are benign, so-called monoclonal gammopathy of undetermined significance (MGUS) [15]. Immunoglobulin involvement may be IgM, non-IgM (IgA, IgG), or light chain [13]. All pose a risk of progression to a malignant disorder. Typically, IgG and IgA MGUS progress to multiple myeloma, IgM MGUS progresses to Waldenström macroglobulinemia or other lymphoproliferative disorders [13]. Some CIDP forms are associated with MGUS. Patients with MGUS require lifelong follow-up, with the intensity of follow-up guided by risk stratification [3].

The aims of the study

- Highlighting the clinical peculiarities of atypical CIDP
- Comparative analysis of NCS parameters (distal motor latency, CMAP amplitude, motor and sensory conduction velocity) in typical and atypical CIDP
- Utility of SSEP to demonstrate the proximal demyelination (at pre or postganglionic levels) in pure sensory CIDP with normal NCS parameters
- Evaluation of the relationship between the presence of MGUS and level of disabilty (Overall Neuropathy Limitation Scale) in patients with CIDP
- The role of superficial peroneal nerve biopsy in the diagnosis of CIDP

Materials and methods

We examined medical records from the Centre of Peripheral Disimunitary Polyneuropathies, Hospital Pitie-Sapletriere, Paris, in the period of time 2010—2014. Two groups of study were identified: 30 patients with typical CIDP and 30 patients with atypical CIDP according to the EFNS/PNS guideline (revised 2010).

Clinical examination included the following scales: Overall Neuropathy Limitation Scale (ONLS), 9-hole peg test, MRC (Medical Research Council). Nerve conduction studies (NCS) were performed in all the patients. A full routine biochemistry, electrophoresis and immunofixation of serum proteins, all spectrum of anti-myeline and anti-ganglioside antibodies were performed. The proximal segments of the sensory peripheral nervous system can only be assessed by somatosensory evoked potentials (SSEPs) [19]. SSEP tests were performed in 10 patients with typical CIDP and 10 patients with sensory CIDP.

SSEPs were considered to be suggestive of proximal demyelination when they revealed: (i) a significant increase in radicular conduction time with normal distal conduction time in at least 1 nerve and/or (ii) absence of N9/N18 potential or N13/N22 potential and/or delayed proximal volleys (N9 or N18) with normal distal conduction time in at least 2 nerves [28].

Cerebral spinal fluid (CSF) macroscopic/microscopic examination was performed in all the patients.

Superficial peroneal nerv biopsies were obtained under local anesthesy from the lateral and inferior part of the shank. 5 patients with typical CIDP and 4 patients with atypical CIDP underwent superficial peroneal nerv biopsies. The 5 centimeters long superficial peroneal nerve specimen was divided into three pieces: one piece was fixated in paraformaldehyde and stained with haematoxylin-eosin; 2nd piece was fixated in glutaraldehyde and the subsequent generationof semi-thin sections were stained with toluidine blue; 3rd piece was frozen in liquid nitrogen and stored at –80 °C — for immunohistological research.

Semi-thin (0.5 μm) sections allow much greater resolution than that provided by specimens embedded in paraffin and allow accurate quantification of demyelination markers: the presence of onion bulbs, decreased number and density of large and small myelinated fibers, decreased thickness of the myelin sheath [12]. Epineural lymphocyte infiltration is seen at the fixing in paraffin, and hematoxylin-eosin staining, or by freezing in isopentane imunoflouriscente samples [23]. Statistical analysis was performed using statistical methods Mann — Whitney and Fisher (SPSS Statistics 20). Cases with $p \leq 0.05$ were considered statistically significant.

Results and discussions

First study group included 30 patients with atypical CIDP, the second group was represented by 30 patients with typical CIDP. The precentage of patients with atypical CIDP was the following: 10 patients with Lewis — Sumner syndrome represent 33 % of patients with atypical CIDP, 6 patients with DADS — 20 % eof patients and 14 patients with sensitive

CIDP — 47 % of patients with atypical CIDP. Our results suggest that sensitive CIDP represents the most frequent form of atypical CIDP.

From the group of 14 patients with sensitive CIDP — 4 patients fulfill the EFNS/PNS Guideline 2010 criteria for NCS demyelination, 10 patients don't fufill these criteria but instead were selected according to the ctriteria of the French Group of CIDP Experts [8]. NCS show no evidence of demyelinating criteria for these 10 patients with sensory CIDP, but these patients show clinical examination abnormalities that are not typical for chronic axonal polyneuropathies like: ataxia, generalized areflexia, distal hypoesthesia progressing toward the proximal portions of the limbs.

According to the sex ratio in the group of patients with atypical PDIC, there were 22 (73 %) men and 8 (27 %) women, with no statistical difference with typical CIDP group: 20 (67 %) men versus 10 (33 %) women ($p > 0.05$).

The average age of patients with atypical CIDP included in the study was 61.83 ± 2.19 years (95 % CI 35.61—79.82) ($p = 0.27$). Most patients, 23 (76.7 %) persons had between 40—70 years, 4 (13.3 %) persons were younger than 40 years, 3 (10 %) persons aged over 70 years. The medium age of onset of symptoms was 53.57 ± 2.36 years (95 % CI 25.52—71.50) for patients with atypical CIDP. Disease duration for patients with atypical CIDP was 99.2 ± 10.9 months (95 % CI 12.45—228.12) which is equivalent to an average 9 years ($p = 0.12$).

Typical CIDP patients analysis shows the average age of these patients was 58.50 ± 2.32 years (95 % CI 31.21—81.34). Most patients — 22 (73.4 %) — had between 40—70 years, 7 (23.3 %) persons were younger than 40 years, 1 person (3.3 %) aged over 70 years. The medium age of onset of disease in typical CIDP group was on average to 51.23 ± 2.41 years (95 % CI 20.33—75.55). Disease duration ranged from 12 months (1 year) to 324 months (27 years), the average being 122.0 ± 13.9 months (95 % CI 12.15—324.15) which is equivalent to an average 10 years ($p = 0.25$).

Our results confirm the recent epidimiological studies regarding CIDP prevalence made in England [18]. They found a total number of 101 patients with CIDP. According to sex ratio males prevailed in their study: there were 66 (65.3 %) males and 35 (34.7 %) females. The mean age at onset was 57.7 years, and the mean age on the prevalence date was 63.7 years. Of 62 patients with available data, 9 (14.5 %) had progressive disease courses, 44 (71 %) had relapsing and remitting disease courses, and 9 (14.5 %) had monophasic disease courses.

In our study, the evolution of the disease in the 2 groups was not statistically different. In the group with typical CIDP 18 (60 %) patients had progressive disease course, 6 (20 %) had relapsing and remitting disease courses, and 6 (20 %) had monophasic disease courses. In the group with atypical CIDP 13 (43.3 %) patients had progressive disease course, 4 (13.4 %) had relapsing and remitting disease courses, and 13 (43.3 %) had monophasic disease courses. Unlike the data from the English epidiomological study, where majority of CIDP patients (71 %) had relapsing remitting disease courses [18], in our study prevail the cases wih progressive disease courses — 31 (51 %) patients with CIDP.

All sensory CIDP patients had clinically pure sensory peripheral neuropathy and normal muscle strength according to MRC scale. In DADS group 3 patients had normal strength, and another 3 only slight distal weakness. Romberg sign was negative in 11 (78 %) cases in sensory PDIC and positive in all DADS patients. Tremor was present in 50 % cases of DADS, and only in 22 % sensory CIDP patients.

Monoclonal gammopathies were found in 13 patients, which represents 22 % of patients with CIDP. In group I with atypical CIDP we have identified 5 cases with monoclonal gammopathies, while in group II — 8 patients ($p > 0.05$) had monoclonal gammopathies.

MGUS type IgM represent a total of 9 (70 %) cases: 6 cases were IgM kappa and 3 cases were IgM lambda. We found 4 (30 %) patients witg IgG MGUS: 3 cases were IgG kappa and 1 case of IgG lambda. The distribution of monoclonal gammopathies in each group is described in fig. 1.

The results obtained in our study match the data recorded by S. Larue et al. in 2010 [14]. 32 (22 %) patients from 146 CIDP patients were detected with monoclonal gammopathies on immunoelectrophoresis. IgM monoclonal gammapthies prevailed in their results: 19 patients had IgM gammapathies and 13 patients had IgG gammapthies [14].

The results presented in table 1 demonstrates the association between the presence of IgM monoclonal gammopathies and higher level of disability in typical CIDP group: average of total ONLS associated with MGUS is 5.00 ± 0.16 compared with total ONLS without MGUS 4.10 ± 0.24 points ($p < 0.05$). Atypical CIDP cases associated with MGUS don't differ by the average ONLS from the rest of the goup not associated with MGUS.

Average values of ONLS in the 2 groups showed the following results:

a) average ONLS in lower limbs is 1.17 ± 0.20 points in atypical CIDP versus 2.23 ± 0.12 points in typical CIDP ($p < 0.001$);

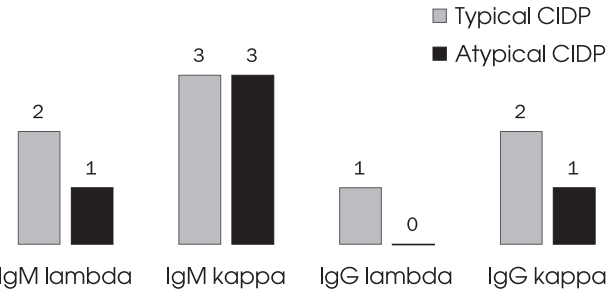

Fig. 1. *Types of gammopathies at patients with CIDP*

b) average ONLS in upper limbs is 1.27 ± 0.18 points in atypical CIDP versus 1.93 ± 0.17 poiints in typical CIDP ($p < 0.11$);

c) average total ONLS in atypical CIDP has a value of 2.43 ± 0.28 points versus 4.17 ± 0.24 points in typical CIDP ($p < 0.001$).

The results of 10 meters test were the following: 6—8 seconds — 21 patients with atypical CIDP and 3 patients with typical CIDP; 9—14 seconds — 8 patients with atypical CIDP and 17 patients with typical CIDP; 15 to 20 seconds — 1 patient with atypical CIDP and 10 patients with typical CIDP ($\chi^2 = 31.288$, $p = 0.002$).

According to the results of 10 meters test, atypical forms of CIDP are less disabling than typical forms of CIDP — 21 (70 %) patients with atypical CIDP can walk without difficulty, while in the group of patients with typical CIDP only 3 (10 %) patients can walk normally.

Patients with a medium degree of disability prevails in typical CIDP: 8 (26 %) patients in atypical CIDP and 17 (56 %) patients with typical CIDP.

The percentage of patients with an advanced degree of disability net prevails in the group of patients with typical CIDP: 10 (33 %) patients with typical CIDP compared with 1 (3 %) patient in the group with atypical CIDP.

In our study, 18 % of all patients with CIDP can walk only with 1 or 2 supports, which corresponds to the data in specialised literature. In a follow-up study over a period of 5 years conducted by S. Kwabara et al. in 2006 [7] — 13 % of patients with CIDP have difficulty in gaining high or are restricted to a wheelchair.

Distal motor latencies, motor conduction velocities, proximal CMAP amplitudes, F-waves latencies of median, ulnar, peroneal and tibial nervs are more preservated in atypical CIDP than in typical CIDP ($p < 0.001$; table 2). These data suggest a less demyelinating and degenerative process in atypical CIDP patients compared with typical cases of CIDP.

NCS show conduction blocks mostly in median and ulnar nerves in patients with Lewis — Sumner syndrome (LSS), but unaffected nerves are strictly normal. NCS in 14 cases with sensory CIDP show normal motor conduction velocity in 10 cases, and diminished only in 4 cases. Also distal motor latency is diminished in 4 cases. Conduction block is present only in one case of sensory CIDP. Sensory conduction velocities in median amd sural nerves were diminshed in 6 cases. The amplitudes of the sensory nerv actions potentials in sural nerves sensory are absolutely normal in 7 patients of 14 with sensitive CIDP (50 % of patients with sensitive CIDP). From these 7 patients 6 of them (43 %) have so-called inverse ratio — amplitude of the sural nerve SNAP is greater than the amplitude of median nerve SNAP, which is an important supportive criteria for diagnosis of CIDP (fig. 2).

SSEP examination were done to 10 patients diagnosed with sensory CIDP but with no signs of demyelination on NCS and compared with SSEP results of 10 patients with typical CIDP. 6 patients with sensory CIDP had prolonged radicular conduction time in at least 1 limb compared to 7 patients in typical CIDP ($p > 0.05$), and 7 had abnormal/delayed N9/N18 potentials and/or absent spinal potential in at least 1 limb compared to 8 patients with typical CIDP ($p > 0.05$). In summary, all patients with sensory CIDP had evidence of proximal demyelination on SSEPs with no statistical difference from the patients with typical CIDP.

Several studies were made to establish an association between the functional scores of disability (ONLS; 10 meters and 9 holes peg test) and clinical, electrophisiological features of patients with CIDP [5, 19, 20]. But no evidence of strong correlation was found. A strong correlation is considered r value of

Table 1

Relationship between persence of monoclonal gammapathies and ONLS levels in typical and atypical CIDP

Patient	Diagnosis	IgM kappa, g/l	IgM lambda, g/l	IgG kappa, g/l	IgG lambda, g/l	Total ONLS*
1	Lewis — Sumner	1.2				1 + 0 = 2
2	Lewis — Sumner		2.0			2 + 2 = 4
3	DADS	1				2 + 0 = 2
4	Sensory CIDP	1				0 + 2 = 2
5	Sensory CIDP			5		3 + 2 = 5
6	Typical CIDP		2.2			2 + 2 = 4
7	Typical CIDP	0.8				3 + 3 = 6
8	Typical CIDP	0.8		0.7		3 + 3 = 6
9	Typical CIDP	2.9				2 + 2 = 4
10	Typical CIDP				9.4	0 + 2 = 2
11	Typical CIDP		10.6			2 + 3 = 5
12	Typical PDIC			1		2 + 2 = 4

** Upper limbs + lower limbs.*

correlation in he range 0.7—0.9; 0.4—0.7 — is considered a medium value; 0.1—0.3 — a weak correlation value. In our study we tried to analyse the relationship between the data obtained using the scores of disabilities in CIDP (ONLS, 9 holes peg test, INCAT sensor score and 10 meters test) and clinical (muscle strength in limbs, absence of deep-tendon reflexes, etc.), paraclinical (NCS studies of motor and sensory nerves, level of proteins in CSF, presence of monoclonal gamapathies) results. We found only medium level correlations in the range 0.4—0.7 with statistical importance or no correlation at all.

The correlation between the average value of MRC and high level of proteins in CSF in typical CIDP

Table 2

Results of NCS in motor nervs in typical and atypical CIDP (M ± SD)

Parameter	Typical CIDP (n = 30)	Atypical CIDP (n= 30)	p
Median nerve			
Motor distal latency, ms	5.40 ± 0.52	4.91 ± 0.49	0.09
CMAP distal amplitude, mV	4.71 ± 0.46	7.25 ± 0.59	< 0.001
CMAP proximal amplitude, mV	2.99 ± 0.40	6.27 ± 0.61	< 0.001
Motor conduction velocity, m/s	31.84 ± 1.83	40.40 ± 2.13	< 0.002
F wave latency, ms	44.11 ± 2.45	35.27 ± 1.73	< 0.003
Ulnar nerve			
Motor distal latency, ms	4.55 ± 0.25	3.61 ± 0.27	< 0.004
CMAP distal amplitude, mV	4.95 ± 0.56	8.18 ± 0.43	< 0.001
CMAP proximal amplitude, mV	3.04 ± 0.38	6.73 ± 0.47	< 0.001
Motor conduction velocity, m/s	31.37 ± 1.88	45.29 ± 2.31	< 0.001
F wave latency, ms	42.31 ± 2.04	34.72 ± 1.14	> 0.05
Peroneal nerve			
Motor distal latency, ms	6.80 ± 0.46	5.11 ± 0.25	< 0.008
CMAP distal amplitude, mV	2.21 ± 0.43	4.09 ± 0.67	< 0.017
CMAP proximal amplitude, mV	1.66 ± 0.41	3.25 ± 0.58	< 0.022
Motor conduction velocity, m/s	28.55 ± 1.70	36.89 ± 1.64	< 0.001
F wave latency, ms	62.84 ± 2.76	50.06 ± 2.20	< 0.001
Tibial nerve			
Motor distal latency, ms	7.64 ± 0.36	5.97 ± 0.35	< 0.001
CMAP distal amplitude, mV	1.65 ± 0.41	5.73 ± 0.79	< 0.001
CMAP proximal amplitude, mV	1.52 ± 0.43	5.41 ± 0.76	< 0.001
Motor conduction velocity, m/s	29.00 ± 1.52	39.11 ± 1.26	< 0.001
F wave latency, ms	65.96 ± 2.07	51.85 ± 2.52	< 0.001

M — average value; SD — standard deviation.

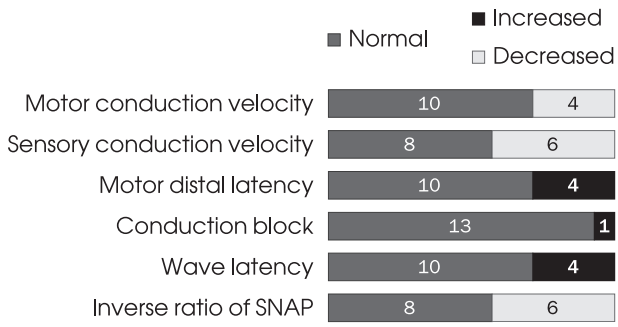

Fig. 2. *NCS findings, electrodiagnostic criteria of sensory CIDP*

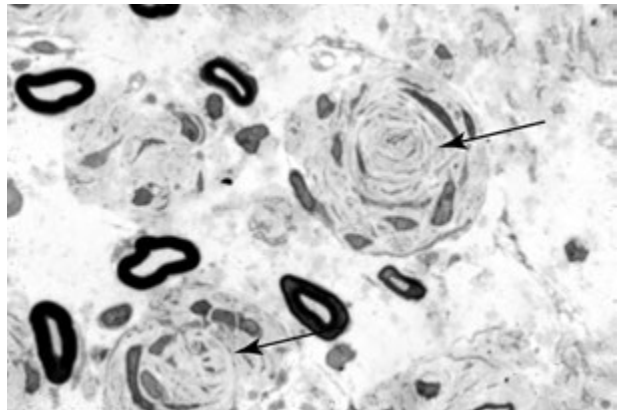

Fig. 3. *Semi thin transversal section of peroneal superficial nerve showing onion bulb formation in a patient with sensory CIDP*

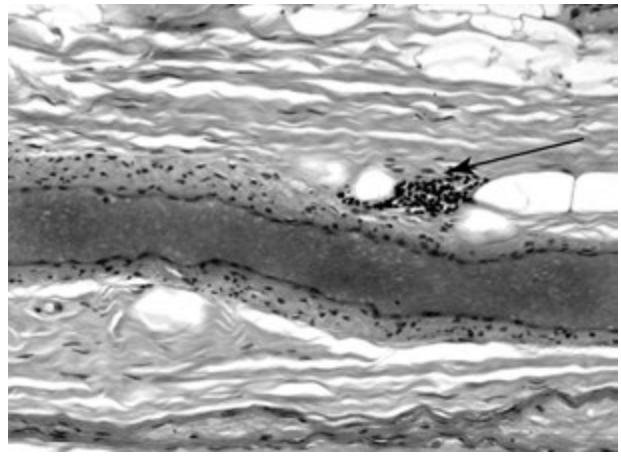

Fig. 4. *Paraffin longitudinal section of fibular nerve in a Lewis—Sumner patient showing perivascular inflammation*

is r = –0.4956 with p = 0.005 compared to r = 0.0716 and p = 0.707 in atypical CIDP. So when the MRC score is low (muscle weakness is increased) we have a higher concentration of proteins in CSF for the patients with typical CIDP. This assocation has no statistical value for patients with atypical CIDP. But in case of patients with aypical CIDP we have another valid association: INCAT score and level of proteins in CSF has r = –0.0934 and p = 0.624 in typical CIDP compared to r = 0.451 and p = 0.012 in atypical CIDP. So the level of muscle weakness in limbs is directly corelated with a higher level of proteins in CSF for the patients with typical CIDP. A higher INCAT score determines a higher level of proteins in CSF in atypical CIDP. Muscle weakness is not so frequent in atypical CIDP, that's why the damage of profound sensitivity and proprioception plays a greater role in atypical CIDP thm muscle weakness.

Nerve biopsy findings were the following: reduction in myelinated fiber density was most frequent (100 %), followed by demyelination (90 %), inflammation (44 %), and onion bulb formation (55 %). Endoneurial inflammation was more frequent in the relapsing-remitting form (fig. 3, 4).

Conclusions

DADS patients have a clinically sensory neuropathy with distal weakness, with ataxia as a predominant feature, frequent generalized areflexia and postural tremor. Gait ataxia is not common in sensory CIDP.

NCS is the most important test used to diagnose demyelinating polyneuropathies. However, NCS are normal when demyelinating lesions are distributed proximally. This may lead to misdiagnosis or mismanagement. SSEPS should be carried out in all cases of atypical sensory polyneuropathy (accompanied by ataxia, areflexia) to demonstrate the proximal demyelination (at pre or postganglionic levels) not accessible for convetional NCS.

ONLS and 9 hole peg tests are efficient to evaluate level of disability in patients with CIDP. According to ONLS scale, patients with typical CIDP are more impaired than sensory atypical CIDP patients.

Serum protein electrophoresis and immunofixation should be always carried out in CIDP patients. In the event of any MGUS, we must exclude the association of this monoclonal gammopathies with a myeloma or lymphoma.

Peroneal nerve biopsy is performed only if the NCS don't bring any demyelinating findings, but the clinical evolution of the disease is progressive and disabling.

There is significant phenotypic variability in the clinical spectrum of CIDP suggesting that there are different immunopathological mechanisms at play. Future research is needed to identify disease markers.

NCS is not a sensitive test to diagnose sensory CIDP, in 70 % cases motor conduction velocities were not affected.

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References

1. Austin J. H. Recurrent polineuropathies and their corticosteroid teatment // Brain. — 1958. — P. 81—92.
2. Ayrignac X., Viala K., Morizot Koutlidis R. et al. Sensory chronic inflammatory demyelinating polyneuropathy: an under-recognized entity? // Muscle Nerve. — 2013. — Vol. 48. — P. 727—732.
3. Bida J. P., Kyle R. A., Therneau T. M. et al. Disease associations with monoclonal gammopathy of undetermined significance: a population-based study of 17,398 patients // Mayo Clin. Proc. — 2009. — Vol. 84 (8). — P. 685—693.
4. Bosboom W. M., Berg L. H., Franssen H. et al. Diagnostic value of sural nerve demyelination in chronic inflammatory demyelinating polyneuropathy // Brain. — 2001. — Vol. 124 (Pt 12). — P. 2427—2438.
5. Camdessanche J. — F., Jousserand G., Ferraud K., Vial C. The pattern and diagnostic criteria of sensory neuronopathy: a case-control study // Brain. — 2009. — Vol. 132. — P. 1723—1733.
6. De Sousa E. A., Chin R. L., Sande H. W. et al. Demyelinating findings in typical and atypical CIDP: sensitivity and specificity // J. Clin. Neuromusc. Dis. — 2009. — Vol. 10. — P. 163—169.
7. Eftimov F., van Schaik I. Chronic inflammatory demyelinating polyradiculoneuropathy: update on clinical features, phenotypes and treatment options // Curr. Opin. Neurol. — 2013. — Vol. 26 (5). — P. 496—502.
8. French CIDP Study Group. Recommendations on diagnostic strategies for chronic inflammatory demyelinating polyradiculoneuropathy // J. Neurol. Neurosurg. Psychiatry. — 2008. — Vol. 79. — P. 115—118.
9. Iijima M. et al. Prevalence and incidence rates of chronic inflammatory demyelinating polyneuropathy in the Japanese population // J. Neurol. Neurosurg. Psychiatry. — 2008. — Vol. 79. — P. 1040—1043.
10. Joint Task Force of the EFNS and the PNS. European Federation of Neurological Societies/Peripheral Nerve Society Guideline on management of chronic inflammatory demyelinating polyradiculoneuropathy: report of a joint task force of the European Federation of Neurological Societies and the Peripheral Nerve Society — First Revision // J. Peripher. Nerv. Syst. — 2010. — Vol. 15 (1). — P. 1—9.
11. Katz J. S., Saperstein D. S., Gronseth G. et al. Distal acquired demyelinating symmetric neuropathy // Neurology. — 2000. — Vol. 54. — P. 615—620.
12. Kulkarni G. B., Mahadevan A., Taly A. B. et al. Sural nerve biopsy in chronic inflammatory demyelinating polyneuropathy: are supportive pathologic criteria useful in diagnosis? // Neurol. India. — 2010. — Vol. 58 (4). — P. 542—548.
13. Kyle R. A., Therneau T. M., Rajkumar S. V. et al. A long-term study of prognosis in monoclonal gammopathy of undetermined significance // N. Engl. J. Med. — 2002. — Vol. 346 (8). — P. 564—569.
14. Larue S., Bombelli F., Viala K. et al. Non-anti-MAG DADS neuropathy as a variant of CIDP: clinical, electrophysiological, laboratory features and response to treatment in 10 cases // Eur. J. Neurol. — 2011. — Vol. 18 (6). — P. 899—905.
15. Leger J. M., Bombelli F., Chassande B. et al. Polyneuropathy associated with monoclonal gammapathy: treatment perspectives // Bull. Acad. Natle. Med. — 2009. — Vol. 193. — P. 1099—1111.
16. Léger J. M., Bombelli F., Tran-Thanh H. et al. Chronic inflammatory demyelinating polyradiculoneuropathy: clinical heterogeneity and therapeutic perspectives // Bull. Acad. Natl. Med. — 2010. — Vol. 194 (4—5). — P. 764—765.

17. Lewis R. A., Sumner A. J., Brown M. J., Asbury A. K. Multifocal demyelinating neuropathy with persistent conduction block // Neurology. — 1982. — 32. — P. 958—964.
18. Mahdi-Rogers M., Hughes R. A. Epidemiology of chronic inflammatory neuropathies in southeast England // Eur. J. Neurol. — 2014. — Vol. 21 (1). — P. 28—33.
19. Merkies I., Schmitz P., Van Der Mechè F., Van Doorn P. Inflammatory Neuropathy Cause and Treatment (INCAT) Group. Psychometric evaluation of a new sensory scale in immune-mediated polyneuropathies // Neurology. — 2000. — Vol. 54. — P. 943—949.
20. Nobile-Orazio E. Chronic inflammatory demyelinating polyradiculoneuropathy and variants: where we are and where we should go // J. Peripher. Nerv. Syst. — 2014. — Vol. 19 (1). — P. 2—13.
21. Rajabally Y. A., Chavada G. Lewis—Sumner syndrome of pure upper-limb onset: diagnostic, prognostic, and therapeutic features // Muscle Nerve. — 2009. — Vol. 39. — P. 206.
22. Sinnreich M., Klein C. J., Daube J. R. et al. Chronic immune sensory polyradiculopathy: a possibly treatable sensory ataxia // Neurology. — 2004. — Vol. 63. — P. 1662—1669.
23. Vallat J. M., Tabaraud F., Magy L., Couratier P. Importance of the nerve biopsy for the diagnosis of atypical forms of chronic inflammatory demyelinating polyradiculoneuritis: 8 cases // Bull. Acad. Natl. Med. — 2003. — Vol. 187 (2). — P. 387—399.
24. Van de Donk N. W., Palumbo A. et al. The clinical relevance and management of monoclonal gammopathy of undetermined significance and related disorders: Recommendations from the European Myeloma Network // Haematologica. — 2014. — Vol. 99 (6). — P. 984—996.
25. Van den Bergh P. Y., Rajabally Y. A. Chronic inflammatory demyelinating polyradiculoneuropathy // Presse Med. — 2013. — Vol. 42 (Pt 2). — P. 203—215.
26. Viala K., Maisonobe T., Stojkovic T. et al. A current view of the diagnosis, clinical variants, response to treatment and prognosis in chronic inflammatory demyelinating polyradiculoneuropathy // J. Peripher. Nerv. Syst. — 2010. — 15 (1). — P. 50—6. — doi: 10.1111/j.1529—8027.2010.00251
27. Viala K., Renié L., Maisonobe T. et al. Follow-up study and response to treatment in 23 patients with Lewis-Sumner syndrome // Brain. — 2004. — Vol. 127. — P. 2010—2017.
28. Yiannikas C., Vucic S. Utility of somatosensory evoked potentials in chronic acquired demyelinating neuropathy // Muscle Nerve. — 2008. — Vol. 38. — P. 1447—1454.

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Нове розуміння атипових форм хронічної запальної демієлінізувальної полінейропатії

Мета — визначити клінічні особливості атипової хронічної запальної демієлінізувальної полінейропатії (ХЗДП), провести порівняльний аналіз параметрів невральної провідності при типовій і нетиповій ХЗДП, оцінити ефективність застосування соматосенсорних викликаних потенціалів для демонстрації проксимальної демієлінізації при сенсорній ХЗДП з нормальними показниками провідності нервів, оцінити роль біопсії малогомілкового нерва в діагностиці ХЗДП.

Матеріали і методи. У дослідження залучили 30 пацієнтів з атиповою ХЗДП і 30 пацієнтів з типовим виявом ХЗДП. Усім хворим здійснювали дослідження невральної провідності, забір крові для біохімічних тестів, а також електрофорез та імунофіксацію білків сироватки крові. Біопсію малогомілкового нерва проведено у 9 пацієнтів (у 4 — з атиповою ХЗДП і у 5 — з типовою ХЗДП). Для оцінки функціональних порушень в усіх пацієнтів використано опитувальник за сумарною шкалою обмежень при нейропатіях (Overall Neuropathy Limitations Scale — ONLS).

Результати. Середнє значення за шкалою ONLS при атиповій ХЗДП становило (2,43 ± 0,29) бала, що було нижче порівняно з типовим виявом ХЗДП ((4,17 ± 0,24) бала). Моноклональні гаммапатії виявлено у 13 (22 %) хворих. Критерій демієлінізації (зменшення кількості мієлінових товстих волокон) найчастіше виявляють при біопсії.

Висновки. Дослідження невральної провідності не вважають золотим стандартом діагностики атипової сенсорної ХЗДП. При оцінці за шкалою ONLS атипові форми ХЗДП є менш інвалідизувальними порівняно з типовими формами ХЗДП. Біопсію малогомілкового нерва при ХЗДП виконують лише тоді, коли електрофізіологічні дослідження не дають змоги виявити ознаки демієлінізації.

Ключові слова: атипова демієлінізувальна полінейропатія, біопсія, діагностичні критерії.

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Новое понимание атипичных форм хронической воспалительной демиелинизирующей полинейропатии

Цель — выделить клинические особенности атипичной хронической воспалительной демиелинизирующей полинейропатии (ХВДП), провести сравнительный анализ параметров невральной проводимости при типичной и нетипичной ХВДП, оценить эффективность применения соматосенсорных вызванных потенциалов для демонстрации проксимальной демиелинизации при сенсорной ХВДП с нормальными показателями проводимости нервов, оценить роль биопсии малоберцового нерва в диагностике ХВДП.

Материалы и методы. В исследование включили 30 пациентов с атипичной ХВДП и 30 пациентов с типичным проявлением ХВДП. Всем больным выполняли исследование невральной проводимости, забор крови для биохимических тестов, а также электрофорез и иммунофиксацию белков сыворотки крови. Биопсия малоберцового нерва проведена у 9 пациентов (у 4 — с атипичной ХВДП и у 5 — с типичной ХВДП). Для оценки функциональных нарушений у всех пациентов использован опросник по суммарной шкале ограничений при нейропатиях (Overall Neuropathy Limitations Scale — ONLS).

Результаты. Среднее значение по шкале ONLS при атипичной ХВДП составляло (2,43 ± 0,29) балла, что было ниже по сравнению с типичными ХВДП ((4,17 ± 0,24) балла). Моноклональные гаммапатии выявлены у 13 (22 %) больных. Критерий демиелинизации (уменьшение количества миелиновых толстых волокон) наиболее часто выявляют при биопсии.

Выводы. Исследование невральной проводимости не считают золотым стандартом диагностики атипичной сенсорной ХВДП. При оценке по шкале ONLS атипичные формы ХВДП являются менее инвалидизирующими по сравнению с типичными формами ХВДП. Биопсию малоберцового нерва при ХВДП выполняют только тогда, когда электрофизиологические исследования не позволяют выявить признаки демиелинизации.

Ключевые слова: атипичная демиелинизирующая полинейропатия, биопсия, диагностические критерии.