ABOUT VALUE OF CSF ANALYSIS AND OPPORTUNITIES OF OTHER RESEARCH METHODS IN DIAGNOSTICS OF CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY: CASE STUDY

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ABSTRACT — The article presents case study of the patient with the first revealed chronic inflammatory demyelinating polyneuropathy (CIDP). Informational content of such methods of diagnostics as stimulation electroneuromyography, computer pallestesiometry, ultrasonography of peripheral nerves and MRT of nervous roots of this pathology has been analyzed. The emphasis on possible non-informative content of albuminocytological dissociation in liquor demyelinating polyneuropathy has been done.

KEYWORDS — chronic inflammatory demyelinating polyneuropathy, diagnostics, cerebrospinal fluid (CSF)

INTRODUCTION

The chronic inflammatory demyelinating polyneuropathy (CIDP) represents the acquired immune-mediated disease of peripheral nervous system with the progressing or relapsing course [1,2]. Classical CIDP is shown by the development of symmetric motor-sensory polyneuropathy with weakness both in proximal, and distal muscles groups of extremities. Most of patients have no reflexes. Sensitive CIDP disorders are shown, as a rule, by vibration sensitivity disorder and to a lesser extent painful and temperature sensitivity disorder. Some patients can have painful dysaesthesia, including cold dysaesthesia [3–8]. According to EFNS/PNS recommendations, it is necessary to consider CIDP diagnosis when there is progressing clinical symptomatology within 8 weeks and more [9] that it delimits this disease from Guillain-Barre syndrome and subacute demyelinating polyneuropathy.

The CIDP diagnosis is based on a definitive clinical picture and is confirmed by identification of demyelinating injury type of peripheral nerves of electromyography (EMG) or nerve biopsy, and also other diseases excluding which can be accompanied by a similar clinical picture [10]. The criterion supporting the CIDP diagnosis is the increase of protein level in CSF more than 45 mg/dl at normal cytosis (albuminocytological dissociation). According to different authors, increase of protein level in CSF is observed in 62-100% of cases [3,10,11]. Though the albuminocytological dissociation is observed among most of patients with CIDP, CSF research is conducted only in 47% of patients [10] that reduces the diagnostic value of this criterion. CIDP atypical forms, including Sensory predominant chronic inflammatory demyelinating polyneuropathy CIDP (SP-CIDP) when patients are revealed at out-patient and polyclinic stage of health care, carrying out a lumbar puncture isn't possible [4–8]. The value of lumbar puncture in disease diagnosis is challenged taking into account CIDP pathogenetic mechanisms with participation of the cellular and humoral immune mechanisms mediating attack of non-identified anti-genes to myelin and/or Schwann cells. It is possible to assume value of this diagnostic method of CIDP atypical form with central nerve system (CNS) affect.

CIDP diagnostics represents a complex challenge as the existing diagnostic criteria are insufficiently specific, clinical picture of the disease is polymorphous, and reliable biomarkers of this disease are absent [12]. So, sensitivity of diagnostic criteria of EFNS/PNS which are most often applied by neurologists makes 34%, and specificity – 99% [10]. The greatest sensitivity (>80%) and specificity (>95%) possess the combined criteria of Koski and others and EFNS that allows to recommend them in clinical practice [1].

EMG-criteria of CIDP diagnostics in practice are revealed among 50-60% of patients with typical clinical symptoms that indicates non-specificity of these criteria [1].

Recently possibilities of the magnetic resonant tomography use (MRT) and ultrasonic research (ultrasonography) in CIDP diagnostics have been widely discussed. Though changes on MRT, such as accumulation of contrast and/or hypertrophy of horse tail,

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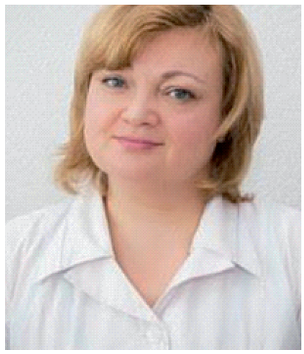

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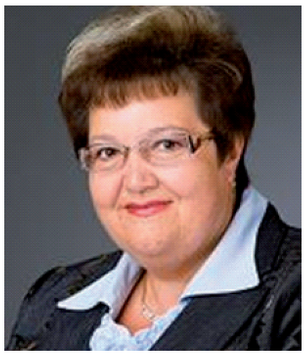

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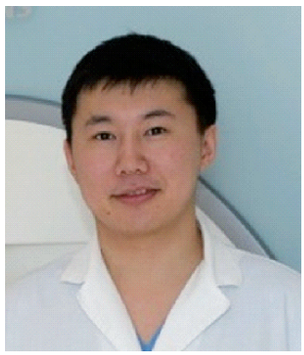

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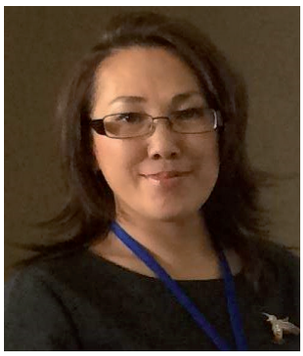

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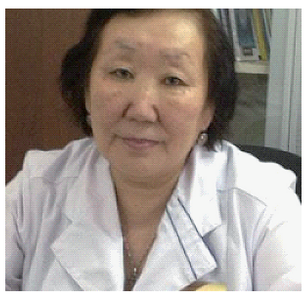

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cervical or lumbar and sacral nerves, or humeral or lumbar and sacral plexuses are included into the supporting criteria on EFNS/PNS, there is a limited number of researches devoted to neurovisualization in CIDP [13,14].

Though ultrasonography of peripheral nerves isn't included into criteria of CIDP diagnostics,

this method is perspective for research of nervous fibers condition. So probably, ultrasonography signs of CIDP can be an identification of increase in cross-sectional area of nerve [15,16].

Classical CIDP in the presence of typical clinical criteria of EFNS is not always kept within other diagnostic criteria, including lack of protein-cellular dissociation in lumbar puncture. All above-mentioned demands revision of diagnostics criteria of classical and CIDP atypical forms. So, in diagnostics of Sensory predominant chronic inflammatory demyelinating polyneuropathy (SP-CIDP) we have offered the new algorithm of neurophysiological diagnostics including EMG, computer pallesteziometry, stabilometry, thermosensometry, transcutaneous oximetry allowing estimating a condition of various sensory fibers of peripheral nerves [18].

We've shown our own case study of the patient with classical CIDP without protein-cellular dissociation in CSF.

CASE STUDY

Patient E., 35-years-old man, unemployed, villager, has admitted to neurological department of Republic hospital 2 — Emergency center of health care in emergency order with complaints to weakness in extremities, more in the lower extremities, movement disorders with use of supportive accessories, numbness of the lower (to the level of knees) and upper limbs (to the level of brushes), muscles weight loss of extremities. The anamnesis has shown that at the end of January, 2016 within several days he was outdoors, protecting horses herd, went by snowmobile much, was exposed to overcooling. There was no any symptoms of flu, diarrhea. After returning home he began to notice feet burning that the patient has connected with influence of low temperatures, without paying any special significance. During February burning began to amplify, especially at night and has extended up to the level of knees. He didn't ask for medical care as there was no any doctor or paramedic in the settlement. A month later, since the first half of March, pain began to be replaced by numbness, sensitivity decrease. By this time the patient felt hands numbness. From the middle of March the increasing weakness in legs has begun to disturb, however the man continued to do housework. The patient denied pains in lumbar, cervical parts of spine. Since the end of March because of the progressing weakness in legs he began to move with a support on cane, he has noticed weakness in hands later. The patient has been sent to Yakutsk and in the emergency order he has been hospitalized in neurologic department Republic hospital №2-Emergency center of health care. He denies the influence of toxic substances and chronic diseases, he doesn't smoke, abuse alcohol. He is married, two children. No hereditary diseases.

Objectively, the general condition of the patient was moderate severity. Skin is pure, usual coloring. Height is 165 cm, weight is 66 kg, IMT 24,24 (within norm). The breath is vesicular in lungs, is carried out by all areas, there are no rales, breath rate is 17 per minute. Tones of heart are rhythmical, clear. AP — 130/80 mm Hg, HR — 78 per min. The stomach is soft, painless palpation. The urination is free, painless. The defecation is regular. Pelvic functions are controlled.

Neurologic status: the consciousness is clear. Mood background is clear. Function of craniocereberal nerves isn't broken. Diffusion muscular hypotonia. Sluggish tetraparesis: hands force is proximally reduced to 3 points, distally — to 4 points, without accurate difference of the sides; in legs proximally muscular force — 3 points, distally — 2 points. The muscular hypotrophy in hands and legs, more expressed in peroneal group of muscles. Reflexes from biceps, triceps, carporadial are low, without asymmetry of the sides. Knee and ankle reflexes aren't caused. A painful and tactile hypesthesia from the level of the lower third of the forearm (as "gloves") and from the level of knee joints (on the golf type). Tuning fork test has revealed decrease in vibration sensitivity at 128 Hz frequency in fingers of hands and feet. The musculoarticulate feeling was reduced in the upper and lower extremities. Coordination sphere: finger-to-nose test with little left past-pointing, he can't carry out knee and calcaneal test because of paresis. He can't stand in Romberg's pose. There is no meningeal and pathological symptomatology. There are no symptoms of nervous tension. The patient walks with crutches support.

RESULTS OF EXAMINATION

The general blood test, biochemical blood test, general urine analysis — without pathology. Coagulogram has revealed moderate decrease in PTI to 74,7% and increase in MNO to 1,12; aPPT — 26 sec. Blood test on RW, HBsAg, antibodies to HIV — negative. Blood test on rheumatoid factors – negative. The analysis of CSF — transparent, cytosis 3/3, protein 0,33 g/l, sugar 2,9 mmol/l, chlorides 118 mmol/l. Microscopic analysis: leukocytes are single, erythrocytes which aren't changed 2–1–2 under review.

ELISA: IgG antibodies to HSV 1:1600 PE/ml, to CMV 4,3 PE/ml (in N to 0,25 PE/ml), to EBV 115 OEd/ml (is normal to 20 OED/ml), antibodies to toxoplasma wasn't revealed.

Electrocardiogram — sinus rhythm with HR 72 beats per min. Electrical axis of the heart is horizontal. Signs of hypertrophy of the left ventricle.

Fibrogastroduodenoscopy: symptoms of superficial gastritis.

Ultrasonography of abdominal organs and kidneys: focal formation of S4 of liver (hemangioma). Echo signs of chronic cholecystitis. Moderately expressed diffusion changes of pancreas parenchyma. Consolidation of both kidneys sinus.

Computer Tomography of abdominal organs: pathological changes weren't revealed (it was carried out for the purpose of differentiation of focal formation of S4 of liver found by ultrasonography).

X-ray analysis of thorax: symptoms of chronic bronchitis.

MRT of lumbar roots: signs of hypertrophy of lumbar roots weren't revealed (fig. 1, fig. 2).

The electromyography has revealed signs of axonal-demyelinating defeat of motor and sensory nervous fibers of peripheral nerves, more expressed in the lower extremities (tab. 1, fig. 3).

The computer pallesteziometry has revealed decrease in vibration sensitivity in a wide range of frequencies both at the level of the upper and lower extremities. In clinical aspect signs of demyelinating defeat of thick myelinating Aβ-fibers like distal departments of peripheral nerves of the upper extremities of moderate degree and expressed degree in the lower extremities were registered (tab. 2, fig. 4).

Ultrasonography of median, ulnar, tibial and peroneal nerves in the longitudinal scan has revealed the uneven contour of the nerve fibers and variegated section of nerves (sections spindles) with isolated hyperechoic lines in different lengths. Ultrasound in the transverse scan has revealed thickening of the nerve fibers sized with an increase in cross-sectional area, mainly due to the presence of increased one or two fasciculi on a background of normal. Thus, it was detected third change the type of nerve fibers. Intensity of these changes prevailed in the nerve fibers of the lower extremities. Fig. 5 shows the ultrasound of the left median nerve.

Thus, the patient has developed the symmetric ascending motor-sensory polyneuropathy, more expressed in the lower extremities. Duration of symptoms development more than 8 weeks has excluded Guillain-Barre syndrome and subacute demyelinating polyneuropathy. The conducted laboratory analyses and also absence of toxic influences, diseases of nervous system among relatives in anamnesis allowed excluding secondary damage of nervous fibers. Abovementioned data and also lengthening of distal latency more than 150%, reduction in the velocity of impulse less than 70% in more than two nerves by EMG results indicated reliable CIDP according to criteria of EFNS/PNS Joint Task Force (2010). Lack of protein-cellular dissociation in CSF pays attention though clinical and electrophysiological picture of disease indicated CIDP classical form. Lack of hypertrophy of nerves by MRT, apparently, is connected with more distal distribution of pathological process. It correlates also with a clinical picture, namely with lack of radicular symptomatology. The intact MRT-picture of nerves doesn't exclude the CIDP diagnosis as MRT changes have the supporting character according to criteria of EFNS/PNS and also due to the results of the conducted researches hypertrophy of nerves were found not in all patients. Ultrasonography of peripheral nerves revealed signs of inflammatory demyelinating affect.

The received clinical-laboratory and tool data has allowed to diagnose the chronic inflammatory demyelinating polyneuropathy, with deep sluggish, predominant distal, tetraparesis; disorders of superficial and deep types of sensitivity by polyneuropathy type.

The patient was given sessions of discrete plasmapheresis, corticosteroid therapy by dexamethasone of 12 mg/day with gradual dose decrease and also massage of extremities, physiotherapy exercises have been held. Positive dynamics in the form of force increase in hands distally to 5 points, proximally practically to 4 points, in legs distally to 4 points, proximally to 5 points was noted after the treatment. On the background of paresis regress the patient has started walking independently. Sensitive disorders in the form of hypesthesia by polyneuropathy type, areflexia at the time of dismissal from hospital have remained.

CONCLUSION

Thus, the presented case study shows informational content of such methods of diagnostics as EMG, computer pallesteziometry, ultrasonography of peripheral nerves of CIDP classical form. Lack of protein-cellular dissociation in CSF relating to the main criteria of CIDP misleads. But a characteristic clinical picture with development of symptoms for more than 8 weeks after the frozen immunocompromising patient, results of neurophysiological researches, affirmative response to pathogenetic therapy (plasmapheresis, corticosteroid preparations) has confirmed classical CIDP.

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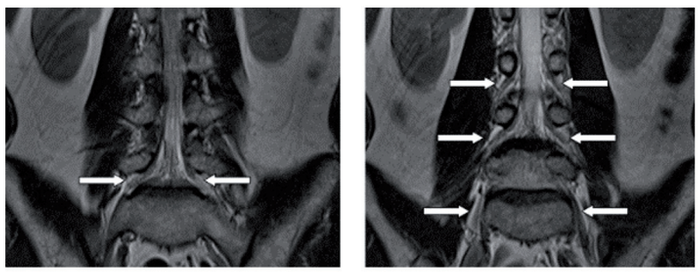

Fig. 1. *MRI of lumbar roots in the coronary projection, T2-WI. The roots are marked by white arrows*

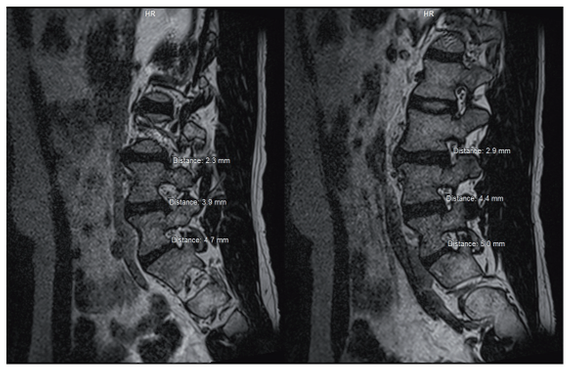

Fig. 2. *MRI of lumbar roots in the sagittal projection, T2-WI. L3-root thickness is 2.3 mm on the right and 2.9 mm of the left; L4-root thickness is 3.9 mm on the right and 4.4 mm on the left; L5-root thickness is 4.7 mm on the right and 5.0 mm on the left.*

Table 1. *Results of ENMG of the patient E., 35 years old*

	Distal latency, ms	Motor nerve action potential, mV	Motor nerve conduction velocity (distal), m/s	Motor nerve conduction velocity (proximal)., m/s	Sensory nerve action potential, mV	Sensory nerve conduction velocity, m/s
N. medianus D	8.0 (N < 3.5)	1.5 (N > 3.5)	48.5 (N > 50.0)	47.2 (N > 50.0)	7.4 (N > 5.0)	42.4 (N > 50)
N. medianus S	6.1 (N < 3.5)	1.5 (N > 3.5)	47.2 (N > 50.0)	33.7 (N > 50.0)	2.9 (N > 5.0)	46.2 (N > 50)
N. ulnaris D	6.1 (N < 3.5)	1.0 (N > 6.0)	41.5 (N > 50.0)	27.1 (N > 50.0)	NR	NR
N. ulnaris S	6.2 (N < 3.5)	1.1 (N > 6.0)	55.9 (N > 50.0)	39.4 (N > 50.0)	NR	NR
N. tibialis D	10.5 (N < 5.0)	0.7 (N > 3.0)	36.3 (N > 40.0)	-	-	-
N. tibialis S	9.7 (N < 5.0)	0.3 (N > 3.0)	23.6 (N > 40.0)	-	-	-
N. peroneus D	9.1 (N < 4.0)	0.3 (N > 3.0)	26.2 (N > 40.0)	-	NR	NR
N. peroneus S	8.8 (N < 4.0)	0.7 (N > 3.0)	30.6 (N > 40.0)	-	NR	NR

NR — no response

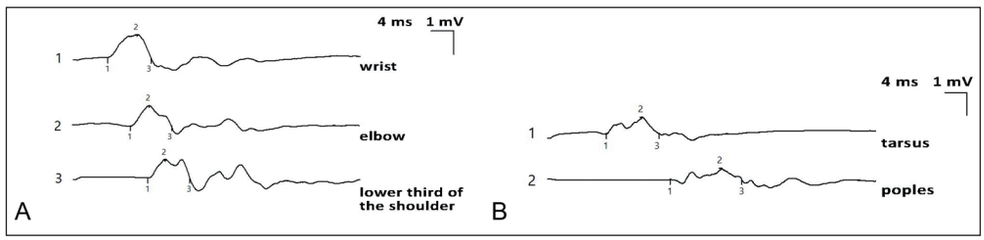

Fig. 3. *Results of EMG of the patient E.*

A *— analysis of motor fibers of the right elbow nerve. Distal latency of motor nerve action potential (MNAP) is 6.2 ms (norm to 3.5 ms). Amplitude of MNAP is reduced, distal is 1.1 mV (norm from 3.5 mV). The polystaging of MNAP increasing in process of stimulation from proximal part of extremity pays attention. Motor nerve conduction velocity (MNCV) distal makes 55.9 m/s, proximal – 39.4 m/s (norm from 50 m/s).*
B *— analysis of motor fibers of the right tibial nerve. Distal latency of MNAP is 10.5 ms (norm from 5 ms). Amplitude of MNAP is reduced, distal makes 0.7 mV (norm from 3.0 mV). MNCV is lowered, makes 36.3 m/s (norm from 40 m/s). Polystaging of MNAP is defined.*

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Table 2. *Results of computer pallestesiometry*

	8 hz	16 hz	32 hz	64 hz	128 hz	250 hz	500 hz
Standards for styloid process	[-16; -9]	[-17; -9]	[-12; -5]	[-15; -7]	[-13; -5]	[-15; -6]	[-13; -3]
Styloid process in the right	13,5	12.75	18	18.75	17.25	15	17.25
Styloid process in the left	12,75	12,75	17,25	18	18	20,25	18
Standards for lateral malleolus	[-9; 1]	[-10; 0]	[-6; 4]	[-9; 1]	[-7; 3,5]	[-7; 6]	[-2; 15,5]
Lateral malleolus in the right	24	24	30	30	30	24	24
Lateral malleolus in the left	24	24	30	30	30	24	24

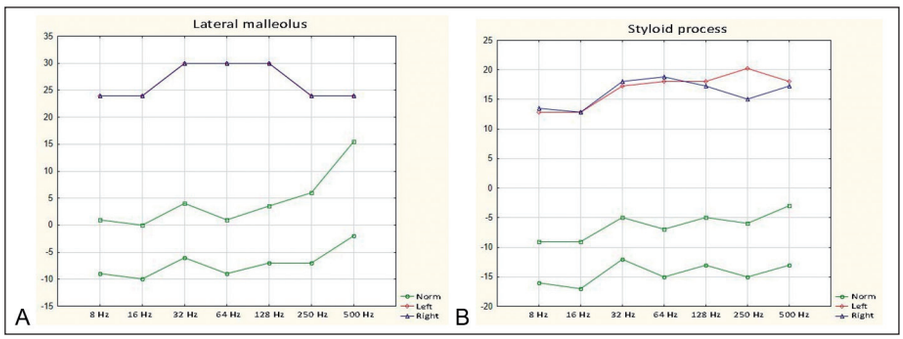

Fig. 4. *Results of computer pallestesiometry of the patient E.*
A *— at the level of lateral malleolus;*
B *— at the level of styloid process (explanation in the text)*

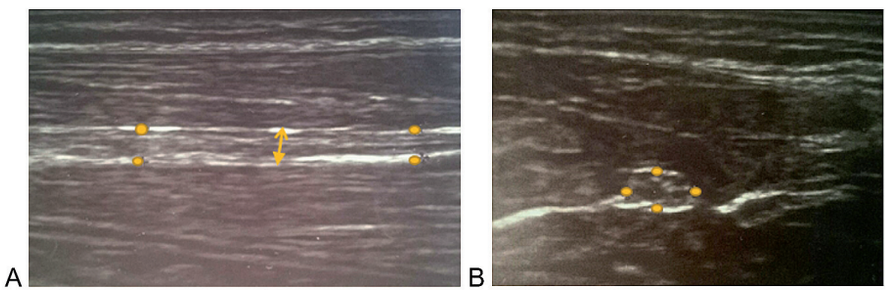

Fig. 5. *Ultrasound of the left median nerve:* ***A*** *— longitudinal scan;* ***B*** *— transverse scan (explanation in the text)*

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