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POLYNEUROPATHY IN PATIENTS WITH CHRONIC BRUCELLOSIS. CASE STUDY

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ABSTRACT — Brucellosis is one of the most common infections that belongs to the group of specifically dangerous zoonoses, which account for a significant share of infectious pathologies affecting humans. The pathogenesis of chronic brucellosis relies on intracellular parasitization of brucella with anti-lysozyme activity. The socio-economic effect of brucellosis problem is due to the specific features of the course that the infection takes, frequently developing into chronic forms, resulting in long-term loss, or even permanent disability. Physically capable population is the group that is affected the most, whereas thew reasons behind this include both professional and social ones. The rate of clinical manifestations pointing at a damage to the nervous system wrought by brucellosis lies within the range of 25% – 90%. This paper presents a clinical case focusing on the nature of the damage chronic neurobrucellosis causes to the peripheral nervous system. We used the MRC, NDS scales as well as electromyography with the identification of the standard conduction parameters for the median, tibial and calf nerves.

KEYWORDS — chronic brucellosis, nerve conduction, polyneuropathy, electromyography, diagnosis.

INTRODUCTION

Brucellosis is a zoonotic infectious disease caused by bacteria known under the common name of *Brucella*, which reveal a high potential for turning chronic and working systemic damage to organs and systems, affecting predominantly the musculoskeletal, the nervous, and the reproductive systems. The epidemiological situation in Russia, in terms of brucellosis prevalence, has remained unfavorable for a long time and can be accounted for by persistent epizootics of brucellosis to be found in small and great cattle, which is the main sources of the brucellosis agent infecting humans. Brucellosis has long been ranked first among occupational diseases of infectious and parasitic etiology. Loss of working capacity or disability in this case explain the socio-economic meaning and relevance of this infection. Another issue is early identification of brucellosis in humans, this being due to a reduced number of laboratory screenings aimed at detecting brucellosis in those who are associated professionally with the risk of contracting brucellosis, as well as due to an increase in the share of cases observed among those who have no association with cattle breeding. A timely diagnosis, though, as well as proper treatment, helps avoid the chronization of the infection and persistent disability [1–4].

The lack of a unified classification for brucellosis nowadays poses a serious obstacle to verifying the diagnosis and studying the disease progress, which is subject to great diversity. Nevertheless, most researchers point at a potentially blurred, low-symptom onset of the disease, where patients seek assistance from various medical experts at a stage, which involves multiple advanced pathologies, all this explaining the relevance of enhancing medical specialists' competence in diagnosing brucellosis [5]. One of the systems involved frequently in the pathological process in case of brucellosis is the nervous system. Neurobrucellosis (NB) is one of the manifestations of general brucellosis, and includes all types of specific damage to the nervous system (NS), all being successive links of a single infectious process affecting the entire body [14]. The frequency of clinically significant manifestations of NB, as different authors note, varies greatly (from 25 to 90%) [6, 8]. Note to be made here that diagnosing NB is a complicated issue due to a number of reasons: lack of pathognomonic symptoms; a wide variety of lesions affecting the NS and its mechanisms. Besides, the diagnosis can be set in case of observing a neurological presentation that is not to be explained by any other neurological health issue [9].

Lesions affecting NS in case of brucellosis can be primary or secondary. The former ones are associated with the direct impact on the tissues that Brucella or products of immune (including immunopathological) responses entail, and is manifested through diffuse encephalopathy and meningoencephalitis; inflammatory peripheral neuropathy and radiculopathy; inflammatory demyelinating syndromes; the optic nerve

disc edema or papillitis with no other focal manifestations; meningomyelitis; posterior cranial fossa syndrome (atactic or stem); neuropsychic syndromes. The secondary type of NB includes effects that earlier chronic brucellosis inflammation has on other organs and systems, and include compression myelopathy and radiculopathy, developing against damage to the osteoarticular system and adjacent soft tissues, as well as cerebral vascular syndromes, which develop on the background of damage to the heart or cerebral vessels [14]. A combination of clinical manifestations of various NB types are a rather frequent phenomenon.

NB is primarily characterized by a damage to the peripheral nervous system (PNS), which is a common development in case of chronic brucellosis (CB), yet has an acute onset and is typically accompanied by the intoxication syndrome (fever, chills, sweating, headache, etc.) [10]. It is to be noted that the use of instrumental methods, in particular electro-neuromyography, as well as clinical and electrophysiological analysis of the peripheral nerve's functional status, allows increasing the level of PNS lesion verification in patients with CB. An in-depth neurological study [7], for instance, revealed the pathology of the PNS in 86% of patients with CB, while a notable thing was that the polyneuropathies or polyradio-neuropathies developing in those patients were caused by a mixed axonal-demyelinating lesion of the motor and sensory branches of peripheral nerves, involving predominantly the pathological process of the axial cylinder of nerves. This was accompanied by a decrease in the motor response amplitude and evoked potentials, as well as emerging axonal blocks at large joints, which occurred against moderate demyelination, and manifested through a slowdown in the conduction of impulses, including at the level of the spinal cord roots.

There is clinical proof available showing that CB, in its progress from active to inactive, features an increase in the depth of pathological changes involving peripheral nerves; axonal blocks to be found in the elbow and knee joints in almost 100% of cases; a decrease in the impulse speed, which is more significant at the level of the lumbosacral spine; a critical decrease in the amplitude of the evoked potentials of nerve sensory branches down to an undetectable level.

The PNS pathology severity often correlates with disorders affecting the regional blood circulation. Yu.N. Linkova [7] in her work, for instance, points at a significant decrease in the pulse blood filling the forearms (2.2 times) and lower thighs (2.8 times) in patients with CB (if compared to similar indicators in healthy individuals), with significant asymmetry of blood supply, increased vascular tone of large caliber, and venous congestion. Disturbed regional blood flow was at its maximum in patients with inactive CB, in case of which, unlike with its active type, the symptoms of impeded venous outflow were aggravated by a drop in the tone of small vessels.

Given the hematogenic, lymphogenic, as well as perineural ways of spreading brucella in the human body, as well as the role that immunopathological processes play in the development of organ pathology in case of brucellosis, the genesis of damage affecting organs and tissues, including peripheral nerves in each case still remains unclear. The value of this understanding, however, is of extreme importance, when it comes to administering proper therapy. Assistance in clarifying the major mechanism of peripheral nerve damage can be found in an additional instrumental study, which can be inferred from the case presented below.

CASE STUDY

Patient P., 54 y.o.; a veterinarian; admitted for inpatient treatment at the occupational diseases clinic (August, 2019); complained of moderate pain in limb large joints, spine, weakness and weight loss in the limbs, a feeling of numbness in the hands and feet. The diagnosis of chronic brucellosis affecting the musculoskeletal system, vegetative and cardiovascular system, was set in 2016 when the patient was seeking medical help for organ lesions, positive serological test results (Wright's test, Heddlson's reaction; RPGA in the titer – 1:320) based on his professional contact with farm animals. Following the treatment, periodic moderate pains in the knee, elbow and wrist joints persisted. The pain worsened under physical strain in the affected joints and at hypothermia. About two years ago, the patient developed weakness and gradual loss of mass in the limbs, which affected the legs more, as well as a feeling of numbness in the hands and feet. For various reasons, did not seek help from doctors.

The current health deterioration has been there for the last two weeks, when, following physical overload, the patient noted intense, stable pain and sharp restriction of movement in the lumbar spine, in the joints (more — in the elbows and knees). Self-administered Ibuprofen, ensured a short-term effect. Furter contacted a local Neurologist who referred him to hospital for treatment.

The specific points that drew attention through the examination were excess weight (BMI — 30.3); skin moisture; pain at palpation along the spinous processes of the spine at the cervical and lumbar sections with restricted movements in the lumbar region and neck; painful palpation and restricted movements in the elbow and knee joints; extended heart boundaries to the left (the left limit is in the intercostal space 1.2 cm inside of *l. mediaclavicularis*) with muffled

heart tones and the second tone accent above the aorta; high blood pressure (150 and 90 mmHg).

The patient had an examined with a GP, a surgeon, a neurologist, and underwent certain instrumental (ECG, elbow and knee joint radiography, lumbosacral spine MRI, echocardiography, rheovasography of the upper and lower extremities), and laboratory, tests (general blood test, biochemical blood test, general urine test), and the analysis of the outcomes, given the respective clinical manifestations, allowed defining the diagnosis. ***Major***: chronic brucellosis, combined type with damage to the musculoskeletal system, the vegetative nervous system, the peripheral nervous system and the cardiovascular system. Polyosteoarthrosis involving the elbow joints (radiologically — Stage 1; function disturbance — 0–1), knee joints (radiologically — Stage 1–2; function disturbance — 1). Polyneuropathy of the upper and lower extremities, chronic lumbosacral radiculopathy. Infectious myocarditis in history. Relative insufficiency of AV valves. ***Minor***: arterial hypertension — Stage 3; risk — 4. Complication: circulatory deficiency 1 (functional class 2). The clinical presentation of the patient with a peripheral form of NB was assessed relying on the topographic features of the hypotrophy and their severity (see Table. 1), the level of muscle weakness (MRC scale) (see Table. 2), changed reflexes and sensitivity based on the neurological disorders Neuropathy Disability Score (NDS) scale (see Table 3). The hypotrophy was assessed based on a 2-point subjective scale: 0 points — no hypotrophy; 1 point — minor degree; 2 points — significant hypotrophy.

Table 1. *Topographic features of limb muscle hypotrophy*

Muscles being tested	Side		Average score
	Right side	Left side	
Muscles of the upper limbs			
M. abductor pollicis brevis	1	0	0.375
M. abductor digiti minimi	1	1	
M. flexor digitorum superficialis	1	1	
M. biceps brachii	0	1	
M. triceps brachii	0	0	
M. deltoideus	0	0	
M. trapezius	0	0	
M. petoralis major	0	0	
Muscles of the lower extremities			
M. rectus femoris	1	0	1
M. adductor femorris magnus	1	0	
M. tibialis antreior	1	2	
M. gastrocnemius	1	1	
M. extensor digitorum brevis	2	2	

As Table 1 shows, the typical signs with the patient in question include a proximal/distal distribution of muscular hypotrophies (with the lower extremities dominating); another notable issue is the asymmetric distribution of their severity.

Besides, there is also a notable decrease in lower extremities strength, the distal parts showing greater severity.

The study of sensitivity issues and reflex changes revealed a moderate degree of sensorimotor polyneuropathy (the patient had an NDS index of 13 points).

To objectify the lesion to the peripheral nerves' motor and sensory fibers, an electromyographic study (EMG) was carried out with an EBNeuro Nemus (Italy) electromyograph following the standard technique. The nerve conduction velocity (NCV), the distal latency (DL), the motor response amplitude (MRA) of the main nerves (median, tibial), and the sensory response amplitude (SRA) of the sural nerve on both sides were evaluated. Needle EMG of the calf muscles was performed this aiming to identify the spontaneous activity, as well as the denervation/reinnervation intensity. The patient was found to have (Table 4) a decrease in NCV along motor and sensory fibers, an increase in DL, which was associated with axon demyelination. The severity of the amplitude decrease in the M-response was associated with the level of fiber conduction slowing, which also serves another proof of the lesion's primary demyelinating nature.

The spontaneous activity manifested as single potentials of acute waves and fibrillation potentials

Table 2. *Muscle weakness (average score, MRC)*

Feature	Side	
	Right side	Left side
Elbow extension	5	5
Elbow flexion	5	4
Finger flexion	5	5
Wrist bending	5	5
Wrist undending	5	5
Opposable thumb	4	4
Spreading fingers	4	4
Hip flexion	5	5
Knee flexion	4	5
Knee extension	4	4
Foot flexion	4	3
Foot extension	3	3

Table 3. *Assessment of sensorimotor issues (NDS scale)*

Sensitivity/reflex test	Right, score	Left, score	Total score
Knee reflex	1	0	5
Achilles reflex	2	2	
Temperature sensitivity	2	2	8
Pain sensitivity	2	2	

in the calf muscles is proof to the denervation of muscle fibers, whereas the restructuring of motor units towards an increase in their amplitude and duration confirms the chronic nature of the process.

DISCUSSION

The pathogenesis of the PNS lesion in case of brucellosis is yet to be studied. Analysis of the respective literature data suggests possible both axonal [11, 12] and demyelinating [13] damage to peripheral nerves in this zoonosis. An assumption can be made that the nature of the injury depends on the type of exposure — brucella and their endotoxins invading the peripheral nerve directly, in case of axonal polyneuropathy, or through immuno-mediated mechanisms of demyelination [14, 15, 16].

CONCLUSION

The medical history described above shows that the clinical nature of neurobrucellosis is of chronic, slowly progressing course. In our case, the effect of a mechanical damage – as a result of the musculoskeletal system pathology, occurring at an earlier stage of the disease – cannot be excluded.

The EMG study allows an objective assessment of the nature, the degree and the prevalence of the peripheral nervous system damage, which makes it a good choice not only to set the diagnosis and opt for a treatment tactics, yet also to assess the dynamics in view of the therapy underway.

Special attention should also be paid to patients with neurological manifestations who live or come from a brucellosis-vulnerable area, so as not to overlook a possible case of neurobrucellosis.

Table 4. *EMG outcomes*

EMG index	Side	
	Right	Left
Average MRA, n. medianus	4.25	4.15
Average MRA, n. tibialis	1.7	1.75
DL, M-response, n. medianus	4.6	4.3
DL, M-response, n. tibialis	5.2	4.3
NCV, n. medianus	45	44.8
NCV, n. tibialis	31.8	33.2
SRA, n. suralis	0.4	0.6
NCV, n. suralis	30.1	32.2
M. rectus femoris	1	0
M. adductor femorris magnus	1	0
M. tibialis antreior	1	2
M. gastrocnemius	1	1
M. extensor digitorum brevis	2	2

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