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Original article

Two-tiered serology in patients with Lyme neuroborreliosis

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Summary

Introduction. Lyme borreliosis is a multisystem infectious disease caused by Borrelia burgdorferi sensu lato complex. It is transmitted by Ixodes ticks. Apart from erythema migrans, other manifestations require laboratory confirmation. The aim of our study was to analyze the results of Two-Tiered Testing in patients with possible Lyme neuroborreliosis (LNB).

Method. We conducted a prospective diagnostic study at the University Clinical Centre of Republic of Srpska from October 2017 to October 2021. The study included 51 patients examined and treated under suspicion of Lyme neuroborreliosis (LNB). We used Two-Tiered Testing through ELISA anti-Borrelia IgM/IgG and confirmatory Immunoblot anti-Borrelia test IgM/IgG.

Results. ELISA anti-Borrelia IgM in serum was positive in 25.5% patients and IgG in 76.47%, while in cerebrospinal fluid (CSF) IgM was positive in 13.7% patients and IgG in 39.2%. Immunoblot test of anti-Borrelia IgM in serum was at the borderline in 7.84% patients, positive in 6.17% and no data for 35.29%, while IgG was positive in 54.9% of patients and no data for 37.25%. A strong correlation between results of ELISA anti-Borrelia IgM in serum and CSF was observed (ρ=0.802, $p<0.001$) and also between ELISA anti-Borrelia IgG and Immunoblot IgG in serum (ρ=0.787, $p<0.001$).

Conclusion. Two-Tiered Testing is very important in patients with possible LNB. False positive and false negative results are possible and test should be interpreted with caution and in correlation with the clinical manifestation and other available tests. More work needs to be done to develop new reliable diagnostic test for LNB, such as detection of CXCL13 in CSF, titrate the interleukin-6 (IL-6) in addition to the CXCL13 chemokine.

Keywords: Lyme Neuroborreliosis, Enzyme-Linked Immunosorbent Assay, Immunoblot test

Introduction

Lyme borreliosis is a multisystem infectious disease caused by spirochete of the Borrelia burgdorferi sensu lato complex and it is transmitted by Ixodes ticks [1–5]. Borrelia burgdorferi sensu lato includes 20 different genospecies. The human infection is caused primarily by three genospecies.

B. burgdorferi sensu stricto, hereinafter referred to as B. burgdorferi, is the sole cause of the disease in the United States (US), whereas Borrelia afzelii and Borrelia garinii are the primary causes in Europe and Asia [6, 7]. Lyme borreliosis is manifested through three stages: 1. early localized infection (erythema migrans-EM), 2. early disseminated infection (a few weeks or months after tick bite, most commonly affecting nervous system, joints, heart, skin), and 3. late disseminated infection stage (a few months or years after tick bite, affecting skin, nervous system, joints) [1, 3, 4, 6, 8].

Apart from EM, which is usually diagnosed clinically, other manifestations require laboratory confirmation [9, 10]. There is no gold standard in the diagnosis of Lyme borreliosis [11]. All evidence-based European or American guidelines recommend a two-stage serological diagnosis, which is performed by detecting antibodies initially using a screening test (enzyme-linked immunoassay-ELISA) and if it is positive or indeterminate, a confirmatory Westernblot (Immunoblot) test is performed [4, 6, 12–16].

In the case of early Lyme borreliosis, Borrelia-specific IgM antibodies can be detected from the third week, and IgG from the sixth week [6, 12, 14]. Interpretation of serological tests (IgM and IgG) can be complicated [17]. A measurable antibody response may be absent in the early, localized manifestation of the disease (EM), in the case of very early antibiotic therapy or reinfection. Persistence of IgM for more than six weeks should be considered a false positive result [14]. IgM antibodies may lack specificity and may be positive in case of cross-reaction with other spirochetes, EBV, CMV, HIV and autoantibodies [17].

A high concentration of IgG antibodies is usually found in late manifestations [6, 12, 14]. Antibodies can remain in cerebrospinal fluid (CSF) for several weeks or in serum for several years [2, 18]. Serology is not adequate for monitoring the results of antibiotic therapy for Lyme borreliosis and is not recommended for this purpose [6, 14]. Treatment success should be assessed based on clinical signs and symptoms [14]. A high level of antibodies can be present in treated patients even several years after recovery [12, 14]. A positive serological result without any clinical signs and symptoms either indicates a serological scar or asymptomatic seroconversion indicating contamination, but not active Lyme borreliosis [14].

In US, the Westernblot (Immunoblot) test is interpreted according to the criteria of the Center for Disease Control and Prevention (CDC) and requires at least two of three significant bands for positive IgM and five of 10 significant bands for positive IgG [4]. However, these criteria cannot be used in Europe, because no set of interpretive criteria gives results of high sensitivity and specificity in all countries, due to the presence of different Borrelia genotypes [19]. Different guidelines have been proposed for traditional Westernblot assays (WB) using, for example, in the US the Bbss 297 strain isolated from a patient with Lyme neuroborreliosis (LNB) and corresponding to the CDC criteria or, in Europe, using the B. afzelii Pko strain isolated from a German erythema migrans. IgM WB should be considered positive if at least two of the following bands are present: p24 (OspC), p39 (BmpA) and p41 (flagellin) using the American strain 297, or at least one of these bands (strong p41 band) and p17 (DbpA), using the European strain Pko. IgG WB should be considered positive if at least five bands are present from p18, p21 (OspC), p28, p30, p39, p41, p45, p58 (not GroEL), p66, and p93 using the strain 297 or at least two bands from p14, p17, p21, OspC, p30, p39, p43, p58, and p83/100 using the strain Pko. Unspecific reactions are frequent with the flagellin antigen (p41). Line blots make it easier to interpret the results of these tests than WB. Line blots based on the use of recombinant Borrelia antigens have been associated with an improvement in sensitivity without loss of specificity in the early disseminated stage, adding recombinant VlsE

and DbpA proteins. Thereby, a new interpretation criterion of Immunoblot has been proposed, which considers a test to be positive when the VlsE band is detected, with a significant improvement in the disseminated early stage diagnosis that may replace IgM Immunoblot testing. In LNB from two European countries, the IgG seroreactivity of VlsE alone surpassed that of other antigens commonly used (p100, p58, p39, OspA, OspC, and p18) compared to control patients. Immunoblot has been recently miniaturized in a microarray format with probable equivalent performances to other commercial immunoblots. Given the diversity of genospecies involved in Lyme borreliosis in Europe compared to the US, almost all of the available IB kits use combinations of recombinant antigens from strains belonging to different species, generally the three main European pathogenic species (B. afzelii, B. garinii, B. burgdorferi ss) possibly associated with B. bavariensis and B. spielmanii, also responsible for some cases of Lyme borreliosis. Considering the intrinsic performance features of Immunoblot alone, European and American meta-analyses have shown that Immunoblot tests are not more sensitive than ELISA tests as a whole, either at the localized stage or in case of Lyme arthritis or neurological manifestations [20].

The aim of our study was to analyze the results of Two-Tiered Testing (ELISA anti-Borrelia IgM/IgG and confirmatory Immunoblot anti-Borrelia test IgM/IgG) in patients with possible LNB.

Methods

We conducted a prospective diagnostic study at the University Clinical Centre of Republic of Srpska from October 2017 to October 2021. The examined group consists of patients who were hospitalized and treated at the University Clinical Centre of Republic of Srpska due to suspicion of LNB.

The inclusion criteria were:

- Neurological manifestations that could correspond to the clinical manifestations of LNB
- Performed lumbar puncture and cytochemical analysis of CSF
- Diagnostic tests performed (ELISA anti-Borrelia IgM/IgG in serum and CSF,
- Immunoblot test anti-Borrelia IgM/IgG in serum)
- Other available medical documentation: anamnestic data (sex, age, occupation, data on previous tick bites or the presence of EM, neurological and other symptoms reported by the subject upon admission to the hospital, comorbidities, duration of symptoms until admission to the hospital, previous antibiotic therapy for Lyme borreliosis, clinical response to antibiotics therapy during hospitalization).

The exclusion criteria were:

- Antibiotic therapy for Lyme borreliosis before lumbar puncture
- Absence of clinical response to antibiotic therapy for LNB during hospitalization
- Diagnosis of another neurological disease
- Withdrawal of the patient from the study.

Initially we analyzed the data of 141 patients hospitalized at the University Clinical Centre of Republic of Srpska due to neuroinfection and in whom LNB was also considered as part of the differential diagnosis. Out of 141 patients, 51 of them met the conditions for participating in our study. The remaining 90 patients were excluded from the study because the CSF was not analyzed due to a contraindication for lumbar puncture, the patient used antibiotic therapy for Lyme borreliosis before the lumbar puncture, there was no favorable clinical response to the applied antibiotic therapy, or the diagnosis of another neurological disease was made.

Blood and CSF samples were taken from all patients in the wards for cytochemical analysis of CSF and microbiological examination of blood and CSF, respecting the principles of asepsis and good clinical and laboratory practice.

Blood for serological diagnostics was extracted by venipuncture into test tubes without anticoagulants and transported at room temperature to the Department of Microbiology, where the blood samples were centrifuged for five minutes at 1600 rpm speed and, after separation of the serum, aliquoted into SARSTEDT micro tubes with a screw cap of 1.5 ml. and stored at -20°C.

CSF was taken by lumbar puncture, two milliliters in sterile test tubes, and one milliliter was urgently transported at room temperature to the Clinical Laboratory Diagnostics for cytochemical analysis (number of cells with the ratio of mononuclear to polymorphonuclear, proteinorrhagia, glycorrhagia) and one milliliter was sent to the Microbiology for serological diagnostics.

Blood and CSF samples for serological diagnosis were taken at the same time:

- Anti-Borrelia ELISA gM and Anti-Borrelia VlsE ELISA IgG in serum and ELISA Anti-Borrelia IgM and IgG in cerebrospinal fluid (EUROIMMUN Analyzer I-2, EUROIMMUN Mediziniche Labordiagnostik AG Lubeck, Germany). The results were interpreted according to the manufacturer's recommendations that the concentration of IgM and IgG antibodies in the serum (with simultaneous determination in the CSF) above 5 RU/ml (relative units per milliliter) was considered positive, and the concentration below 5 RU/ml was considered negative.

- Anti-Borrelia EUROLINE RN-AT- adv IgM and Anti-Borrelia EUROLINE RN-AT IgG were performed as confirmatory EUROLINE Immunoblot tests in serum for all subjects for whom the mentioned ELISA tests in serum and/or CSF were positive or indeterminate in IgM and/or IgG class (EUROIMMUN EUROLINE BLOT, EUROIMMUN Mediziniche Labordiagnostik AG Lubeck, Germany).

Data were presented with standard descriptive statistical measures in accordance with the type of data. The analysis and comparison of the investigated groups were done in accordance with the type of data. Frequencies were compared using the appropriate chi-square test. The correlation of the results was determined by the Spearman correlation coefficient. The connection of the results was established by the Dice similarity coefficient, on the basis of which the dendrogram was created. The statistical significance of the examined differences was established for $p<0.05$. Statistical analysis and graphical presentation of data were done with the help of the statistical software package SPSS 22 (IBM, 2013).

Results

This prospective diagnostic study included 51 subjects who were examined and treated under suspicion of LNB at the University Clinical Center of Republic of Srpska from October 2017 to October 2021.

Information about previous tick bites was not available for the largest number of our patients (64.71%) and 37 (72.55%) did not have data on previous skin changes - EM.

The main symptoms of our patients at admission were numbness and weakness of the extremities followed by headache, vision impairment, and dizziness. Disorders of consciousness, speech, facial nerve paresis and lower back pain were less present.

The largest number of patients had symptoms lasting up to three months before being admitted to the hospital. By far the largest number of patients complained about symptoms for exactly one month.

Out of 51 patients, 18 (35.3%) had pleocytosis with a significant predominance of lymphocytes, 15 of them had values of the total number of cell elements from 5 to 100, and

three of them had values from 100 to 1000. Elevated protein values in the CSF were present in 19 (37.25%) of our patients, and the range of elevated values was from 0.48 to 3.6 g/L.

Out of 51 of our patients, 13 (25.5%) had positive anti-Borrelia IgM antibodies in the serum by ELISA, and 39 (76.47%) had IgG antibodies.

Anti Borrelia IgM ELISA test in CSF was positive in seven of our patients (13.7%) and anti Borrelia IgG ELISA in 20 of them (39.2%).

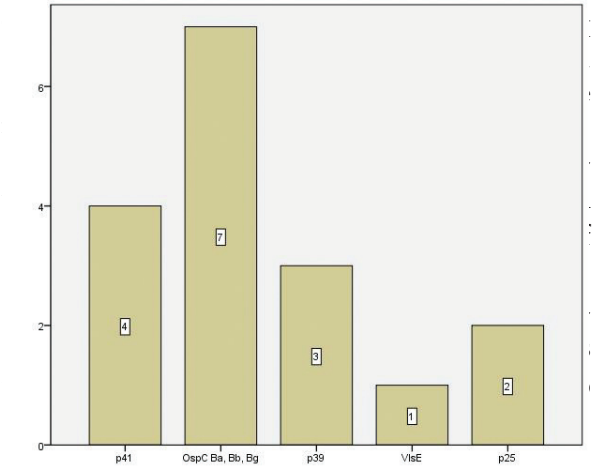

Figure 1. Immunoblot serum anti Borrelia burgdorferi IgM positive antibodies to individual specific antigens of Borrelia burgdorferi

Figure 2 shows which antibodies to individual specific antigens of Borrelia were positive in our patients in whom the Immunoblot test of anti Borrelia IgG in the serum was positive.

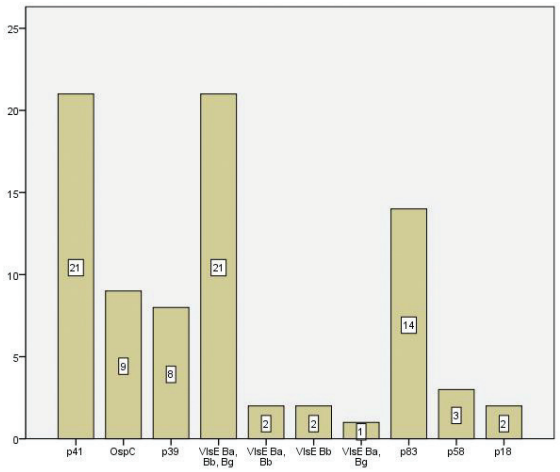

Figure 2. Immunoblot serum anti Borrelia burgdorferi IgG positive antibodies to individual specific antigens of Borrelia burgdorferi

Analyzing the correlation of the results of individual serological tests (Table 1), a strong correlation between the results of ELISA anti Borrela IgM in serum and CSF can be observed (ρ=0.802, p<0.001). A strong relationship is also

Table 1. Correlation of serological test results

		ELISA serum anti BB IgM	ELISA CSF anti BB IgM	ELISA serum anti BB IgG	ELISA CSF anti BB IgG	Immunoblot anti BB IgG
Immunoblot anti BB IgM	coeff. cor.	.447**	.478*	.112	.181	0.000
	p	.009	.010	.534	.357	1.000
	N	33	28	33	28	32
ELISA serum anti BB IgM	coeff. cor.		.802**	-.206	.050	-.029
	p		.000	.147	.750	.877
	N		44	51	44	32
ELISA CSF anti BB IgM	coeff. cor.			-.242	.102	-.120
	p			.114	.510	.552
	N			44	44	27
ELISA serum anti BB IgG	coeff. cor.				.463**	.787**
	p				.002	.000
	N				44	32
ELISA CSF anti BB IgG	coeff. cor.					.433*
	p					.024
	N					27

BB - Borrelia burgdorferi, CSF - cerebrospinal fluid

Table 2. Index of agreement of the results of individual tested tests (Dice's index, 100% agreement is 1)

	ELISA CSF anti BB IgG	ELISA serum anti BB IgM	ELISA CSF anti BB IgM	Immunoblot anti BB IgM	Immunoblot anti BB IgG
ELISA serum anti BB IgG	.778	.296	.231	.467	.978
ELISA CSF anti BB IgG		.421	.333	.455	.757
ELISA serum anti BB IgM			.889	.615	.286
ELISA CSF anti BB IgM				.500	.222
Immunoblot anti BB IgM					.452

BB - Borrelia burgdorferi, CSF - cerebrospinal fluid

Table 3. Correlation between certain clinical manifestations in subjects and antibodies to certain specific antigens of B. burgdorferi

		p41	OspC	p39	VlsE Ba, Bb, Bg	VlsE Ba, Bb	VlsE Bb	VlsE Ba, Bg	p83	p58	p18
numbness and weakness of the extremities	coeff. cor.	-.207	.091	-.406**	-.207	.137	-.081	.096	-.342*	-.011	-.299*
	p	.145	.524	.003	.145	.339	.572	.504	.014	.941	.033
	N	51	51	51	51	51	51	51	51	51	51
headache	coeff. cor.	.169	.109	.267	.169	-.143	.286*	-.100	.217	0.000	.071
	p	.236	.446	.058	.236	.317	.042	.485	.125	1.000	.618
	N	51	51	51	51	51	51	51	51	51	51
vision impairment	coeff. cor.	-.215	-.271	-.129	-.215	-.118	.114	-.083	-.360**	-.146	-.118
	p	.130	.055	.369	.130	.409	.427	.564	.010	.306	.409
	N	51	51	51	51	51	51	51	51	51	51
dizziness	coeff. cor.	.477**	.264	.298*	.245	-.081	.213	.355*	.521**	.142	.507**
	p	.000	.061	.034	.083	.574	.133	.011	.000	.319	.000
	N	51	51	51	51	51	51	51	51	51	51
disorders of consciousness	coeff. cor.	-.096	.248	-.126	-.096	-.059	-.059	-.041	-.016	-.073	-.059
	p	.503	.080	.379	.503	.681	.681	.774	.911	.611	.681
	N	51	51	51	51	51	51	51	51	51	51
disorders of speech	coeff. cor.	-.244	-.135	-.126	-.244	-.059	-.059	-.041	-.179	-.073	-.059
	p	.084	.345	.379	.084	.681	.681	.774	.208	.611	.681
	N	51	51	51	51	51	51	51	51	51	51
nervousness	coeff. cor.	.241	.171	.191	.241	-.041	-.041	-.029	.102	-.051	-.041
	p	.088	.229	.180	.088	.776	.776	.842	.476	.725	.776
	N	51	51	51	51	51	51	51	51	51	51
lower back pain	coeff. cor.	.129	-.116	.121	.129	-.051	-.051	-.035	-.154	-.063	-.051
	p	.365	.419	.396	.365	.725	.725	.805	.281	.663	.725
	N	51	51	51	51	51	51	51	51	51	51

observed between ELISA anti Borrelia IgG in serum and Immunoblot anti Borrelia IgG (ϱ=0.787, p<0.001).

The expected grouping by IgG and IgM type is observed. However, the results of ELISA in serum and Immunoblot are in the best agreement for IgG, while for IgM the best agreement of test results is observed between ELISA in serum and ELISA in CSF (Table 2).

Although there are some statistically significant relationships, the correlation coefficient between certain clinical manifestations and antibodies to certain specific antigens of Borrelia is low and therefore these relationships are not significant for practical analysis (Table 3).

Discussion

Our research on serological diagnosis of LNB is the first research of this type in Republic of Srpska.

The diagnosis of LNB in our research was defined by the clinical picture with positive serological tests. According to literature, diagnostic criteria for borreliosis of the nervous system include the possibility of exposure to ticks, clinical features associated with LNB and accompanying laboratory findings [21, 23, 24]. Diagnosing LNB is a challenge because the clinical picture is very diverse and neurological symptoms often reveal borreliosis without the reported tick bite or skin lesion [25]. Even among our patients with the clinical picture of LNB, only 31.37% of them gave information about the tick bite, even less than 9.8% saw the change on the skin corresponding to EM and those subjects knew about the previous tick bite. According to the current European case definitions, EM is diagnosed clinically and does not require laboratory testing, while the diagnosis of LNB implies the analysis of CSF and the determination of serum antibodies to Borrelia [26]. ELISA is the first line test, and then in patients with positive or borderline ELISA test, a confirmatory Immunoblot test is performed [21, 25, 26]. Out of a total of 51 patients, the ELISA serum anti Borrelia IgM test was positive in 13 of them, and IgG in 38 of them; ELISA CSF anti Borrelia IgM was positive in seven patients, IgG in 20, and for seven patients we had no data for either IgM or IgG. Immunoblot test of serum anti Borrelia IgM was borderline in four patients, positive in five, and no data were available for 18 patients; while IgG was positive in 28 patients and there were no data for 19. Both IgG and IgM positive antibodies were present in the serum of eight patients, and in the CSF in four of them. By analyzing the correlation of the results of individual serological tests of our patients, a strong correlation between the results of ELISA anti Borrelia IgM in serum and CSF was observed (ϱ=0.802, p<0.001). A strong relationship was also observed between ELISA anti Borrelia IgG in serum and Immunoblot anti Borrelia IgG (ϱ=0.787, p<0.001). A strong relationship was also observed between ELISA anti Borrelia IgG in serum and Immunoblot anti Borrelia IgG (ϱ=0.787, p<0.001). Of our 18 patients with pleocytosis, two of them had positive both IgM and IgG antibodies by ELISA test in both serum and CSF and by confirmatory Immunoblot test; four patients had positive only IgG antibodies by ELISA test in both serum and CSF, two of them also on the confirmatory Immunoblot test, and for two we had no data; in four patients only IgG antibodies were positive by ELISA test in the serum and in two of them also in the confirmatory Immunoblot test, and for two we had no data.

Positive test results do not always lead to a diagnosis of Lyme borreliosis, and negative tests do not definitively exclude the diagnosis, uninfected people may have immunity and test positive, while infected people may have a delayed antibody response and may be negative [21, 24, 25, 27]. Maintenance of positive serological tests for Lyme borreliosis in CSF may be due to delayed clearance

of CSF proteins rather than persistent intrathecal synthesis, leukocytes are rarely found, and IgG titers may remain elevated [28].

If the symptoms of the disease last a month or longer, there is no need to do ELISA test for IgM, because of false positive results, which is called the one-month diagnostic rule for Lyme borreliosis [25]. In the case of early Lyme borreliosis, Borrelia-specific IgM antibodies can be detected from the third week, and IgG antibodies from the sixth week, and then the serological test is considered to be associated with more than 90% sensitivity and specificity [6, 12, 14]. Antibodies can persist for months to years, even after successful antibiotic treatment and cure of the disease [25].

Although there are some statistically significant relationships, the correlation coefficient between certain clinical manifestations and antibodies to certain specific antigens of Borrelia in the Immunoblot test was low and its clinical significance was not proven.

Analyzing the presence of antibodies to certain specific antigens of Borrelia Immunoblot test in the IgM class, the most represented was ospC in seven patients, then p39, p25 and in one patient VlsE, while in the IgG class the most represented VlsE in 26, p41 in 21, then p83 in 14 patients, ospC in nine patients, then p58 and p18. According to the literature, for the interpretation of the Immunoblot test it is important to know the antigenic characteristics of individual proteins, p41 is extremely immunogenic but has relatively little diagnostic value due to cross-reaction with the flagellin of other bacteria, p25 is a marker of the early phase of immunity, VlsE is a variable surface lipoprotein that is common to different borrelia species, an immunogen in the early and late stages of the disease [29].

Further work is needed to develop new reliable and unambiguous diagnostic test for LNB. Various studies suggest that the detection of CXCL13 in CST is a useful marker in the diagnosis of early LNB. Its CSF level is high even before specific antibodies which levels can be very low at early LNB stage. Its level rapidly declines after antibiotics treatment, while CSF pleocytosis remains elevated and antibody level remains positive for years after treatment. But, it is nonspecific for LNB and should be interpreted with care. Increased CSF values have also been found in patients affected by neurosyphilis, CNS lymphomas or also in immunocompromised patients and patients with an autoimmune disorder. To overcome this limit, a recent study proposed to titrate the interleukin-6 (IL-6) in addition to the CXCL13 chemokine. High concentrations of IL-6 have been found in CSF samples from patients suffering from neuroinfections due to bacterial or viral etiology, while lower levels have been detected in CSF specimens from cases of LNB. To overcome this limit, the recent study proposed to titrate the interleukin-6 (IL-6) in addition to the CXCL13 chemokine. However, the use of CXCL13 and IL-6 needs to be evaluated further in future studies [30].

Conclusion

Two-step serological diagnostic tests (ELISA, Immunoblot) are very important in patients with possible LNB, but false positive and false negative results are possible. They should be interpreted with caution and in correlation with the clinical manifestation and other available tests (epidemiological data-information about previous tick bites; previous skin changes; the analysis of CSF; effectiveness of antibiotics treatment). The expected grouping by IgG and IgM type is observed. However, for IgG, the results of ELISA in serum and Immunoblot in serum are in the best agreement, while for IgM, the best agreement of test results is observed between ELISA in serum and ELISA in CSF. The correlation between certain clinical manifestations of LNB and the presence of antibodies to certain specific antigens of Borrelia in the Immunoblot

test is low and has no significance in establishing the diagnosis. More work needs to be done to develop new reliable diagnostic test for LNB, such as detection of CXCL13 in CSF, titrate the interleukin-6 (IL-6) in addition to the CXCL13 chemokine.

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Ethical approval. The Ethics Committee of the University Clinical Centre of Republic of Srpska, Banja Luka, Republic of Srpska, Bosnia and Herzegovina, approved the study and informed consent was obtained from all individual respondents. The research was conducted according to the Declaration of Helsinki.

Conflicts of interest. The authors declare no conflict of interest.

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Dvostepena serološka dijagnostika kod pacijenata sa lajmskom neuroboreliozom

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Uvod. Lajmska borelioza je multisistemska infektivna bolest uzrokovana kompleksom Borrelia burgdorferi sensu lato. Prenose je Ixodes krpelji. Osim erythema migrans, druge manifestacije zahtijevaju laboratorijsku potvrdu. Cilj našeg istraživanja bila je analiza rezultata dvostepene serološke dijagnostike kod pacijenata sa mogućom lajmskom neuroboreliozom (LNB).

Metod. Od oktobra 2017. do oktobra 2021. godine u Univerzitetskom kliničkom centru Republike Srpske sproveli smo prospektivnu dijagnostičku studiju. Studijom je obuhvaćen 51 pacijent koji je liječen pod sumnjom na LNB. Koristili smo dvostepenu serološku dijagnostiku pomoću ELISA anti-Borrelia IgM/IgG i potvrdnog Immunoblot anti-Borrelia testa IgM/IgG.

Rezultati. ELISA pozitivan anti-Borelia IgM u serumu imalo je 25,5% pacijenata, a IgG 76,47%, dok je u cerebrospinalnoj tečnosti (CSF) pozitivan IgM imalo 13,7% pacijenata, a IgG 39,2%. Immunoblot test anti-Borrelia IgM u serumu je bio graničan kod 7,84% pacijenata, pozitivan kod 6,17%, za 35,29% pacijenata nije bilo podataka, dok je IgG bio pozitivan kod 54,90%, a nema podataka za 37,25% pacijenata. Može se uočiti značajna korelacija između rezultata ELISA anti-Borrelia IgM u serumu i likvoru (ρ=0,802, p<0,001), kao i u serumu između ELISA anti-Borrelia IgG i Immunoblot IgG (ρ=0,787, p<0,001).

Zaključak. Dvostepena serološka dijagnostika (ELISA, Immunoblot) je veoma važna kod pacijenata sa mogućom LNB, ali mogući su lažno pozitivni i lažno negativni rezultati, i rezultate treba tumačiti s oprezom i u korelaciji sa kliničkom manifestacijom i drugim dostupnim testovima. Potrebni su novi pouzdani dijagnostički testovi za LNB, npr. detekcija CXCL13 u CSF, određivanje interleukin-6 (IL-6) uz CXCL13 hemokin.

Ključne riječi: lajmska neuroborelioza, enzimski imunosorbentni test, Immunoblot test