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LYME-BORELIOSIS IN UKRAINE (LITERATURE REVIEW)

Abstract. *The article deals with the analysis of recent literature on Lyme disease (tick-borne borreliosis). It is proved that this zoonotic disease affects the skin, nervous, musculoskeletal and cardiovascular systems and also the statistical data on the number of registered cases of infection with this disease are presented here.*

Keywords: *Lyme disease, borreliosis, antigenic structure, symptoms, course of the disease, statistics.*

In recent years there has been an intensification of natural foci of zoonoses that are especially dangerous to humans, such as tick-borne encephalitis, Lyme disease (tick-borne borreliosis), and a significant increase in the incidence of the diseases in Ukraine, as well as other countries worldwide.

Environmental changes (first of all, global warming) are among the causes of this phenomenon contributing to the increase of ticks as vectors of infections and the exposure of the population to them while visiting endemic areas.

Nowadays, Lyme disease is a serious medical-biological and medical-social problem due to the predisposition to chronicity and development of lesions of the central nervous system, musculoskeletal system, cardiovascular system leading to adverse consequences - long-term disability and incapacity of people of any age and sex. Every year, the study of such pathology in medical practice becomes more relevant. Much attention is paid to detecting lesions of the musculoskeletal system among non-erythematous forms, which are difficult to diagnose and most of which are able to simulate various diseases. In general, Lyme disease or tick-borne borreliosis is a bomb with a clock mechanism that can destroy human health.

Lyme Disease (La Maladie De Lyme in French, Die Lyme-Krankheit in German) is an infectious transmissible naturally focal disease caused by spirochetes transmitted by Ixodes and is characterized by propensity to the prolonged and chronic course of disease predominantly with lesions of the skin, nervous, musculoskeletal and cardiovascular systems.

The causative agents of borreliosis are spirochetes of the genus *Borrelia*, which belong to gram-negative microorganisms. They contain two main protein components – specific flagellin and non-specific HSP60. By the structure, they are labile spirochetes resembling a spiral helix of 20-30 microns long and 0.2-3.0 microns thick.

A distinctive feature of the *Borrelia* is the absence of mitochondria in them. A significant antigenic polymorphism is specific to pathogens of Lyme disease. Genomic differences can have a clinical significance since they determine the antigenic structure of pathogens. The symptom complex of the disease depends on it to a certain extent. In Europe and the United States of America, there are some differences in the prevalence of different strains of the pathogen. Thus, the *B.garinii* and *B.afzelii* genotypes are prevalent mostly in the European part of the post-Soviet area. In the United States, strains of pathogenic *Borrelia* belong to one genotype - *B.burgdorferi sensu stricto*, which has arthrogenic properties. In Europe, the most pathogenic genotypes of *Borrelia* are known, which lead to the development of arthritis, meningoradiculitis, and acrodermatitis:

1. *B.burgdorferi* (causing arthritis).
2. *B.garinii* (causing meningoradiculitis).
3. *B.afzelii* (causing acrodermatitis).

These gram-negative spirochetes growing in a culture medium that contains amino acids, vitamins, and animal serum. They consist of 2 main protein components – specific flagellin and HSP60 protein. The antigenic structure of the *Borrelia* is represented by:

- surface proteins Osp (A, B, C, D, E, F);
- flagellar antigen;

- cytoplasmic antigen.

Within the genotype, there is also variability in the composition of superficial proteins OspA and OspC. Most of the antigenic determinants of the outer membrane are similar to the antigenic determinants of other *Borrelia* species and even some bacteria, which explains the possibility of cross-immunological reactions.

Borrelia, isolated in different geographical zones, differ in morphology and protein composition (this is typical for Eurasia). Different genetic species have a different DNA nucleotide sequence. It has been found that it is possible to detect *Borrelia* belonging to two different genotypes in a single tick. Cases of simultaneous infection with borreliosis and tick-borne encephalitis virus are known in medical practice. The main transmission of infection is vector-borne one, that is, through the bite of *Dermacentor marginatus* tick of the *Ixodes* genus.

The pathogen enters the human body with tick saliva. The primary lesion develops in the place of penetration, which is clinically manifested by the development of erythema. Hematogenous dissemination begins after the penetration of the *Borrelia* through the dermis and into the vessels, characterized by spirochetemia of short duration with a small number of spirochetes. The pathogen enters the viscera, joints, central nervous system through the hematogenous and lymphogenous way. In dissemination, the *Borrelia* penetrate into macrophages, endothelial cells of various organs and systems, which is clinically manifested by the development of multiple organ dysfunction. The ability of the pathogen to intracellular parasitism provides the possibility of a chronic course of the disease with late relapses and prolonged persistence of *Borrelia* in the body (over 10 years). When the *Borrelia* die, they excrete endotoxin, which causes an immunopathological cascade.

The vast majority (81.7%) of new cases of borreliosis is recorded in May-September, that is, it occurs in the spring-summer-autumn period.

Symptoms in Lyme disease

The clinical picture of Lyme disease is characterized by polymorphism of manifestations: lesions of skin, musculoskeletal, nervous, and cardiovascular systems, general intoxication. In clinical practice, the development of the disease is divided into 4 stages:

- localized (the stage of the primary lesion);

- disseminated (generalized);
- persistent (chronic);
- residual (post-treatment Lyme disease syndrome).

Often the course of the disease becomes chronic and relapsing. The acute course (from a few weeks to 6 months) involves two successive stages - early localized and disseminated. The chronic form of the disease may last be lifelong with periods of exacerbation and remission.

Stages of the disease (may overlap or appear simultaneously, all of the symptoms do not usually appear together):

1. Early limited stage:

1) flu-like symptoms;

2) erythema migrans - usually occurs in ≈ 7 (3-30) days from the tick bite; first reddish spot or papule rapidly enlarges in diameter, diameter >5 cm, ring-shaped with enlightenment in the center (could be monochromatic), the contours are clearly delineated, remains at the skin level being painless and not itchy;

3) rarely lymphocytic lymphoma of the skin - painless, reddish-blue node, most often on the auricle, nipple or scrotum. Erythema migrans and systemic symptoms disappear within 4-12 weeks in patients untreated with antibiotics; less intense symptoms may persist in some patients for several years or chronic symptoms of the late stage develop (there may be the first and only symptom of borreliosis, even a few years after infection, such as arthritis).

2. Early disseminated stage (organ) - can develop from several weeks to several months after infection:

1) arthritis – most often mono-, sometimes oligoarthritis of large joints (knee, ankle, elbow), typically without an intensive systemic inflammatory reaction, despite the predominantly significant effusion in the joint capsule, periodic exacerbations (from several days to several weeks) eventually occurring less often, becoming shorter and milder; arthritis may become chronic if left untreated;

2) myocarditis ($\approx 5\%$ of patients) – sudden AV blockade or other conduction and rhythm disturbances; usually, articular and neurological symptoms are present at the same time;

3) nervous system lesions (neuroborreliosis) – simultaneous or gradual lesions of the central and

peripheral nervous systems at different levels: lymphocytic meningitis (usually mild, headache may be the only symptom) and neuritis of the cranial nerves (paresis or paralysis, most often of the facial nerve, which may be bilateral).

3. Late stage:

1) chronic erythematous erythroderma of the extremities – reddish-blue, usually asymmetric changes of the skin of the distal limbs, appear several years after infection; at first, inflammatory edema, then dominated by atrophy (thin depilous

skin with a purple shade), the pain of adjacent joints and paresthesia are often present;

2) chronic arthritis, the prolonged lesion is less common; light myositis, bursitis or tendonitis;

3) chronic neuroborreliosis (very rare) – inflammation of the nerve roots and peripheral nerves, peripheral polyneuropathy, chronic encephalitis, and myelitis.

The main clinical manifestations of Lyme disease, depending on the stage of the disease, are given in Table 1.

Table 1.

Clinical manifestations of Lyme disease at different stages of the infectious process (according to L.M. Vovk, 2011)

Lesions of organs and systems	Early localized infection	Early disseminated infection	Chronic infection
General detoxification manifestations	Flu-like syndrome	Pronounced general weakness	Syndrome of chronic fatigue
Lymphatic system	Regional lymphadenitis	Generalized lymphadenopathy	-
Skin	Erythema migrans	Secondary erythema and exanthema	Benign lymphocytoma of skin, chronic erythematous erythroderma
Cardiovascular system	-	Atrioventricular blockade, myocarditis	-
Nervous system	-	Meningitis, neuritis of the cranial nerves, meningoencephalitis, radiculoneuritis, Bannwarth syndrome	Encephalomyelitis, radiculopathy, vasculitis
Musculoskeletal system	Myalgia	Erratic pain in bones, joints, muscles, first arthritis attacks	Chronic polyarthritis

There are five variants of common lesions of organs and systems in Lyme disease: 1) skin; 2) nervous system; 3) bone and joint system; 4) cardiovascular system; 5) mixed variant.

The incubation period of the disease lasts from 1 to 50 days from the time the pathogen enters the body, accounting for an average of 10 - 12 days.

During the course of the disease, there are 3 periods:

The first period lasts up to 7 days. It is characterized by skin lesions and infectious manifestations: headaches, nausea, drowsiness, rapid fatigability, weakness, myalgia, and arthralgia.

The main symptom of this disease is the presence of erythema at the site of the tick bite in the form of a red spot or papule, which may reach the size of 10-60 cm gradually increasing. There are often

unpleasant sensations in the field of erythema, itching, moderate pain.

Skin redness is often accompanied by weakness, chills, heat, fever to 39 - 40° C, headache, and muscle ache. Sometimes nausea and vomiting, dry cough, runny nose, rarely itchy throat are noted.

The second period lasts 2-6 weeks. Characteristic neurological and cardiac complications, marked neurological symptoms are usually manifested after erythema disappears by the following: serous meningitis, encephalitis, neuritis of the cranial nerves, lesions to the peripheral nervous tissue, manifested in 10-25% of the infected patients.

The most common neurological disorder in Lyme disease is Bannwarth syndrome, which includes serous meningitis with lesions of the spinal nerves of the cervical and thoracic spine. A month later,

neurological disorders resolve, but they can recur, becoming chronic. Moreover, the following symptoms and syndromes with CNS lesions will occur:

- 1) mono-, polyneuritis;
- 2) lymphocytic meningitis;
- 3) chorioretinitis;
- 4) meningoradiculoneuritis;
- 5) myelitic paraplegia;
- 6) myeloradiculoneuritis;
- 7) focal or common meningitis;
- 8) paroxysmal disturbances of consciousness;
- 9) epileptic seizures;
- 10) cerebral vasculitis with cerebral infarctions;
- 11) progressive encephalomyelitis.

The development of cardiac disturbances is possible on the fifth week of the disease: disturbances of heart contractions, cardiac pain, pericarditis, myocarditis, heart failure, cardiac conduction disorder. The duration of symptoms is up to 6 weeks. Erratic pain in the muscles, joints, bones, weakness remain in patients with borreliosis during the second period.

The third period lasts from 2 months up to 2 years. Lesions of large joints are specific to this period. The disease then becomes chronic, which is represented by the alternation of recurrence and remission periods or resembles a continuous relapse. Chronic Lyme disease is manifested by arthritis, osteoporosis, thinning of cartilage, degenerative changes.

Typical symptoms of the late stage of the disease are:

1. Chronic acrodermatitis;
2. Neuroborreliosis (a combination of progressive chronic encephalomyelitis and polyneuropathy).
3. Benign lymphoma.

Outbreaks of Lyme disease in the Chernivtsi region

2015 – 10 cases registered;

2016 – 13 cases registered (three children aged 1 y. 10 m., 4 years and 5 years among the infected patients);

2017 – 4 patients registered.

In the Lviv region for the period from 2010 to 2017, 461 cases of Lyme borreliosis were registered. If 9 cases were registered in 2010, then in 2011 – 28, 2012 – 53, 2013 – 48, 2014 – 44, 2015 – 126, 2016 – 153, 2017 – 169 cases.

Consequently, the Ixodes are the main vectors of the pathogen of Lyme disease, as well as the reservoir of the pathogen at the same time. The ticks are aggressive towards humans. Migratory birds can carry Ixode tick-borne borreliosis to other continents.

Therefore, tick-bite victims should certainly consult an infectious disease physician who is obliged to prescribe a preventive treatment to the patient, regardless of whether the tick is infected, or not. After all, the risk of becoming infected with Lyme disease is real, even though it is small considering there are only 4 out of 5 ticks are the vectors.

Conclusions. Timely antimicrobial therapy is important to prevent dissemination of infection and the development of organ lesions. Therefore, specific serological studies should be conducted for patients with an unknown cause of the disease in the presence of medical history data confirming tick bite.

Significant prevalence of the disease in Ukraine (on studying ticks, their infection with *Borrelia* was detected in 18.3%, that is, every fifth tick is a vector of *Borrelia*).

In particular, during the period from 2000 to 2010, the incidence of Lyme borreliosis in Ukraine has increased by 21.9 times from 58 to 1,275 cases (0.12 to 2.77 rate per 100,000 population). The total number of officially registered cases for this period has been 4,596. The trend for further growth is predicted. This is evidenced by the fact that 13,061 cases were registered in Ukraine for the period from 2011 to 2017, that is, the incidence has increased dramatically for a shorter period.

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