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REVIEW ARTICLE

Lyme Disease: A Review

EL Fane Mouna*, Sellam I and Lemkhente Z

MIBCM, Faculty of Medicine and Pharmacy, University Ibn zohr, Agadir, Morocco

***Corresponding author:** El Fane Mouna, Faculty of Medicine and Pharmacy, University Ibn zohr, Agadir, Morocco, Tel: 212 660832362, E-mail: elfanemouna@gmail.com

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Abstract

Lyme disease or Lyme borreliosis is a spirochetosis transmitted by tick bite. The most common clinical manifestation is erythema migrans. It is the most common tick-borne disease in the northern hemisphere. It is a systemic disease, caused by a flagellate bacterium close to treponema pallidum syphilis of the genus Borrelia burgdorferi sensu lato (essentially *B. garinii, B. afzelii, B. burgdorferi sensu stricto*), transmitted by the bite of a tick of the genus Ixodes (Ixodes ricinus in Europe). The pathogen can spread haematogenously to various tissues and organs, including primarily the nervous system, joints, and skin. Diagnosis is based on anamnestic, clinical and biological arguments. Biological tests, mainly based on serology, are essential for the diagnosis of the disease, with the exception of erythema migrans, the diagnosis of which must remain strictly clinical. The treatment is based on the use of one of the following 3 classes of antibiotics: β-lactams, cyclins or macrolides, for a duration of 2 to 4 weeks depending on the clinical context. In addition to the protection against tick bites, the most effective individual preventive measure is, in case of exposure, early detection and removal of ticks attached to the skin.

Keywords: Lyme Disease; Borrelia Burgdorferi; Ixodes; Erythema Migrans

Introduction

Lyme disease (borreliosis) is one of the most common vector-borne diseases worldwide. Its incidence and geographic expansion has been steadily increasing in the last decades [1]. Its incidence and geographic expansion has been steadily increasing in the last decades. Lyme disease is caused by Borrelia burgdorferi sensu lato, a heterogeneous group of which three genospecies have been systematically associated to Lyme disease: *B. burgdorferi* sensu stricto Borrelia afzelii and Borrelia garinii [1]. It is characterized by a large clinical polymorphism, evolving schematically in three phases, primary focal cutaneous infection, secondary tissue infection focused, and tertiary where the focal manifestations evoke a dual mechanism, infectious and / or inflammatory, even dysimmunity [2]. Its severity is related to cardiac and neurological disorders, as well as to potential lymphomas that can complicate the evolution of borreliosis. Joint or eye damage can lead to significant morbidity. Indeed, as the most prevalent vector-borne disease in the Northern Hemisphere, Lyme disease is increasingly recognized as escalating public health threat that demands innovative strategies for prevention and care [3]. The objective of this article is to review the clinical diagnosis and treatment of *B. burgdorferi* infection for the front-line clinician.

Causal Agent

Lyme borreliosis is caused by spirochetes, spiral bacteria belonging to the order Spirochaetales, the family Spirochaetaceae and the genus Borrelia. The species responsible for Lyme borreliosis are grouped in the complex Borrelia burgdorferi sensu lato (*B. burgdorferi sl*) [4]. It has species and one genomospecies. Three species are pathogenic in humans: *B. burgdorferi ss*, *B. garinii* and *B. afzelii*. In the United States, *B. burgdorferi* ss is the only species isolated by culture of human samples. In Europe: *B. garinii* and *B. afzelii* are more often at the origin of the disease and are also most often found in the vector tick [5]. The bacteria of the genus Borrelia have a helicoidal morphology and a characteristic mobility, with a length of 4 to 30 µm and a diameter of 0.2 to 0.5 µm with a particular ultrastructure which consists, from the inside towards outside, by the protoplasmic cylinder, the periplasmic space and the outer membrane [4].

The flagella exist under the outer membrane, allowing the spirochaetes to move [6]. The Borrelia wall structure has similarities to the Gram-negative bacterial wall, but does not gram-free with lipopolysaccharide. The genetic material of *B. burgdorferi* is polymorphic with presence of both a chromosome and linear plasmids [4]. Their distinct organotropism is well documented: *B. burgdorferi ss*: readily causes arthritis, more common in the United States than in Europe. *B. garinii*: its neurotropism accounts for the high frequency of neurological forms in Europe, particularly in France *B. afzelii*: is the predominant agent of chronic atrophic acrodermatitis observed only in Europe [5].

Epidemiology

Incidence and Geographical Distribution

Lyme borreliosis is the most common vector-borne disease in the northern hemisphere. It occurs in Europe, North America, Asia and some Maghreb countries, following the geographical distribution of its vector. It appears as an emerging disease, in the United States, with increasing incidence, and a concentration of cases in a dozen northern states [5]. Rare cases have been reported in tropical Africa, the first in Côte d'Ivoire, followed by Burkina Faso, South Africa, Zimbabwe, Mozambique, and Europeans [5,6]. The total number of confirmed cases is more than 30,000 annually [7]. Professional activities (forestry), recreational activities in wooded and humid areas expose to contamination. The favorable period extends from May to August, when ticks are on the lookout for their food, a period of peak tick activity from early spring to late autumn [4,8,9].

The interhuman contaminations are exceptional: transplacental, by blood transfusion, after autologous transplantation of chondrocytes, but not by breastfeeding [5]. Information from surveillance data regarding the sex of cases indicated that most cases were male individuals (56.7%). The vast majority were white (89.7%) followed by other race (6.8%), black (1.6%), Asian/Pacific Islander (1.5%), and American Indian/Alaska Native (<1%) [9]. Patient age was available in 89.6% of the records and indicated a bimodal distribution with peaks at ages 5 to 9 years and 50 to 55 years [9].

Vectors, Hosts and Germ Reservoirs

Lyme disease is commonly caused by the spirochete Borrelia burgdorferi in the United States. This bacterial spirochete occurs most frequently in small vertebrates and is transmitted to humans via bites by the Ixodes scapularis or Ixodes pacificus ticks, commonly known as deer ticks or black-legged ticks [9]. The hosts are small mammals, rodents. In the United States, the main reservoir of sprouts is the white-footed mouse, Peromyxes leucopus. In Europe, the fauna concerned seems very diverse (mammals, birds, reptiles). Survival of tick vectors requires that they protect themselves from desiccation under green cover in wooded rural areas, peri-urban areas, gardens, hedges, recreational areas and even public parks [5]. The hard tick is infested during its meal on an infected mammal and then Borrelia will develop in the mite [10].

Disease transmission to humans requires the need for the tick to ingest a blood meal to transform to their next stage of development. Once attached to the host, the tick inserts its central piercing agent, called a hypostome, into the host's skin. Ixodes ticks secrete a cementing material to the skin for additional attachment, as well as anticoagulants, immunosuppressive, and anti-inflammatory substances [9]. These substances allow the pathogens to pass to the host and also may alter the host's awareness to the tick bite. The tick needs to remain in place between 24 and 48 hours for transmission of the pathogen to occur.

Pathogenesis

Contamination: Circumstances and Mechanisms

Human, terminal host for the germ, will most often be contaminated by the bite of nymphs as their small size (1 mm). The germ is initially fixed on the cells of the midgut of the tick vector by the OspA protein (outer surface protein A) which is anchored on a receptor TROPSA (tick receptor for OspA). The arrival of hot blood causes the replication of the germ and its migration into the salivary glands of the tick. The meal also causes the expression of proteins allowing the colonization of the host: OspC, various adhesins, CRASP (complement regulator-aquiring surface protein) ... while the expression of OspA is reduced. In the United States, for the risk of contamination to become important, the process of migration and 83 adaptation of the germ would require at least 48 hours of attachment. scapularis to his new host; in Europe the time required for contamination is poorly known and may be shorter [4,5,10].

Dissemination of the Germ

In the skin and then in the organs, Borrelia interacts with a wide variety of specialized immune cells. It is devoid of intrinsic proteolytic activity, the bacterium diverts for its own benefit the own systems of destruction of the host extracellular matrix. Activation of plasminogen to plasmin allows the bacterium to destroy adjacent components of the extracellular matrix and basement membranes, thereby promoting tissue migration and vascular penetration of the spirochaete [5]. Tick saliva is an essential element of the transmission and initiation phases and increases the virulence of transmitted spirochetes [4].

Late Forms of the Disease

In late forms of the disease, particularly in chronic arthritis or arthritis resistant to antibiotic therapy, the pathogenesis remains uncertain. Evidence of the persistence of a small number of germs in the joint is sometimes provided by the detection of their genome in the synovium, by gene amplification [11]. The role of immune mechanisms is also discussed in late and chronic manifestations of the disease or the absence of germs contrast with the intensity of inflammatory phenomena and immune response [12].

Natural History of the Disease

Lyme disease presents in 1 of 3 general stages. Each stage has distinct symptomatology, although clinical features may overlap, contributing to difficulty in diagnosis. The stages of Lyme disease are as follows: early localized disease, early-disseminated disease, and late-disseminated disease. The most common presentation is early localized disease [1,9]. Erythema migrans (EM) is the classic sign of early infection, indicating a focal cutaneous infection [9]. The disseminated early phase corresponds to the most florid phase of the disease where cutaneous, rheumatological, neurological, cardiological, ocular manifestations can occur. Late manifestations of germ dissemination are chronic atrophic acrodermatitis and extracutaneous signs, especially neurological and articular.

Erythema Migrant

Erythema migrans, originally coined as erythema chronicum migrans by Azfelius, is the most frequent dermatologic manifestation of Lyme disease. It is present in 70–95% of affected patients during the first 3 weeks of inoculation. It is more frequent in children than in adults. It presents as red to bluish-red, round or oval patch with centrifugal expansion that may present central clearing. It should measure 5 or more cm although maximum size is highly variable. Topography varies depending on the bitten site. In children, the most common regions affected are head and neck, and in adult extremities or pelvis area. Systemic symptoms such as malaise, lymphadenopathy, and fever may accompany erythema migrans. Without treatment, the lesions may persist for weeks to months [13].

The lesion develops a few days to a few weeks after infection, spreads spontaneously in several weeks, then disappears in a few months. The migration of EM is observed only once in four in the United States and seems even more unusual in France [5]. If the diagnosis was not made at the initial stage of the infection, the bacterium can spread by hematogenous means, giving rise to a fugitive bacteremia most often asymptomatic. It can result in headaches or fugitive and migratory arthromyalgia. The resolution of the lesion is done in a few weeks, even in the absence of treatment. It disappears more rapidly, within a few days, after initiation of antibiotic therapy and may leave a pigmental sequel [3].

Lyme Neuroborreliosis (LNB)

The neurologic manifestations of B. burgborferi infection usually present in the early disseminated stage [1]. It is the most common complication in Europe, occurring in approximately 15% of untreated patients [13]. LNB has a slight preponderance in males and has a bimodal peak affecting children/adolescents and adults over 50 years [14]. LNB is mainly marked by meningoradiculitis with lymphocytic meningitis. In children, isolated peripheral facial palsies are frequent manifestations of neuroborreliosis. Central lesions such as meningoencephalitis and myelitis are rarer [2].

Meningoradiculoneuritis

Garin-Bujadoux-Bannwarth syndrome (meningoradiculoneuritis) is the most common manifestation of acute Lyme borreliosis in adults in Europe after erythema migrans. The symptoms of radiculitis develop on average 4-6 weeks (1-18) after the tick bite or after the erythema migrans. Segmental pain occurs first, which intensifies at night and whose localisation can change. Often the pain is initially localised in the extremity where the tick bite or erythema migrans was first observed. The patient experiences pain that is burning, nagging, stabbing or tearing in nature and responds only slightly to conventional analgesics. It often peaks within a few hours or days. Three-quarters of patients develop neurological deficits after 1-4 weeks, and pareses are more frequent than sensory disorders [15]. Meningitis Isolated acute meningitis present only 4 to 5% of NBL. The meningeal syndrome, if it exists, is never as intense as in purulent meningitis. Meningitis is characterized by moderate headache, nausea, photophobia, neck stiffness [13]. Because of clinical poverty, these meningitis can initially go unnoticed and thus become chronic [10].

Polyneuropathy

Polyneuropathy/polyneuritisis linked to a Borrelia infection in European patients only in association with acrodermatitis chronic a atrophicans (ACA) in 48–64% of the cases. Isolated polyneuropathies/polyneuritis without other clear symptoms of Lyme borreliosis have been identified in 39-52% of American patients with Lymeborreliosis [15].

Achievement of Cranial Nerves

About 60 % of patients with Bannwarth's syndrome have cranial nerve deficits. All cranial nerves may be involved with the exception of the olfactory nerve. The facial nerve is affected in over 80 % of cases where there is cranial nerve involvement [15].

Involvement of the Central Nervous System (CNS)

Involvement of the CNS is rare and occurs in only around 4% of Lyme neuroborreliosis cases. Its onset is gradual and it is frequently chronic. The most common manifestation is myelitis with spastic atactic gait disturbance and bladder dysfunction. Symptoms can develop overdays or several months. Some patients suffer from severe tetra- or paraparesis [15]. Other late LNB

manifestations include chronic meningitis and encephalitis. Vasculitis central nervous involvement and stroke has also been increasingly recognized as a late complication of Lyme disease.

Joint Manifestations

Arthralgia

Erratic arthralgia, often accompanied by entheseal pain, myalgia, and a flu-like state can be seen in the EM stage. They often precede authentic arthritis. These arthralgias will then be difficult to relate to their cause in the absence of EM identified in the antecedents. Finally, the "post-Lyme" syndrome, close to fibromyalgia, includes chronic pain symptomatology including arthralgia, myalgia, asthenia [5].

Lyme Arthritis

Lyme arthritis is the second most common clinical finding in American patients. If left untreated, patients with EM develop arthritis in close to 60% of cases in an average time of 6 months. Characteristically, the joint swellingis severe, while the pain is moderate to mild. Serum white-blood cell count is usually within normal range, while inflammatory markers are usually high. Imaging study's findings are unspecific [1]. Arthrocentesis should always be performed in monoarticular arthritis to rule out septic arthritis or crystal arthropathy. Negative Gram staining and culture, absence of crystal detection in polarize light microscopy, negative serum rheumatoid factor, and anticitrullinated protein antibodies should raise suspicious of Lyme arthritis. Synovial liquid white blood cell count ranges from 10,000 to 25,000 cells/mm^3. Anti-Borrelia antibody detection, history of previous erythema migrans, or PCR detection in synovial liquid warrant treatment [1]. The transition to chronicity is observed in approximately 10% of patients (in the United States). It mainly affects the knee, and osteocartilaginous erosions can develop. But the evolution remains finally favorable after several years [5]. These complicated cases could benefit with treatment similar to other chronic inflammatory arthritis like methotrexate and hydroxychloroquine.

Dermatological Manifestations

Borrelian Lymphocytoma (LB)

It is a nodule or a firm plate of pink, purple or blue color, of variable size, measuring 1 to 5 cm, located at the lobule of the ear in the child and on the areola breast at adults. It occurs a few weeks to a few months after the tick bite. The histological differential diagnosis should be done with cutaneous B-cell lymphoma, therefore a borreliosis test treatment is recommended for all primary B-cell lymphoma.

Chronic Atrophic Acrodermatitis (ACA)

This is the dermatological manifestation of the late phases of borreliosis. It starts several months to several years after infection. It begins with purplish-blue erythema, associated with edema, predominant at the extremities and opposite articular surfaces. The lesions are characterized by atrophic zones giving the skin a fine and shiny appearance. Homolateral lymphadenopathy, especially sensitive neuropathy, as well as musculoskeletal manifestations of the affected limb, can be observed. These lesions evolve progressively towards a final 195 atrophy. At this stage, the treatment no longer modifies the clinical aspect. The occurrence of cutaneous immunophenotype B lymphoma may complicate the evolution of ACA.

Muscular Manifestations

The muscular manifestations of Lyme borreliosis are relatively poorly documented. They usually reduce to myalgias, which are common, but cases of myositis have been reported.

Myalgia

Migratory myalgia is an early sign of germ dissemination, is associated with elevated serum levels of creatine phosphokinase, or is part of the sequelae of Lyme borreliosis. They are often associated with a set of general signs: fatigue, headache, fever, "flu-like" syndrome that seem less frequent and less pronounced in Europe than in the United States. Their cause is uncertain; they are possibly related to the local presence of the germ. Finally, myalgia is part of the sequelae manifestations of Lyme borreliosis. The "post-Lyme syndrome" includes asthenia, memory problems, concentration, sleep, arthralgia and myalgia. This syndrome is manifested especially when the initial symptomatology has shown signs of neurological dissemination and when antibiotic therapy was late [11].

Myositis

The occurrence of myositis is rare, characterized by their clinical polymorphism and frequent association with other manifestations of the disease. The attack is often localized [2]. The signs of myositis are associated with other manifestations of the disease, often of neighborhood: neurological involvement, arthritis, acrodermatitis chronic atrophiante. The electromyogram proves to be of little contribution to the diagnosis, especially in case of neurological involvement. Serum creatine phosphokinase levels remain generally

normal or low. Gallium-67 scintigraphy would better detect muscle damage. Pathological examination remains essential. It confirms and clarifies muscle damage by showing interstitial myositis with or without muscle fiber changes. Several cases of orositis of the orbit are reported. The evolution is favorable under treatment. The germ has sometimes been directly demonstrated in the muscle by immunohistology and silver impregnation techniques. Finally, the interest of the MRI must currently be considered. Evolution is slowly favorable after antibiotic therapy and the beneficial effect of corticosteroids is discussed [5].

Poly- and Dermatomyositis

Some observations suggest that *B. burgdorferi* could trigger an authentic dermatomyositis. These observations are similar to those of other cases of connectivitis, eosinophilic fasciitis, scleroderma, triggered or aggravated by *B. burgdorferi* [5].

Lyme Carditis

The term Lyme carditis groups the cardiovascular manifestations of Lyme disease. Cardiac involvement is reported in 1–2% of Lyme disease cases. Lyme carditis presents in the second stage (early disseminated infection) 2–5 weeks after EM. Symptoms include palpitations, syncope or pre-syncope, dyspnea, and chest pain. The most common manifestation of Lyme carditis is cardiac conduction abnormalities. Atrioventricular (AV) block may rapidly progress to a third degree one. A common finding is myocarditis and changes in surface electrocardiography. Diffuse myocardial involvement frequently results in ST segment changes [1]. Cases of myocarditis and pericarditis have been reported and *B. burgdorferi* has been isolated from the myocardium in chronic cardiomyopathy [5].

Psychiatric Manifestations

Psychiatric illnesses caused by Lyme disease are relatively varied, they include developmental disorders, autism spectrum disorders, schizoaffective disorders, bipolar disorder, depression, anxiety disorders (panic disorder, social anxiety disorder, generalized anxiety disorder, posttraumatic stress disorder, intrusive symptoms), eating disorders, decreased libido, sleep disorders, addiction, opioid addiction, cognitive impairments, dementia, suicide, violence, anhedonia, depersonalization, dissociative episodes, derealization and other impairments. These impairments result in diminished quality of life, lost productivity, disability, caregiver burden, violence, and suicide from untreated and inadequately treated Lyme disease. Lyme disease causes an estimated 1200 suicides, 31,000 suicide attempts and 15,000 self-harm events in the United States per year [16].

Diagnostic Tests for Lyme Borreliosis

Diagnostic Techniques

Serological Tests

The biological diagnosis of lyme disease is thus based in practice on the detection of serology. All guidelines recommend the two-tier serology for the serodiagnosis of Lymeborreliosis. The two-tier serology is first based on an immunoen-zymatic technique (ELISA) and then, if positive or equivocal, on a confirmatory immunoblot test (western blot, WB) with increased specificity. ELISA tests should be used as first-line tests [17]. Several studies demonstrated that one-tier (ELISA test alone) and two-tier strategies (ELISA ± WB) had similar performances. No study hasever demonstrated the superiority of ELISA test alone versus the two-tier strategy (ELISA ± WB). Seroconversion occurs within six weeks approximately, with IgG detection. Six weeks after symptoms onset, the serological test is associated with > 90% sensitivity and specificity [17]. Serology remains positive and even after effective treatment, anti-Borrelia antibodies may persist for months or even years after healing. It is therefore of no use for monitoring treated patients, and the presence of IgM is not synonymous with an active Borrelia infection. Also the direct detection of Borrelia in the blood during the phase of bacteremia is not indicated because it is not sensitive enough [4].

Direct Biological Diagnosis

Culture

Culture is the reference biological diagnostic method, with 100% specificity but with limited sensitivity because of the small numberof bacteria at the sampling sites. There is no healthy carriageof *B. burgdorferi* sensu lato: isolation of the bacterium indicatesactive Lyme borreliosis [17]. Culture is performed in specialized labora-tories. The culture medium is specific (BSK), enriched, and it mayeasily be contaminated by commensal bacteria. Culture takes time (usually 2–8 weeks), and negative results are available only afterthree months. Spirochetes cannot be detected by Gram stainingat direct microscopic examination. A dark-field or phase-contrastmicroscope is required or direct immunofluorescence should beused (moderate sensitivity and specificity).

Diagnosis by Polymerase Chain Reaction (PCR)

The specificity of *B. burgdorferi* DNA PCR detection should be close to 100%. The PCR sensitivity varies depending on the disease stage and its localization. PCR testing is useful for difficult-to-establish diagnoses for cutaneous (PCR test on skin biopsy) or joint manifestations (PCR test on synovial fluid or synovial biopsy). It is however point less in patients presenting with neurological manifestations for more than six weeks (poor sensitivity). Look-ing for *B. burgdorferi* sensu lato by PCR test in urine and blood samples is not recom mended as studies reported highly contradictory results [17].

Choice of Techniques according to Stage of Infection

The kinetics of the bacterial spread and the antibodies that it generates direct the choice of the analyzes to be prescribed. Thus, the anamnesis is essential for the good conduct of the diagnosis [2].

Isolated Tick Bites

No serological examination is indicated at this stage. Only clinical monitoring is useful 280 because not all bites are infective. It is recommended to regularly observe the site of the bite, for at least one month, in search of the possible appearance of erythema migrans [2].

Erythema Migrant

At this stage, the diagnosis must remain strictly clinical because the lesion is pathognomonic and does not require any additional biological examination. Conventional epidemiological arguments such as exposure during a stay in an endemic area and the notion of a tick bite are useful for the diagnosis [1]. Serology is useless at this stage of the disease because its sensitivity is too weak. Specific anti-Borrelia antibodies are only detectable in 20 to 60% of patients. A negative result should lead to a second serum 3 to 4 weeks later. When the lesion is atypical, specific PCR can be used on skin biopsy [2].

Borrelian Lymphocytoma

Positive serology is sufficient to make the diagnosis if the skin lesion is typical and the anamnestic data is consistent. In case of doubt, the recommended complementary examinations are the pathological examination and the direct search for Borrelia in the lesion. Histology confirms the diagnosis of benign lymphocytoma; the positivity of the PCR or culture makes it possible to posit the diagnosis with certainty [4].

Chronic Atrophic Acrodermatitis (ACA)

The sensitivity of the serology is close to 100%. The immunoblot reveals the presence of 298 antibodies against a very large number of Borrelia antigens. PCR has the advantage here of a better sensitivity than culture and should be preferred in this indication.

Arthritis

The diagnosis is based on the combination of a serum positive serology and a bundle of compatible clinical and anamnestic arguments. Seropositivity approaches 100%. The cytochemical analysis of the articular fluid confirms the inflammatory character of the effusion with a very variable rate of leukocytes, on average of about 20 000 and the standard bacteriological examination makes it possible to eliminate a septic arthritis. Histopathological examination of a synovial biopsy shows hyperplastic synovitis distinguished by abundant deposits of fibrin and aspects of endarteritis obliterans. PCR is often positive on synovial samples. Microscopic techniques have yielded few positive results [5].

Neuroborreliosis

The biological diagnosis of neuroborreliosis requires the performance of a lumbar puncture. CSF contains about a hundred lymphocyte elements. Glycorachia is normal, proteinase is moderately increased to around 1 g / l. Serology is positive in serum in the acute phase in 80 to 95% of cases, and the rate of positivity in the CSF is higher. The presence of specific antibodies in the CSF can not be sufficient for diagnosis in case of neurological manifestations, because of the possible passive transfer of these antibodies. The European criteria therefore recommend the proof of an intrathecal synthesis of these specific IgGs. In case of diagnostic doubt, PCR or CSF culture can be discussed despite their low sensitivity except in case of early neuroborreliosis or in the context of immunosuppression (corticosteroids) [17].

Cardiac and Ocular Manifestations

The responsibility of a Lyme borreliosis in these types of attacks is difficult to prove. Nevertheless serology in serum is generally positive and antibodies are present at high titres [4].

Treatment

The treatment is based on antibiotic therapy. The active molecules used in clinical practice belong to three families of antibiotics: β-lactams, cyclins and macrolides, all of which have good in vitro activity on the different Borrelia species. The cutaneous and articular tissue diffusion of these 3 families of antibiotics is equivalent; in contrast, CSF diffusion of third-generation injectable cephalosporins is better than for other molecules. The choice of the molecule, its mode of administration and the duration of treatment depend on the stage of evolution of the infection; therapeutic recommendations have been established by type of clinical manifestation [14]. Doxycycline should not be used in children under 8 years of age, or in pregnant or lactating women.

Erythema Migrant

The treatment of a ME is based on the administration of antibiotics of the beta-lactam class (mainly amoxicillin) or cyclins (doxycycline) for 14 to 21 days. In the case of beta-lactam intolerance, doxycycline or azithromycin should be favored. The signs of the skin can not disappear until one month after the start of treatment without any sign of a therapeutic failure [18].

Joint Disorders

The treatment of arthritis is based on the prescription of oral doxycycline or amoxicillin over a period of 30 days on average. The effect of corticosteroid therapy remains poorly defined; it has been used in cases of rebel arthritis, in case of antimicrobial resistance. Sometimes used intra-articularly [18].

Late Stages of the Disease

The first line treatment of neuroborreliosis is ceftriaxone for 21 to 28 days, oral treatment is recommended only in cases of isolated facial paralysis [18].

Monitoring

The best follow-up is based on the evolution of the clinical symptomatology and its complete resolution. A partial improvement should involve at least two options: an antibiotic whose mode of action would be different from the first antibiotic used or a recontamination. A new antibiotic treatment must be proposed [14]. The serological follow-up of the treated patients is most often useless in view of the fact that a serological scar persists most often. The patient must be informed of the risk of recurrence in case of new tick bites [10].

Prevention

Primary Prevention

Is essential, wearing pants and long-sleeved shirts is preferable; in addition, clear clothing will allow better identification of ticks during routine inspection. This inspection will also include the skin and the scalp, regular examination of the integuments with regard to the bite in the following weeks to institute early a curative treatment in case of appearance of a ME. Repellents have limited efficacy and especially contact toxicity [12].

Secondary Prevention

In case of sting, the tick should be removed as soon as possible associated with local skin disinfection and simple clinical monitoring of the stung area for a month in search of further development of a possible MS are sufficient. Ether, alcohol or any other chemical are absolutely not recommended to extract the tick because these products increase the risk of regurgitation of the tick. The ideal is to use a tick (tick-tick) forceps. Careful disinfection of the wound with an antiseptic solution is essential. The site of the bite must be monitored for seven to twenty days after the bite [18]. Only one study demonstrated the benefit of single-dose antibiotic therapy with 200 mg once-daily doxycycline within 72 hours of a tick bite in an endemic area. This prevention is used only on a case-by-case basis, only in endemic areas, and if the tick has remained on the subject for more than 48 hours [10]. It can be considered: if the duration of attachment of the tick is greater than 48-72 hours; if the duration of implantation of the tick is unknown but the parasite is gorged with blood at the time of withdrawal; in pregnant women and children under 8 years of age, especially if the stings are multiple and the duration of attachment exceeds 48 hours and in immunocompromised patients [18].

Strengths

- The diagnosis of Lyme Borreliosis should be evoked on clinical manifestations 382 associated with a possible tick bite, recalling that specific anti-SR immunity does not prevent re-infection
- EM is less common in Europe than in North America, neurological manifestations are more common in Europe and joint involvement in North America, probably due to genomic differences in spirochete
- Neurological forms (meningoradiculitis) are early and common in Europe
- Lyme arthritis, later, usually presents as a recurrent oligoarthritis or monoarthritis (knee)
- The biological diagnosis is based mainly on the serology, ELISA then western blot of confirmation
- It is important to remember the importance of bacteriological evidence, direct examination at the joint or skin level
- The presence of specific antibodies in the CSF can not be sufficient for diagnosis in 395 case of neurological manifestations, because of the possible passive transfer of these 396 antibodies. The European criteria therefore recommend the proof of an intrathecal synthesis of these specific IgGs.
- Therapeutic proposals are based on the very good sensitivity of spirochetes to beta-lactams, cyclins and macrolides, as well as to the clinical determination of the disease, giving priority to third-generation parenteral cephalosporins in case of neuroborreliosis

- Antibiotic treatment of EM ensures healing and prevents the occurrence of late manifestations
- The pathogenesis of chronic arthritis remains uncertain and their treatment poorly codified
- Prevention is based mainly on systematic research and immediate removal of the tick 406 after the activities exposed. It will avoid many prescriptions of antibiotics, useless and not innocuous
- The systematic serological control of the treated patients is not based on any scientific reasoning since a well-conducted antibiotic treatment allows the complete eradication of Borrelia, and avoids progression to late forms.

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