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Lyme Disease

Issue Description

Lyme disease is the most common tick-borne disease in the Northern Hemisphere. Borrelia is transmitted to humans by the bite of infected ticks belonging to certain species of the genus Ixodes (the hard-bodied 'hard ticks'). Early manifestations of infection may include fever, headache, fatigue, depression, and a characteristic skin rash called erythema migrans. Left untreated, late manifestations involving the joints, heart, and nervous system can occur. In most cases, the infection and its symptoms are eliminated with antibiotics, especially if diagnosis and treatment occur early in the course of illness. Late, delayed, or inadequate treatment can lead to late manifestations of Lyme disease which can be disabling and difficult to treat.

Other Names

Borreliosis

Symptoms

Lyme disease can affect multiple body systems, producing a range of potential symptoms. Not all patients with Lyme disease will have all symptoms, and many of the symptoms are not specific to Lyme disease but can occur in other diseases as well. The incubation period from infection to the onset of symptoms is usually 1–2 weeks, but can be much shorter (days), or much longer (months to years). Symptoms most often occur from May through September because the nymphal stage of the tick is responsible for most cases. Asymptomatic infection exists but is found in less than 7% of infected individuals in the United States. Asymptomatic infection may be much more common among those infected in Europe.

Stage 1 – Early localized infection

The classic sign of early local infection is a circular, outwardly expanding rash called erythema chronicum migrans (also erythema migrans or EM), which occurs at the site of the tick bite 3 to 32 days after being bitten. The rash is red, and may be warm, but is generally painless. Classically, the innermost portion remains dark red and becomes indurated; the outer edge remains red; and the portion in between clears – giving the appearance of a bullseye. However, the partial clearing is uncommon, and thus a true bullseye occurs in as few as 9% of cases.

Erythema migrans is thought to occur in about 80% of infected patients. Patients can also experience flu-like symptoms such as headache, muscle soreness, fever, and malaise.

Lyme disease can progress to later stages even in patients who do not develop a rash.

Stage 2 – Early disseminated infection

Within days to weeks after the onset of local infection, the borrelia bacteria may begin to spread through the bloodstream. Erythema migrans may develop at sites across the body that bear no relation to the original tick bite. Another skin condition, which is apparently absent in North American patients, is borrelial lymphocytoma, a purplish lump that develops on the ear lobe, nipple, or scrotum. Other discrete symptoms include migrating pain in muscles, joint, and tendons, and heart palpitations and dizziness caused by changes in heartbeat.

Acute neurological problems, which appear in 15% of untreated patients, encompasses a spectrum of disorders. One is facial or Bell's palsy, which is the loss of muscle tone on one or both sides of the face. Another common neurologic manifestation is meningitis, characterized by severe headaches, neck stiffness, and sensitivity to light.

Radiculoneuritis causes shooting pains that may interfere with sleep and abnormal skin sensations. Mild encephalitis may lead to memory loss, sleep disturbances, or changes in mood or affect. In addition, simple altered mental status as the sole presenting symptom has been reported in early neuroborreliosis.

Stage 3 – Late persistent infection

After several months, untreated or inadequately treated patients may go on to develop severe and chronic symptoms affecting many organs of the body including the brain, nerves, eyes, joints and heart. Myriad disabling symptoms can occur.

Chronic neurologic symptoms occur in up to 5% of untreated patients. A polyneuropathy manifested primarily as shooting pains, numbness, and tingling in the hands or feet may develop. A neurologic syndrome called Lyme encephalopathy is associated with subtle cognitive problems such as difficulties with concentration and short term memory. Such patients may also experience profound fatigue. Other problems such as depression and fibromyalgia are no more common in people who have been infected with Lyme than in the general population. Chronic encephalomyelitis, which may be progressive, may involve cognitive impairment, weakness in the legs, awkward gait, facial palsy, bladder problems, vertigo, and back pain. In rare cases, frank psychosis has been attributed to chronic Lyme disease effects, including mis-diagnoses of schizophrenia and bipolar disorder. Panic attack and anxiety can occur, also delusional behavior, including somatoform delusions, sometimes accompanied by a depersonalization or derealization syndrome similar to what was seen in the past in the prodromal or early stages of general paresis.

Lyme arthritis usually affects the knees. In a minority of patients arthritis can occur in other joints, including the ankles, elbows, wrist, hips, and shoulders. Pain is often mild or moderate, usually with swelling at the involved joint. Baker's cysts may form and rupture. In some cases joint erosion occurs.

Acrodermatitis chronica atrophicans (ACA) is a chronic skin disorder observed primarily in Europe.[20] ACA begins as a reddish-blue patch of discolored skin, usually in sun-exposed regions of the upper or lower limbs. The lesion slowly atrophies, and the skin may become so thin that it resembles wrinkled cigarette paper.

Cause

Lyme disease is caused by Gram-negative spirochetal bacteria from the genus *Borrelia*. At least 11 *Borrelia* species have been described, 3 of which are Lyme related. The *Borrelia* species known to cause Lyme disease are collectively known as *Borrelia burgdorferi sensu lato*, and have been found to have greater strain diversity than previously estimated.

Three closely-related species of spirochetes are well-established as causing Lyme disease and are probably responsible for the large majority of cases: *B. burgdorferi sensu stricto* (predominant in North America, but also in Europe), *B. afzelii*, and *B. garinii* (both predominant in Eurasia). Some studies have also proposed that *B. bissettii* and *B. valaisiana* may sometimes infect humans, but these species do not seem to be important causes of disease.

Transmission

Hard-bodied ticks of the genus *Ixodes* are the primary vectors of Lyme disease. The majority of infections are caused by ticks in the nymph stage, since adult ticks are more easily detected and removed as a consequence of their relatively large size. Transmission is relatively rare, with only about 1% of recognized tick bites resulting in Lyme disease: this may be due to the fact that an infected tick has to be attached for at least a day for transmission to occur.

In Europe, the sheep tick, castor bean tick, or European castor bean tick (*Ixodes ricinus*) is the transmitter.

In North America, the black-legged tick or deer tick (*Ixodes scapularis*) has been identified as the key to the disease's spread on the east coast. Only about 20% of people who become infected with Lyme disease by the deer tick can remember having been bitten, making early detection difficult in the absence of a rash. Tick bites often go unnoticed because of the small size of the tick in its nymphal stage, as well as tick secretions that prevent the host from feeling any itch or pain from the bite. The lone star tick (*Amblyomma americanum*), which is found throughout the Southeastern United States as far west as Texas, is unlikely to transmit the Lyme disease spirochete *Borrelia burgdorferi*, though it may be implicated in a related syndrome called southern tick-associated rash illness, which resembles a mild form of Lyme disease.

On the West Coast, the primary vector is the western black-legged tick (*Ixodes pacificus*). The tendency of this tick species to feed predominantly on host species that are resistant to *Borrelia* infection appears to diminish transmission of Lyme disease in the West.

While Lyme spirochetes have been found in insects other than ticks, reports of actual infectious transmission appear

to be rare. Sexual transmission has been anecdotally reported; Lyme spirochetes have been found in semen and breast milk, however transmission of the spirochete by these routes is not known to occur.

Congenital transmission of Lyme disease can occur from an infected mother to fetus through the placenta during pregnancy, however prompt antibiotic treatment appears to prevent fetal harm.

Diagnosis

Lyme disease is diagnosed clinically based on symptoms, objective physical findings (such as erythema migrans, facial palsy, or arthritis), a history of possible exposure to infected ticks, as well as serological tests. When making a diagnosis of Lyme disease, health care providers should consider other diseases that may cause similar illness. Most but not all patients with Lyme disease will develop the characteristic bulls-eye rash, and many may not recall a tick bite. Laboratory testing is not recommended for persons who do not have symptoms of Lyme disease.

Because of the difficulty in culturing *Borrelia* bacteria in the laboratory, diagnosis of Lyme disease is typically based on the clinical exam findings and a history of exposure to endemic Lyme areas. The EM rash, which does not occur in all cases, is considered sufficient to establish a diagnosis of Lyme disease even when serologies are negative. Serological testing can be used to support a clinically suspected case but is not diagnostic.

Diagnosis of late-stage Lyme disease is often difficult because of the multi-faceted appearance which can mimic symptoms of many other diseases. Lyme disease may be misdiagnosed as multiple sclerosis, rheumatoid arthritis, fibromyalgia, chronic fatigue syndrome (CFS), lupus, or other autoimmune and neurodegenerative diseases.

Prevention

Attached ticks should be removed promptly. Protective clothing includes a hat and long-sleeved shirts and long pants that are tucked into socks or boots. Light-colored clothing makes the tick more easily visible before it attaches itself. People should use special care in handling and allowing outdoor pets inside homes because they can bring ticks into the house.

A more effective, community wide method of preventing Lyme disease is to reduce the numbers of primary hosts on which the deer tick depends such as rodents, other small mammals, and deer. Reduction of the deer population may over time help break the reproductive cycle of the deer ticks and their ability to flourish in suburban and rural areas.

An unusual, organic approach to control of ticks and prevention of Lyme disease involves the use of domesticated guineafowl. Guinea Fowl are voracious consumers of insects and have a particular fondness for ticks. Localized use of domesticated guineafowl may reduce dependence on chemical pest-control methods. Many victims of ticks and others with concern often turn to the Guinea Fowl Breeders Association for advice on this topic.

Management of host animals

Lyme and all other deer-tick-borne diseases can be prevented on a regional level by reducing the deer population that the ticks depend on for reproductive success. This has been demonstrated in the communities of Monhegan, Maine and in Mumford Cove, Connecticut. The black-legged or deer tick (*Ixodes scapularis*) depends on the white-tailed deer for successful reproduction.

For example, in the US, it is suggested that by reducing the deer population to levels of 8 to 10 per square mile (from the current levels of 60 or more deer per square mile in the areas of the country with the highest Lyme disease rates), the tick numbers can be brought down to levels too low to spread Lyme and other tick-borne diseases. However, such a drastic reduction may be impractical in many areas.

Vaccination

A recombinant vaccine against Lyme disease, based on the outer surface protein A (OspA) of *B. burgdorferi*, was developed by GlaxoSmithKline. In clinical trials involving more than 10,000 people, the vaccine, called LYMErix, was found to confer protective immunity to *Borrelia* in 76% of adults and 100% of children with only mild or moderate and transient adverse effects. LYMErix was approved on the basis of these trials by the U.S. Food and Drug Administration (FDA) on December 21, 1998.

Following approval of the vaccine, its entry in clinical practice was slower than expected for a variety of reasons including its cost, which was often not reimbursed by insurance companies. Subsequently, hundreds of vaccine

recipients reported that they had developed autoimmune side effects. Supported by some patient advocacy groups, a number of class-action lawsuits were filed against GlaxoSmithKline alleging that the vaccine had caused these health problems. These claims were investigated by the FDA and the U.S. Centers for Disease Control (CDC), who found no connection between the vaccine and the autoimmune complaints.

Despite the lack of evidence that the complaints were caused by the vaccine, sales plummeted and LYMERix was withdrawn from the U.S. market by GlaxoSmithKline in February 2002 in the setting of negative media coverage and fears of vaccine side effects. The fate of LYMERix was described in the medical literature as a "cautionary tale"; an editorial in *Nature* cited the withdrawal of LYMERix as an instance in which "unfounded public fears place pressures on vaccine developers that go beyond reasonable safety considerations," while the original developer of the OspA vaccine at the Max Planck Institute told *Nature*: "This just shows how irrational the world can be... There was no scientific justification for the first OspA vaccine [LYMERix] being pulled."

New vaccines are being researched using outer surface protein C (OspC) and glycolipoprotein as methods of immunization.

Tick removal

Many old wives' tales exist about the proper and effective method to remove a tick, however it is generally agreed that the most effective method is to pull it straight out with tweezers. Data have demonstrated that prompt removal of an infected tick, within approximately 36 hours, reduces the risk of transmission to nearly zero; however the small size of the tick, especially in the nymph stage, may make detection difficult.

Treatment

Antibiotics are the primary treatment for Lyme disease; the most appropriate antibiotic treatment depends upon the patient and the stage of the disease. The antibiotics of choice are doxycycline (in adults), amoxicillin (in children), and ceftriaxone. Alternative choices are cefuroxime and cefotaxime. Macrolide antibiotics have limited efficacy when used alone.

Results of a recent double blind, randomized, placebo-controlled multicenter clinical study, done in Finland, indicated that oral adjunct antibiotics were not justified in the treatment of patients with disseminated Lyme borreliosis who initially received intravenous antibiotics for three weeks. The researchers noted the clinical outcome of said patients should not be evaluated at the completion of intravenous antibiotic treatment but rather 6–12 months afterwards. In patients with chronic post-treatment symptoms, persistent positive levels of antibodies did not seem to provide any useful information for further care of the patient.

In later stages, the bacteria disseminate throughout the body and may cross the blood-brain barrier, making the infection more difficult to treat. Late diagnosed Lyme is treated with oral or IV antibiotics, frequently ceftriaxone for a minimum of four weeks. Minocycline is also indicated for neuroborreliosis for its ability to cross the blood-brain barrier.

Prognosis

For early cases, prompt treatment is usually curative. However, the severity and treatment of Lyme disease may be complicated due to late diagnosis, failure of antibiotic treatment, and simultaneous infection with other tick-borne diseases (co-infections) including ehrlichiosis, babesiosis, and bartonella, and immune suppression in the patient.

A meta-analysis published in 2005 found that some patients with Lyme disease have fatigue, joint or muscle pain, and neurocognitive symptoms persisting for years despite antibiotic treatment. Patients with late stage Lyme disease have been shown to experience a level of physical disability equivalent to that seen in congestive heart failure. In rare cases, Lyme disease can be fatal.

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