Overview on the treatment of Lyme disease in pregnancy

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ABSTRACT

Lyme disease is a tick-borne illness, which is typically caused by *Borrelia Burgdoferi*. Over time, a typical Borreliosis skin reaction takes shape, *i.e.* the formation of an annular erythema that tends to expand centrifugally with erythematous edges whose diameter can reach up to 20 cm. The symptoms of Lyme disease are not only cutaneous but there may be a systemic involvement. Obviously, this disease can also affect pregnant women and for this reason this review aims to summarize the main ways of treatment to avoid worsening of the clinical condition in the mother and an eventual, albeit rare, involvement of the fetus.

KEY WORDS: Lyme neuroborreliosis; Skin diseases, infectious; Dermatology.

The term Lyme disease was coined in the mid-1980s and refers to an infectious disease caused by Borrelia. It belongs to the family of spirochaetes of which three types are known to date: *B. burgdorferi*, *B. afzelii* and *B. garinii*. The former is more frequent in America, while in Europe the latter prevail. The vector of the disease is represented by a tick (species *Ixodes ricinus*) whose nymphs are the source of infection for humans. Ticks live in rural environments such as woods, meadows, hilly areas and can "bite" humans to feed on blood. The bite of the tick may remain unknown, the skin in fact reacts with a non-specific inflammatory reaction. Over time, a typical Borreliosis skin reaction takes shape, *i.e.* the formation of an annular erythema that tends to expand centrifugally with erythematous edges whose diameter can reach up to 20 cm. The symptoms of Lyme disease are not only cutaneous but there may be a systemic involvement. Obviously, this disease can also affect pregnant women and for this reason this review aims to summarize the main ways of treatment to avoid worsening of the clinical condition in the mother and an eventual, albeit rare, involvement of the fetus.

Borrelia infection during pregnancy

Currently, in literature is described very little about Lyme borreliosis in pregnancy, transplacental transmission and the possible consequences of the infection on the fetus.

Borrelia is a bacterium similar to Treponema and Leptospira species, belonging to the family of Spirochaetes, whose infection, as known, can be transmitted to the fetus.

Although transplacentary transmission has been demonstrated in some animal studies,[1, 2] nowadays, there is still no certain association between congenital borrelia infection and any adverse pregnancy outcomes; moreover, there are no reported cases of transmission of *B. Burgdorgeri* through breast milk.[3]

Transmission of Lyme infection during pregnancy is more frequent in the first months of gestation than in the last.

Schlesinger et al in 1985 described the first case of Borrelia infection with fatal consequences for the fetus in a pregnant woman who had developed, during the first trimester of pregnancy, migrant erythema, arthralgia and headache.[4]

In the following years cases of abortion,[5] fetal malfor-

mations, such as ventricular septum defect, malformations of the cardiac[6] or genitourinary system[7] and brain damage, were reported in mothers with Lyme disease despite antibiotic therapy.[8]

In 1999 Maraspin *et al.* reported a case series of 105 pregnant women with erythema migrans: 88.6% of newborns were born healthy, 5.7% preterm and 1.9% had birth defects and, of these, 2 newborns died a few hours after birth due to heart abnormalities.

Despite these cases described in the literature, birth congenital defects and early death could not be clearly linked with fetal infection by *B. Burgdoferi*.[9-11]

Epidemiological studies have researched the correlation between seropositivity for borrelia during pregnancy and the possibility of consequences for the fetus without any significant finding,[12] even in areas where the infection is endemic.

Waddell *et al.* in a recent systematic review analyzed the potential role of gestational Lyme disease on adverse birth outcomes and the possible vertical transmission of *B. burgdoferi* to the fetus. They showed less impact of adverse events if mothers are treated promptly and effectively.[6]

Prophylaxis

Several oral or parenteral therapeutic regimens are available for the treatment of Lyme borreliosis based on the clinical stage, systemic symptoms and period since the tick bite.

In the past, antibiotic prophylaxis following a tick bite was thought to protect against the possible development of infection and the onset of disease. Nowadays, according to the US center for disease control and prevention and the infectious disease society of America guidelines,[13] the routine use of prophylaxis with antibiotics is not recommended.

In a recent meta-analysis by Warshafsky *et al.*, it was recommended to use a 10-day prophylactic treatment with amoxycillin in pregnant women to be started if: 1) the tick has been in contact with the skin for more than 36 hours; 2) no more than 72 hours have elapsed since the bite; 3) location in an endemic area with a risk of infection greater than 20%. This type of treatment has been defined by the authors of the article as "likely to be effective, although the precise benefit has not been established."[14]

Treatment

Lyme borreliosis presents a good response to antibiotic therapy, especially if it is carried out at an early stage.[15] Antibiotic therapy not only reduces the duration of erythema migrans but also prevents the progression of the disease.

Antibiotic treatment of pregnant women should be performed if there is strong evidence of ongoing bacterial infection. The treatment of Lyme borreliosis involves the use of different classes of antibiotics including tetracyclines (usually doxiclyne), penicillins, second and third generation cephalosporins and, in patients allergic to beta-lactams, the use of macrolides. The skin manifestations of Lyme disease in Stage 1 respond well to therapy with doxycycline 100 mg 2 per day for 3 weeks. This drug, however, is contraindicated in pregnancy and during lactation for a considerable risk of bone growth disruption, permanent yellowing of the teeth, cardiac abnormalities and occasionally liver failure.[16] Therefore, depending on the clinical manifestation and severity of the infection, the antibiotics of choice during gestational Lyme borreliosis are penicillins and cephalosporins.[17]

Given the possibility, as mentioned above, of adverse events to the fetus, most studies in the literature propose an intravenous antibiotic therapy with ceftriaxone 2 g per day for 14 days for all gestational Lyme borreliosis. There is no indication for pregnancy termination, at any stage of the disease.[10]

Conclusions

Based on literature review and the data analyzed, a relationship between maternal infection with *Borrelia burgdoferi* and any adverse events on the fetus cannot be defined with certainly.

However, a reduced incidence of adverse events on the fetus of mothers with Lyme disease, promptly treated with antibiotic therapy, is certainly demonstrated.

The recommendation is therefore to treat any pregnant woman suffering from Lyme disease with the correct antibiotic therapy, remaining confident that further studies can definitively clarify the correlation between adverse events at birth and infection with *Borrelia Burgdoferi*.

Therefore, in conclusion, following the worldwide guidelines it is recommended to undertake antibiotic therapy with ceftriaxone in pregnant women with Lyme disease.

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