Erythema Migrans

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KEYWORDS

• Lyme disease • Erythema migrans • *Borrelia burgdorferi*

KEY POINTS

- Erythema migrans (EM) is the most common objective manifestation of *Borrelia burgdorferi* infection. It is associated with systemic symptoms in most but not all cases. Despite a characteristic appearance, EM should not be considered pathognomonic for Lyme disease because it must be distinguished from other similar-appearing skin lesions, including local reactions to uninfected arthropod bites in endemic areas, and southern tick-associated rash illness in nonendemic areas.
- An evaluation for early Lyme disease by health care practitioners should include a complete skin examination with all patient clothes removed, in order to uncover EM skin lesions that may otherwise go unrecognized.
- EM should be considered a clinical diagnosis, and serologic and polymerase chain reaction assays are not necessary.
- Leukopenia and thrombocytopenia are not characteristic of Lyme disease and should be considered to indicate either an alternative diagnosis or a coinfection with the agents of human granulocytic anaplasmosis or babesiosis.
- EM has an excellent prognosis when appropriate antimicrobial treatment is initiated promptly.

INTRODUCTION

Erythema migrans (EM; previously known as erythema chronicum migrans), the distinctive skin lesion of early Lyme disease, has a unique appearance, so early investigators were able to describe the clinical manifestations of Lyme disease years before the discovery of the causative pathogen, *Borrelia burgdorferi*, or the development of the first diagnostic laboratory assays. Transmission by an *Ixodes* tick vector was recognized after noting that EM develops at the exact site of a tick bite that occurred days to weeks earlier.[1–5] EM is the most common objective manifestation of Lyme disease, accounting for about 90% of cases.[1,6–8]

Historical Perspective

Two Connecticut mothers, Polly Smith and Judith Mensch, can be credited with spurring the investigations that eventually led to the recognition of the clinical manifestations and,

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ultimately, the pathogenesis and treatment of Lyme disease. They were skeptical of the diagnosis of juvenile rheumatoid arthritis given to their children and many others by physicians in October 1975, and requested a formal investigation from Connecticut health authorities and the US Centers for Disease Control and Prevention (CDC).[3] As a result, it was found that, in Old Lyme, Connecticut, an inflammatory joint syndrome occurred at a frequency more than 100 times that of juvenile rheumatoid arthritis. It was preceded in many cases by a characteristic skin rash that was noted by some patients to follow an arthropod bite after a median of 12 days. A team of researchers led by Dr Allen Steere realized that this skin lesion was reminiscent of the European erythema chronicum migrans (ECM) lesion, initially described in 1909,[3,4] which had been associated with the bite of the *Ixodes ricinus* tick. A quarter of a century before Dr Steere's investigation, some European physicians had observed a favorable response of ECM to penicillin treatment, as might be expected with a bacterial illness.[9] By 1982, a previously unrecognized spirochete, subsequently named *B burgdorferi*, was isolated from *Ixodes dammini* (now known as *Ixodes scapularis*) ticks from Shelter Island, New York, and also from the blood, skin, and cerebrospinal fluid of human patients with Lyme disease, finally establishing the cause and vector.[3] Treatment studies soon confirmed the efficacy of certain antimicrobial medications in improving patient outcomes.[10]

CLINICAL DIAGNOSIS

Primary EM is an expanding erythematous skin lesion, usually round or oval, that develops at a site where ticks belonging to certain *Ixodes* species have inoculated the spirochete *B burgdorferi*, 7 to 14 days (range, 1–36 days) earlier.[2,5,11–13] Secondary EM lesions may develop after *B burgdorferi* spreads from the site of the tick bite through the blood and back to other areas of skin (discussed later). In order to increase the specificity of the diagnosis, the CDC and others have designated 5 cm in largest diameter as a minimum size for primary EM lesions.[14] Use of this cutoff is helpful in differentiating EM from other lesions; in particular, a localized and transient inflammatory reaction to the bite of an arthropod that is not associated with infection and, in contrast with EM, resolves spontaneously within a day or two.[2,15–17] The 5-cm size limitation is useful for increasing accuracy in the clinical diagnosis of Lyme disease and, in particular, in clinical and epidemiologic studies, but should not be used alone to exclude the diagnosis of EM in individual patients with otherwise suggestive clinical and epidemiologic features.[2,6,14,16]

Tick Bite

Only about 25% (range, 14%–32%) of US patients with EM recalled the preceding tick bite that transmitted the infection.[12,16,18] One explanation for this is that the nymphal stage of *I scapularis*, the principal vector for Lyme disease in the United States, is only about the size of a poppy seed, and most tick bites are unassociated with pruritus or pain.[2,16,19] In addition, tick bites that result in infection occur at body sites such as the back or posterior thigh in adults or the hairline of children, where the tick can feed for days without being noticed.[2,12,20] The reason for this is that the transmission of *B burgdorferi* takes at least 36 hours, during which time the spirochete must move from the tick midgut to the salivary glands before it can be transmitted to the skin of the human host.[21] The locations of primary EM lesions in one study of 79 adult patients whose EM was culture confirmed are listed in **Table 1**.[12]

Evolution of Erythema Migrans and Central Clearing

EM begins as a small macule or papule at the tick bite site and progresses into a slowly enlarging erythematous patch over days.[5,11,13,22] A depressed or raised area (punctum)