Mini Erythema Migrans –
A Sign of Early Lyme Borreliosis

Klaus Weber\textsuperscript{a} Bettina Wilske\textsuperscript{b}

\textsuperscript{a}Dermatological Practice and Krankenhaus der Missionsbenediktiner, Tutzing, and
\textsuperscript{b}Max von Pettenkofer Institute for Hygiene and Medical Microbiology, National Reference Center for Borreliae,
Ludwig Maximilian University, München, Germany

\textbf{Introduction}

Erythema migrans (EM) is the hallmark of Lyme borreliosis. The typical primary EM is a ring-shaped or homogeneous erythematous and usually peripherally expanding skin lesion caused by \textit{Borrelia burgdorferi} sensu lato \cite{1, 2}. In Europe \cite{1, 3–6} and in the USA \cite{7–9}, the median or mean maximum diameter of the primary EM varies between 10 and 20 cm with a range of 1–85 cm.

EM lesions with a size of less than 5 cm had previously been noted \cite{1, 3–9}. This is not in agreement with the US case definition stating that an EM should have a size of at least 5 cm \cite{10}. In Europe, a case definition allows for the diagnosis of an EM if its size is less than 5 cm \cite{11}, but diagnostic criteria for such small lesions have not been discussed. In another European study, however, the isolation of \textit{B. burgdorferi} sensu lato from 3 EM lesions with a size of 2–4 cm has been reported \cite{1}.

In this study, we present more details about the clinical and laboratory investigations of our patients with what we call mini EM.

\textbf{Patients and Methods}

\textbf{Definition and Diagnosis}

We defined a mini EM to be a cutaneous erythema with a maximum diameter of 2 up to less than 5 cm, remaining smaller than 5 cm and being due to \textit{B. burgdorferi} sensu lato. The essential cri-
terion for the diagnosis of the mini EM was the identification of *B. burgdorferi* sensu lato by culture and/or PCR within the erythema.

**Patients, Study Design, Follow-Up and Treatment**

We carried out a retrospective study of 257 consecutive patients with the objective to study patients with mini EM in more detail. The 257 patients came from several German dermatological centers in which they were seen between 1978 and 1991 [3, 4, 12–14]. After the first visit, the patients were usually followed for 3–12 months, sometimes for years. All patients with established EM received systemic antibiotic treatment [4, 12–15].

*Cultivation and Subtype Analysis of B. burgdorferi sensu lato*

Up to 1991, an attempt had been made to culture borreliae from fresh biopsy material of the suspected mini EM lesions in the laboratory of Prof. Vera Preac-Mursic [16, 17]. In 2003, the *Borrelia* isolates from patient 1 and from a patient with a typical expanding EM could be re-cultivated and subjected to subtype analysis using outer surface protein A (OspA) PCR with subsequent analysis by sequencing [18] and restriction fragment length polymorphism [19] of the amplicons.

**Serology**

The sera of our patients were tested for the presence of IgM and IgG antibodies against *B. burgdorferi* by ELISA according to Wilske et al. [20] and by immunoblot according to Schulte-Spechtel et al. [21].

**Results**

**Patients with a Small EM at the First Visit**

Five patients (2%) had a small EM with a size of less than 5 cm at the first visit. Three of these patients (1.2%) developed typical ring-shaped peripherally expanding EM lesions with a size of 10, 20 and 21 cm in diameter, respectively, within the next 4 weeks. *B. afzelii* was identified in 1 of these 3 patients.

**Patients with Mini EM**

The remaining 2 patients were found to have a definite (patient 1) and a questionable (patient 2) mini EM. The erythema in these patients was bright red, homogeneous, nonindurated, nonraised and nonscaling. From both mini EM lesions, *B. burgdorferi* sensu lato could be cultivated. Species and subtype analysis from the isolate of patient 1 yielded *B. garinii* OspA type 6. The isolate of patient 2 could not be re-cultivated for typing. None of the patients with mini EM had elevated antibody titers against *B. burgdorferi* (confirmed by repeated serological testing performed in 2002).

*Case Report of the Patient with Definite Mini EM.* Patient 1, a 26-year old woman, presented with an asymptomatic erythema with a size of 2 by 2.5 cm at the first visit. She had observed the lesion on the left thigh for 1 week. A tick bite had not been noted. She complained of fatigue and abdominal pain. A biopsy from the erythema to culture borreliae was done at the first visit. The lesion did not change in size until it subsided spontaneously 6 weeks after the first visit. The patient was seen by one of us (K.W.) at the first visit and after 2, 4 and 7 weeks. At the follow-up after 7 weeks, she received amoxicillin 500 mg with clavulanic acid 3 times daily for 2 weeks because the culture had revealed growth of *B. burgdorferi* sensu lato. Fatigue and abdominal pain subsided within a few weeks after therapy. There were no signs and symptoms related to Lyme borreliosis during the next 12 months.

![Fig. 1. EM of 3 days’ duration on the right lower leg, 2.5 × 4 cm in diameter, in patient 2; from Weber et al. [1, colorplate I].](image-url)
Case Report of the Patient with Questionable Mini EM. Patient 2, a 43-year old man, presented with an asymptomatic erythema with a size of 2.5 by 4 cm at the first visit. The lesion had been noted on the right lower leg for 3 days (fig. 1). A tick bite had not been observed. He suffered from fatigue. A biopsy from the erythema to culture borreliae was performed 4 days after the first visit. The patient decided to start taking doxycycline 200 mg daily for 2 weeks after the second visit although at that time the result of the culture was not yet available. As ascertained by his wife, a physician, several times during the 3-week period and by one of us (K.W.) after 2 weeks, the EM did not change in size until it disappeared within 2 weeks after therapy. The fatigue subsided within a few days of therapy. Follow-up for 3 more years showed that he developed no later signs or symptoms related to Lyme borreliosis.

Discussion

Our observations on 257 consecutive patients have revealed that a small EM with a size of less than 5 cm seen at the first visit can develop into two directions. First, the small EM may peripherally expand into a typical EM. Secondly, the small EM may not reach a size of 5 cm in diameter at any time to represent a mini EM.

One of our patients with mini EM could be observed for 7 weeks without treatment. This time period appears to be sufficiently long to assure that the patient did not develop a typical expanding EM. However, early antibiotic treatment could have prevented the development of a typical expanding EM in our patient 2 so that this case appears to be questionable.

EM lesions can strongly vary in size. The mini EM apparently represents an EM which stops to expand after some time, expands so slowly or disappears so soon that it does not reach a size of 5 cm. The other extreme variant is an EM which spreads over large parts of the skin [1–9] and rarely even over the entire skin within about 4 months as reported in a single patient [22].

Early European Lyme borreliosis is occasionally associated with another erythematous lesion which is usually smaller than 5 cm in diameter, borrelial lymphocytoma. However, borrelial lymphocytoma is a raised, indurated, tumor-like lesion preferentially occurring at certain sites such as the ear lobe or nipple [23, 24].

Contrary to a typical EM, a mini EM represents a considerable diagnostic problem [1, 25]. A couple of other dermatoses such as a nonspecific tick bite reaction, eczema, granuloma anulare, tinea corporis, fixed allergic drug reaction, the initial lesion of pityriasis rosea or erysipelas might be considered. On the other side, an erythema following a tick bite and not expanding to more than 1 cm in diameter most likely indicates a nonspecific tick bite reaction rather than a mini EM.

The diagnosis of a mini EM rests on the identification of B. burgdorferi sensu lato within lesional skin. In Europe, most EM lesions are now known to be associated with B. afzelii [2, 6, 18, 25–28]. Yet, B. garinii OspA type 6 was identified in one of our patients with mini EM. This was somewhat surprising considering the recent findings of Logar et al. [6], who obtained hints that EM lesions due to B. garinii expand more rapidly than EM lesions due to B. afzelii. In their study however, the subtype (OspA type) has not been determined. For example, OspA type 4 is more often found among isolates from cerebrospinal fluid than among isolates from ticks [17] indicating differences of pathogenicity regarding different OspA types of B. garinii. Further work appears to be necessary to determine which species or subtype of B. burgdorferi sensu lato predominates in association with the mini EM.

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References


