

Serologically Diagnosed Lyme Disease Manifesting Erythema Migrans in Korea

Lyme disease is a vector-borne infection, primarily transmitted by *Ixodes* ticks, and caused by *Borrelia burgdorferi*. It has a wide distribution in the northern hemisphere. In Korea, however, only one human case has been reported, although *B. burgdorferi* was isolated from the vector tick *I. persulcatus* in the region. A 60-year-old male and a 45-year-old female developed the clinical sign of erythema migrans. Each patients were bitten by a tick four weeks and five weeks, respectively, before entering the hospital. On serologic examination, significantly increased IgM and IgG antibody titers to *B. burgdorferi* were observed in consecutive tests performed at an interval of two weeks. They responded well to treatment with tetracycline.

Key Words : Lyme disease; *Borrelia burgdorferi*; *Ixodes*; *Erythema chronicum migrans*

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INTRODUCTION

Lyme disease is caused by the tick-borne spirochete, *Borrelia burgdorferi* (1-3). It is the most common vector-borne disease of bacterial origin in the United States and Europe (2,7). However, in Korea only one human case has been recognized (4). This fact is very doubtful and interesting because *B. burgdorferi* was isolated from the vector tick *I. persulcatus* in Korea (5, 6).

The spirochete affects multiple organs, such as the skin, joints, nervous and cardiovascular systems. In particular, erythema migrans, the principal cutaneous mark of Lyme borreliosis, starts at the site of the tick bite (1, 2, 9, 10). We report two cases of Lyme disease that had the typical features of erythema migrans, past history of tick bite, and positive serologic studies.

CASE REPORT

Case 1

A 60-year-old man presented with a ten-day history of an enlarging, annular, and erythematous lesion in the right anterior chest wall and an intermittent arthralgia of the left knee for ten days. The patient stated the central plaque of the annular lesion was the site of a tick bite he received four weeks before admission to the hospital. The lesion had

begun as an asymptomatic, erythematous macule that soon developed into a plaque. The patient noticed that a ring of redness had developed for some distance around the original plaque. Physical examination showed nothing unusual except for a reddish, ringed lesion in the right anterior chest wall that consisted of an erythematous band and surrounded an erythematous plaque 1.5 cm in diameter. Both the central and peripheral parts of the lesion were slightly raised and had a smooth surface. Between them the skin appeared clinically normal (Fig. 1). Biopsy specimens were taken from both the enlarged band and from the central plaque. In ELISA, significantly increased IgM and IgG antibody titers to *B. burgdorferi* were found in consecutive tests performed at an interval of 2 weeks (Table 1). All results from other tests were either negative or normal.

The histopathology showed a superficial and deep perivascular infiltrate composed mostly of lymphocytes at the peripheral band (Fig. 2A). Plasma cells and eosinophils

Table 1. Seroreactivity of the patients by ELISA

	Case 1		Case 2	
	IgM	IgG*	IgM	IgG*
first visit	0.17	0.14	0.41	0.25
After 2 weeks	0.22	0.43	0.21	0.31
After 2 months	0.22	0.06	—	—

*The control value of IgG in 200 healthy people residing in Seoul, Korea : 0.083±0.054



Fig. 1. The well-demarcated annular erythema (thin arrow) is separated from the central reddish plaque with the punctum (thick arrow) by the normal appearing skin at the right anterior chest, "target shape" (Case 1).

were seen in the specimen taken from the band at the central plaque (Fig. 2B).

The patient was treated with tetracycline (250 mg orally three times per day) for 14 days. The lesion cleared completely and did not recur.

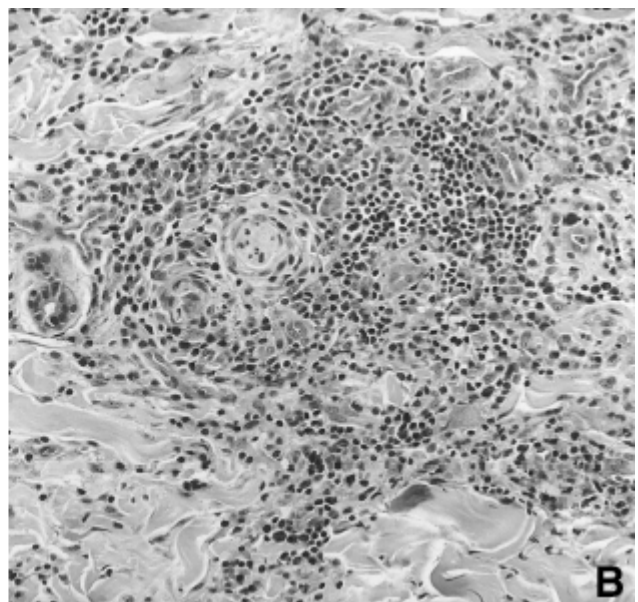
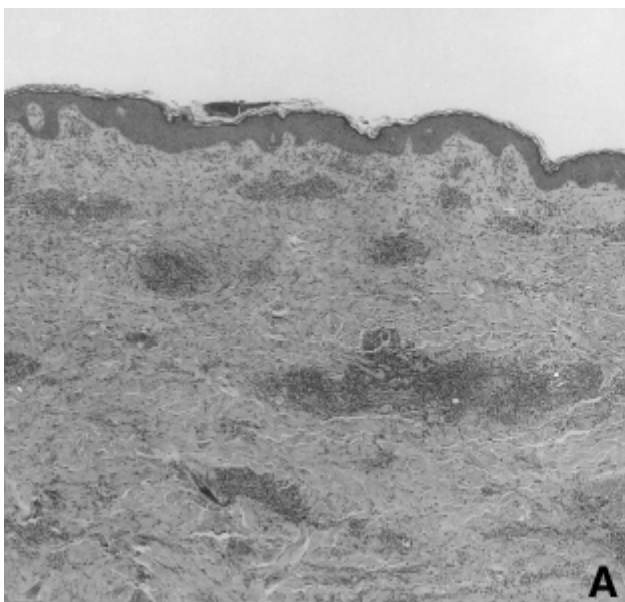


Fig. 2. A: Relatively dense superficial and deep perivascular infiltrate composed mostly of lymphocytes at the peripheral band (H&E, $\times 40$). B: Infiltrate of lymphoid cells, plasma cells and a few eosinophils at the central plaque (H&E, $\times 400$).

Case 2

A 45-year-old female had complained the progression of erythematous skin lesion on the right flank seven days ago. The annular area of edema and erythema was present, extending from the right flank to the right back. On the posterior axillary line there was a tender, and reddish punctuate plaque at the site of the tick bite sustained five weeks after camping. She recalled that after removing the tick from the skin, a coin-sized erythema appeared on the bite site. On examination, an annular, centrifugally expanding, erythematous lesion was observed on the right back (Fig. 3). Biopsy specimens were taken from both the peripheral erythematous lesion and from the central plaque. CBC, liver function test, urinalysis, and ANA were either normal or negative. Serologic examination revealed markedly increased levels of IgM and IgG antibodies to borrelial antigen. The histopathology showed similar findings to those of case 1.

The patient was treated with tetracycline (250 mg orally three times per day) for 14 days. The skin lesion cleared completely after 7 days of treatment.

DISCUSSION

Lyme disease is caused by a spirochete, *Borrelia burgdorferi*. It is transmitted by ticks and is primarily a zoonosis in which mammals, particularly humans, are innocent victims (1, 2).



Fig. 3. An annular, centrifugally expanding, erythematous lesion on the right back (Case 2).

Lyme disease has been documented in North America, Europe, and Asia including China and Japan where *Ixodes* species of ticks are found (1, 2, 7, 9). However, in Korea, although *B. burgdorferi* was isolated from the vector tick *I. persulcatus* in the region (5-6), only one human case has been reported (4).

The basic elements in the life cycle of *B. burgdorferi* are the organism itself, animal reservoirs of infection, and ticks infesting the animals. Small animals, particularly rodents, maintain a reservoir of infection and an enzootic cycle. Three stages of vector ticks, larva, nymph and adult, each feeding once on a different host, transmit the organism to the hosts. All stages may parasitize humans; nymphs and adult females are the most common vectors (1-3). Our patients had a history of removing the tick from the skin while traveling in rural areas.

The clinical spectrum of Lyme disease includes a mild nonspecific flu-like illness to a severe multisystem disease. The disease has an early localized phase characterized by erythema migrans and a disseminated phase. During the early disseminated phase various organ systems, such as the cardiovascular, central and peripheral nervous, and musculoskeletal, are commonly involved. The late phase (the infection lasting more than 12 months) is characterized by chronic cutaneous, central nervous system, and articular manifestations (1-3).

Erythema migrans (previously known as "erythema chronicum migrans"), the only pathognomonic feature of Lyme disease, typically appears as a flat erythematous lesion with reinforced borders expanding over a period of a few days.

The involved area can be solid red, ring-shaped with central clearing, or appear as a bull's eye. The incubation period may vary from a few days to three months but is usually 1 to 3 weeks (1, 2, 9, 10).

Most patients have normal hemoglobin and leukocyte count and normal liver function test. Cerebrospinal fluid analysis is used in patients with meningeal symptoms. Its findings are typical of aseptic meningitis (2). Serology continues to be the standard for the diagnosis of Lyme disease despite its inadequacies. Several techniques have been used to detect antibodies to borrelial antigens, including immunofluorescence, ELISA, and Western blot. Measuring antibody levels by means of ELISA is quick, reproducible, and relatively inexpensive; however, the false positivity rates are high, mainly as a result of cross-reactivity (1, 2). So, it is recommended that laboratories use a two-test approach for the serologic diagnosis of Lyme disease. Specimens should be tested first by using the more sensitive ELISA or indirect immunofluorescence assay. Specimens that are positive or equivocal should be tested with the more specific IgG and IgM Western blot (11). ELISA test of our cases showed elevated levels of IgM and IgG responses to *B. burgdorferi*, but we could not perform the Western blot because we did not have the specific antigens of *B. burgdorferi*.

Most patients with Lyme disease can be treated successfully with antibiotics such as tetracycline, doxycycline, minocycline, and second generation of cephalosporin (1-3). Our patients responded well to treatment with tetracycline.

Although Lyme borreliosis is a disease with a wide distribution in the northern hemisphere, one human case has been recognized in Korea. However, spirochetes were isolated from *Ixodes* ticks and rodents (*Apodemus agrarius*) collected from some provinces in Korea (6). These results demonstrate the potential for human Lyme disease to occur in Korea.

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