

CONCISE COMMUNICATION

Case of tick-associated rash illness caused by *Amblyomma testudinarium*

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ABSTRACT

We report a case of tick-associated rash illness (TARI), a new clinical entity of erythema migrans associated with a tick bite without infection of Lyme borreliosis agent. The patient, a 53-year-old man, went hiking in a mountainous area of Minoh City, Osaka Prefecture in October 2012. An erythematous macule with itching and a biting tick was found on his left thigh 2 days later, which gradually expanded. On the first visit to our department at the fifth day after hiking, an erythematous macule of 10 cm was recognized around the bite site. He had no systemic symptoms, and laboratory data were within normal limits. The tick was identified as a nymph of *Amblyomma testudinarium*. Histopathologically, perivascular infiltrates, mainly consisting of T lymphocytes, were seen in the dermis. The skin rash disappeared within 2 weeks with no treatment. Serum antibody titers against Lyme disease borrelial and rickettsial agents on the first visit and 2 weeks later were negative. These results indicate that the skin lesion of TARI was not associated with borrelial or rickettsial infection but a T-cell-mediated allergic reaction to salivary gland substances of the tick.

Key words: *Amblyomma testudinarium*, erythema migrans, Lyme disease, tick bite, tick-associated rash illness.

INTRODUCTION

As tick-transmitted infections in Japan, Lyme disease, Japanese spotted fever and severe fever with thrombocytopenia syndrome are well known. Among them, Lyme disease is a borrelial infection transmitted by *Ixodes persulcatus* and clinically characterized by erythema migrans (EM) centering at the tick bite site. In the USA, tick bite-associated annular erythema, which is indistinguishable from EM in Lyme disease, is observed and called southern tick-associated rash illness (STARI).^{1–4} STARI is considered to develop due to a bite from *Amblyomma americanum* that is distributed throughout the southeastern USA, but its pathogenesis is still unclear. In Japan, EM sometimes develops after a bite from *A. testudinarium*, classified in the same genus as *A. americanum*, and we termed this condition tick-associated rash illness (TARI).⁵ We encountered a patient with TARI, and performed histopathological examination.

PATIENT

A 53-year-old Japanese man went hiking in a mountainous area of Minoh City, Osaka Prefecture in October 2012, and was bitten on his left thigh by a tick. An erythematous macule

with itching developed at the bite site after 2 days, and gradually expanded to the surrounding area. After 5 days, because the erythematous lesion had expanded further, he visited our department. During this period, no systemic symptoms such as fever, malaise or arthralgia were observed.

At the time of the first consultation, an erythematous macule (~10 cm in diameter) was present on the left thigh, and, at its center, a blood-sucking tick was observed (Fig. 1). The left inguinal lymph node was not swollen. The tick was approximately 2 mm in length, and identified as a nymph of *A. testudinarium* based on its morphological characteristics. Blood analysis was performed at the time of the first consultation and after 2 weeks. The blood cell counts, liver function and renal function were normal, and C-reactive protein was negative. Serum samples obtained at the first consultation and after 2 weeks were examined for seroreactivity to antigens of Lyme disease *Borrelia* using a commercial kit (recomLine Borrelia IgG/IgM; Mikrogen, Neuried, Germany), but were determined to be negative. An indirect immunofluorescent antibody assay against rickettsial agents (spotted fever group, *Rickettsia japonica* and *Rickettsia conorii*; typhus group, *Rickettsia typhi* and *Rickettsia prowazekii*, and *Orientia tsutsugamushi* serotype Karp and Gilliam) was also negative. The DNA of the borrelial flagellin gene (*flaB*) and rickettsial gene (*gltA* and genus

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Figure 1. Clinical finding. An erythematous macule of approximately 10 cm in diameter was present on the left thigh and, at its center, a blood-sucking tick was observed.

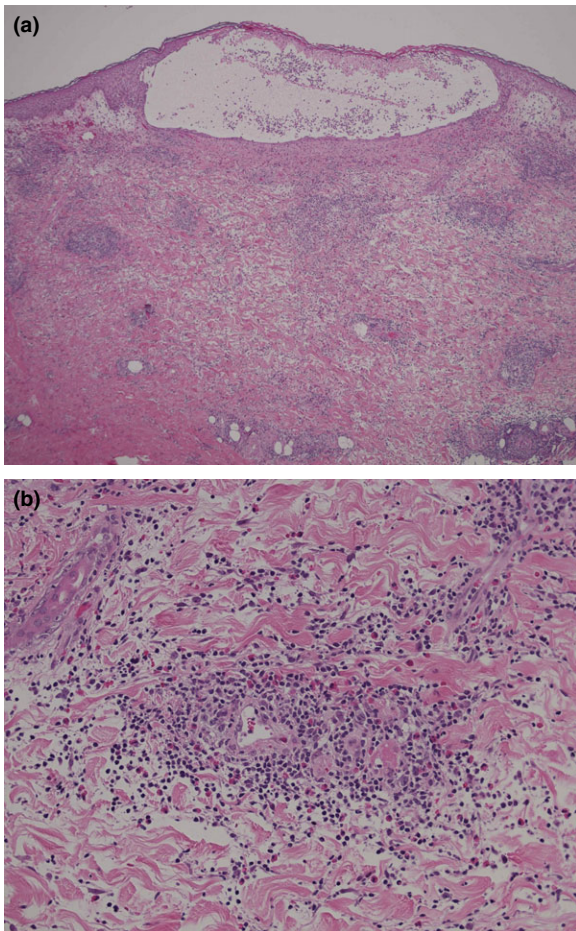


Figure 2. Histopathological findings. (a) Epidermal bullae and the infiltration of inflammatory cells in the dermis were seen. (b) The infiltration in the upper dermis consists of many lymphocytes and a few eosinophils in perivascular areas (hematoxylin–eosin, original magnifications: [a] $\times 40$; [b] $\times 200$).

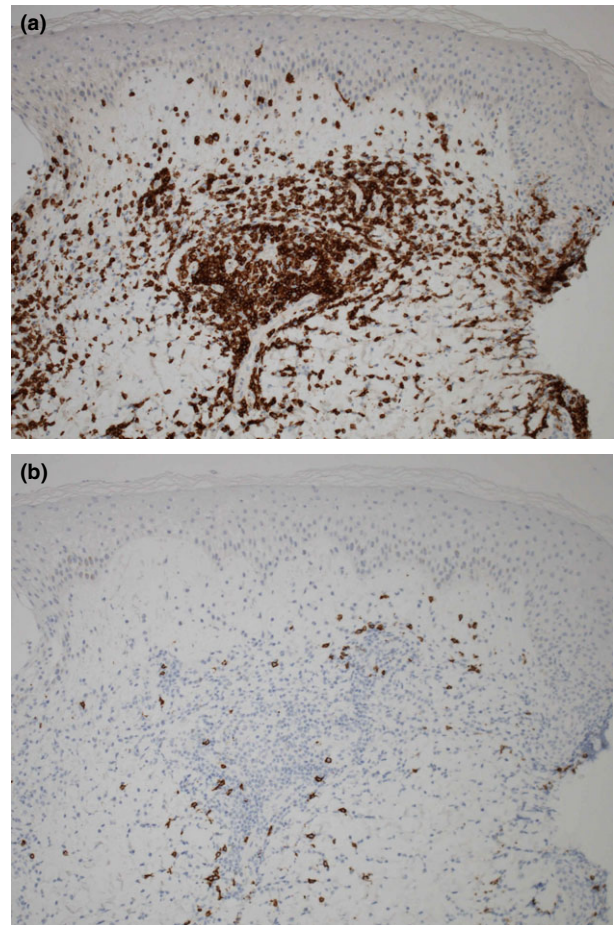


Figure 3. Immunohistological findings. (a) The infiltrated cells in the dermis were CD3-positive. (b) There were few CD20-positive cells in the dermis (original magnifications: [a] $\times 100$; [b] $\times 100$).

Rickettsia-specific outer membrane gene) were not detected from the skin lesion or serum samples with nested polymerase chain reaction assay.⁶

At the first consultation, skin biopsy of the central area of the erythematous macule together with the tick revealed epidermal bullae and the infiltration of inflammatory cells consisting of many lymphocytes and a few eosinophils in perivascular areas in the upper dermis (Fig. 2). As a result of immunohistological evaluation, most infiltrative cells in the dermis were CD3-positive and CD20-negative (Fig. 3a,b), suggesting T lymphocytes. As T lymphocytes, CD4-positive cells were mixed with CD8-positive cells, and the former were predominant. In this patient, the course was observed without treatment, and the erythema had mostly disappeared after approximately 2 weeks.

DISCUSSION

Erythema migrans is an early lesion characteristic of Lyme disease. In general, EM appears a few to 14 days after infection

with Lyme disease-related *Borrelia*. Clinically, an annular erythematous lesion with a diameter of at least 5 cm (generally, 10–16 cm) is observed in many cases. In Lyme disease-endemic areas, the presence of EM strongly suggests Lyme disease.^{7,8} Lyme disease develops due to *Borrelia afzelii* or *Borrelia garinii* infection transmitted by *I. persulcatus* in Japan and due to *Borrelia burgdorferi* infection transmitted by *Ixodes scapularis* in the USA.⁹ However, in the southeastern USA, the development of EM resembling Lyme disease following a bite by *A. americanum* is a problem, and this disease is called STARI or Masters disease.^{1–4} In recent years, in the northeastern USA where Lyme disease occurs, patients with STARI have also been reported.¹⁰ Concerning the pathogenesis of STARI, *Borrelia lonestari* or *Rickettsia amblyommii*, present in some *A. americanum* ticks, were previously considered to be pathogens. However, this speculation was refuted because subsequent studies showed the absence of these bacteria in patients with STARI.³ Therefore, the pathogenesis of STARI is unclear, but the possibility that a certain pathogen in ticks is involved still remains.

In Japan, *A. testudinarium* is widely distributed in the mountainous areas of temperate regions. Tick bites due to this species are often observed in southwestern Japan.¹¹ In some cases, erythema with itching develops 2–3 days after a tick bite, but no anti-*Borrelia* antibody is detected. We proposed that such cases should be called TARI.⁵ The pathogenesis of TARI is unclear, but the possibility of borrelial or rickettsial infection may be excluded. In the patient reported in this study, histopathological examination showed inflammatory cell infiltration, mainly T-lymphocyte infiltration, in the dermis. This finding suggests the involvement of a delayed-type allergic reaction to tick salivary gland substances in the development of TARI. To treat TARI, antimicrobials are not necessary, and a topical steroid was useful in our previously reported patient.⁵ The patient in the present study improved without antimicrobials or topical steroids. Therefore, in treatment for TARI, observation of the natural course also may be an option.

In the future, it will be necessary to clarify the pathogenic mechanism of TARI and evaluate treatments and methods of differentiation from Lyme disease.

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CONFLICT OF INTEREST: None declared.

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