Rickettsia africae Infection in a Japanese Traveller with Many Tick Bites

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Accepted November 6, 2011.

African tick bite fever (ATF) is caused by *Rickettsia africae*, and is endemic in sub-Saharan Africa and the eastern Caribbean (1, 2). Cattle ticks of the *Amblyomma* genus act as both reservoirs and vectors (1), and the rate of *R. africae* infection in *A. hebraeum* is 70% in endemic areas (2). Indigenous cases typically occur during agricultural work (1), and 26.9% of adult residents have antibodies to *R. africae* in rural areas of Cameroon (3). Although ATF presents as an acute febrile disease frequently accompanied by headache, myalgia, lymph node swelling, and maculopapular eruption with inoculation eschars, it is basically a self-limited, mild disease (2). Nevertheless, it has also been reported that reactive arthritis may complicate 5% of travel-associated ATF cases, and some patients may develop subacute cranial or peripheral neuropathy (4). In contrast, we report here a case of ATF in a Japanese woman without any general symptoms, in spite of a large number of tick bites.

CASE REPORT

A 61-year-old Japanese woman noticed more than 100 small arthropods on her extremities and trunk the night she returned to Japan (day 1) following an 11-day trip to South Africa; she had stayed in the Kruger National Park for 3 days. Although she removed the ticks as far as possible, 16 brown-grey-, red-, or yellow-coloured ticks, 2 × 3 mm in size were found on her skin (Fig. 1a, c) when she consulted our hospital on the fourth day (day 4); the remaining ticks were removed (Fig. 1b). On day 19, multiple red papules, which were not itchy, appeared in the different areas affected by tick bite on the 4 extremities and trunk (Fig. 2a, b). The number of papules increased over the following week, but no symptoms, such as fever, myalgia, fatigue, or lymph node swelling, were evident. Although she was given minocycline 200 mg/day, she took it only once. The eruption had developed to pigmentation by day 31. Laboratory examination data were within normal ranges on both days 4 and 20. The ticks were identified as *A. hebraeum* by morphology and by sequencing of the tick *mt-rrs* and tick 12S rRNA gene (5, 6). Using PCR method for rickettsial agents (7), identical sequences with *R. africae* of 17-kDa antigen, *gltA* and *ompA* genes were detected in the body of the ticks and the crust of the eschar on the patient's skin. Because an immunofluorescence assay for *R. africae* was not available in Japan, antibodies to *R. conorii*, which cross-reacts with *R. africae* (8), was tested by immunoperoxidase assay. Positive conversion of antibodies to *R. conorii* were detected on day 20; with IgM titres of 80 and 320, and IgG titres of < 40 and 1,280 on days 4 and 20, respectively. Based on these findings, a diagnosis of *R. africae* infection via *A. hebraeum* was made.

Histopathological findings of the eruption on day 4 included perivascular infiltration of mostly lymphocytes and a few

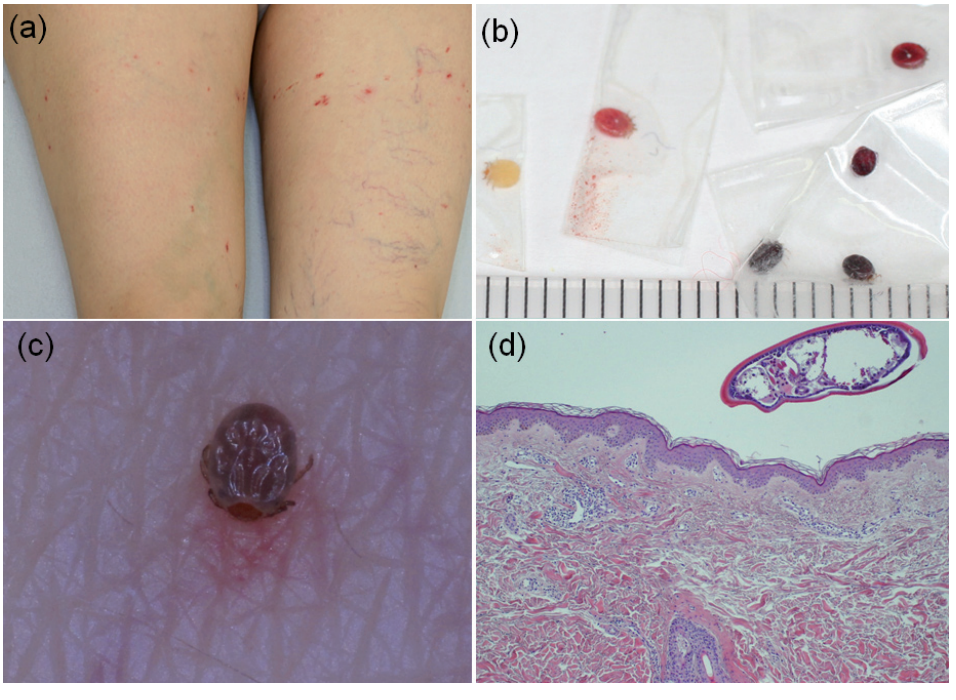

Fig. 1. Clinical findings on day 4, including (a) the appearance of the thighs, (b) some of the removed ticks, (c) a tick on the skin, and (d) histological findings from a section of skin bitten by a tick (haematoxylin and eosin stain, original magnification × 100).

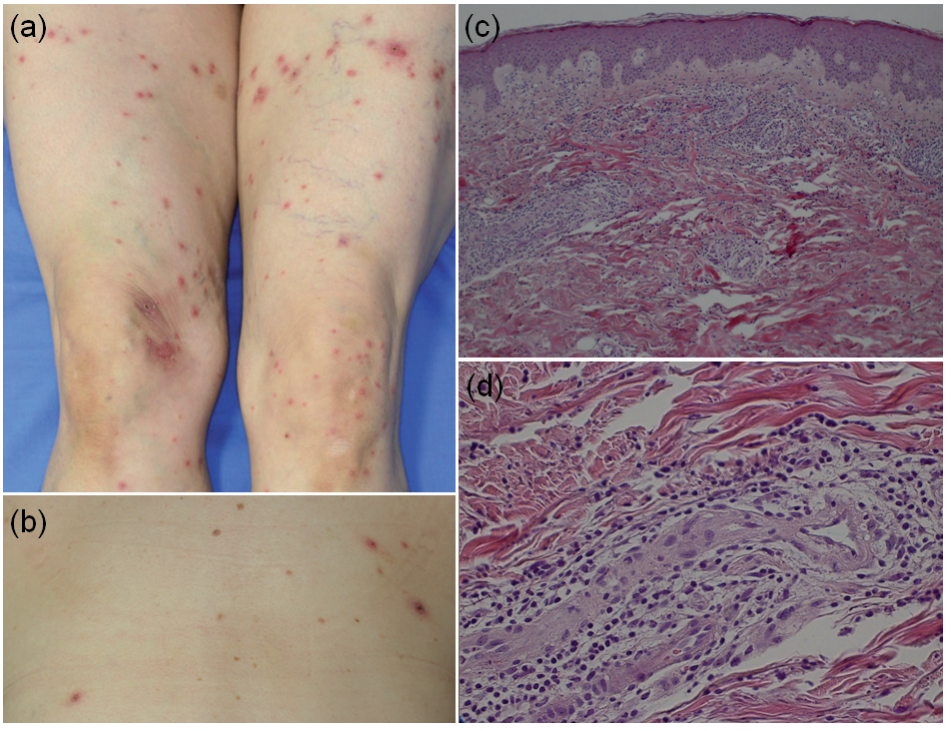

Fig. 2. Clinical findings on day 19, including (a) the appearance of the lower extremities and (b) back, and (c, d) histological findings from the skin eruption (haematoxylin and eosin stain, original magnification: (c) × 100 and (d) × 200).

eosinophils in the upper dermis at the site of epidermal tick bite (Fig. 1d). However, when papules appeared on day 19, lymphocyte infiltration was evident not only around the capillaries, but also between collagen bundles, and swelling of capillary endothelial cells was observed through the middle dermis (Fig. 2c, d). These lymphocytes constituted mostly $CD3^+$, $CD4^+$, $CD8^-$ and $CD25^-$ cells.

DISCUSSION

Most patients with ATF exhibit flu-like symptoms. The incubation period from tick bite to the onset of symptoms is usually 5–7 days. In the present case, the tick bites were presumed to have occurred 2–3 days before she noticed the tick on her skin, probably originating in the Kruger National Park and the incubation period to onset of multiple papules was 21–22 days, which is longer than that described in previous reports. In addition, the eruptions in the present patient were not typical of maculopapular eruption usually seen in rickettsiosis, which is more widely distributed.

In rickettsiosis after tick bite, rickettsial pathogens are known to infect endothelial cells, inducing subsequent perivascular infiltration of T cells and macrophages, resulting in vasculitis. Histological findings in ATF eruption are varied; one report showed more abundant neutrophil infiltration than that seen in Mediterranean spotted fever caused by *R. conorii* (9), but another showed only mononuclear cells, but not neutrophils, infiltrating into the dermis (10). In the present case, most infiltrated cells were immunohistochemically identified as helper T lymphocytes.

REFERENCES

1. Jensenius M, Fournier PE, Raoult D. Rickettsioses and the international traveler. Clin Infect Dis 2004; 39: 1493–1499.
2. Jensenius M, Fournier PE, Kelly P, Myrvang B, Raoult D. African tick bite fever. Lancet Infect Dis 2003; 3: 557–564.
3. Ndip LM, Biswas HH, Nfonsam LE, LeBreton M, Ndip RN, Bissong MA, et al. Risk factors for African tick-bite fever in rural central Africa. Am J Trop Med Hyg 2011: 84; 608–613.
4. Jensenius M, Fournier PE, Vene S, Hoel T, Hasle G, Henriksen AZ, et al. African tick bite fever in travelers to rural sub-Equatorial Africa. Clin Infect Dis 2003; 36: 1411–1417.
5. Beati L, Keirans JE. Analysis of the systematic relationships among ticks of the genera Rhipicephalus and Boophilus (Acari: Ixodidae) based on mitochondrial 12S ribosomal DNA gene sequences and morphological characters. J Parasitol 2001; 87: 32–48.
6. Ushijima Y, Oliver JH Jr, Keirans JE, Tsurumi M, Kawabata H, Watanabe H, et al. Mitochondrial sequence variation in Carios capensis (Neumann), a parasite of seabirds, collected on Torishima Island in Japan. J Parasitol 2003; 89: 196–198.
7. Ando S, Kurosawa M, Sakata A, Fujita H, Sakai K, Sekine M, et al. Human Rickettsia heilongjiangensis infection, Japan. Emer Infect Dis 2010; 16: 1306–1308.
8. Fournier PE, El Karkouri K, Leroy Q, Robert C, Giumelli B, Renesto P, et al. Analysis of the Rickettsia africae genome reveals that virulence acquisition in Rickettsia species may be explained by genome reduction. BMC Genomics 2009; 10: 166.
9. Lepidi H, Fournier PE, Raoult D. Histologic features and immunodetection of African tick-bite fever eschar. Emerg Infect Dis 2006; 12: 1332–1337.
10. Kim J, Smith KJ, Naefie R, Skelton H. Histopathologic features of and lymphoid populations in the skin of patients with the spotted fever group of rickettsiae: southern Africa. Int J Dermatol 2004; 43: 188–194.