

# Analysis of *Rickettsia*-related pathogens for the identification of unknown rickettsiosis-like fever in Japan

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Rickettsiosis is a tick-borne febrile infectious disease which is caused by an obligatory intracellular bacterium belonging to the genus *Rickettsia*. In Japan, "Japanese spotted fever disease (JSFD)" is well-known as a severe rickettsiosis caused by *Rickettsia japonica*. The epidemic area for JSFD is western Japan. In recent years, there are clinical cases with unknown fever similar to, but not, JSFD. *Rickettsia*-related bacteria such as unidentified spotted fever group (SFG) rickettsia, *Ehrlichia* species, and *Anaplasma phagocytophilum* are thought to be candidates for the causative agents of such unknown fever. In this study, we investigated these *Rickettsia*-related bacterial infections in humans, Japan.

In 2010, a total of 211 blood samples were collected from human patients with suspicious rickettsiosis in 7 prefectures (Kochi, Miyazaki, Kagoshima, Wakayama, Fukuoka, Hyogo, and Nagasaki). The total DNA was prepared from these blood samples and PCR was performed for the detection of SFG rickettsia *gltA* gene, *A. phagocytophilum p44* gene, and *Ehrlichia* species *p28* gene. Three blood samples tested were PCR-positive for *A. phagocytophilum p44* genes. One of the three positive samples was also positive for SFG rickettsiae *gltA* gene. These results strongly suggest the infection with *A. phagocytophilum* alone as well as the co-infection with *R. japonica* and *A. phagocytophilum* in humans, Japan. None of the samples were PCR-positive for *Ehrlichia* species *p28* gene.

As far as we know, in Europe and the US, the co-infection with Lyme disease borreliae and *A. phagocytophilum* occurs, but the co-infection with SFG rickettsiae and *A. phagocytophilum* has not been reported. However, as mentioned above, we found the co-infection of *R. japonica* and *A. phagocytophilum* in this study. Because western Japan is epidemic for JSFD, we think that the potential co-infection with these two pathogens still more exists in this endemic area. We tried to isolate *A. phagocytophilum* from the patient blood using tissue culture system in this study, but could not succeed in the attempt. In general, it is so hard to isolate *Rickettsia*-related bacteria including *A. phagocytophilum*. However, we will continue to try the isolation, because this attempt is very important for the understanding of unknown rickettsiosis-like fever, probably caused by such unidentified *Rickettsia*-related pathogens.