Ehrlichia chaffeensis and Rochalimaea Antibodies in Kawasaki Disease

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Sera from 38 patients with Kawasaki disease were tested for immunofluorescent antibodies to Ehrlichia chaffeensis, Rochalimaea henselae, and R. quintana Oklahoma. Only 2.5% of the patients tested positive for E. chaffeensis, and 5% were positive for R. henselae and R. quintana Oklahoma. Our data suggest that Ehrlichia and Rochalimaea spp. do not play a unique role in the etiology of Kawasaki disease.

Kawasaki disease (KD), mucocutaneous lymph node syndrome, is a multisystem vasculitis of infants and young children and a leading cause of acquired pediatric coronary artery disease throughout the world (4, 10). The disorder is characterized by fever, mucosal inflammation, polymorphous exanthema, cervical lymphadenopathy, edema of the hands and feet, and peringuinal desquamation. The epidemiologic features, including seasonality and peak disease incidence between 1 and 2 years of age, and the clinical and pathological features suggest an infectious etiology. Serologic evidence of an association with infections with numerous bacteria (7) (Propionibacterium acnes, streptococci, and staphylococci), spirochetes (7) (leptospires and Borrelia burgdorferi), mycoplasmas (7), rickettsiae (7, 10) (Coxiella burnetii and Ehrlichia spp.), Toxoplasma gondii (7), human parvovirus (10), and herpesviruses (6, 9) (Epstein-Barr virus, cytomegalovirus, human herpesvirus 6, varicella-zoster virus, and herpes simplex virus) has been sought and not obtained. Childhood ehrlichiosis has been confused clinically with KD (1). Ehrlichia chaffeensis, the recently identified etiologic agent of human ehrlichiosis (1), and Rochalimaea spp., etiologic agents of bacillary angiomatosis, bacillary peliosis hepatitis, relapsing fevers, and cat scratch disease (13), has been strongly associated with vascular lesions. Rochalimaea spp. elicit a hyperplastic lymphoid response reminiscent of that seen in KD (13). We investigated the role of E. chaffeensis and Rochalimaea spp. in the etiology of KD.

Paired (acute- and convalescent-phase) sera from 18 clinically confirmed KD patients and single sera from 20 additional KD patients were tested for immunofluorescent antibodies to Rochalimaea henselae, R. quintana, and E. chaffeensis.

R. henselae (Houston-1 isolate) (11) and R. quintana (OK-90-268 isolate) (14) were cultivated with Vero cells to inhibit autoagglutination of Rochalimaea organisms commonly seen with such bacilli cultivated on erythrocyte-enriched agar (12). E. chaffeensis was propagated in DH82 cells until 90 to 100% of the cells were infected (2). Infectious organisms were inactivated by gamma irradiation. Antigen and antisera were prepared for immunofluorescent-antibody testing by standard techniques.

The immunofluorescent-antibody test was performed by diluting serum samples 1:64 in 0.01 M phosphate-buffered saline. When distinct staining of the organism was observed at this dilution, serial twofold dilutions were made. Serologic results were reported as the reciprocal of the highest dilution at which specific fluorescence of Ehrlichia or Rochalimaea sp. organisms was observed. Antisera from individuals with culture-confirmed R. henselae, R. quintana, or E. chaffeennis infections were used as positive controls.

Of the 20 patients for whom only acute-phase sera were tested, one each tested positive for antibodies to E. chaffeensis, R. henselae, and R. quintana Oklahoma. Of the 18 patients for whom both acute- and convalescent-phase sera were available, one showed positive antibody responses to R. henselae and R. quintana. Both patients with positive Rochalimaea serologic results had exposure to a household pet, one a cat and the other a dog.

The patient who was seropositive for E. chaffeensis had a single titer of 1:256 in an acute-phase serum specimen. He was a 4-year-old child who had a history of 5 days of fever, conjunctival injection, and red, swollen lips. He had no evidence of streptococcal infection. The other two patients showed significant antibody responses to both R. henselae and R. quintana OK-90-268. The first of these, for whom only acute-phase serum was available, had titers of 1:512 and 1:2,048 to R. henselae and R. quintana OK-90-268, respectively. He was a 3.5-year-old boy who fulfilled the criteria for KD (4). The other patient showed a rise in antibody titers to both R. henselae and R. quintana Oklahoma between her acute- and convalescent-phase sera. The titer of antibodies to R. henselae increased from <1:64 in the acute-phase serum to 1:1,024 in the convalescent-phase serum. The acute- and convalescent-phase titers of antibodies to R. quintana OK-90-268 were <1:64 and 1:2,048, respectively. This 3-month-old child developed "atypical" KD with extensive coronary artery aneurysms. Since diagnosis in 1991, these aneurysms have continued to resolve. She is currently doing well.

Infections with Ehrlichia and Rochalimaea spp. have been recognized increasingly more frequently in both immunocompetent and immunocompetent individuals, although...
their disease spectrum remains incomplete. Although we made no attempt to culture either *E. chaffeensis* or *Rochalimaea* spp. from our patients with KD, the serologic data do not support a major causative role for either infectious agent. Further studies are necessary to define the etiology and pathogenesis of KD.

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REFERENCES


