A CASE OF CAT SCRATCH DISEASE DIAGNOSED BY INDIRECT FLUORESCENT ANTIBODY ASSAY OF IGM SPECIFIC FOR A JAPANESE STRAIN OF Bartonella henselae

Sho-Hei Uchi, MD,* Ryoji Yanai, MD, PhD,* Hidehiro Tsuneoka, PhD,† Ken-ichiro Otsuyama, PhD,† Koh-Hei Sonoda, MD, PhD,‡ Kazuhiro Kimura, MD, PhD*

Purpose: To report a case of cat scratch disease–associated retinitis diagnosed with an indirect fluorescent antibody (IFA) assay for immunoglobulin M (IgM) specific for a strain (YH-01) of Bartonella henselae recently identified in Japan.

Methods: Case report of a 24-year-old pregnant woman presented with general fever, fatigue, as well as blurred vision, and a central visual field deficiency in her right eye and was suspected as cat scratch disease because she had started to feed a feral dog a month ago.

Results: The patient’s serum tested negative, however, with an IFA assay for IgG or IgM specific for the Houston-1, common strain of B. henselae. Further testing with an IFA assay for IgM specific for the YH-01 strain yielded a positive result. On the basis of the clinical findings and the IFA results, we were thus able to make a definitive diagnosis of cat scratch disease.

Conclusion: An IFA assay based on the YH-01 or combination of both YH-01 and Houston-1 strains of B. henselae may show increased sensitivity for the diagnosis of cat scratch disease in Japan.

From the Departments of *Ophthalmology, †Clinical Laboratory Science, Faculty of Health Science, Yamaguchi University Graduate School of Medicine, Yamaguchi, Japan; and ‡Department of Ophthalmology, Kyushu University Graduate School of Medical Sciences, Fukuoka, Japan.

Cat scratch disease (CSD) is a zoonotic infectious disease caused by Bartonella henselae, a Gram-negative bacillus, and is transmitted to humans from domestic animals such as cats and, more rarely, dogs.1 It is characterized by general fever, lymphadenitis, or neuroretinitis,2 the latter encompassing inflammation of the optic nerve and retina that results from travel of the bacteria to the eye and which gives rise to blurred vision. Swelling of the optic nerve head and macular star are typical signs of neuroretinitis associated with CSD, although their absence in some cases may make diagnosis difficult, especially in the early phase of the disease. Diagnosis of CSD can be made on the basis of various tests including indirect fluorescent antibody assay (IFA) of serum, biopsy of lymphoid tissue, polymerase chain reaction analysis of cerebrospinal fluid, and more western-blot bands.3 Indirect fluorescent antibody assays for immunoglobulin G (IgG) or IgM specific for B. henselae are widely applied to CSD diagnosis, with the Houston-1 strain of B. henselae isolated in the United States or the Marseille strain isolated in Europe being the standard strains adopted for these tests worldwide. Given that these two strains differ in their antigenicity, some IFA kits for CSD rely on both strains to increase test sensitivity. However, even these tests have still been found to yield some false-negative results.4
We have previously described a Japanese-specific strain of B. henselae named YH-01, which was originally isolated from a Japanese patient with CSD-induced valve endocarditis. Here, we present for the first time a case of CSD with atypical eye signs that was diagnosed with an IFA assay for IgM based on YH-01, with the patient testing negative for Houston-1–specific IgG or IgM. Our results suggest that testing for YH-01 infection may increase the sensitivity of IFA assays for CSD diagnosis.

**Case Report**

A 23-year-old pregnant woman (35 weeks of pregnancy) visited the Department of Ophthalmology at Yamaguchi University Hospital complaining of blurred vision and a central visual field deficiency in her right eye. She had experienced a general fever and fatigue for 2 weeks. Clinical examination revealed her left eye to be normal, but the right eye showed loss of visual acuity (20/400), a reduced critical flicker frequency (11 Hz, compared with 43 Hz in the left eye), and a white exudate at the central macula without macular star (Figure 1). Optic disk swelling, a relative afferent pupillary defect, and cells or flare in the anterior chamber were not detected at this time. Spectral domain optical coherence tomography (SD-OCT) revealed a subretinal exudate only at the macula (Figure 2). Given her general fever, the infectious white exudate at the macula, and her mentioning that she had started to feed a feral dog a month ago, we suspected CSD as a likely diagnosis.

According to the eye symptoms and signs, as unilateral retinitis with macula exudate, we believed differential diagnosis as follows: CSD, tuberculosis, toxoplasma, and toxocara as infectious disease, and renal failure, macular dystrophy, sarcoidosis, Bechet disease, and diabetic retinopathy as noninfectious disease. We started a differential diagnosis for these disease with blood screening. In that screening, we tested the patient’s serum for IgG and IgM specific for the Houston-1 strain of B. henselae with an IFA assay, but the result was negative. However, a similar test revealed her serum to be positive (1:40 titer) for IgM specific for the YH-01 strain.
strain, whereas IgG was negative. The combination of clinical findings and serodiagnosis with the latter IFA assay for IgM allowed us to make a definitive diagnosis of CSD.

Given the risk to the fetus associated with drug or other agent administration, with the patient’s agreement, we decided not to perform fluorescein angiography or to prescribe topical antibiotics or subconjunctival or sub–Tenon capsule injection of prednisolone acetate. We instead monitored the exudate for any change in size before deciding on a course of treatment. The development of macular star with radial exudates surrounding the right macula was apparent after 1 month of observation (Figures 3 and 4). The patient’s general fever subsequently abated, however, and the macular star was slowly reabsorbed, resulting in an improvement in her visual acuity. She gave birth 7 weeks after her initial visit (42 weeks of pregnancy) to a baby showing no congenital anomalies, and no infectious complications were apparent for the mother or baby.

Six months after the initial visit, the patient tested negative for both *B. henselae* YH-01–specific IgM and IgG. A clinical examination showed improved visual acuity (20/40), although a few precipitates of macular exudate remained (Figures 5 and 6). The left eye continued to show no sign of infection or visual loss.

**Discussion**

We here describe the first diagnosis of CSD with an IFA assay for IgM titer based on the YH-01 strain of *B. henselae*. Strains of this bacterium are classified on the basis of 16S rRNA genotype as either 16S Type I/Houston-1 or 16S Type II/Marseille.7 Both genotypes are widely distributed, with 16S Type I being more common in Asia including Japan. On the other hand, multispacer typing (MST), a nucleotide sequencing–based genotyping method, has resulted in the classification of *B. henselae* into Clusters 1 to 4,8 with Houston-1 being in MST Cluster 2 and Marseille in MST Cluster 3. Most infected cats in Japan harbor *B. henselae* 16S Type I in their blood.9 Measurement of *B. henselae*–specific IgG or IgM by IFA tests in Japanese hospitals is thus usually performed with the Houston-1 strain only. Recent studies revealed that all *B. henselae* strains iso-
Current IFA serodiagnosis kits for CSD are often based on both Houston-1 and Marseille strains, which differ in both 16S rRNA genotype and MST cluster, to increase sensitivity. We suggest that such tests based on the YH-01 or combination of YH-01 and Houston-1 strains may be more appropriate for use in Japan, even in ophthalmologic field.

**Key words:** cat scratch disease, *Bartonella henselae*, IFA, Houston-1, YH-01.

**References**