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Short survey

Feline bartonellosis and cat scratch disease

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Abstract

Bartonella species are important emerging zoonotic pathogens. Transmission of these organisms in nature may be much more complex than is currently appreciated. Cats can be infected with five *Bartonella* species, including, *Bartonella henselae*, *Bartonella clarridgeae*, *Bartonella bovis*, *Bartonella koehlerae* and *Bartonella quintana*. In addition to cats, numerous domestic and wild animals, including bovine, canine, human, and rodent species can serve as chronically infected reservoir hosts for various intra-erythrocytic *Bartonella* species. In addition, an increasing number of arthropod vectors, including biting flies, fleas, keds, lice, sandflys and potentially ticks have been implicated in the transmission of various *Bartonella* species to animals or human beings. In the reservoir host, *Bartonella* species cause chronic intra-erythrocytic and vascular endothelial infections, with a relapsing bacteremia documented in experimentally infected cats. Although the immunopathology induced by *Bartonella* infection requires additional study, the organisms can localize to the heart valve (endocarditis), cause granulomatous inflammation in lymph nodes, liver or spleen, induce central nervous system dysfunction with or without cerebrospinal fluid changes, and may contribute to inflammatory polyarthritis. Hematological abnormalities are infrequent, but thrombocytopenia, lymphocytosis, neutropenia, and eosinophilia have been reported in *B. henselae*-infected cats. Serology, PCR and culture can be used to support a diagnosis of feline bartonellosis, however, due to the high rate of sub-clinical infections among various cat populations, documenting causation in an individual cat is difficult, if not impossible. Response to treatment can be used in conjunction with serology or organism isolation to support a clinical diagnosis of feline bartonellosis. As fleas are involved in the transmission among cats, the use of acaracide products to eliminate fleas from the environment is of critical importance to decrease the risk of *B. henselae* transmission among cats and to humans.

Keywords: Cat; Bartonella; Cat scratch disease; Epidemiology

The genus *Bartonella* is currently comprised of at least 20 species and subspecies of vector-transmitted, fastidious, gram-negative bacteria that are highly adapted to one or more mammalian reservoir hosts (Boulouis et al., 2005). *Bartonella henselae* and *Bartonella clarridgeae* have evolved to cause persistent intravascular infection in domestic cats and wild felid species, while *Bartonella vinsonii* subspecies *berkhoffii* has evolved to cause persistent intravascular infection in dogs and wild canines, including coyotes and foxes (Breitschwerdt and Kordick, 2000). Other *Bartonella* species have evolved to cause persistent blood borne infection in rodents, small mammals, or ruminants.

Epidemiological evidence and transmission studies support an important role for fleas in the transmission of *B. henselae* and *B. clarridgeae* among cats (Chomel et al., 1996). Three other *Bartonella* species, *B. koehlarae*, *B. bovis* and *B. quintana* have been isolated from cat blood, but the modes of transmission and the reservoir potential of these species in felids have not been

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definitively established (Boulouis et al., 2005; Droz et al., 1999). Although there is clinical and epidemiological evidence to support tick transmission of *B. vinsonii* subspecies *berkhoffii* to dogs and coyotes, the mode of transmission of any *Bartonella* species to canines has not been proven through controlled experimental vector transmission studies (Chang et al., 2001).

Numerous domestic and wild animals, including bovine, canine, feline, human, and rodent species can serve as chronically infected reservoir hosts for various *Bartonella* species (Kordick and Breitschwerdt, 1998). An increasing number of arthropod vectors, including biting flies, fleas, keds, lice, sandflies, and ticks have been implicated in the transmission of *Bartonella* species (Halos et al., 2004). Considering the diversity of *Bartonella* species and subspecies, the large number of reservoir hosts, and the spectrum of arthropod vectors, the clinical and diagnostic challenges posed by *Bartonella* transmission in nature may be much more complex than is currently appreciated in human and veterinary medicine (Jacomo et al., 2002).

Once an animal is infected by a bite, a scratch, or arthropod transmission, *Bartonella* species localize to erythrocytes and endothelial cells, which facilitates a potentially unique strategy for bacterial persistence within the blood stream of reservoir or non-reservoir species. *In vitro* infection of human CD34 +progenitor cells with *B. henselae* suggests that these bacteria are capable of infecting bone marrow progenitor cells, which may contribute to ongoing erythrocytic infection (Mandle et al., 2005). Infection of bone marrow progenitor cells followed by non-hemolytic intracellular colonization of erythrocytes would preserve *Bartonella* organisms for efficient vector transmission, protect *Bartonella* from the host immune response, facilitate widespread vascular dispersion throughout the tissues of the body, and potentially contribute to decreased antimicrobial efficacy (Dehio, 2001; Rolain et al., 2001, 2002).

1. Feline bartonellosis

B. henselae bacteremia can be documented in 25–41% of healthy cats in different regions throughout the world (Jameson et al., 1995; Maruyama et al., 2001). Self-limiting febrile illness of 48–72 h duration, mild to moderate transient anemia, and transient neurologic dysfunction were reported in cats experimentally infected with *B. henselae* by blood transfusion (Kordick et al., 1999). Self-limiting fever can also occur in *B. henselae* bacteremic cats following minor surgical procedures. Although unproven, it is likely that stress, such as surgery or trauma, can induce transient disease manifestations in cats, including self-limiting fever, mild anemia and neurological dysfunction. Due to the high percentage of chronically bacteremic healthy cats in the United States (Jameson et al., 1995; Pedersen and Koehler, 1995), establishing a cause and effect relationship between disease manifestations and bacteremia in cats will require large epidemiological studies in *Bartonella* endemic regions. Several recent epidemiologic studies suggest that fever, lymphadenopathy, stomatitis and gingivitis are significantly associated with seroreactivity to *B. henselae* antigens (Breitschwerdt and Kordick, 2000). Immunosupression associated with FeLV or FIV appears to increase the pathogenicity of *B. henselae* infection in cats. In experimentally infected cats, fever, lymphadenopathy, mild neurological signs and reproductive disorders have been reported. In experimentally infected cats, gross necropsy results are unremarkable; however, histopathological lesions can include peripheral lymph node hyperplasia, splenic follicular hyperplasia, lymphocytic cholangitis/pericholangitis, lymphocytic hepatitis, lymphoplasmacytic myocarditis, and interstitial lymphocytic nephritis (Kordick et al., 1999). These findings would indicate that antibiotic treatment should be considered in seroreactive or bacteremic cats with these disease manifestations.

The diagnosis of *Bartonella* infection should be confirmed by culturing the organism from blood or tissues such as lymph node or heart valve (endocarditis) or by amplifying *Bartonella*-specific DNA sequences from tissues using PCR (Clarridge et al., 1995). *B. henselae*, *B. quintana* and *B. bacilliformis* can be visualized within erythrocytes using confocal or electron microscopy. Cell lysis, using a commercially available lysis centrifugation technique or by freezing the blood sample prior to plating, facilitates bacterial isolation from blood. Although organisms within the genus *Bartonella* are fastidious and slow-growing, they can be cultured successfully with agar plates containing 5% defibrinated rabbit or sheep blood, that are maintained at 35 °C in a high humidity chamber with a 5% CO_2 concentration. In our experience, bacterial colonies may not be visible until 10–56 days after inoculation of the agar plate. As cats maintain a higher level of bacteremia, culturing *B. henselae* or *B. clarridgeiae* from aseptically obtained blood samples is much more likely to be successful than culturing *B. henselae* from a dog or human blood sample. The recent introduction of a liquid growth medium (*Bartonella* alpha *Proteobacteria* growth medium) has facilitated the successful isolation of *B. henselae* from dog and