

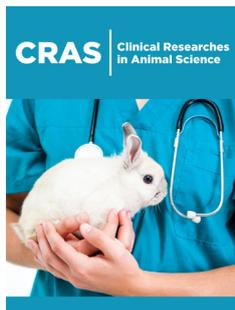
Cat Scratch Disease: Literature Review

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Abstract

Cat scratch disease is a zoonosis transmitted by the bite or scratch of the domestic cat (*Felis catus*). The disease is most commonly caused by the bacterium *Bartonella henselae*, which is transmitted to animals by fleas (*Ctenocephalides felis*). In cats, the disease has low pathogenicity. In humans, the infection may have a benign course or evolve to a systemic form and be lethal, especially in immunocompromised patients. The treatment of cats mainly includes vector control with the aim of preventing the transmission of the disease to humans.

Keywords: *Bartonella spp.*; Feline; Zoonosis; Prevention

Literature Review

The cat scratch disease, also known as bartonellosis or benign lymphoreticulosis, is caused by small gram-negative and hemotropic bacilli, belonging to the order Rickettsiales, family Bartonellaceae and genus *Bartonella sp.* *Bartonella henselae* is the most known species, but *B. quintana*, *B. clarridgeiae*, *B. koehlerae*, *B. elizabethae*, *B. rochalimae*, *B. vinsonii*, and *B. berkhoffii* have also been identified [1,2]. All of these species have been associated with the disease in cats (*Felis catus*) and have zoonotic potential [3].

The members of the genus *Bartonella spp.* are facultative intracellular bacteria and are adapted to a wide range of mammalian hosts [4]. Each species seems to have evolved with a specific primary host, which has become a source of infection for accidental hosts in natural exposure conditions [1]. The distribution of this bacterium is wide, occurring mainly in hot and humid regions [5].

The main clinical syndromes associated with infection by *Bartonella spp.* in humans include Cat scratch disease (*Bartonella henselae*), Bacillary angiomatosis, Liver peliosis (*B. henselae*, *B. quintana*), Endocarditis (*B. henselae*, *B. quintana*, *B. vinsonii*, *B. alsatica* and *B. rochalimae*), Carrion's disease (*B. bacilliformis*), Trench fever (*B. quintana*), Retinitis (*B. henselae*, *B. grahamii*), Myocarditis (*B. washoensis*), and Splenitis (*B. rochalimae*) [6]. Although in some cases the infection has a benign course, some of these diseases can be lethal, especially in immunocompromised patients [7]. In general, bartonellosis, with the exception of Carrion's disease (*B. bacilliformis*), are self-limiting zoonosis. Due to the non-specific clinical picture, can be considered as differential diagnoses, different infectious, lymphoproliferative or autoimmune diseases Cabral [8].

Bartonellosis caused by *B. henselae* can affect animals, with humans being accidental hosts [5]. The disease is characterized as subacute and is transmitted by direct inoculation of the bacteria through scratching, biting, or contact with the saliva of healthy carrier cats of *B. henselae*, affecting mainly children and young people [9]. The domestic cat is a reservoir of *B. henselae* [10]. According to [11], epidemiological studies have shown worldwide distribution of the infection in these animals, in which the transmission of bacteria between cats occurs through fleas [12,13]. Fleas (*Ctenocephalides felis*) are described as vectors of *B. henselae*,

acquiring the bacteria during the blood meal in infected animals. The bacteria remain and replicate in the intestine of fleas [14] and are eliminated viable in the feces, contaminating the feline digits, nails, and teeth [12].

It is a consensus that transmission among cats occurs only in the presence of the vector [15]. The range of vectors involved in the transmission of the disease to other mammals has not yet been fully clarified [12,16]. However, it is mentioned that lice, flies, mosquitoes and ticks can transmit the agent [7], since the intra-erythrocyte location of bacteria in the hosts would increase the possibility of being captured by hematophagous arthropods [17]. Moreover, it allows a prolonged bacteremia without resulting in disease, which is an adaptive strategy of persistence of the bacteria in the host [14,15].

Cat scratch disease has a high prevalence and low pathogenicity in cats, making it difficult to report specific signs of infection [18]. In addition, although *Bartonella spp.* is common in felines, its relationship with the pathogenesis of other diseases in the species is also unclear [19]. It is known that stressful conditions, such as malnutrition, overpopulated environments with inadequate hygiene, absence of vaccination and co-infections by the Feline Immunodeficiency Virus (FIV) disease, Feline Leukemia Virus (FeLV) infection Or Feline Infectious Peritonitis (PIF), make animals immunosuppressed and increase the pathogenicity of the infection [17,20]. Thus, cats with *B. henselae* may be asymptomatic or present clinical signs, such as fever, lethargy, anorexia, regional lymphadenopathy and myocarditis [17], neurological signs and reproductive disorders [14]. Regarding alterations in laboratory exams, the occurrence of eosinophilia in cat's positive for different species of *Bartonella spp.* has been described [2].

In humans, infections by *Bartonella spp.* may not result in clinical manifestations. When they do occur, the signs depend on the strain virulence that is causing the infection and, on the host, immunocompetence, which may have severe systemic disease, especially when it has other concomitant diseases and is under conditions that favor immunosuppression, such as malnutrition [21,3]. After 3 to 10 days of inoculation of the bacteria by the cat, approximately 60 to 80% of people develop an erythematous papule on the spot in the scratch or bite. The erythematous papule evolves to a vesicopustular lesion [22, 21], which is the most common manifestation of the disease [23].

Once the bacterium invades red blood cells, leading to hemolysis, persistent bacteremia occurs, which can induce proliferation of endothelial cells in blood vessels and granulomatous and suppurative inflammatory response in immunocompetent patients or Vaso-proliferative response in immunosuppressed patients [24]. In some cases, lymphadenopathy can occur from 7 to 12 days after the occurrence of the bite or scratch, mainly on the head, cervical region, and upper limbs. Lymphadenopathy is the most important clinical sign of the disease and leads the patient to seek medical attention [5]. Lymphadenopathy can lead to the occurrence of

fever, affecting approximately 50% of patients [18]. In addition, headache, anorexia, weight loss, nausea, vomiting, sore throat, and splenomegaly may also occur (REGNERY and TAPPERO, 1995). Atypical manifestations like ocular, hepatosplenic and neurologic clinical signs are also reported and can be develop in 5 to 20% of patients with increased risk for hospitalization [25]. Among the ocular signs there is the Parinaud's Syndrome, characterized by conjunctival granuloma at the inoculation site and preauricular lymphadenopathy [23].

The occurrence of the systemic presentation of the disease is more severe and more likely to affect immunosuppressed patients and possibly arises from an immune-mediated response [18,26], affecting about 2% of patients and leading to signs of sudden change in mental status, seizures, myelitis, radiculitis, polyneuritis, paraplegia, neuro-retinitis and cerebral arteritis [23].

The diagnosis of bartonellosis is a challenge, both in cats and in humans, and it is based on epidemiological data, clinical signs, serology, molecular exams, and culture of lymph nodes aspirate or regions with suppuration [27,28]. Serological IgM and IgG dosages showed low sensitivity with high specificity using Indirect Immunofluorescence (IFA) and Enzyme-Linked Immunosorbent Assay (ELISA). PCR test presented 100% and 93% of sensitivity and specificity, respectively [29]. Although, as it is a condition with nonspecific clinical signs, it is probably underdiagnosed [30].

In infected cats, treatment includes control of ectoparasites in order to reduce the risk of disease transmission. Even though antibiotic therapy is indicated in animals with clinical manifestation of the disease and a confirmed diagnosis, a standardized therapeutic protocol is not described [21]. However, some recommendations are advised, with the main objective of reducing the risks of antimicrobial resistance, such as not treating healthy animals and keeping sick animals under treatment for at least 4 to 6 weeks [31]. Furthermore, macrolides are not indicated as the first choice of treatment because, although effective, it is known that strains of *B. henselae* develop rapid resistance to this class of drugs [3].

In human cases, there is also no therapeutic consensus regarding the need to use antibiotics, which is restricted to systemic presentations of the disease, with visceral, bone, ocular or central nervous system involvement [27]. When necessary, the drugs of choice are macrolides such as azithromycin and erythromycin. Other drugs like doxycycline, rifampicin, trimethoprim-sulfamethoxazole, and quinolones may also be used [29,32,33].

Conclusion

Vaccines against infections caused by *Bartonella spp.* are not available. The most effective way to prevent the disease is through the control of ectoparasites, in addition to avoiding playing with animals aggressively, especially if there are previous skin injuries. Regular evaluation of pet cats is also indicated, and in cases of accidents due to bites or scratches, immediate washing of the area and medical attention is recommended.

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