

Cat-Scratch Disease—A New Tick-Borne Disease?

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ABSTRACT

A broad outline of the different *Bartonella* species is presented. The epidemiology, pathology, and clinical presentation of *Bartonella henselae* is covered. Co-infection rates of 327 patients tested for tick-borne illnesses revealed that more patients were positive for *Bartonella henselae* (92/327) than for *B burgdorferi* (64/327); 22 patients were positive for

both. This correlates with the infection rates found in ticks analyzed in 2001. Of those patients with positive *Bartonella* polymerase chain reaction, 83% had positive antibodies. A patient with both *Bartonella* and Lyme disease is presented. This patient developed a sarcoid-like presentation as a complication of her infection.

Key words: *Bartonella*, tick-borne infections, sarcoid

INTRODUCTION

Cat-scratch disease, caused by the bacterial organism *Bartonella*, has been recognized since 1950. It was always thought to be transmitted by a cat scratch, a puncture wound, a previous break in the skin or, rarely, the bite of a cat or other animal. It was postulated in several articles, though, that it can be transmitted by an insect vector. It was in the 1990s that the organism responsible for this disease was identified as *Bartonella henselae*.

A recent article published by Eskow and Mordecai¹ demonstrates the coexistence of both Lyme disease and *Bartonella* in several cases. This has raised the possibility that *Bartonella* is yet another infection that can be transmitted by deer ticks.

Other species of *Bartonella* are responsible for several other vector-borne infectious diseases, namely:

- Carrion's disease: *Bartonella baccilliformis* transmitted by sand flies.
- Trench fever: *Bartonella quintana* transmitted by human lice.
- Several new species identified in animals, mites, and ticks.

Epidemiology

The epidemiology of cat-scratch disease is interesting because 72% of cases in the United States were seen between June and December. This seasonality would not be explained if the disease were transmitted only by cat scratches alone.

Over the past 1 to 2 years, several studies have been published wherein the relationship between *B henselae* and tick-borne illnesses has been studied. In July 1999, a study of deer ticks conducted in the Netherlands found polymerase chain reaction (PCR) evidence of *Bartonella* in 70% of ticks tested compared with a 45% positivity for *Ehrlichia* and a 13% positivity for *Borrelia*.² A subsequent study performed in the United States on deer ticks in California demonstrated an infection rate of 19%.³ This organism has been isolated from a wide range of mammals, many of which also carry *Borrelia*, *Ehrlichia*, and *Babesia*. A study in the midwestern United States revealed that the white footed mouse, a common reservoir of Lyme disease, was 46% positive for *B burgdorferi* by culture, 12% positive for *Babesia* by PCR, 5 to 10% positive for *Bartonella* by culture.⁴ In an ongoing study in New Jersey, we currently estimate that 20% of deer ticks are positive by PCR (unpublished).⁵

Prevalence statistics of *Bartonella* in cats specifically are: California, 85.7%; North Carolina, 89.5%; and Hawaii, 42.3%.⁶ Although transmission of this disease by

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Table 1. Analysis of 327 patients tested by polymerase chain reaction (PCR) for Bartonella species.

Total Patients	327
Positive Bartonella PCR	92
Positive Lyme and Bartonella PCR	22
Positive Lyme PCR	64

ticks has not been conclusively established, we know that it is transmitted in the feline population by fleas.⁷

MATERIALS AND METHODS

Data on the clinical presentation of cat-scratch disease consists of one large review of cases published by Carithers in 1985⁸ and numerous case reports found in ophthalmology, neurology, infectious disease, and rheumatology literature. The initial rash in the classic description of cat-scratch disease is described as a papule that progresses through a vesicular, crusty stage (resembling the lesions seen in chickenpox) over a period of several days. Within 1 to 2 weeks, regional lymphadenopathy appears. In 75% of cases, the illness is mild and self-limiting. Biopsies of lymph nodes reveal pathology often indistinguishable from sarcoidosis. There also are reports of biopsies strongly suggestive of lymphoma. Atypical or unusual manifestations reported in the literature include:

- Oculoglandular syndrome: preauricular adenopathy and conjunctivitis associated rarely with suppurative lymph nodes.
- Encephalopathy occurring 1 to 6 weeks after the initial infection.⁸⁻¹¹ Ten percent overall had some residual neurologic deficits. The cause has been postulated to be both infectious¹² and vasculitis, as seen in several reports demonstrating beading of the cerebral arteries.¹³
- Myelitis including 1 case of transverse myelitis.¹⁴
- Pradiculitis.
- Sarcoid-like presentation.
- Osteolytic lesions.
- Erythema nodosum (notably associated with sarcoidosis).
- Ophthalmologic manifestations: peripapillary angioma, branch retinal artery occlusion with vision loss,¹⁵ Bartonella neuroretinitis.¹⁶
- Arthritis.¹⁷
- Chronic demyelinating polyneuropathy.¹⁸

Analysis of 327 Patients Tested for Tick-borne Infections

Table 1 demonstrates that of the 327 patients tested for tick-borne infections, 92 tested positive by PCR for Bartonella species. This number exceeds those who tested positive for *B burgdorferi* (64). Additionally, 22 patients

Table 2. Polymerase chain reaction (PCR) sensitivity.

	+PCR	-PCR
+AB	48 (83%)	62 (76%)
-AB	10 (17%)	19 (24%)

tested positive for both infections. These data are similar to studies done in ticks in 2001, wherein a higher percentage of ticks tested positive for Bartonella, than for *B burgdorferi* (unpublished).

Table 2 illustrates the sensitivity and specificity of antibody production in patients with a positive PCR. Of those patients with a positive PCR for Bartonella, 83% had positive antibodies. Of those with negative PCRs, however, 76% also had positive antibodies. The presence of antibodies cannot, therefore, be used as the sole criterion for establishing a clinical diagnosis. While the sensitivity is 83%, the specificity is only 24%. Of 3 patients who underwent a spinal tap, 3/3 had a positive PCR for Bartonella. One of these 3 also had a positive PCR for *B burgdorferi*.

CASE REPORT

A 30-year-old female was diagnosed by a dermatologist as having erythema migrans rash. She was placed on oral doxycycline. Within a week, the rash became vesicular and crusty and antiviral medication was added. Within 2 weeks, the patient had progressive loss of balance, bilateral symmetrical leg weakness, loss of bladder control, headaches, and neck stiffness. A MRI revealed enhancing lesions in the thoracic and cervical spinal cord. The brain was normal. Both blood and cerebral spinal fluid were positive for Bartonella PCR. Subsequent serologies for *Bartonella henselae* were strongly positive. The patient has had a protracted course with an initial response to 3 months of intravenous antibiotics. This was followed by a relapse in which she developed total paralysis of both legs, traverse myelitis, and hilar lymphadenopathy. Hilar node biopsy was consistent with sarcoidosis. Protracted treatment with a combination of steroids and intermittent antibiotics has resulted in substantial improvement. The patient does have residual weakness and is currently experiencing some relapsing symptoms associated with another positive Bartonella PCR (which had become negative after treatment).

Other Bartonella Infections

The most comprehensive review of Carrion's disease was recently reported by Maguina et al¹⁹ based upon a review of 145 patients from Peru. The organism responsi-

ble for this illness is *Bartonella bacilliformis*. In this disease, cases are separated by clinical criteria into two groups: hematic phase (47%) and eruptive (verruca) phase (53%).

The hematic phase is usually associated with fever, lymphadenopathy, and hepatomegaly (with abnormal liver enzymes). Of these patients, 17% had ophthalmological findings including flame-shaped hemorrhages, cotton wool exudates, and papilledema. Twenty-six percent had central nervous system symptoms and/or findings. In 30%, cardiomegaly was present on a chest roentgenograph. Intraerythrocytic organisms were present in 100% of patients, visible on a blood smear stained with Giemsa. Only 71% grew positive cultures and the average time to yield a positive culture was 18 days. Most patients were anemic with an elevated bilirubin. The death rate in this group was 9%.

The eruptive phase is generally benign and usually associated with skin lesions, most commonly miliary lesions on the lower extremities.

CONCLUSION

Bartonella is an emerging infectious disease that is carried by deer ticks, isolated in animal reservoirs known to also be reservoirs for Lyme disease, and is being found in association with *B Burgdorferi* in patients. It is being isolated from a substantial number of deer ticks in New Jersey, and has been tested in several patients this year in whom both the infecting tick and the patient had positive PCRs.

It would be advisable to consider this infection in the same light as the other more recently discovered infections transmitted by the bite of deer ticks, even in the absence of conclusive proof that it is transmitted by tick bites. Further studies should be performed in laboratory animals to gain better knowledge of this issue.

The relevance of testing for this infection would lie in the different treatment approaches. Some of the first line choices of antibiotics for the treatment of Lyme disease would not be the first choice in *Bartonella*.

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