Inoculation Bartonellosis in an Adult: A Case Report

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Cat-scratch disease (CSD) and bacillary angiomatosis (BA) are caused by a gram-negative bacilli classified under the genus Bartonella *(formerly* Rochalimaea*). Patient history, symptoms, and histopathology often fall along a continuum; therefore, both conditions should be considered in the differential diagnosis.*

We report a case of an 83-year-old immunocompetent woman who presented with a pyogenic granuloma–like lesion on her dorsal left wrist. The histologic differential diagnosis included an inoculation site from a cat scratch infected with Bartonella *and BA. Because the patient had only 1 lesion at the site of a prior cat scratch, the lesion was diagnosed as inoculation bartonellosis. We also review the epidemiologic, clinical, and histopathologic features of CSD and BA.*

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Currently there are at least 24 species or subspecies in the genus *Bartonella* (formerly *Rochalimaea*) and approximately half are pathogenic to humans.[1-3] One of the more common infections caused by *Bartonella*, specifically *Bartonella henselae*, is cat-scratch disease (CSD).[4] This organism also is responsible for approximately half the cases of bacillary angiomatosis (BA), with the other half caused by *Bartonella quintana*. Moreover, *B quintana* has been implicated as the causative organism for trench fever. In addition, depending upon the immune status of the individual, *B henselae* and *B quintana* also can cause bacillary peliosis hepatis, persistent or relapsing bacteremia, and endocarditis.[4] *Bartonella bacilliformis* is another species of *Bartonella*, but it is primarily restricted to South America and causes bartonellosis (also known as Carrión disease). *Bartonella elizabethae* and *Bartonella clarridgeiae* have been associated with several human infections; however, only isolated reports exist.[1-4] Table 1 summarizes the major *Bartonella* infections in humans.[1-7]

We report a case of an 83-year-old immunocompetent woman who presented with a pyogenic granuloma–like lesion on her dorsal left wrist. Histologically, the lesion consisted of a lobular proliferation of small blood vessels, some with plump reactive endothelial cells, admixed with inflammatory cells. A Warthin-Starry silver stain demonstrated clumps of rod-shaped organisms with a classic Chinese letter configuration consistent with a diagnosis of BA.

Case Report

An 83-year-old immunocompetent woman presented to the dermatology department upon referral from her primary care physician with an asymptomatic, red, blisterlike lesion on her wrist of 5 days' duration that was concerning for nonmelanoma skin cancer. The lesion gradually increased in size, and although the patient denied any specific trauma to the area, she reported a history of cat exposure and prior scratches. Physical examination revealed a 1-cm, pearly, erythematous, firm, nontender nodule on her dorsal left wrist with a collarette of scale (Figure 1). There were no other cutaneous lesions or evidence of lymphadenopathy.

Histologic evaluation of a shave biopsy specimen revealed a lobular proliferation of small blood vessels with plump reactive endothelial cells. Admixed among the vascular proliferation were inflammatory cells consisting of lymphocytes and histiocytes with rare neutrophils (Figure 2). Warthin-Starry silver stain revealed clumps of organisms that showed a classic configuration with the bacilli arranged in a Chinese letter–like

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Table 1.

Major Differentiating Features of *Bartonella* Infections in Humans

Disease	Species	Vector	Clinical Presentation
Cat-scratch disease	*Bartonella henselae*	Domesticated cat scratches or bites, or cat fleas *(Ctenocephalides felis)*	Classically seen in immunocompetent patients, with disseminated disease seen in immunocompromised patients; regional lymphadenopathy +/− mild fever and erythematous nodule at inoculation site
Parinaud oculoglandular syndrome	*B henselae*	Domesticated cat scratches or bites, or cat fleas *(C felis)*	Most common in immunocompetent patients; unilateral conjunctival granuloma with preauricular lymphadenopathy
Bacillary angiomatosis	*B henselae, Bartonella quintana*	Domesticated cat scratches or bites, cat fleas *(C felis)*, and human body louse *(Pediculus humanus* var *corporis)*	Typically seen in immunocompromised patients; erythematous papules and nodules; frequently regional lymphadenopathy, fever, chills, malaise, headache; can have disseminated disease
Bartonellosis Acute phase: Oroya fever or Carrión disease Chronic phase: verruca peruana	*Bartonella bacilliformis*	Sandfly *(Phlebotomus verrucarum)*	Found only in Andes Mountains in Peru, Ecuador, and southwestern Colombia at elevations 800–2500 m Acute phase: high fever, chills, myalgia, nausea, headache, hemolytic anemia, thrombocytopenia; fatality rate, 40%–90% Chronic phase: rapidly enlarging, reddish purple nodules and papules that are friable; can be associated with necrosis of liver and spleen
Trench fever	*B quintana*	Human body louse *(P humanus* var *corporis)*	Typically seen in epidemics; prolonged or recurrent fever, chills, myalgia, headache, eye pain, bone pain notably in tibia, brief maculopapular eruption
Bacillary peliosis hepatis	*B henselae, B quintana*	Same as bacillary angiomatosis	Occurs primarily in immunocompromised patients; fever, abdominal pain, hepatosplenomegaly
Persistent or relapsing bacteremia	*B henselae, B quintana*	Same as bacillary angiomatosis	Occurs in both immunocompetent and immunocompromised patients; prolonged fever, malaise, anorexia, weight loss and headache, leg pain, thrombocytopenia
Endocarditis	*B henselae, B quintana, Bartonella elizabethae*	Same as bacillary angiomatosis	Occurs in both immunocompetent and immunocompromised patients; fever, cardiac murmur, dyspnea, bibasilar lung rales, embolic phenomena

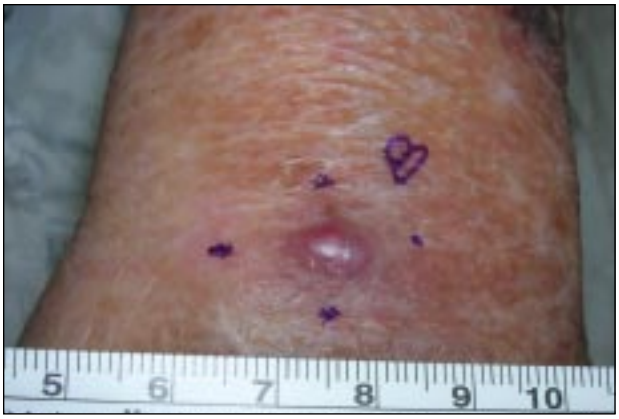

Figure 1. Pearly erythematous nodule on the dorsal wrist.

formation (Figure 3). The histologic differential diagnosis included inoculation bartonellosis and BA. Because the patient had localized disease restricted to the site of a prior cat scratch, the lesion was diagnosed as inoculation bartonellosis.

Following a 10-day course of erythromycin, complete resolution of the lesion was noted. The site was completely healed at the 6-month follow-up visit.

Comment

The clinicopathologic and microbiologic spectrum of skin disease due to *Bartonella* species has been well-defined over the past 2 decades.[5-13] In 1988, the Armed Forces Institute of Pathology announced that they identified a novel bacterial agent in the lymph node of a patient with CSD and named the organism *Afipia felis*.[10] However, other laboratories were able to recover additional isolates. Subsequently, a similar gram-negative organism was identified in BA, and at the time, it was hypothesized that BA might represent a disseminated form of CSD in immunocompromised patients.[11] Later, DNA extracted from BA lesions were amplified utilizing polymerase chain reaction and showed that the organisms identified were related to bacteria in the *Rochalimaea* genus. However, ensuing genotype evaluation showed that the organisms were more closely related to the *Bartonella* genus, thus the change in nomenclature.[9] As serologic testing became more widely available, multiple studies have confirmed that 81% to 100% of patients with suspected classic CSD are seropositive for *B henselae*.[4,12] The causative agents for BA have been identified to be *B henselae* and *B quintana*, with approximately equal frequency.[13]

It is unknown why some patients develop BA rather than CSD following a cat scratch, but it is hypothesized that it is due to differences in host immunity.[14] Originally, a cat scratch or bite was thought to precede BA in only 20% of cases compared to 90% of cases of classic CSD[15]; however, a more recent case-controlled study found that of a long list of environmental agents, only a cat scratch or bite was strongly associated with BA.[4] Cat-scratch disease and BA have several features in common. Each has the same causative agent (*B henselae*), a recent history of cat exposure, large numbers of organisms in lesions demonstrated by Warthin-Starry silver staining, and electron microscopy showing similar bacilli, yet they differ in clinical and histologic presentation.

Cat-scratch disease is a benign self-limited condition characterized by painful regional lymphadenopathy at the site of a cat scratch, most commonly from a kitten.[16] Most cases occur in immunocompetent patients within the first 2 decades of life.[5] Typically, 25% to 60% of patients will report a

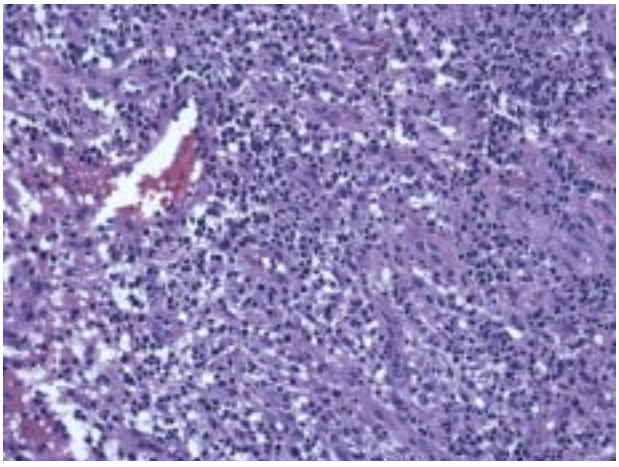

Figure 2. Lobular proliferation of small blood vessels admixed with inflammatory cells (H&E, original magnification ×20).

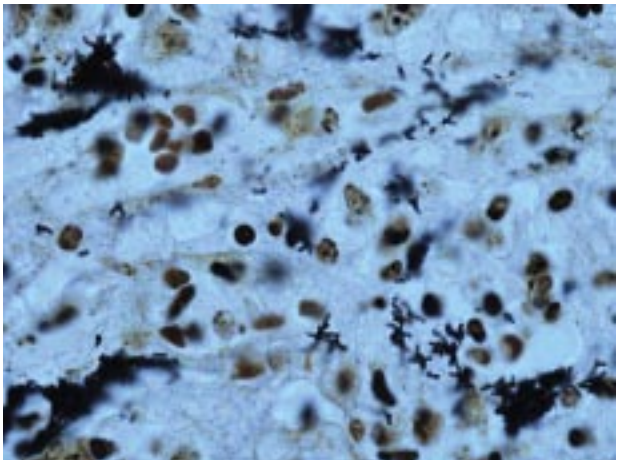

Figure 3. Clumps of organisms with a classic Chinese letter configuration (Warthin-Starry silver, original magnification ×100).

Table 2.

Differential Diagnosis of Chronic Lymphadenopathy

Infectious Disease	Neoplastic Disease	Other
AIDS	Leukemia	Benign sinus histiocytosis
Bartonellosis	Lymphoma	Chronic pseudolymphomatous lymphadenopathy
Coccidioidomycosis	Metastatic disease	Connective tissue diseases
Cryptococcosis		Hemopoietic disease
Cytomegalovirus or infectious mononucleosis		Kikuchi disease
Histoplasmosis		Sarcoidosis
Lymphogranuloma venereum		
Sporotrichosis		
Tuberculosis		
Tularemia		
Typical or atypical *Mycobacterium* infections		

primary inoculation lesion, which is usually a red-brown, nontender papule that presents 3 to 10 days after being scratched.[9] Over the next few weeks, the patient develops regional lymphadenopathy with at least 1 enlarged tender lymph node. Late in the course, approximately 10% of patients will develop overlying erythema and fluctuation resulting in a suppurative lymph node.[4] Although many patients appear well, only exhibiting lymphadenopathy, approximately 50% of patients have constitutional symptoms such as low-grade fever and malaise. Other findings include headache, anorexia, weight loss, nausea, vomiting, sore throat, and splenomegaly.[4,9] If a biopsy is performed, it typically shows classic stellate necrosis within the lymph node, with central necrosis surrounded by a suppurative granulomatous reaction. The histologic findings at the inoculation site of CSD differ from those found in the lymph node. They more closely resemble the cutaneous lesions of BA.

Traditionally, the diagnosis of CSD requires the presence of 3 of 4 criteria: (1) history of contact with a cat, (2) a positive skin test for *B henselae*, (3) negative studies for other causes of lymphadenopathy, and (4) characteristic histopathologic findings.[5] However, because skin testing and lymph node biopsy are no longer routinely performed due to increased morbidity, suspected cases typically undergo serologic evaluation to determine the presence of antibodies. When evaluating a suspected case of CSD, other causes of chronic lymphadenopathy must be considered in the differential diagnosis, including multiple infectious causes as well as neoplastic disease (Table 2).[12,17] These entities can be differentiated by clinical presentation, histologic features, and special stains, along with polymerase chain reaction, immunofluorescence, and/or enzyme-linked immunosorbent assay testing.

Lymphadenopathy usually lasts weeks to months and tends to be benign, following a self-limiting course without the need for antibiotics. Immunocompromised patients, such as those with AIDS, can develop severe systemic symptoms due to disseminated disease. In these cases, antibiotics may be needed.

Bacillary angiomatosis, on the other hand, is a systemic disease that can present in any age group. Although it primarily occurs in immunocompromised patients, most commonly those with human immunodeficiency virus (HIV) and a low CD4 lymphocyte

Table 3.

Clinical and/or Histologic Differential Diagnosis of Cutaneous Lesions of Bacillary Angiomatosis

Amelanotic melanocytic lesions (Spitz nevus, nodular melanoma)
Angiokeratoma
Basal cell carcinoma
Cherry hemangioma
Dermatofibroma
Epithelioid hemangioma
Hemangioma
Kaposi sarcoma
Pyogenic granuloma
Squamous cell carcinoma

count, there have been several case reports of BA occurring in immunocompetent patients.[7] At least 3 to 4 different clinical presentations have been described for BA.[4,18] The most common presentation is an erythematous papule or nodule often surrounded by a collarette of scale, thereby having a similar appearance to pyogenic granuloma. Other lesions that can occur include those resembling Kaposi sarcoma as well as less distinctive lesions that appear as lichenoid, violaceous, indurated plaques.[18] There are subcutaneous lesions that present as flesh-colored nodules up to several centimeters in diameter that may erode onto the skin surface. Regardless of the morphology, the host immune status will influence the number and distribution of lesions.[19] Immunocompetent hosts may have only a single lesion, whereas immunocompromised patients may have hundreds.

A diagnosis of BA is most often made by an assessment of the clinical features coupled with a biopsy. The biopsies may exhibit some or all of the following distinct histologic features. Classically the lesion consists of a dome-shaped papule with an epithelial collarette within which is a lobular proliferation of small blood vessels lined by large epithelioid endothelial cells, edematous stroma, scattered neutrophils, and nuclear debris. Admixed within the areas of inflammation is a purple haze, which consists of clumps of bacteria that is best appreciated with the use of a Warthin-Starry silver stain.[20] In addition to a biopsy, blood cultures should be obtained and incubated for a prolonged period of time to evaluate for bacteremia. Suspected cases of BA with extracutaneous involvement should undergo appropriate laboratory evaluation and radiologic imaging.

Treatment with erythromycin is highly effective in most cases of cutaneous BA; however, if left untreated, BA can be life threatening and even fatal.[20,21] Erythromycin 500 mg taken 4 times daily for at least 4 weeks has been successful for cutaneous lesions; however, the optimal duration of therapy remains unknown.[14,18] After 4 to 7 days of therapy, the lesions substantially resolve, and they are usually completely resolved after 1 month.[20] Treatment should extend for days to weeks after the lesions have cleared to decrease the likelihood for relapse.[5] For patients who have a relapse, a 3-month course of antibiotics or continuous suppressive therapy may be useful. It is important for the clinician to consider each case of BA individually by clinical presentation, severity of the disease, level of immunosuppression, and the response to initial treatment. Treatment may need to last for months or even years in immunocompromised patients and/or in those with systemic involvement.

Failure of clinical improvement may be attributable to antibiotic resistance. A coexisting pathology and/or other diagnoses also should be considered. The clinical and/or histologic differential diagnosis of cutaneous lesions of BA includes a variety of soft tissue neoplasms that can readily be differentiated by their histologic features (Table 3).[7,20,21]

Conclusion

Careful judgment based on clinical presentation, disease severity, level of immunosuppression, and exposure to cats is necessary when evaluating cases such as the one presented herein. This case was unusual in that the patient had a solitary lesion limited to the site of inoculation, rather than presenting with no lymphadenopathy. Histologically, the lesions closely resembled BA, but because it was an isolated lesion restricted to the site of the presumed inoculation, a more appropriate diagnosis was inoculation bartonellosis. Although the patient was treated with a 10-day course of erythromycin, in retrospect the shave biopsy probably would have been a sufficient treatment.

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