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ID TEACHING CASES

Bartonella quintana Infection Manifesting as Leucocytoclastic Vasculitis Rash

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We present the first case described in the literature of leucocytoclastic vasculitis due to *Bartonella quintana* infection. A 73-year-old woman presented to the hospital with persistent fevers, retro-orbital headache, generalized weakness, and left lower thigh pain for 1 week. She was found to have truncal and proximal lower extremity papules and small plaques. Serology revealed *Bartonella quintana* immunoglobulin M (IgM) titer of 1:256 with undetectable *Bartonella quintana* immunoglobulin G (IgG) and undetectable *Bartonella henselae* IgG and IgM. Skin biopsy of an abdominal lesion revealed fibrinoid necrosis of vessel walls in the superficial and mid-dermis consistent with leucocytoclastic vasculitis. Doxycycline 100 mg orally twice daily was initiated, after which she had defervescence within 36 hours and rapid improvement of other presenting symptoms.

Keywords. bartonella; rash; vasculitis.

Bartonella quintana infection, otherwise known as trench fever, was previously a widespread disease, thought to have infected more than 1 million soldiers during World War I, which was attributed to poor hygienic conditions due to its vector of *Pediculus humanus corporis*, the body louse. Reported cases have dramatically diminished since that time; however, in recent years it has reemerged primarily in vulnerable populations such as those experiencing homelessness [1].

CASE REPORT

A 73-year-old woman with a history of well-controlled type II diabetes mellitus and cirrhosis of undetermined etiology presented to the hospital in the fall of 2020 with persistent fevers, retro-orbital headache, generalized weakness, and left lower thigh pain for 1 week. She was initially evaluated as an outpatient for a pulsatile sensation in her right ear and was provided medication for suspected migraine, which did not improve her symptoms.

Other medical history included 4 prior cesarean sections and a remote surgery for carpal tunnel release. She was born in Mexico and traveled there for a short period of time in early 2020. She had recently moved from Houston, where she was living with her son, to Dallas to live with her daughter. She also lived with 2 dogs at home. She had no other animal exposures or notable outdoor activities. She did not recall any recent insect bites. She consumed dairy products only from reputable grocery stores. She had no history of homelessness, living in a group setting, or living in unsanitary conditions. She had no history of tobacco, alcohol, or recreational drug use. She had no family history of malignancy or autoimmune disorders.

Her initial labs were notable for thrombocytopenia of 103 000 platelets/mL, hyponatremia of 124 mmol/L, and slight transaminitis with aspartate transaminase of 55 units/L and alanine aminotransferase of 48 units/L. Transthoracic echocardiogram did not show valvular abnormalities, and a total of 4 sets of blood cultures sent over 2 consecutive days in the absence of antimicrobials were observed for 5 days and remained without growth.

During her hospitalization, she was noted to have truncal and proximal lower extremity papules and small plaques (Figure 1A). Due to her constellation of symptoms and lab abnormalities, primarily headache, rash, and daily persistent fevers up to 39.4°C in the setting of transaminitis and thrombocytopenia, a variety of acute and subacute infectious etiologies were considered, including *Rickettsia typhi* (endemic to Texas), *Rickettsia rickettsii*, *Bartonella henselae*, *Bartonella quintana*, *Brucella*, *Coxiella burnetii*, and viral syndromes such as respiratory viral infection or acute hepatitis. Punch biopsy of the skin was performed to further evaluate for potential infectious and noninfectious etiologies. Empiric doxycycline 100 mg orally twice daily was initiated, and defervescence was achieved after 36 hours with rapid improvement of symptoms and normalization of all initial laboratory abnormalities noted above.

Initial serology revealed *Bartonella quintana* immunoglobulin M (IgM) titer of 1:256 with undetectable *Bartonella quintana* immunoglobulin G (IgG) and undetectable *Bartonella*

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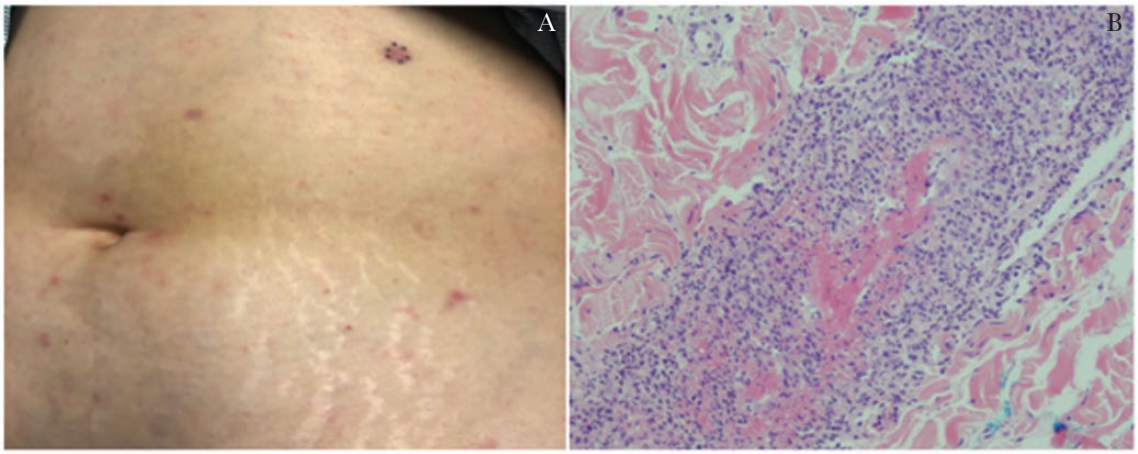

Figure 1. A, Abdominal skin lesions during hospitalization with left upper quadrant lesion status post recent biopsy. B, Skin biopsy sample of the abdomen (hematoxylin and eosin stain at 20× magnification) showing fibrinoid necrosis of vessel walls in the superficial and mid-dermis consistent with leucocytoclastic vasculitis. Warthin-Starry stain did not reveal any organisms.

henselae IgG and IgM. *Bartonella* serologies performed 5 weeks after initial serology showed *Bartonella quintana* IgG of 1:64, undetectable *Bartonella quintana* IgM, and undetectable *Bartonella henselae* IgG and IgM.

At the time serologies returned indicating *Bartonella quintana* infection, she already had dramatic improvement, and thus she was continued on doxycycline monotherapy to complete a 14-day course with sustained resolution of symptoms at an appointment several weeks later.

Broad testing for other diagnoses returned entirely negative, including hepatitis B surface antigen, surface antibody, core antibody, hepatitis C antibody, fourth-generation HIV-1/2 antibody and antigen, nasopharyngeal SARS-CoV-2 polymerase chain reaction (PCR) by ePlex followed by nasopharyngeal SARS-CoV-2 PCR by Roche nearly 48 hours later, *Coxiella burnetii* IgG and IgM, *Brucella* total antibody, *Rickettsia typhi* IgG and IgM, *Rickettsia rickettsii* IgG and IgM, T-SPOT.*TB* test, throat culture, and nasopharyngeal respiratory virus PCR panel, which included adenovirus, *Bortadella pertussis*, *Chlamydophila pneumoniae*, coronavirus 229E, HKU1, NL63, and OC43, influenza A and B, *Mycoplasma pneumoniae*, parainfluenza 1, 2, 3, and 4, and respiratory syncytial virus.

Pathology from punch biopsy of an abdominal lesion (Figure 1B) showed fibrinoid necrosis of vessel walls in the superficial and mid-dermis consistent with leucocytoclastic vasculitis. Warthin-Starry stain did not reveal any organisms.

DISCUSSION

Leucocytoclastic vasculitis is a small vessel vasculitis that is induced by a variety of potential underlying etiologies, including hypersensitivity drug reactions, connective tissue diseases, systemic vasculitis, malignancies, and, though less commonly recognized, bacterial and viral infections, including hepatitis B, hepatitis C, acute HIV, *Streptococcus*, *Staphylococcus aureus*, gonorrhea, and both tuberculous and nontuberculous mycobacteria [2]. We present the first case described in the literature of leucocytoclastic vasculitis due to *Bartonella quintana* infection. However, several manifestations of vasculitis and related syndromes have been associated with *Bartonella* infection (usually infections due to *Bartonella henselae*) including antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis and glomerulonephritis [3-5], Henoch-Schönlein purpura [6], retinitis [7], and uveitis [8].

Cutaneous manifestations of bartonellosis can take several forms, including purpura, morbilliform rash, erythema nodosum, erythema marginatum, papules, and nodules [9]. Diagnosis of leucocytoclastic vasculitis is made from skin biopsy pathology with resolution generally following treatment of the underlying etiology [2].

Due to its vector, the body louse, *Bartonella quintana* infection is generally considered to be a disease affecting those in poor sanitary conditions; however, it should be considered in patients with a similar clinical presentation, even in the absence of known risk factors. Leucocytoclastic vasculitis is an underrecognized manifestation of many systemic etiologies, and when identified, knowledge of the associations may lead to more rapid diagnosis and treatment of occult infection.

Literature Review

A literature review was conducted using PubMed, most recently in June 2021, with the following keywords: "*Bartonella* and vasculitis" yielded 63 articles. "*Quintana* and vasculitis" yielded 36 articles. "*Bartonella* and leukocytoclastic" yielded 8 articles. "*Bartonella* and leucocytoclastic" yielded 2 articles. "*Quintana* and leukocytoclastic" yielded 4 articles. "*Quintana* and leucocytoclastic" yielded no articles. These articles were examined. Although there were reports of several manifestations of vasculitis in the setting of bartonellosis, primarily associated

with *Bartonella henselae*, none described leucocytoclastic vasculitis in the setting of *Bartonella* infection.

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