

Bacillary angiomatosis with atypical clinical presentation in an immunocompetent patient

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ABSTRACT

Bacillary angiomatosis is a recently described infectious disease that usually affects immunosuppressed hosts with a previous history of contact with cats. We report a rare case of bacillary angiomatosis in an immunocompetent 59-year-old woman with no history of previous exposure to cats, and atypical clinical features (fever and subcutaneous nodules with ulceration on the left ankle). Histopathology of the lesion showed extensive ulceration and reactive tumor-like vascular proliferation of the blood vessels with swollen endothelial cells and an inflammatory infiltrate including neutrophils and lymphocytes in the dermis and subcutis. Staining with the Warthin-Starry method demonstrated the presence of clustered bacilli located in the extracellular matrix adjacent to the proliferating endothelial cells. Diagnosis was confirmed with the detection of *Bartonella* spp. DNA in the affected skin and in bone marrow using polymerase chain reaction.

Key words: Bacillary angiomatosis, bartonella quintana, bartonella henselae, immunocompetent

INTRODUCTION

The spectrum of Bartonella infections has expanded rapidly since the first HIV-infected patient with bacillary angiomatosis (BA) was described in 1983. Of the 19 species of Bartonella described until now, only 10 were acknowledged as human pathogens; *B. bacilliformis*, *B. quintana*, and *B. henselae* are the most frequently described.^[1,2] BA usually affects immunosuppressed hosts, especially HIV-infected patients with a decrease in the CD4 lymphocyte count.^[1-6] Hepatic peliosis is exclusively associated with *B. henselae* infection. BA caused by *B. quintana* can develop lytic bone lesions and subcutaneous masses.^[2]

There are very few reported cases of BA in immunocompetent patients.^[3-11] The skin is the most frequently affected site, presenting as papules, warts, pedunculated and subcutaneous nodules (rarely ulcerated or bleeding), or hyperkeratotic plaques.^[1,2] Most patients with BA have been exposed to cats.^[1-5,12,13] We describe an atypical case of BA in an

immunocompetent woman with no previous exposure to cats.

CASE REPORT

A 59-year-old woman was admitted to our hospital with a four-week history of a painful skin lesion localized on the backside of the left ankle. The first two days she had suffered a high grade fever which remitted spontaneously. However, cutaneous lesions progressed despite empiric treatment with amoxicillin plus clavulanate. The patient denied having had direct contact with cats or wild animals, had no previous illness and received no medication. Physical examination revealed a lobulated and ulcerated plaque with an easily bleeding surface. Slight swelling of the left calf was evident [Figure 1a]. No lice infestation was detected.

Blood count, CD4 count, blood chemistry, urine analysis, erythrocyte sedimentation rate, X-ray and abdominal ultrasonography were normal. Doppler-

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ultrasonography of the left leg showed internal saphenous vein thrombosis at the level of the knee. Two sets of blood cultures, as well as a skin-biopsy culture (processed for aerobic and anaerobic bacteria, fungi, and mycobacteria), were negative. Serotesting for HIV by enzyme-linked immunoassay was negative. Serology, using an indirect immunofluorescence assay (IFA), detected an antibody titer of 1:64 (IgG) against *B. henselae*. IgM against *B. henselae* was negative. Serotesting (IFA) against *B. quintana*, *C. burnetii*, and *Chlamydia* were negative.

Histopathological examination of the skin lesion showed extensive ulceration, and a tumor-like vascular proliferation of the blood-vessels with

swollen endothelial cells in the dermis and subcutis, predominating in the upper dermis. The dermis and subcutis showed an inflammatory infiltrate including neutrophils, and lymphocytes intermingled with the blood vessels [Figure 2]. Staining with the Warthin-Starry method demonstrated the presence of clustered bacilli located in the extracellular matrix adjacent to the proliferating endothelial cells [Figure 3]. Staining for fungi, cytomegalovirus and mycobacteria were negative.

Bartonella spp. DNA was detected in the skin lesion and bone marrow by polymerase chain reaction (PCR) [Figure 4]. DNA was purified from bone marrow and epithelial cells by a DNA purification kit (Qiagen).



Figure 1: (a) Before treatment: subcutaneous nodules with ulceration and an easily bleeding surface on the backside of the left ankle. (b) After treatment: Healed plaque with residual hyperpigmentation

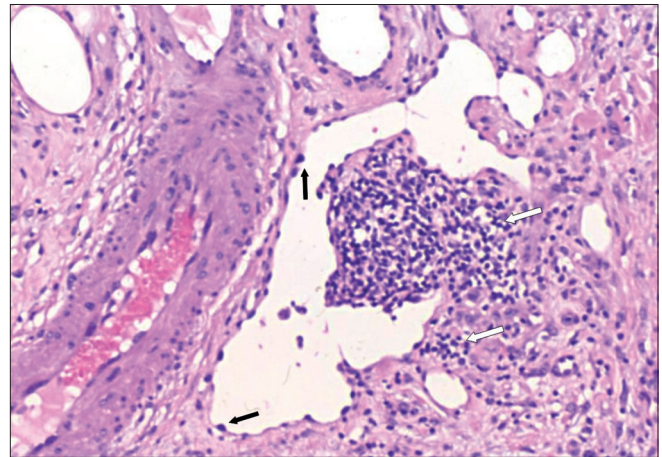


Figure 2: Tumor-like lobular proliferation of the blood-vessels in the dermis with swollen endothelial cells (black arrows). Inflammatory infiltrate (white arrows) including neutrophils, and lymphocytes intermingled with the blood vessels (H and E, x40)

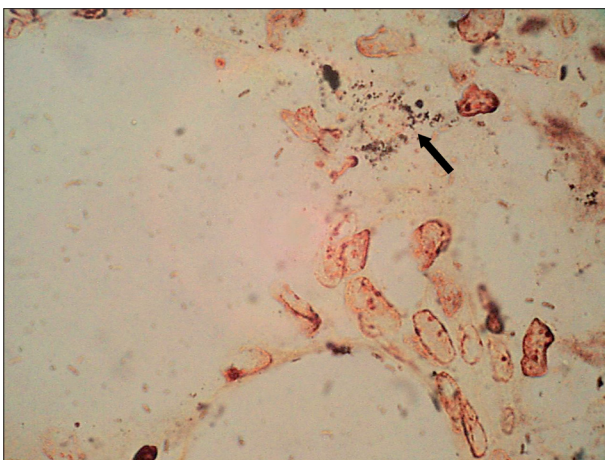


Figure 3: Solitary or clustered bacilli (arrow) located in the extracellular matrix adjacent to the proliferating endothelial cells (Warthin-Starry stain, x100)

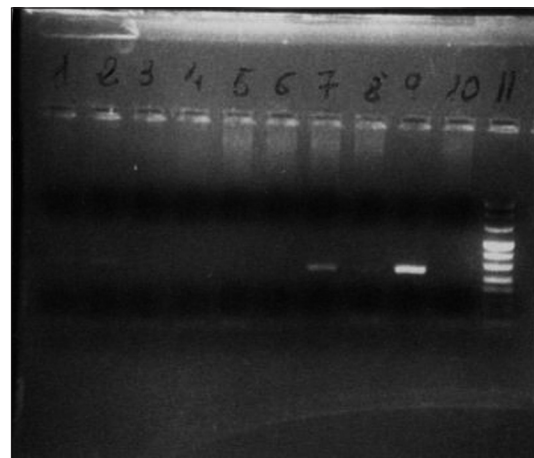


Figure 4: Detection of *Bartonella* spp. by polymerase chain reaction. Lanes from left to right: 1-4, patient's skin DNA; 5-8, patient's bone marrow DNA; 9, *Bartonella* spp. DNA; 10, negative control; 11, molecular size marker

PCR was performed using 1 µg DNA over 35 cycles consisting of 15 s at 95°C, 15 s at 50° and 45 s at 72°C in a reaction volume of 50 µl containing 0.5 units Taq polymerase, 10 mM Tris HCl pH 8.8, 50 mM KCl, 1.5 mM MgCl₂, 0.1 % Triton X-100, 33 µM of each dNTPs, and 0.5 µM of each primer. Primers P24E 5'-CCT CCT TCA GTT AGG CTG G-3' and P12B 5'-GAG ATG GGT TTT GGA GAG TA-3' were used as specific primers. DNA from *B. henselae* and *B. quintana* was used as control for discrimination purposes.

Oral doxycycline (100 mg/12 h) was given for two months. The lesion regressed leaving a hyperpigmented plaque [Figure 1b]. In a follow-up period of 12 months, there was no recurrence. The absence of recurrence was demonstrated with a second histopathological study of the hyperpigmented plaque.

DISCUSSION

Clinical presentation of BA as subcutaneous nodules with ulceration in an immunocompetent host is unusual.^[8] It is generally accepted that human infection occurs directly or by an arthropod vector (*Ctenocephalides felis* for *B. henselae*, and still unknown for *B. quintana*). However, one third of the patients with BA deny having had any previous contact with cats.^[1,2,12-16] The absence of direct contact with cats and the atypical clinical presentation made the diagnosis especially difficult in this case. Clinical differential diagnosis included infections with sporotrichoid dissemination (nocardiosis, mycobacteria, and sporothrix among others) and pyogenic granulomas. Histopathological features in our patient [Figure 2] distinguished BA from Kaposi's sarcoma (lack of spindle cells, atypically shaped vascular channels and hyaline globules) and pyogenic granuloma (endothelial cells were large and polygonal, with a prominent inflammatory infiltrate with polymorphonuclear leukocytes scattered throughout the lesion, as opposed to classic pyogenic granuloma in which polymorphonuclear leukocytes are near the surface). Histopathological findings, serological results, the regression of the lesion with oral doxycycline, and the detection of *Bartonella* spp DNA in the skin lesion and bone marrow all confirmed the diagnosis of BA in our patient.

The culture of the skin lesion processed for aerobic and anaerobic bacteria, fungi, and mycobacteria was negative. Culture in blood agar (5% defibrinated rabbit

blood) incubated at 37°C in 5% CO₂ could not be done due to lack of laboratory facility. However, the vast majority of BA cases are diagnosed histologically, with identification of the causative bacteria by Warthin-Starry staining. *Bartonella* spp. is an extremely fastidious Gram negative rod, and requires special culture conditions for isolation; hence culture is not routinely performed for diagnosis.^[1,2] Serological tests, using an indirect immunofluorescence assay (IFA), show relatively high specificity to the genus level against *Bartonella* spp., but are not species specific. It is well known that *Bartonella* spp. cross-react with other genera and species, such as *C. burnetii* and Chlamydia. However, in our patient, serological (IFA) tests against *B. quintana*, *C. burnetii*, and Chlamydia were negative.^[17,18] PCR can be very useful in demonstrating *Bartonella* spp. DNA in clinical samples, enabling an early therapeutic approach.^[1,2]

Endocarditis and asymptomatic bacteremia caused by *B. henselae* and *B. quintana* in the absence of BA, and other evidence of primary inoculation site have been previously described in both immunosuppressed and immunocompetent patients.^[1,2,18-21] In this sense, *Bartonella* spp. DNA found in our patients' bone marrow and the presence of low specific IgG titers against *B. henselae* could easily have been a sign of a past infection with hematogenous dissemination. We do not know whether the skin lesion was the primary inoculation site in this case, or on the contrary, a secondary manifestation of a previous asymptomatic bacteremia.

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