Case Report

Bacillary Angiomatosis and Bacteremia due to *Bartonella quintana* in a Patient with Chronic Lymphocytic Leukemia

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We present a 63-year-old man treated with alemtuzumab for chronic lymphocytic leukemia who developed multiple angiomatous papules and fever. Real-time polymerase chain reaction (RT-PCR) from a skin lesion and blood sample revealed *Bartonella quintana* as causative agent confirming the diagnosis of bacillary angiomatosis with bacteremia. Treatment with doxycycline, initially in combination with gentamicin, led to complete resolution of the lesions. This case shows the importance of considering bacillary angiomatosis as a rare differential diagnosis of angiomatous lesions in the immunocompromised patient, particularly in chronic lymphocytic leukemia and following lymphocyte depleting treatments as alemtuzumab.

1. Introduction

Bacillary angiomatosis is a rare vasculoproliferative disorder due to *Bartonella henselae* or *Bartonella quintana*. The disease usually manifests as cutaneous angiomatous tumors. Lesions may be solitary or multiple and dissemination to visceral organs can occur. Bone lesions and subcutaneous masses are associated with *B. quintana*, whereas peliosis hepatitis and lymph node lesions are associated with *B. henselae* [1]. Cases were usually described in HIV infected individuals. Although less common, the infection was reported in immunocompetent patients and in otherwise immunocompromised conditions such as solid organ transplantation and oncology patients, particularly in chronic lymphocytic leukemia [2, 3]. Because of its potentially life-threatening course, early diagnosis and adequate treatment are crucial. To our knowledge, we describe the first case of bacillary angiomatosis and bacteremia due to *B. quintana* in a patient with chronic lymphocytic leukemia.

2. Case Presentation

A 63-year-old man was admitted for evaluation of multiple nonpruritic skin lesions that had been present for 1 month on his arms, legs, trunk, and face. His medical history was significant for chronic lymphocytic leukemia with long-standing profound neutropenia, anemia, and thrombocytopenia. He had previously been treated with chlorambucil and prednisone, as well as cladribine, rituximab, and bendamustine. At the time of presentation, he had been receiving alemtuzumab for 4 months. Current medication included prophylaxis with trimethoprim sulfamethoxazole as well as valacyclovir, and treatment with voriconazole for probable invasive pulmonary aspergillosis diagnosed during a previous febrile neutropenic episode. There had been several other episodes of neutropenic fever without specific infectious focus.

Physical examination showed multiple nontender cutaneous papules and nodules, resembling angiomatous lesions up to 10 mm in diameter (Figure 1). Some were crusted, and some surrounded by an erythematous halo (Figure 2). On the right forearm, there were signs of superinfection. Fever up to 39°C was noted.

The white blood count was 2600/μL (absolute neutrophil count 2500/μL, lymphocytes 70/μL, CD4 cells 10/μL, 12%, eosinophils 0/μL, monocytes 100/μL), CRP was 117 mg/L, and chemistry panel and urine analysis were otherwise unremarkable. Computed tomography revealed known
hilomediastinal and axillary lymphadenopathy, unchanged splenomegaly without focal lesions, and minimal residual pulmonary infiltrates and caverness from the formerly diagnosed aspergillosis.

Biopsy of the skin revealed features of pyogenic granuloma with lobular proliferation of small vessels and mixed cell, predominantly neutrophilic inflammation (Figures 3 and 4). No microorganisms were detected on special stains as Warthin-Starry, Giemsa, Gram, or Grocott. There were no morphological signs of Kaposi sarcoma or of a vascular tumor such as hemangioendothelioma.

Routine culture of skin and blood specimens showed no bacterial growth. However, RT-PCR for B. quintana [4, 5] was positive in a skin biopsy as well as from a blood specimen (Figure 5), confirming bacillary angiomatosis with bacteremia. To rule out endocarditis, echocardiography was performed, which showed no relevant valvulopathies or vegetations.

We started antibiotic treatment with doxycycline and gentamicin. In addition, amoxicillin/clavulanate for superinfection of the right forearm was administered for 10 days. Gentamicin was stopped after two weeks, followed by doxycycline of 6 months duration. The patient defervesced promptly and all the lesions resolved within few weeks.

3. Discussion

The causative organism of bacillary angiomatosis in different case series was found to be B. henselae in 28% and 53%, respectively, and B. quintana in 64% and 47%, respectively [6, 7]. B. quintana infection in bacillary angiomatosis is associated with homelessness, low socioeconomic status and exposure to lice [7]. B. quintana was first recognized as an etiological agent of trench fever, a recurrent fever transmitted by body lice occurring in troops during World War I, whereas cat scratch disease is mainly attributed to B. henselae. B. quintana and B. henselae have worldwide distribution. Other clinical features of B. quintana are chronic bacteremia, endocarditis, and lymphadenopathy. Relapses of trench fever can occur many years after the initial illness or the patients may be bacteremic but have no clinical signs, as was noted in outbreaks of urban trench fever among homeless people [8]. Prolonged bacteremias in patients with B. quintana infections possibly contribute to the development of endocarditis and bacillary angiomatosis [9]. In contrast to B. henselae, B. quintana can cause endocarditis in previously intact heart valves. Our patient was a retiree originating from Macedonia who had lived in Switzerland for 33 years working as a bricklayer. There was no history of cat exposure, homelessness, pediculosis, or alcoholism in our patient. Unfortunately we could not establish if it was a relapse of a previous disease or if the relapsing neutropenic fever episodes were also due
As in our case, the diagnosis of bacillary angiomatosis can be confirmed by detection of *Bartonella species* DNA in biopsy extracts by PCR. Identification of *Bartonella* by culturing is fastidious and not sensitive. Although detection of the organism in conventional cultures as performed in our patient is possible, the sensitivity could have been improved by subculture, special media, and prolonged incubation [6]. Serology may be unreliable in immunocompromised patients due to lack of antibody response [14]. Histopathology can help establishing diagnosis of cutaneous bacillary angiomatosis.

In vitro and in vivo activities of antibiotics against *Bartonella species* often differ. In epidemiological investigation trimethoprim sulfamethoxazole, ciprofloxacin, penicillins, and cephalosporins were not protective against *Bartonella* infections whereas doxycycline, tetracycline, rifampin or a macrolide were [7]. Gentamicin and rifampin were the only agents found to be bactericidal against *B. quintana* [15]. Erythromycin or doxycycline for the duration of 3 months are the drugs of choice for the treatment of bacillary angiomatosis. We preferred an initial combination of doxycycline and gentamicin because of bacteremia, as outlined in treatment recommendations for trench fever, chronic bacteremia, or endocarditis [16]. Based on the increased risk of relapse by ongoing immunosuppression in our patient, the following treatment period with doxycycline was extended to 6 months.

In conclusion, bacillary angiomatosis should be considered a differential diagnosis in immunosuppressed patients presenting with cutaneous angiomata-like lesions. Particular attention should be addressed to conditions such as chronic lymphocytic leukemia and T-cell depleting therapies.

**Conflict of Interests**

The authors have no conflict of interests.

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