CASE REPORT

Bacillary angiomatosis by *Bartonella quintana* in HIV-infected patient: molecular confirmed case in Iran

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Abstract

Bartonella is an infrequent yet important pathogen in immunocompromised patients. *Bartonella* infections can cause serious morbidity and mortality in people living with human immunodeficiency virus (PLWH), particularly those with advanced immunosuppression. The prevalence of clinically evident *Bartonella* infections among PLWH is relatively low. Here, we reported a bacillary angiomatosis (BA) case in a homeless HIV-positive patient. A 31-year-old man with acquired immunodeficiency syndrome (AIDS) and advanced immunosuppression, who had discontinued antiretroviral therapy (ART) one year ago, referred to the hospital. At the admission, he had nausea, vomiting, anorexia, weight loss, occasional sputum cough, subjective fevers, and multiple skin lesions. Lesions' biopsies were non-diagnostic for routine bacterial, tuberculosis, and fungal infection. However, the diagnosis of *Bartonella quintana* was confirmed by serum polymerase chain reaction (PCR). After receiving a long course of antibiotic therapy, skin lesions resolved. The patient had a favorable outcome with supportive care and continuation of ART and doxycycline. While easily treated, an infection due to *Bartonella* may be clinically unrecognized, if skin lesions are absent or overlooked, and microbiologically unrecognized, if appropriate protocols are not followed. Because the fever caused by *Bartonella* infection is easily treated, it is essential that suspected clinical signs of *Bartonella* infection in immunocompromised hosts should be reported to the microbiology laboratory. *Bartonella* quintana infection can result in a broad range of often non-specific clinical manifestations; therefore, patients must be evaluated for suspected bacteremia, and clinical wariness is required for diagnosis.

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Key words: HIV/AIDS, cutaneous lesion, *Bartonella quintana*, bacillary angiomatosis.

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Introduction

Bartonella infections caused by *B. henselae* or *B. quintana* in immunocompromised patients, primarily present as a systemic illness that may be identified by angioproliferative lesions of the skin, liver, and spleen [1].

Bacillary angiomatosis (BA) vasoproliferative mass lesions in multiple organs and fever are the most common manifestations of *B. henselae* and *B. quintana* in patients with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS). Other clinical manifestations include cutaneous vascular lesions, subcutaneous nodules, vascular-proliferative disease of the liver and spleen, systemic illness with fever, bacteremia, and weight loss [2].

Isolation of *Bartonella* bacteria from blood and tissue is difficult, requiring prolonged incubation. The organisms can be seen on Warthin-Starry staining of histopathologic specimens. Also, polymerase chain reaction (PCR) assay can be used in detecting *Bartonella* DNA in the tissue [3].

For the first time in Iran, we reported bacillary angiomatosis caused by *B. quintana* in an HIV-positive patient.

Case report

A 31-year-old homeless man with HIV presented to an emergency room (ER) of Imam Khomeini Hospital, with a seven-day history of nausea, vomiting, anorexia, weight loss (22 kg) over the preceding 12 months, occasional sputum cough, and subjective fever. He had been suffering from a fever for the past week and had a prominent skin lesion, 3 cm in diameter, in the left region of the hemithorax. He had a history of intravenous drug use (IDU), and had tuberculosis (TB) 4 years ago, which was treated. He had started antiretroviral therapy (ART) 4 years ago when he was diagnosed with HIV, and had stopped it last year.

On examination, the patient had oral thrush, inguinal lymphadenophaty on both sides, and several enlarged lymph nodes that were detected within the anterior cervical region as well as mild splenomegaly. Intravenous fluconazole was prescribed for oral candidiasis for 21 days, which resulted in the improvement of dysphagia and odynophagia.

In the examination of the left hemithorax lesion, tenderness and discharge with no erythema were observed (Figure 1). Moreover, a striking cutaneous lesion, 2 cm in diameter, was found in the left scapula, without erythema, discharge, and tenderness (Figure 2). Other physical symptoms were not significant during the examination. Laboratory results were notable for a white blood cell count of $2.7 \times 10^3/\mu l$, with 61% polymorphonuclear cells, 32% lymphocytes, and a hemoglobin level of 8.9 g/dl. Liver function test results were normal. There were two negative blood cultures. Besides, the erythrocyte sedimentation rate (ESR) and

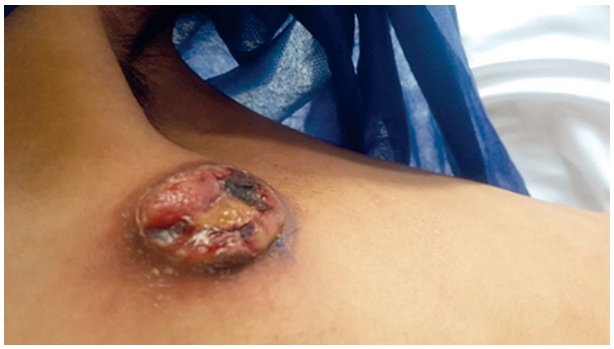

Figure 1. Photograph of the left hemithorax lesion after biopsy

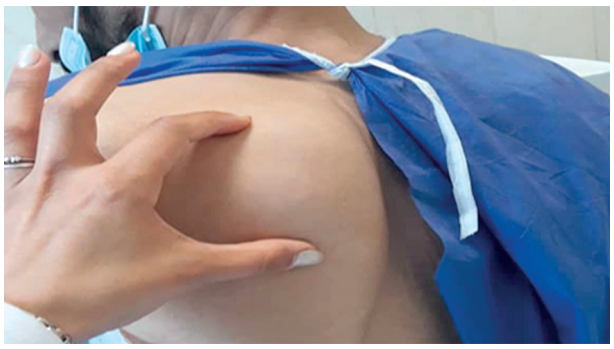

Figure 2. Photograph of the cutaneous lesion, located in the left scapula

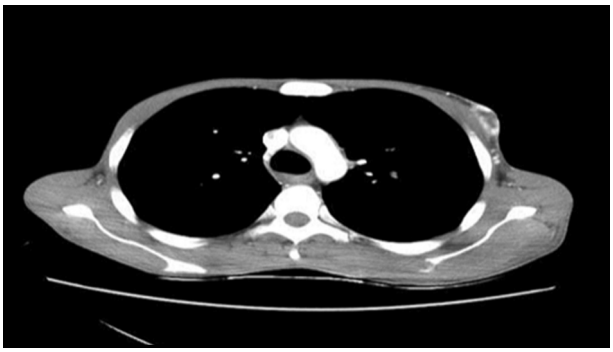

Figure 3. A contrast-enhanced computed tomography scan of the chest, demonstrating left hemithorax lesion

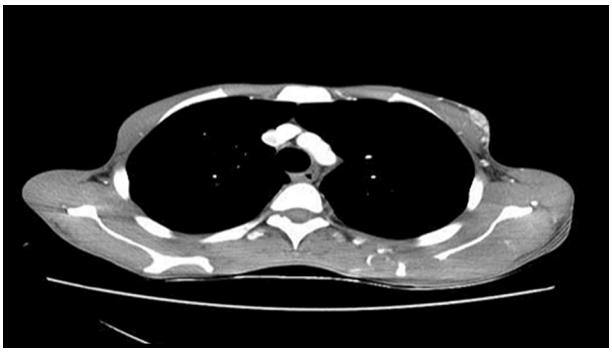

Figure 4. A contrast-enhanced computed tomography scan of the chest demonstrating skin lesion on the left hemithorax that has invaded the rib bone in the back

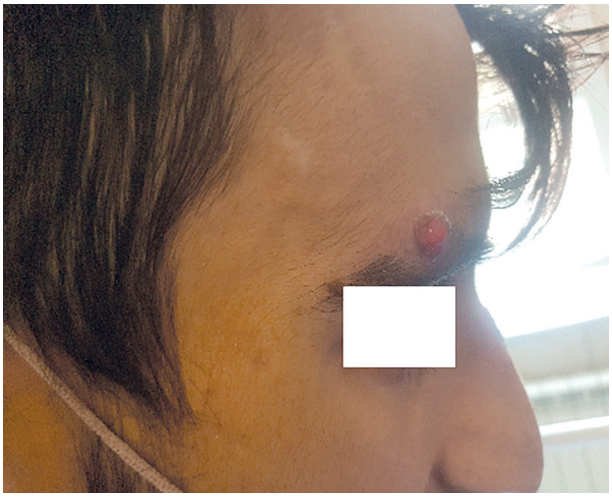

Figure 5. Photograph of a purple lesion on the forehead

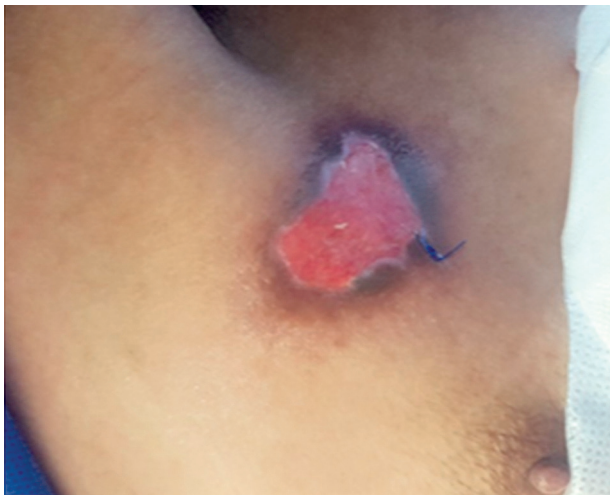

Figure 6. This image shows a left hemithorax lesion after treatment that is completely healed

C-reactive protein (CRP) level were elevated up to 75 mm/h (normal range, 0-15 mm/h) and 45 mg/l (normal range, < 3.1 mg/l), respectively. At the time of admission, the patient's CD4+ T cell count was 4 cells/µl, and his HIV RNA level was 12,683.404 copies/ml. In the patient's contrasted chest computed tomography (CT) scan, a cutaneous lesion, which invaded rib bone was detected (Figures 3 and 4).

Subsequently, a biopsy of the left hemithorax lesion was taken that was non-diagnostic and all bacterial, mycobacterial, and fungal tests were negative. Since histopathology of this lesion was not diagnostic, a biopsy was taken from the lesion located in the scapula, but histopathology of this lesion was not diagnostic also. However, in the description of operation, the surgeon reported that the lesion was vascular. In addition to the above-mentioned lesions, the patient had a prominent purple lesion on the forehead, as shown in the photo (Figure 5). Surgeon's descriptions of the lesion being vascular as well as the discovery of a new lesion, raised suspicions about *Bartonella*.

Mycobacterium tuberculosis gamma interferon release assay was also negative. The patient had two negative sputum results by smear and culture for acid-fast bacilli (AFB) as well as GeneXpert. Moreover, in the chest CT scan, there was no parenchymal involvement in favor of TB.

During the hospitalization, the patient had a seizure. Ptosis was also found on the left side and the pupil on the same side had a reduced response to light. With suspected opportunistic infections, brain magnetic resonance imaging (MRI) and lumbar puncture (LP) were performed, both of which were within range. Cerebrospinal fluid was tested for BK, JC viruses, fungal, CMV, and VDRL, which all were negative.

Due to strong clinical suspicion of *Bartonella* infections, we initiated empiric treatment with doxycycline (100 mg, p.o., BD) and rifampin (300 mg, p.o., daily) and at the same time, a sample was sent for *Bacillus* PCR test. The prescribed medicines effectively resulted in complete healing of the skin

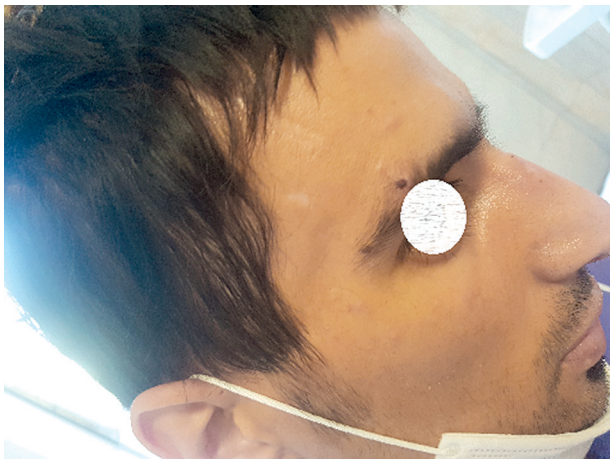

Figure 7. This image shows a completely healed lesion on the forehead after treatment

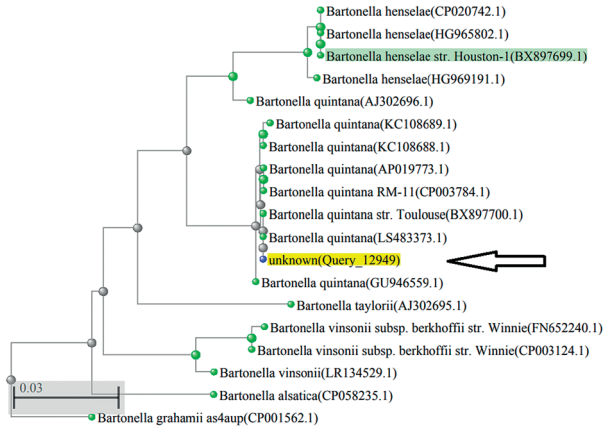

Figure 8. Neighbor-joining tree based on the batR gene nucleotide sequences of *Bartonella quintana*. The arrow indicates the bacterium identified in this report

lesions and ptosis for two weeks (Figures 6 and 7). PCR test for *B. quintana* was performed on the pathology sample and it was positive (Figure 8).

Discussion

Bartonella infections in HIV-infected patients can cause serious morbidity and mortality, especially in those with significant immunosuppression [4]. Two species cause clinical infections in HIV-infected patients, including *B. henselae*, which usually appears in patients with a history of cat exposure, and *B. quintana* that usually in occurs in homeless individuals with body lice. The clinical manifestations include BA, lesions of the liver (hepatic peliosis), splenitis, osteomyelitis, bacteremia, subcutaneous masses, and hemophagocytic lymphohistiocytosis [5]. BA is a common presentation in HIV-infected individuals with advanced immunosuppression, characterized by violaceous, friable, and vascular lesions that bleed profusely with trauma. Most frequently, these lesions involve the skin, but can also appear in internal organs, including the liver and spleen [6]. While both *B. henselae* and *B. quintana* typically cause skin lesions, subcutaneous masses and bone lesions are more likely to be due to *B. quintana*, and bacillary peliosis and lymph node involvement are more likely to result from *B. henselae* [7]. Also, constitutional symptoms are reported by almost all patients with BA. Fever caused by *Bartonella* species is likely under-recognized, particularly if skin lesions are absent or few, and the presentation is non-specific [8].

AIDS patients with CD4 cell counts of less than 100 cells/l are at increased risk of infection due to *Bartonella* species [9]. *Bartonella* infections can be diagnosed by histopathological examination of tissue with Warthin-Starry silver stain, special *Bartonella* blood culture analysis (unavailable in most hospital laboratories), serological assays, and increasingly, PCR amplification of DNA extracted from biopsy tissue [2]. However, definitive diagnosis can be challenging, since *Bartonella* species generally do not grow in routine cultures. Also, isolation of the fastidious, slow-growing, and Gram-negative organisms is difficult, requiring specific laboratory conditions to enhance the yield of culture [10]. Detection of *Bartonella* DNA in tissue specimens via PCR assay is diagnostic, but the sensitivity is very low, especially when the duration of illness continues for more than 6 weeks [11].

All HIV-positive patients who are diagnosed with *Bartonella* infection should receive antibiotic therapy. No randomized controlled trials have evaluated the optimal treatment regimen for *Bartonella* in people living with HIV; however, patients generally responded well to prolonged courses of either erythromycin or doxycycline [10].

Bartonella is an infrequent but important pathogen in immunocompromised patients. While easily treated, infection due to *Bartonella* may be clinically unrecognized if skin lesions are absent or overlooked, and microbiologically unrecognized, if appropriate, protocols are not followed [12]. Because the fever caused by *Bartonella* infection is easily treated, it is essential that the suspected clinical signs of *Bartonella* infection in immunocompromised hosts must be reported to the microbiology laboratory [13]. Moreover, *B. quintana* infection can result in a broad range of often non-specific clinical manifestations [5]. Therefore, clinical wariness is required for diagnosis.

Conflict of interest

The authors have no conflict of interest.

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