Acta Dermatovenerol Croat 2014;22(4):294-297 CLINICAL ARTICLE

Bacillary Angiomatosis in a HIV-positive Patient with Poor Adherence to Antiretroviral Therapy

Leonor Lopes[1], João Borges-Costa[1], Nuno Janeiro[2], Diana Neves[2], Luís Soares Almeida[1], Paulo Filipe[1]

[1]Department of Dermatology; [2]Department of Infectious Diseases, Centro Hospitalar Lisboa Norte – Hospital de Santa Maria, Lisbon, Portugal

Corresponding author:
Leonor Neto Lopes, MD
Avenida Prof. Egas Moniz, 1649-028
Lisboa
Portugal
leonorlopes@gmail.com

Received: November 27, 2013
Accepted: September 1, 2014

SUMMARY Bacillary angiomatosis is a systemic disease caused by *Bartonella (B.) henselae* and *B. quintana*. Today it is a rare disease that occurs predominantly in patients with poor adherence to antiretroviral therapy or with late diagnosis of human immunodeficiency virus (HIV). We report on the case of a 40-year-old Caucasian female with HIV-1 and hepatitis B virus (HBV) co-infection diagnosed 17 years ago. She presented to the emergency department with an erythematous, painless nodule located on the left naso-genian fold. In the next few weeks the disease disseminated to the oral and left tarsal mucosa and to the palm of the left hand. The histopathological findings were suggestive of bacillary angiomatosis which was confirmed by polymerase chain reaction (PCR). The patient was treated with clarithromycin 500 mg bid per os for 3 months, with complete remission of the mucocutaneous lesions. Bacillary angiomatosis is a potentially fatal disease. Early diagnosis and treatment are critical in reducing the morbidity and mortality associated with it.

KEYWORDS: bacillary angiomatosis; *Bartonella henselae*; clarithromycin; antiretroviral therapy

INTRODUCTION

Bacillary angiomatosis is a systemic disease caused by *Bartonella (B.) henselae* and *Bartonella quintana*, which are small gram-negative rods in the *Bartonellaceae* family (1). This condition is included in category B of the CDC classification for persons infected by human immunodeficiency virus (HIV) (2). Its incidence has reduced with the use of antiretroviral and prophylactic antibiotic therapies (3). Despite representing a rare diagnosis in patients with HIV infection on antiretroviral therapy, it is still observed in patients with poor adherence to therapy or in patients with late HIV diagnosis.

CASE REPORT

We report on the case of a 40-year-old Caucasian female, former intravenous drug user, with HIV-1 and hepatitis B virus (HBV) co-infection diagnosed in 1996, with weakened immune status due to non-adherence to antiretroviral therapy (ART). In this context, the patient had a personal history of *Salmonella typhimurium* sepsis, pneumocystosis (in 2008) and periorbital cellulitis (in 2009). Between 2008 and 2010, there was a gradual improvement of the immune system and a reduction of viral replication under therapy with atazanavir/ritonavir, efavirenz, and tenofovir/emtric-

Acta Dermatovenerol Croat
2014;22(4):294-297

itabine. Between June 2010 and February 2013, she suspended ART. In February 2013 she presented to the emergency with an erythematous, painless nodule, 1×1 cm in diameter, with rapid growth in the last 15 days, located at the left naso-genian fold (Fig. 1a). An excisional biopsy was performed and sent to histopathological examination with the following diagnostic hypotheses: pyogenic granuloma, Kaposi's sarcoma, or bacillary angiomatosis. The hematoxilin-eosin staining revealed lobular vascular proliferation with epitelioid endotelial cells and an inflammatory infiltrate with multiple neutrophils (Fig. 2a). The immunohistochemistry showed a granular interstitial material suggestive of bacillary angiomatosis (Figure 2b). *Bartonella henselae* infection was confirmed by PCR (Fig. 3). Meanwhile, the patient missed the follow-up visit and it was not possible to establish further contact.

One month after the first observation, the patient presented to the dermatology department due to recurrence of erythematous papules on the left naso-genian fold. The presence of new erythematous papules on the oral and left tarsal mucosa and on the palm of the left hand was also observed (Fig. 1b). The patient reported no fever, night sweats, chills, prostration, abdominal pain, or diarrhea. She reported being bitten on the first finger of the right hand by an abandoned cat, three weeks before the appearance of the first lesion. The patient had started the last antiretroviral regimen on her own when the lesions appeared and was medicated with clarithromycin 500 mg bid per os for 3 months.

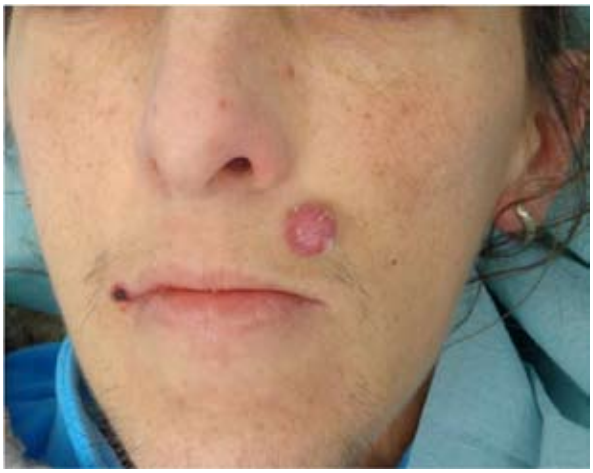

Figure 1 a: Bacillary angiomatosis, clinical presentation: Erythematous, painless, nodule located to the left naso-genian fold.

The laboratory assessment performed 3 weeks after starting therapy showed: Hb-10.3 g/dL (12-15); leukocytes-10.01x10^9/L (4-11); neutrophils-76.3% (40-60); platelets-630x$10^{9/}$L(150-450), CD4+-25.9 cells/µL [1.6% (29-59)]; HIV viral load-656 copies/ml; GGT-162 U/L (<38); FA-312 U/L (45-129); CRP-7.99 mg/dL (<0.5); anti-*Bartonella henselae* IgM and IgG were equivocal. The chest X-ray revealed no changes. As the patient reported no systemic symptoms, she refused to perform an abdominal ultrasound to exclude liver and spleen involvement. The patient achieved complete remission of the mucocutaneous lesions, two months after onset of therapy. However, therapy was continued for another month to reduce recurrences.

DISCUSSION

Bartonella infections manifest depending on the patient's immune status and, most likey, strains virulence (3). In immunocompetent persons, *B. henselae* can cause an acute infection called cat scratch disease, while in immunocompromised patients *Bartonella* species produce a wide range of clinical manifestations such as bacillary angiomatosis, peliosis hepatitis, splenitis, osteomyelitis, endocarditis, and bacteremia (4,5).

Figure 1b - Bacillary angiomatosis, clinical presentation: Erythematous papules on the oral and left tarsal mucosa and on the palm of the left hand.

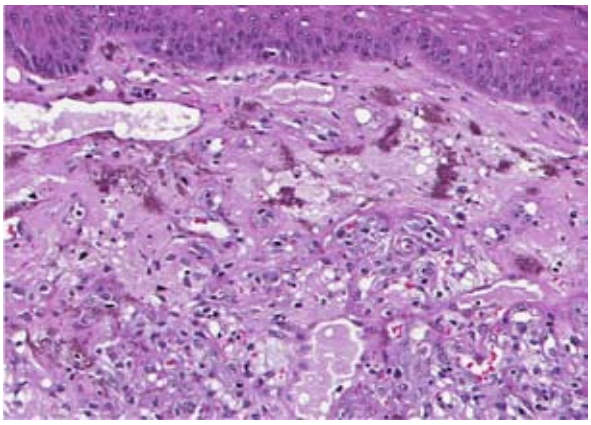

Figure 2a – Bacillary angiomatosis, histopathologic examination: lobular vascular proliferation with epithelioid endotelial cells and an inflammatory infiltrate with multiple neutrophils (H&E 100x)

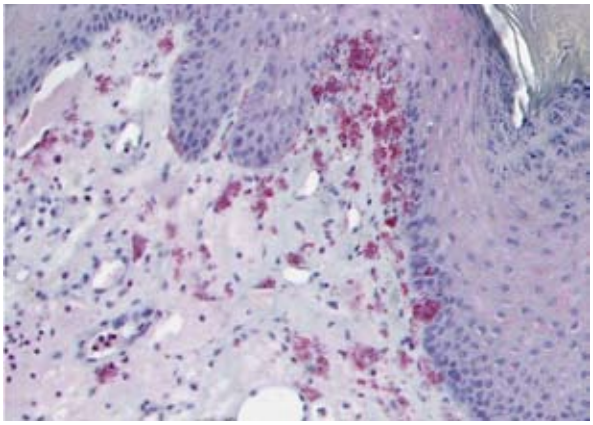

Figure 2b – Granular interstitial and perivascular material suggestive of bacillary angiomatosis (IHQ 100x)

Bacillary angiomatosis is an opportunistic infection first described in 1983 by Stoler *et al.* (6). It is mainly observed in HIV patients, especially when the $CD4^+$ count drops to less than 200 cells/mm^3 (1,2), and less frequently, in patients with other types of immunosuppression (3,5,7,8). Clinical cases have been described in immunocompetent patients only rarely (1,9).

Epidemiological studies revealed that the most common clinical feature of bacillary angiomatosis are skin lesions which occur in 55-90% of the patients (3). This disease may present with several patterns such as: globular angiomatous papules or nodules, subcutaneous nodules, large exophytic masses, and hyperpigmented indurated plaques on the extremities (1,7,9). It may be preceded or accompanied with constitutional symptoms such as malaise, fever, night sweats, headache, cough, anorexia, bloody stool, weight loss, and lymphadenopathy (1,2,9). Potentially fatal infections with organ involvement, such as: liver, spleen, gastrointestinal and respiratory tract, bone, bone marrow, and central nervous system infections, can also occur (3,5,7).

It is clinically difficult, but important, to distinguish between Kaposi's sarcoma and bacillary angiomatosis (3,7); the latter often has a peeling colarette on the basis of the lesions (8). Other diseases that should be considered in the differential diagnosis of bacillary angiomatosis are: pyogenic granuloma, histiocytoid hemangioma, lobular capillary hemangioma, angiosarcoma, glomangioma, angiokeratoma, cutaneous lymphomas, atypical mycobacteria infections, or histoplasmosis (1,7).

Histopathological examination is essential to confirm the diagnosis; and includes findings of circumscribed lobular proliferation of small blood vessels with "epitelioid" endothelial cells, central necrosis, a mixed inflammatory infiltrate with predominance of neutrophils, and, occasional, interstitial leukocytoclasia of non-ulcerated lobules (1,3,10). Silver staining or electron microscopy can show the interstitial granular material, revealing the bacilli that can also confirm the diagnosis (1,7).

In some cases it may be necessary to do other tests such as: culture, serology, or molecular methods (PCR). In immunocompromised patients, serology tests may have low sensitivities due to: cross-reactions between *Bartonella* sp. and *Coxiella burnetii* or *Chlamydia* sp., and the inability of these patients in producing antibody response (5), as in the case re-

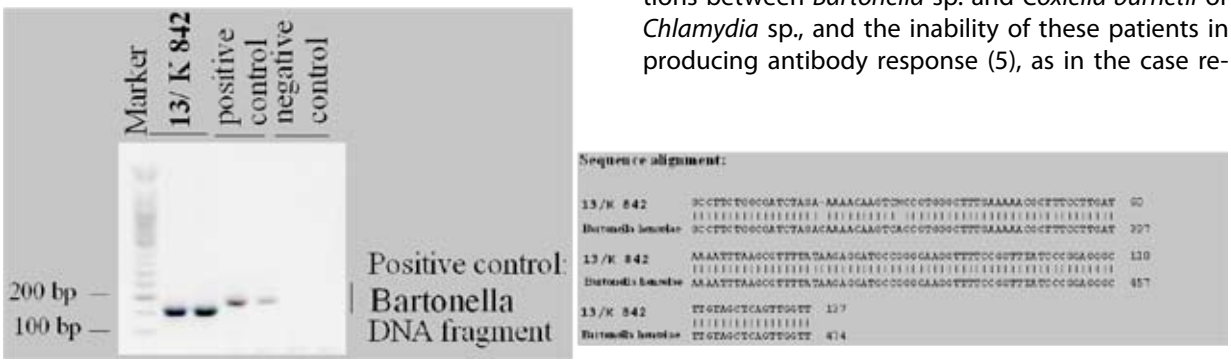

Figure 3 – Polymerase Chain Reaction study confirmed Bartonella henselae infection.

Acta Dermatovenerol Croat
2014;22(4):294-297

ported. The treatment of bacillary angiomatosis depends on the infective species, the clinical course, and the immunological status of the patient (4). Erythromycin 500 mg four times a day or doxycycline 100 mg twice a day should be the first options (4,10). Clarithromycin also showed good efficacy, fewer gastrointestinal side effects, (8) and a tissue-serum ratio greater than that of erythromycin in the skin after oral administration (8). The optimal duration of treatment is not yet defined. The cutaneous lesions regress completely after one month of therapy (1) and the treatment should be maintained for at least 2 months (5). In immunodeficient patients it is recommended to maintain therapy for 3-4 months, to reduce the risk of recurrences (10).

CONCLUSION

Bacillary angiomatosis should be considered in the differential diagnosis of angiomatous lesions in immunosuppressed patients. Since this is a potentially fatal disease with high morbidity and mortality, early diagnosis and treatment are essential to achieve a favorable prognosis.

References

1. Zarraga M, Rosen L, Herschthal D. Bacillary angiomatosis in an immunocompetent child: a case report and review of the literature. Am J Dermatopathol 2011;33:513-5.
2. Gazineo JL, Trope BM, Maceira JP, May SB, Coelho JM, Lambert JS, *et al.* Bacillary angiomatosis: description of 13 cases reported in five reference centers for AIDS treatment in Rio de Janeiro, Brazil. Rev Inst Med Trop Sao Paulo 2001;43:1-6.
3. Chian CA, Arrese JE, Piérard GE. Skin manifestations of *Bartonella* infections. Int J Dermatol 2002;41:461-6.
4. Prutsky G, Domecq JP, Mori L, Bebko S, Matzumura M, Sabouni A, *et al.* Treatment outcomes of human bartonellosis: a systematic review and meta-analysis. Int J Infect Dis 2013;17:e811-e9.
5. Gasquet S, Maurin M, Brouqui P, Lepidi H, Raoult D. Bacillary angiomatosis in immunocompromised patients. AIDS 1998;12:1793-803.
6. Stoler MH, Bonfiglio TA, Steigbigel RT, Pereira M. An atypical subcutaneous infection associated with acquired immune deficiency syndrome. Am J Clin Pathol 1983;80:714-8.
7. Amsbaugh S, Huiras E, Wang NS, Wever A, Warren S. Bacillary angiomatosis associated with pseudoepitheliomatous hyperplasia. Am J Dermatopathol 2006;28:32-5.
8. Milde P, Brunner M, Borchard F, Südhoff T, Burk M, Zumdick M, *et al.* Cutaneous bacillary angiomatosis in a patient with chronic lymphocytic leukemia. Arch Dermatol 1995;131:933-6.
9. Turgut M, Alabaz D, Karakaş M, Kavak M, Aksaray N, Alhan E, *et al.* Bacillary angiomatosis in an immunocompetent child with a grafted traumatic wound. J Dermatol 2004;31:844-7.
10. Velho PE, Souza E, Cintra ML, Mariotto A, Moraes A. Bacillary angiomatosis: literature review and iconographic documentation. An Bras Dermatol 2003;78:601-9.