

# Diagnosis of Bacillary Angiomatosis and Kaposi's Sarcoma in the same Skin Lesion in a Patient with Recent HIV/AIDS Diagnosis

Correa J<sup>1,2\*</sup>, Villafane MF<sup>1,2</sup>, De Carolis L<sup>1,2</sup>, Corti M<sup>1,2</sup>, Sforza R<sup>1</sup>, Maronna E<sup>3</sup>, Giamperetti S<sup>4</sup> and Bare P<sup>5</sup>

<sup>1</sup>HIV/AIDS Division, Infectious Diseases F. J. Muniz Hospital, Argentina

<sup>2</sup>Department of Medicine, University of Buenos Aires, Argentina

<sup>3</sup>Histopathology Laboratory, Infectious Diseases F. J. Muniz Hospital, Argentina

<sup>4</sup>Zoopathology Laboratory, Infectious Diseases F. J. Muniz Hospital, Argentina

<sup>5</sup>Virology Laboratory, National Academy of Medicine, Argentina

## ARTICLE INFO

### Article history:

Received: 21 September 2017

Accepted: 27 November 2017

Published: 05 December 2017

### Keywords:

Bacillary angiomatosis;  
Kaposi's sarcoma;  
HIV/AIDS

**Copyright:** © 2017 Correa J et al.,  
Clin Dermatol Res Ther

This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**Citation this article:** Correa J, Villafane MF, De Carolis L, Corti M, Sforza R et al.. Diagnosis of Bacillary Angiomatosis and Kaposi's Sarcoma in the same Skin Lesion in a Patient with Recent HIV/AIDS Diagnosis. Clin Dermatol Res Ther. 2017; 1(1):113.

## ABSTRACT

Kaposi's Sarcoma (KS) is polyclonal multifocal disease of endothelial origin, with four clinical and epidemiological well described variants. AIDS-related KS has a variable clinical course, ranging from minimal disease located to the skin and presenting as an incidental finding to a rapidly progressing neoplasm with skin, mucosal, and visceral compromise that can result in significant morbidity and mortality, depending upon the specific sites of involvement.

Bacillary Angiomatosis (BA) is a rare manifestation of infection caused by *Bartonella* species, which leads to vasoproliferative lesions of skin and other organs. Bacillary angiomatosis affects individuals with advanced HIV disease or other immune compromised individuals. There are two conceptually distinct *Bartonella*-associated syndromes: bacteremia (in the absence of focal tissue vascular proliferative response) and the tissue infection associated with angiogenic response.

A major challenge in the diagnosis of cutaneous BA is the diverse presentation of lesions. The most important clinical differential diagnosis of cutaneous lesions includes KS.

Here, we present an HIV/AIDS patient that developed concomitant KS and BA in the same skin lesion diagnosis by histopathological examination of biopsy sample and biomolecular diagnosis methods.

## Introduction

Kaposi's sarcoma (KS) and Bacillary Angiomatosis (BA) are the two more frequent angiomatous lesions associated with Human Immunodeficiency (HIV) infection. Kaposi's sarcoma was recognized early in the acquired immunodeficiency syndrome epidemic because it occurred much more frequently than had been previously seen in non-HIV infected persons. On the other hand, BA first described by Stoler et al in 19831, represents a *Bartonella henselae* or *quintana* infection causing angioproliferative lesions in immune compromised persons, especially those with advanced HIV disease and severe immune suppression [1,2]. The main clinical differential diagnosis for cutaneous and mucosal BA lesions is KS.

### Correspondence:

**Dr. Jorge Correa,**

Division "B", Infectious Diseases F.J.  
Muñiz Hospital, Uspallata 2272,  
CABA, Argentina,

Email: jercorrea@gmail.com

Here, we present an HIV/AIDS patient that developed concomitant KS and BA in the same skin lesion diagnosis by histopathological examination of biopsy sample and biomolecular diagnosis methods.

### Case Report

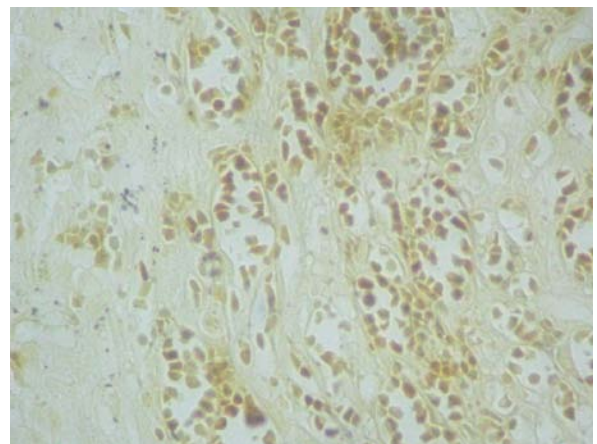
A 59-year-old man, with recent diagnosis of HIV infection, was admitted to our Department of HIV/AIDS with a one month history of wasting syndrome, night sweats and weight loss (17 kg in the last three months). He acquired HIV infection secondary to unprotected heterosexual intercourse. He was not receiving Highly Active Antiretroviral Therapy (HAART). On presentation, the CD4-T-cell count was 6 cells/ $\mu$ L (3%) and the plasma viral load was 334.000 copies/mL (log<sub>10</sub> 5.5). As an epidemiological background, the patient worked in a cemetery and had contact with felines. Physical examination revealed an indurated and violaceous nodule located on the face near the left labial commissure (Figure 1). Relevant laboratory findings included: haematocrit 24%, haemoglobin 8.3g%, white blood cell count  $3.3 \times 10^3$ /L, platelets  $125 \times 10^6$ , erythrocyte sedimentation rate 40 mm/1st h. Renal and liver function were normal. HCV and HBV serology were negative. CMV-pp65 antigen test was positive (18 cells/200.000).



**Figure 1:** Erythematous nodular lesion near the labial commissure.

For direct pathogen identification a skin biopsy was performed; hematoxylin-eosin stain showed a leukocyte infiltration, Warthin Starry stain was negative for

microorganisms (Figure 2). An EDTA blood sample and tissue sample of the nodular skin lesion were analyzed in polymerase chain reaction (PCR) assays. A PCR for Bartonella species was positive in both the cutaneous and in blood. For the identification of Bartonella, DNA from suspensions of bacterial colonies or from blood or tissue samples was extracted with the blood and tissue QIAampDNA Mini kit (Qiagen, Germany) as per the manufacturer's recommendations. Primers for Bartonella PCR were designed to target segments of the rib C gene that were well conserved among Bartonella species but not with unrelated microorganisms. Each reaction was performed in a total volume of 50  $\mu$ L PCR on a Bio-Rad MyCycler with cycles and primers as previously described for G. Johnson et al. (2003). A 10  $\mu$ L volume of each amplicon was subjected to electrophoresis on 1.5% agarose gels containing



**Figure 2:** Biopsy specimen showing the negative of Warthin Starry stain.

SYBR Safe DNA gel stains (Invitrogen, USA). In each PCR run, an aliquot of phosphate-buffered saline was also subjected to DNA extraction as a negative control.

The histopathology of skin biopsy showed dermal proliferation of spindle cells with hyperchromatic nuclei arranged in fascicles and forming irregular vascular structures with extravasation of erythrocytes and presence of hemosiderophages; diagnosis of Kaposi's sarcoma was confirmed. HHV-8 was positive in the biopsy sample. The detection of DNA HHV-8 was performed by PCR in biopsy sample by tissue disruption

to perform the DNA extraction, DNA purification by spectrophotometry analysis and DNA amplification with specific oligonucleated primers.

Antibiotic treatment for Bartonellosis based on chlarytromycin and ciprofloxacin was commenced with improvement of the skin lesions within the second week of treatment. Because of the patient's poor clinical condition, he couldn't receive chemotherapy for KS.

## Discussion

BA, first described by Stoler et al in 1983, is a multisystem bacterial infectious vasculoproliferative disorder caused by *Bartonella henselae* and *Bartonella quintana* and is most commonly seen in HIV-infected individuals with CD4 counts less than 200 cells/ $\mu$ L [1,3]. Infection is spread to mammals by arthropod vectors, including ticks, biting flies, fleas, and body lice [4,5]. BA commonly presents in the skin but may affect almost any visceral organ, including liver (peliosis), spleen, or the oral mucosal and nasal cavities [6].

The typical cutaneous lesions of BA appear as single or multiple bright red to deep purple dome-shaped papules, nodules, or plaques. Cutaneous lesions have a variety of morphologies, including papular, nodular, pedunculated, or verrucous forms, which often appear as small red-purple papules before enlarging. The lesions may bleed profusely with trauma and are usually singular or several in number but may rarely appear in disseminated form [7,8]. Additionally, BA is accompanied by an unspecific infectious syndrome with fever, myalgias, arthralgias, anorexia, night sweats and weight loss. Clinical manifestations of BA can include oral cavity mucosal involvement with similar lesions to the skin, liver compromise named as hepatic peliosis and more rarely spleen lesions. Hepatic peliosis is characterized by the presence of multiple blood-filled lacunae lesions. Eventually, liver peliosis can be the only or the first manifestation of the disseminated disease. The clinical differential diagnosis for a lesion of cutaneous BA may include KS, pyogenic granuloma, cherry angioma, dermatofibroma, hemangioma, mycobacterial infection such as tuberculosis, coccidioidomycosis, cryptococcosis, and histoplasmosis [9].

KS is a malignant neoplasm, described by Moritz Kaposi in 1872 [10]. It originates from the endothelium and it is a low grade and indolent malignancy, considered rare until the discovery of the AIDS epidemic. Epidemiologic evidence indicated that AIDS-associated KS may have an infectious etiology. Since the initial detection of human

herpes virus type-8 (HHV-8) in KS biopsy smears, some serological evidence implicates this viral agent with the development of the neoplasm as we could find in our patient. However, HHV-8 infection is a necessary factor but not sufficient in the etiology of all clinical forms of KS (classic, endemic, iatrogenic or postransplant and epidemic). Despite the fact that each of them has a distinct clinical course, they all have in common the participation of HHV-8 or the Kaposi's sarcoma associated herpes virus (KSHV), although other factors are necessary for the develop of the neoplasm [11,12]. KS, like BA, is also seen in HIV-infected patients with low CD4 T cell counts. With less frequency patients with KS also present with B symptoms.

The overlapping constellation of cutaneous manifestations of BA and KS make them clinically indistinguishable from each other when presenting as a single or multiple violaceous papules, nodules, plaques or tumors [6]. Occasionally, clinical clues can lead toward one diagnosis or the other. KS lesions may cause prominent lymphedema of the legs, eyelids, lips and scrotum, and with frequent involvement of oral cavity with lesions that compromise frequently the hard and soft palate and the gingiva. BA may have a very rapid onset with swift growth of lesions, which may occur with immune reconstitution inflammatory syndrome, further complicating the difficulty in distinguishing these entities without histopathological confirmation. However, KS can also develop rapidly in severely immunocompromised patients and during immune reconstitution, and BA can have oral lesions that mimic KS. In addition, other HIV-associated dermatologic conditions, such as disseminated mycobacterial or fungal infections can have similar presentations to those of KS or BA [13,14].

In the literature review, Berger et al described two cases of concurrent BA and KS in the same lesions of two AIDS

patients. The authors emphasize that these two conditions may occur simultaneously, and in this stage they are clinically, histologically, and pathogenically distinct, and respond differently to treatment [15].

Colesional pathology may easily be overlooked in skin biopsies from patients with HIV/AIDS, especially when the primary pathological lesion dominates the histological picture [16]. It is, therefore, essential that in this clinical context histological specimens are always examined carefully to ensure that a second (or perhaps even a third) infective organism is not overlooked.

Differentiating BA from KS is largely reliant on skin biopsy with histopathologic examination, which, for BA, demonstrates protuberant endothelial cells surrounded by clumps of bacilli that are visible with Warthin-Starry staining [17]. BA lesions have well-developed capillaries and inflamed the cutaneous stroma that harbors clumps of basophilic bacilli and with an acute inflammatory infiltrate. On the other hand, KS is characterized of ill-developed vasculature with slit-like spaces, prominent spindle cells, many extravasated erythrocytes, siderophages and extracellular haemosiderin deposits. These features are less commonly seen in BA. Additionally, KS often has an abundance of plasma cells, in contrast to the mixed infiltrate, with a predominance of neutrophils that often can often be seen in BA [18].

The use of PCR-based tests has played an important role in studies and reports of Bartonella-associated infections because of the difficulty in isolating Bartonella species from tissue samples. The PCR test generally can distinguish among the different Bartonella species. In our patient PCR for Bartonella species was positive not only in serum but also in biopsy smears.

Although there is no consensus treatment for BA, clinicians experienced in treating this condition recommend therapy with oral erythromycin or doxycycline for 8 to 12 weeks to avoid relapses [7].

Care for patients with KS must take into account the type of KS, the extent of the tumor mucocutaneous lesions and the organs involved, especially gastrointestinal tract and lungs, but also its potential effect on the patient's overall clinical condition and virological, immune, and

hematological status. A recent review of four available staging systems for epidemic KS confirmed the importance of CD4 cell counts and other HIV-related prognostic factors for predicting survival in KS. For limited disease, defined as less than 10 skin lesions with no proximal edema and no or minimal

mucosal involvement, HAART alone is preferred, with strict clinical monitoring to detect progression of KS, which is rare but has been reported in both patients with immune restoration and patients without immune restoration. Adjuvant local therapies can be used to treat patients who experience such progression [19]. Indications for systemic chemotherapy include widespread skin involvement (more than 10 lesions), extensive oral involvement, marked symptomatic edema, rapidly progressive disease, symptomatic visceral KS, and KS flare. Currently, liposomal anthracyclines and taxanes are the backbone of systemic cytotoxic therapy against KS [20].

In conclusion, the coexistence of BA and KS in the same cutaneous lesions has been rarely reported in the literature. BA misdiagnosed as KS can have 2 consequences: failure to treat BA, which can affect bone and viscera and may be life threatening, and unnecessary administration of highly toxic chemotherapeutic agents intended to treat KS. Treatment with appropriate antibiotic therapy (current recommendations favor either doxycycline or erythromycin for 3 months) typically leads to complete resolution of BA. Failure to treat often results in death from hepatic or pulmonary failure.

## References

1. Stoler MH, Bonfiglio TA, Steigbigel RT, Pereira M. (1983). An atypical subcutaneous infection associated with acquired immune deficiency syndrome. *Am J ClinPathol.* 80: 714–718.
2. Corti M, Metta H, Trione N, Nicita D, Romer Y, et al. (2014). Angiomatosis bacilar por Bartonella Henselae en un paciente con SIDA: Presentación de un caso y revisión de la literatura. *Rev Argent Dermatol.* 95: 2-8.

3. Mohle-Boetani JC, Koehler JE, Berger TG, LeBoit PE, Kemper CA, et al. (1996). Bacillary angiomatosis and bacillary peliosis in patients infected with human immunodeficiency virus: clinical characteristics in a case-control study. *Clin Infect Dis*. 22: 794-800.
4. Billeter SA, Levy MG, Chomel BB, Breitschwerdt EB. (2008). Vector transmission of *Bartonella* species with emphasis on the potential for tick transmission. *Med Vet Entomol*. 22: 1–15.
5. Cotté V, Bonnet S, Le Rhun D, Le Naour E, Chauvin A, et al. (2008). Transmission of *Bartonella henselae* by *Ixodes ricinus*. *Emerg Infect Dis*. 14: 1074–1080.
6. Schwartz RA, Nychay SG, Janniger CK, Lambert W. (1997). Bacillary angiomatosis: presentation of six patients, some with unusual features. *Br J Dermatol*. 136: 60-65.
7. Koehler JE, Tappero JW. (1993). Bacillary angiomatosis and bacillary peliosis in patients infected with human immunodeficiency virus. *Clin Infect Dis*. 17: 612–624.
8. Tappero JW, Perkins BA, Wenger JD, Berger TG. (1995). Cutaneous manifestations of opportunistic infections in patients infected with human immunodeficiency virus. *Clin Microbiol Rev*. 8: 440–450.
9. Cortes EE, Saraceni V, Medeiros D, Ribeiro I. (2000). Bacillary angiomatosis and Kaposi's sarcoma in AIDS. *AIDS Patient Care and STDS*. 14: 179–182.
10. Kaposi M. (1872). Idiopathisches multiples Pigmentsarkom der Haut. *Archiv fur Dermatologi und Syphilis*. 3: 265–273.
11. Moore PS, Chang Y. (1995). Detection of herpesvirus-like DNA sequences in Kaposi's sarcoma in patients with and those without HIV infection. *N Engl J Med*. 332: 1181-1185.
12. Corti M, Villafane MF, Metta H, Trione N, Bare P, et al. (2015). Detection of Kaposi's sarcoma-associated human herpes virus type 8 DNA in biopsy smears of human immunodeficiency virus-infected patients. *Glob Dermatol*. 3: 238-240.
13. Tiussi RM, Caus ALO, Diniz LM, Lucas EA. (2012). Sarcoma de Kaposi: clinical and pathological aspects in patients seen at the Hospital Universitário Cassiano Antônio Moraes - Vitória - Espírito Santo - Brazil. *An Bras Dermatol*. 87: 220-227.
14. Rodriguez O, Campbell LR, Bacha JM, Kovarik CL. (2016). Successful treatment of bacillary angiomatosis with oral doxycycline in an HIV-infected child with skin lesions mimicking Kaposi sarcoma. *JAAD Case Rep*. 2: 77-79.
15. Berger TG, Tappero JW, Kaymen A, LeBoit PE. (1989). Bacillary (epithelioid) angiomatosis and concurrent Kaposi's sarcoma in acquired immunodeficiency syndrome. *Arch Dermatol*. 125: 1543-1547.
16. Grayson W. (2011). Recognition of dual or multiple pathology in skin biopsies from patients with HIV/AIDS. *Patholog Res Int*.
17. LeBoit PE, Berger TG, Egbert BM, Beckstead JH, Yen TS, et al. (1989). Bacillary angiomatosis. The histopathology and differential diagnosis of a pseudoneoplastic infection in patients with human immunodeficiency virus disease. *Am J Surg Pathol*. 13: 909–920.
18. Forrestel AK, Naujokas A, Martin JN, Maurer TA, McCalmont TH, et al. (2015). Bacillary angiomatosis masquerading as Kaposi's sarcoma in East Africa. *J Int Assoc Provid AIDS Care*. 14: 21–25.
19. Antinori A, Izzi I, Ammassari A, Camilli G, Murri R, et al. (1992). Evaluation of different staging systems for Kaposi's sarcoma in HIV-infected patients. *J Cancer Res Clin Oncol*. 118: 635–643.
20. Radu O, Pantanowitz L. (2013). Kaposi Sarcoma. *Arch Pathol Lab Med*. 137: 289–294.