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Bacillary Angiomatosis Associated Immune Reconstitution Inflammatory Syndrome

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Abstract

Identifying cutaneous lesions among persons living with human immunodeficiency virus (HIV) can present as a diagnostic challenge. Bacillary angiomatosis (BA) is a rare disease characterized by neovascular proliferation of the skin, presenting as tumor-like masses[1]. Since the advent antiretroviral therapy (ART), bacillary angiomatosis have been rare amongst patients with HIV [1]. We present a case of a 37-year-old male, coming in with 2 year history of generalized multiple violaceous plaques, with exophytic nodules on the lower extremities, that bleed easily when disturbed. An immunocompromised condition was considered after admission for pneumonia and persistence of cutaneous lesions. After testing positive for HIV, he was started on Lamivudine/Tenofovir/Efavirenz (LTE) with good compliance. Worsening of his lesions were observed 1 month after ART, prompting referral to our HIV and AIDS Core Team (HACT) Clinic. He was initially treated as plaque psoriasis with seborrheic dermatitis, but biopsy revealed bacillary angiomatosis. Significant improvement of cutaneous lesions were observed 1 month post oral erythromycin therapy.

Keywords: Bacillary Angiomatosis, Human Immunodeficiency Virus, Immune Reconstitution Inflammatory Syndrome, Bacillary Associated Uveitis

1. Introduction

Bacillary angiomatosis (BA) is a rare disease characterized by neovascular proliferation of the skin or the internal organs, presenting as tumor-like masses[1]. Stoller and colleagues first described this disease in 1983 in an HIV-infected patient with multiple subcutaneous nodules[2]. The earliest, most common lesion appears as discrete pinpoint red–purple papules which may ulcerate and become crusted [3]. It may enlarge to an exophytic or pedunculated nodules [4]. They are often dome shaped, vascular lesions, and they may be surrounded by erythema or a collarette of scale [4]. The lesions are friable, and can bleed profusely due to extensive vascularization [5].

This disease is now known to occur in other immunocompromised states such as organ transplant recipients, but may also occur in immunocompetent persons [1]. During the pre-Highly Active Anti-retroviral Therapy (HAART) era, the incidence of BA was 1.2/1000 patients[1]. Currently, this disease have been rare amongst HIV patients occurring predominantly among HIV patients with a CD4 cell counts below 200 cells/uL [5].

BA is an infectious, pseudo neoplastic cutaneous vascular disorder caused by the genus Bartonella, most commonly *Bartonella Quintana and Bartonella henselae* [3]. The bacillus remained refractory to isolation attempts for years until 1992 [2]. Since then, the Bartonella genus has expanded from a single species to 29 officially recognized species [2]. About 50% of patients with bacillary angiomatosis are infected with B. henselae, and the remaining cases are caused by *B. Quintana* [6]. Transmission of the disease is through flea-infested cats which transmits the organism to humans through bites or scratches [6]. *B. Quintana* can also be transmitted through body louse among homeless, impoverished and low socioeconomic populations [1]. *B. Quintana* causes cutaneous bacillary angiomatosis with occasional involvement of the subcutaneous tissues, and bone while *B. henselae* causes cat-scratch disease and peliosis of the liver and spleen [1,7].

2. Case Report

A 37-year-old male was referred to our HIV and AIDS Core Team (HACT) Clinic due to multiple cutaneous lesions associated with blurring of vision, occasional productive cough and exertional dyspnea. Two years prior, he had multiple erythematous papules on the face. In the interim, his facial lesions gradually extended to his extremities and torso. This prompted consultation at a HACT clinic where he tested positive for HIV. He was started on Lamivudine/Tenofovir/Efavirenz (LTE) combination tablets. However, 1 month after LTE, his rashes worsened, now increasing

towards the extremities, with the appearance of friable exophytic pedunculated nodules. He denies exposure to cats but is now homeless, jobless and living in poverty.

On physical examination, there were multiple erythematous to violaceous round papules and plaques with scales and crusting scattered all over, mostly on the upper and lower extremities, sparing the palms and soles (Figure 1). There were five nodular, pedunculated exophytic masses 2-5 cm which bled easily when disturbed. The eyes were erythematous with no discharge.

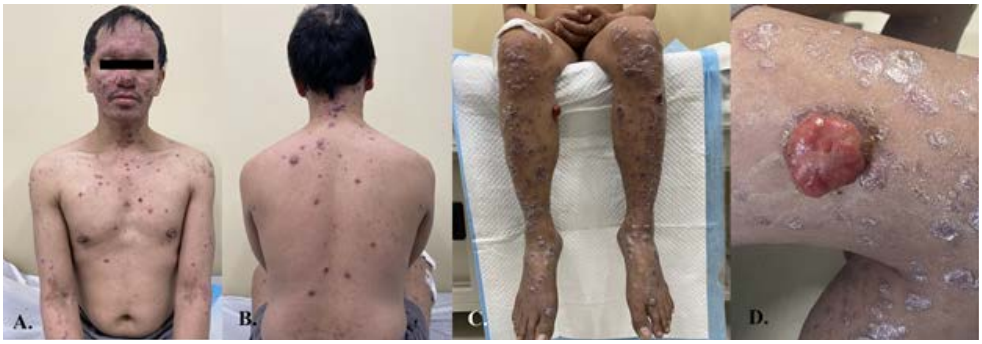

Figure 1: Presentation of the Cutaneous Lesions on the (a) Anterior, (b) Posterior Trunk and Lower Extremities (c) Prior to Erythromycin Therapy. an Exophytic Pedunculated Mass on the Left Lateral Leg where the Biopsy was Taken (d)

Baseline CD4 count was 72 cells/uL, HIV Viral load was unavailable. Biopsy of exophytic mass showed diffuse proliferation of blood vessels surrounded with mixed infiltrates of lymphocytes, histiocytes, and neutrophils. Adjacent to neutrophils are bluish-violaceous granular collections highly suggestive of bacillary angiomatosis (Figure 2). The purplish grey colonies surrounded with numerous neutrophilic infiltrates stained positive on the GMS Stain. WarthinStarry Stain and HHV 8 however were unavailable in the locality. Wound gram stain and culture was positive for Methicillin Resistant Staphylococcus Aureus (MRSA) but was negative for Acid Fast Bacilli (AFB). Blood cultures on both arms showed positive for *Staphylococcus cohnii.*

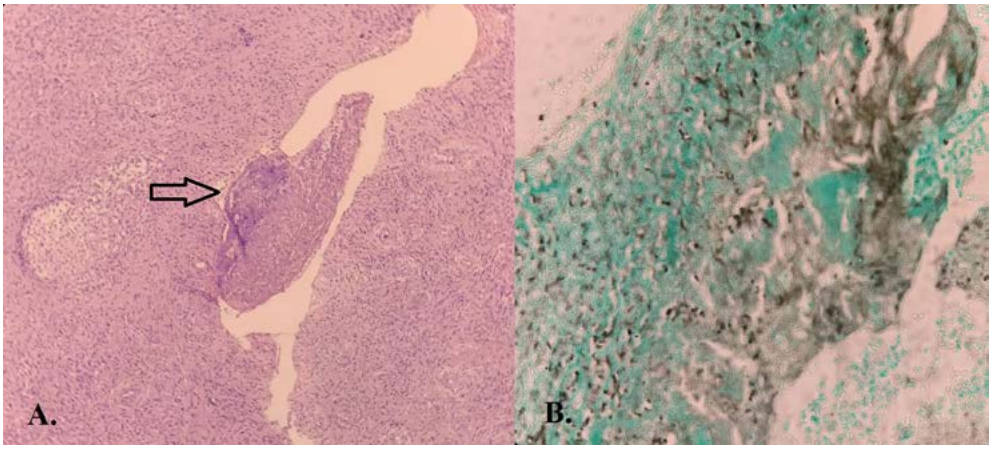

Figure 2: Hematoxylin and Eosin Stain (A) Demonstrating Diffuse Proliferation of Blood Vessels Surrounded with Mixed Infiltrates of Lymphocytes, Histiocytes, and Neutrophils (Arrow). Bluishviolaceous Granular Collections Highly Suggestive of Bacillary Angiomatosis. Grocott Methenamine Silver (GMS) Stained Positive (B)

Work-up revealed reactive for Hepatitis B surface antigen and anti-Treponema Pallidum, with high quantitative Treponema pallidum hemagglutination test at 25.50, confirming concomitant Hepatitis B and Syphilitic infection. Chest radiograph showed bronchitis, but sputum gene expert was negative for acid fast bacilli. Complete blood count, kidney and liver function tests were all normal.

He was started on Erythromycin 500 mg tablet every 6 hours, Penicillin G 2.4 million units' intramuscular injection weekly for 3 doses and Amoxicillin Clavulanic Acid for acute bronchitis. LTE was continued and Trimethoprim Sulfamethoxazole was started as prophylaxis. He was seen by Dermatology, where additional diagnosis of seborrheic dermatitis and androgenic alopecia was made. A referral to Ophthalmology was done which revealed anterior uveitis. Retina was not visualized due to anterior synechia prohibiting retinal examination. He was then started on Prednisone tablet. One month after taking erythromycin there was significant improvement of his lesions (Figure 3), with noticeable flattening of the lesions and clearing of plaques and crusting. Furthermore, the exophytic nodules regressed to <2 cm in largest diameter.

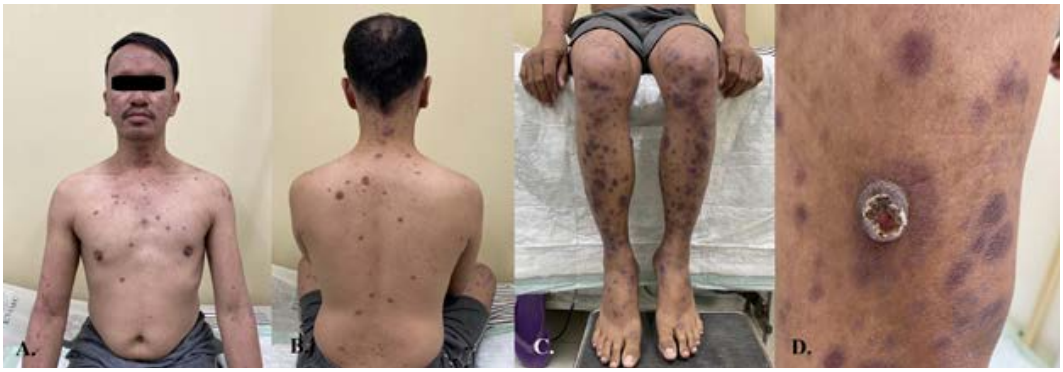

Figure 3: One Month after Erythromycin Therapy, Notice that the Lesions Started Clearing and the Plaques Started to Resolve (A-C). The Exophytic Mass Started to Regress (D)

3. Discussion

Bacillary angiomatosis can occur in the setting of non-compliance with ART or late diagnosis of HIV infection [1]. Disease course may be insidious to subacute in the immunocompromised, but can also be sudden among immunocompetent individuals [5]. Different skin lesions seen in this disease are: (1) globular angiomatous papules or nodules resembling pyogenic granuloma, (2) violaceous nodules resembling Kaposi sarcoma, (3) a lichenoid violaceous plaque, or (4) a subcutaneous nodule with or without ulceration [6]. Histologically, it presents as lobular proliferation of capillaries lined with prominent large endothelial cells, inflammatory infiltrate with neutrophils, and aggregates of bacillary bodies demonstrable on Warthin-Starry silver stain [4]. Histologically, lesions of BA can present similarly to Pyogenic granuloma however, the presence of granular clumps of pinkish to purplish rods is an important clue for a microbiologic diagnosis [8]. Histopathologic examination also differentiates the clinically similar lesions of BA and Kaposi Sarcoma.

The causative agents of bacillary angiomatosis are fastidious, gram-negative, facultative intracellular *bacilli, B. quintana and B. henselae*, with a tropism for erythrocytes and endothelial tissue [9,10]. It initiates a neoproliferative process based on the production of angiogenetic molecules, like vascular endothelial growth factor (VEGF) and IL-8 [6]. Furthermore, there is production of proteins (BepA and BepA2) that induce an antiapoptotic state in endothelial collagen tissue, facilitating vascular proliferation [10]. The treatment of choice for mild cutaneous bacillary angiomatosis is erythromycin or doxycycline for 12 weeks [1]. The response usually seen by three to four weeks [1]. Erythromycin is effective as first-line treatment probably due to both its anti-bacterial and anti-angiogenic effects [9].

Immune Reconstitution Inflammatory Syndrome (IRIS) is the unmasking or worsening of an underlying infection following antiretroviral therapy (ART) initiation [11]. It usually appears days or weeks following the start of HAART, but can also be seen several months later [11]. There have been reports of dramatic exacerbation of bacillary angiomatosis secondary to IRIS in HIV-infected patients [4]. A review revealed five cases with low CD4 counts <100 [1]. One case of *Bartonella quintana* bacillary angiomatosis resulted to death in an HIV-infected man during the immune restoration phase due to external tracheal compression of a lateral neck mass [11].

This case also presented with bilateral blurring of vision and eye redness. This could be secondary to bartonella associated uveitis; however, the ophthalmologic examination was limited by anterior synechiae. The first published description of Bartonella-associated uveitis was that of a nongranulomatous anterior uveitis without posterior segment findings [12]. Bartonella-associated uveitis can either be unilateral or bilateral; anterior, intermediate, or posterior; granulomatous or nongranulomatous [13]. A study by Brydak-Godowska showed specific IgG-class antibody in 33.3% of the patients with uveitis, thus recommending screening for Bartonella spp. in the workup for uveitis [14,15].

4. Conclusion

Here we describe a 37-year-old HIV patient presenting with multiple cutaneous lesions with worsening post HAART initiation. This could be due to an unmasking secondary to immune reconstitution inflammatory syndrome. Biopsy showed bacillary angiomatosis. Rapid improvement of skin lesions were observed post erythromycin therapy.

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