

# A Case Report of Bacillary Angiomatosis in a Patient Infected With Human Immunodeficiency Virus

Cindy F. Hoffman, DO; Dimitria Papadopoulos, DO; Debbie M. Palmer, DO; Craig Austin, MD; Charles A. Gropper, MD

## GOAL

To gain a complete and detailed understanding of bacillary angiomatosis

## OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Discuss the clinical manifestations of bacillary angiomatosis.
2. Explain the histologic findings of bacillary angiomatosis.
3. Describe the treatment for bacillary angiomatosis.

CME Test on page 210.

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*A man infected with human immunodeficiency virus (HIV) presented with a few-month history of an enlarging friable growth on the medial area of the left foot and a one-week history of bilateral lower extremity edema. Clinical and histologic examination led to a diagnosis of bacillary*

*angiomatosis, and the patient responded to antibiotic therapy. We provide an overview of bacillary angiomatosis, a rare disorder that affects immunocompromised patients with CD4 cell counts less than 100/ $\mu$ L.*

## Case Report

A 45-year-old black man whose medical history included human immunodeficiency virus (HIV) infection, endocarditis, congestive heart failure, intravenous drug abuse, end-stage renal disease, sinusitis, and pneumonia presented with a few-month history of a progressively enlarging growth on the left foot (a growth that bled with mild trauma)

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From the Department of Dermatology, Saint Barnabas Hospital, Bronx, New York. Dr. Hoffman is Director of the Dermatology Residency Program and Associate Attending Physician.

Drs. Papadopoulos and Palmer are Dermatology Residents. Dr. Austin is Assistant Clinical Professor of Dermatopathology. Dr. Gropper is Chief of Dermatology.

Reprints: Cindy F. Hoffman, DO, Third Ave and 183rd St, Bronx, NY 10457 (e-mail: erderm@aol.com).



A well-circumscribed hemorrhagic nodule on the medial area of the left foot.

and a one-week history of bilateral lower extremity edema. The patient's medications included methadone, temazepam, zolpidem, calcium carbonate, calcitriol, folic acid, multivitamin, ferrous sulfate, and trimethoprim-sulfamethoxazole.

On physical examination, the patient was afebrile and had normal mucous membranes, brittle fingernails, generalized xerosis, "track marks" on the left upper extremity, bilateral lower extremity pitting edema that was tender and warm to the touch, and a 1-cm well-circumscribed hemorrhagic nodule on the medial area of the left foot (Figure).

Results of laboratory studies were a leukocyte count of  $7.3 \times 10^3/\mu\text{L}$  (reference range,  $4.8\text{--}11 \times 10^3/\mu\text{L}$ ), a CD4 lymphocyte count of 107 cumulative cells (reference range, 400–1770 cumulative cells), a CD8 lymphocyte count of 2292 cumulative cells (reference range, 240–1200 cumulative cells), and no growth of any organisms in 3 serial serum blood cultures. Findings from bilateral lower extremity x-rays and Doppler ultrasounds were normal. The differential diagnoses that were considered included pyogenic granuloma, hemangioma, Kaposi sarcoma, papular angiokeratoma, arteriovenous malformation, hemangiopericytoma, vasculitis, thrombophlebitis, and an infectious etiology.

A biopsy specimen taken from the nodule on the medial area of the left foot contained a lobe of proliferating capillaries, venules, and neutrophils and an interstitial bacillary deposit. A Warthin-Starry silver stain tested positive for bacilli.

An initial diagnosis of cellulitis was made, and the patient was treated with amoxicillin. After a final diagnosis of bacillary angiomatosis was made, the antibiotic regimen was changed to erythromycin 500 mg 4 times a day. The hemorrhagic nodule cleared after 8 weeks of therapy. The patient was then lost to follow-up.

#### Comment

First described in 1983 by Stoler et al,<sup>1</sup> bacillary angiomatosis is an angioproliferative disease that often occurs with severe immunodeficiency, as in advanced acquired immunodeficiency syndrome.<sup>2,3</sup> This disease has been found in patients with acute myeloblastic leukemia, chronic lymphocytic leukemia, and organ transplants.<sup>2-4</sup> Bacillary angiomatosis usually manifests as cutaneous tumors but also may manifest as systemic disease.<sup>4</sup> The name of this disease was derived from the proliferating blood vessels seen in histologic specimens and from the presence of numerous bacillary organ-

isms detected with Warthin-Starry silver stain or electron microscopy.<sup>2</sup>

Although *Bartonella* infections are not uncommon, bacillary angiomatosis is a rare (or underdiagnosed) disorder—1.2 cases per 1000 patients infected with HIV.<sup>2</sup> Patients affected most are those with CD4 cell counts less than 100/ $\mu$ L.<sup>2</sup> Regular use of antibiotics may account for the rarity or underdiagnosis of this disease in patients infected with HIV.<sup>2</sup>

The first reported case of infection with organisms of *Rochalimaea* genus, now known as *Bartonella*, occurred during World War I and was termed *trench fever*.<sup>2</sup> Transmission was through the bite of the human body louse.<sup>5</sup> In 1990, Relman et al<sup>6</sup> recognized a relation between trench fever and *Rochalimaea quintana*, now known as *Bartonella quintana*, the cause of bacillary angiomatosis. Transmission through the body louse vector accounts for the association of *B quintana* infection with homelessness.<sup>2</sup> In 1992, another member of the genus *Bartonella*, *B henselae*, also was recognized as an etiologic agent of this illness.<sup>2</sup> *B henselae* is transmitted to humans through direct contact with cats or cat fleas, *Ctenocephalides felis*.<sup>2</sup> *B quintana* is responsible for most cases of subcutaneous infection, deep soft-tissue disease, and lytic bone lesions.<sup>5</sup> Liver and lymph node involvement have been associated with *B henselae* infection.<sup>5</sup> *Bartonella* species are fastidious gram-negative bacteria.<sup>3</sup>

Bacillary angiomatosis can present typically and atypically. Typical presentation is an inflammatory disease most often involving the skin.<sup>2</sup> One or multiple skin lesions can develop, and these can be localized in cutaneous and subcutaneous tissues.<sup>2</sup> The usual lesion is an angiomatous papule or nodule resembling a pyogenic granuloma or a subcutaneous nodule with or without ulceration.<sup>7</sup> Atypical presentation resembles Kaposi sarcoma or papular angiokeratoma.<sup>7</sup> Other areas of involvement could include the oral, anal, conjunctival, and gastrointestinal mucosal surfaces, as well as the brain, respiratory tract, liver, spleen, bone, bone marrow, and lymph nodes.<sup>2,5</sup> Lesions evolve slowly over several weeks, and patients usually complain of fever, weight loss, chronic lymphadenopathy, and, sometimes, abdominal pain.<sup>2,4</sup>

Typical findings of the histologic examination of bacillary angiomatosis consist of an atrophic or ulcerated epidermis with pseudo-epitheliomatous hyperplasia and lobes of proliferating small blood vessels containing cuboidal endothelial cells with or without atypical nuclei.<sup>2,7</sup> Also found is a

mixed inflammatory cell infiltrate predominated by vessel-surrounding neutrophils.<sup>2,7</sup> Blood vessels can proliferate superficially or deep.<sup>7</sup> Superficially proliferating vessels resemble a pyogenic granuloma or papular angiokeratoma<sup>7</sup>; deep-proliferating vessels resemble a histiocytoid hemangioma with a proliferation of small blood vessels lined by protuberant endothelial cells adhering to one another in an “epithelioid” pattern.<sup>7</sup> The granular material found beside blood vessels is bacteria, which stains black with Warthin-Starry silver stain.<sup>7</sup> Bacteria also may be detected with immunohistochemistry, using anti-*Bartonella*-species immune serums.<sup>4</sup> Positive factor XIIIa dermal dendrocytes have been found in bacillary angiomatosis.<sup>7</sup> Fibrous long-spacing collagen, a distinct ultrastructural collagen present in normal tissue, is abundant in various tumors, including those of bacillary angiomatosis.<sup>8</sup> This collagen is found adjacent to *Bartonella* organisms and to endothelial cells.<sup>8</sup>

The diagnosis of bacillary angiomatosis is established by clinical and histologic examination of affected tissues.<sup>2</sup> Culture of *Bartonella* species from serum is insensitive, and very few isolates are available worldwide.<sup>4</sup> Polymerase chain reaction amplification is another method used in detecting *Bartonella* species in biopsy specimens.<sup>4</sup>

Bacillary angiomatosis can be cured with appropriate antibiotic therapy.<sup>4,5</sup> Erythromycin 2 g/d is the treatment of choice, and doxycycline 100 mg twice a day is alternative therapy.<sup>2,4</sup> Treatment of immunocompromised patients should be continued for 2 to 3 months.<sup>2,4</sup> Not uncommonly, patients with bacillary angiomatosis relapse after withdrawal of antibiotic therapy.<sup>4</sup> Precautionary measures that should be taken with immunocompromised patients include avoidance of contact with cats, fleas, and lice.<sup>4</sup> Permethrin 1% dusting powder, the agent of choice for delousing, should be applied to clothing and bedding.<sup>4</sup>

Maintaining a high level of clinical suspicion is the most important aspect of diagnosing bacillary angiomatosis in immunocompromised patients. As this disease can be cured, recognition is important; untreated, bacillary angiomatosis can be fatal.

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