Actinobacillus actinomycetemcomitans Isolated From a Case of Cutaneous Botryomycosis

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Cutaneous botryomycosis is an uncommon chronic suppurative bacterial skin infection that can mimic a fungal infection both clinically and histopathologically. Causative bacteria, most commonly Staphylococcus aureus, *aggregate to form characteristic granules. We report the case of a 52-year-old black man who developed cutaneous botryomycosis of the hand following trauma. Routine bacterial cultures grew* S aureus *and* Actinobacillus actinomycetemcomitans, *a fastidious gram-negative bacillus known to cause periodontal disease, endocarditis, and actinomycosislike soft tissue infections. Despite culture-proven eradication of* S aureus *with long-term appropriate antibiotic therapy, the lesion resolved only after fluoroquinolone treatment directed against* A actinomycetemcomitans, *suggesting that* A actinomycetemcomitans *was of etiologic significance.*

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Cutaneous botryomycosis is an uncommon chronic skin infection that appears as a localized suppurative plaque or nodule with superficial crusting or ulceration. Although clinically suggestive of a deep fungal or atypical mycobacterial infection, botryomycosis is bacterial in origin. *Staphylococcus aureus* is the most frequent organism cultured; however, gram-negative bacilli including *Pseudomonas aeruginosa*, *Proteus* species, and *Escherichia coli* also have been isolated from botryomycotic infections.[1] Histologic examination reveals characteristic granules with basophilic centers composed of clumped nonfilamentous bacteria surrounded by an eosinophilic periphery (Splendore-Hoeppli phenomenon). Foreign bodies, impaired host immunity, and virulent organisms are possible pathogenic factors.

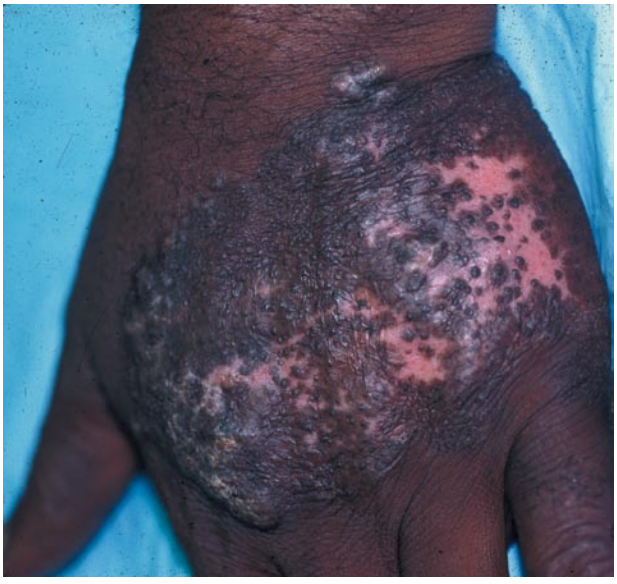

Figure 1. Erythematous verrucous plaque with some mild crusting on the dorsal left hand.

Case Report

A 52-year-old black man presented with a 1-year history of a gradually enlarging tender lesion that initially appeared after trauma caused by hauling tree branches. A 5×6-cm erythematous verrucous plaque with some mild crusting was present on the dorsal left hand without evidence of ulceration (Figure 1). Histologic examination of biopsy specimens obtained at the time of presentation and one month later showed pseudoepitheliomatous hyperplasia with acute and chronic inflammation. Neither fungal nor

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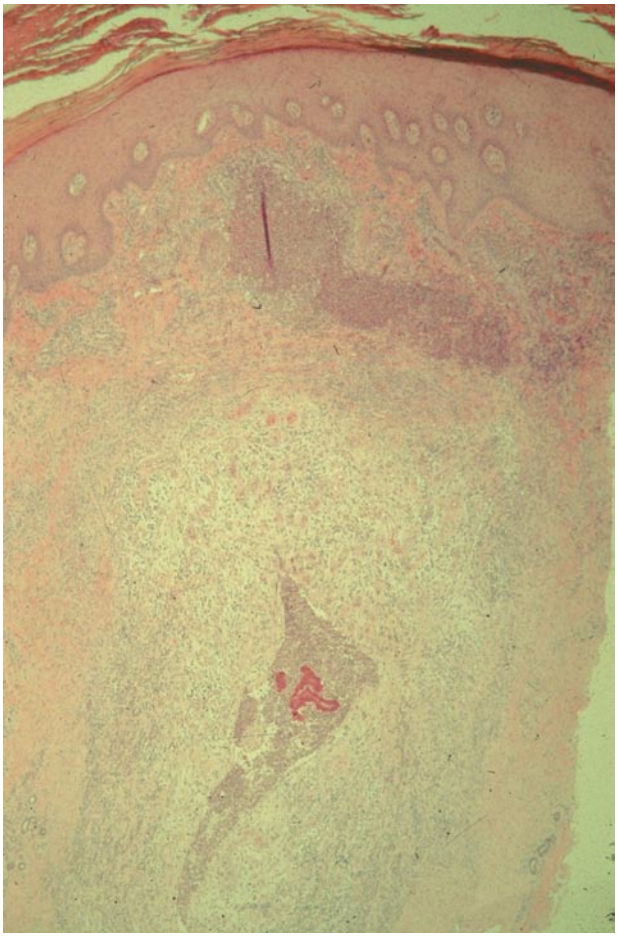

Figure 2. Dermal microabscesses surrounded by fibrosis and granulation tissue (H&E, original magnification ×20).

acid-fast organisms were found on special stains or tissue culture. Routine bacterial cultures grew *S aureus* susceptible to tetracycline and resistant to methicillin and ciprofloxacin hydrochloride. The patient was treated with minocycline hydrochloride 100 mg twice daily but failed to improve. Results of a repeat biopsy 2 months later again showed pseudoepitheliomatous hyperplasia with inflammation. Results of repeat fungal and mycobacterial stains and cultures were negative, and bacterial cultures grew only scant *Staphylococcus epidermidis*. Minocycline hydrochloride was continued and empiric oral itraconazole was added. Due to persistent disease, a fourth biopsy specimen was obtained 11 months after initial presentation. Biopsy results revealed dermal microabscesses with collections of organisms surrounded by an eosinophilic capsule typical of botryomycosis (Figures 2 and 3). Although special stains again failed to demonstrate fungi or mycobacteria, bacterial tissue culture grew abundant *Actinobacillus actinomycetemcomitans* susceptible to quinolones. The lesion resolved after 15 weeks of monotherapy with oral ciprofloxacin (1500 mg/d).

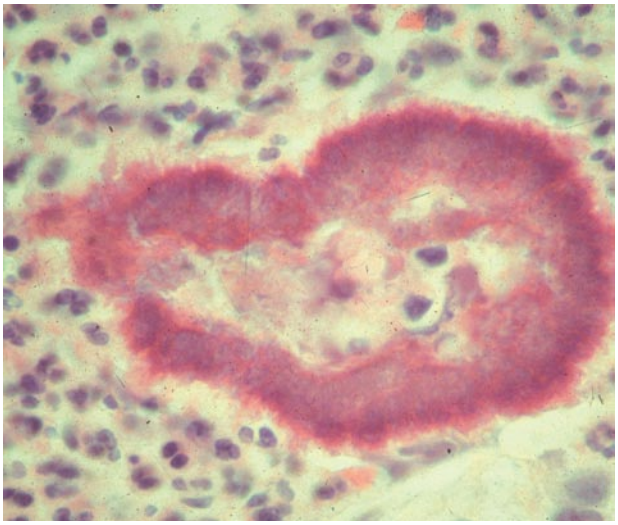

Figure 3. Granule of nonfilamentous bacteria with an eosinophilic periphery (H&E, original magnification ×400).

Comment

In 1884, Rivolta[2] was the first to use the term *botryomycosis*, believing that the causative organism was a true fungus. It was not until 1919 that a bacterial etiology was definitively proved.[3] The misleading nomenclature has resulted in some confusion in the literature because botryomycosis is only 1 of several granulomatous infectious diseases of the skin that forms granules. Mycetoma is characterized by tumefaction and draining sinuses with an exudate containing grains or granules. The granules of botryomycosis and mycetoma are composed of tightly packed colonies of causative organisms; however, mycetoma granules usually are filamentous. Mycetomas can be subdivided into 2 categories: (1) eumycotic mycetomas caused by true fungi such as *Pseudallescheria boydii* and (2) actinomycotic mycetomas caused by filamentous aerobic bacterial organisms such as *Nocardia* species or *Actinomadura* species. Anaerobic filamentous bacteria, especially *Actinomyces israelii*, can cause actinomycosis, a chronic infection of the cervicofacial, thoracic, and abdominal tissues characterized by draining sinuses that also discharge granules composed of aggregates of bacterial filaments. There can be considerable overlap of the clinical appearance and tissue response of mycetoma, actinomycosis, and botryomycosis. When granules are found in tissue sections, fungal or actinomycotic infections often are considered before botryomycosis, and isolation of nonfilamentous bacteria on culture is essential to confirm the diagnosis of botryomycosis.[4] Berger et al[5] suggested that the term *bacterial actinophytosis* be substituted for the term *botryomycosis* to avoid confusion, but this nomenclature has never been adopted.

The pathogenesis of botryomycosis is not completely understood but is thought to involve a balance between the virulence of the organism and the resistance of the host. Providing an intermediate concentration of inoculum is important. A weak inoculum will eradicate too few organisms, and a powerful inoculum could cause an overwhelming or necrotizing infection.[6] Although many hosts have no apparent immune deficits, botryomycosis has been reported in association with human immunodeficiency virus infection[7,8] and Job syndrome.[9] As in our case, a history of trauma providing a route of entry for organisms into the skin is frequently but not uniformly present.[1,10] Other factors that might play a role in the pathogenesis of botryomycosis include the presence of a foreign body[11] or underlying generally debilitating medical conditions, including diabetes mellitus,[10,12] alcoholism,[10] and cystic fibrosis.[13]

A actinomycetemcomitans is a nonfilamentous fastidious gram-negative bacillus known to cause periodontal disease, endocarditis, and actinomycosislike soft tissue infections. As with *A israelii*, *A actinomycetemcomitans* is part of the normal oral flora and can be isolated in association with *A israelii* or as a sole pathogen. Because of its slow growth, correct diagnosis of disorders resulting from *A actinomycetemcomitans* often is delayed or missed entirely if laboratories discard the culture after the first week of incubation.[14,15] Although multiple reports of soft tissue abscess formation directly caused by *A actinomycetemcomitans* exist in the English language literature,[16-18] few exhibit the characteristic granule of botryomycosis. In 1948, Auger[19] reported a patient with botryomycosis of the kidney from which *Actinobacillus lignieresii* was isolated. Thirty years later, a case was reported of botryomycosis caused by a previously unidentified gram-negative organism, most likely thought to be a member of the genus *Actinobacillus*.[20] In 1989, Kaplan et al[16] described a cervical abscess–containing granule following dental extractions that grew *A actinomycetemcomitans*. No fungi or *Actinomyces* species were cultured in any of these cases. Therefore, actinobacilli may be considered an extremely rare cause of the clinicopathologic entity known as botryomycosis.

In this case, *S aureus* could represent a cocausative organism, a superinfection from the initial trauma, or an overgrowth superimposed on actinobacillary botryomycosis. *S aureus* is not likely to be the primary cause of this case of botryomycosis given that the lesion failed to improve despite culture-proven eradication of this organism with appropriate antibiotic therapy (minocycline hydrochloride). Instead, the patient cleared only after administration of ciprofloxacin, to which the staphylococcal organisms were resistant. Isolation of multiple organisms is not unusual in botryomycosis; however, only one organism typically is considered to be the casual agent.[1]

Treatment of *A actinomycetemcomitans* infections can be difficult. Its slow growth and fastidious nature often prevent in vitro susceptibility testing. Susceptibility to ampicillin and penicillin is variable, and the organism usually is resistant to methicillin, vancomycin, erythromycin, and clindamycin.[16] Although cephalosporin and tetracycline can be effective,[16] our patient did not respond to 9 months of therapy with minocycline hydrochloride. Susceptibility testing of fluoroquinolones has shown promising results in periodontal infections,[21] and ciprofloxacin has been successfully used to treat endocarditis caused by *A actinomycetemcomitans*.[22] Ciprofloxacin also was effective in our patient.

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