Botryomycosis Secondary to *Staphylococcus simulans* Masquerading as Mycetoma in a 46-year-old Filipino Female

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ABSTRACT

Botryomycosis is a rare pyogenic disease that presents with chronic suppurative and granulomatous skin lesions, commonly caused by *Staphylococcus aureus*. We report a case of botryomycosis presenting similarly to mycetoma, secondary to the emerging cutaneous pathogen *Staphylococcus simulans.* A 46-year-old female who previously worked in a wet market presented with a 13-year history of suppurative papules on a gradually enlarging right foot, and pain on ambulation. She had no systemic symptoms or co-morbidities, and does not recall preceding trauma. Physical examination showed brawny edema of the right foot with multiple sinus tracts draining purulent discharge. The clinical diagnosis at presentation was mycetoma. Magnetic resonance imaging showed a soft tissue mass involving the right foot and ankle with osseous destruction. Biopsy revealed suppurative granulomatous dermatitis; staining with Grocott methenamine silver did not highlight fungal elements. Potassium hydroxide mount of the purulent discharge did not show grains or hyphal elements. Tissue cultures showed growth of co-trimoxazole-susceptible *Staphylococcus simulans*. The patient was managed as a case of botryomycosis and treated with co-trimoxazole for 12 months. There was a significant decrease in right foot circumference along with scarring and resolution of associated pain. Repeat biopsy showed no evidence of infection. This is the first reported case of botryomycosis in the Philippines as well as the first report citing *Staphyloccocus simulans* as a causative agent. Botryomycosis is an important differential in patients clinically presenting as mycetoma. Animal pathogens may need to be considered as etiologic agents in at-risk patients with chronic subcutaneous infections.

Keywords: botryomycosis, mycetoma, Staphylococcus simulans, coagulase-negative streptococci

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INTRODUCTION

Cutaneous botryomycosis is a rare suppurative granulomatous disease that frequently affects trauma-prone areas such as the extremities. It manifests as papules, nodules, abscesses, ulcers or sinus tracts, with draining seropurulent exudate.[1] This morphologic presentation can be similar to that of other chronic cutaneous infections such as actinomycosis, mycetoma, nocardiosis, sporotrichosis, and cutaneous tuberculosis. Hence, botryomycosis is an important differential for chronic, purulent subcutaneous infections. Most cases are caused by *Staphylococcus aureus*, but other reported etiologic agents include *Pseudomonas aeruginosa, Streptococcus spp.*, *Escherichia coli,* and coagulase-negative staphylococci.[2] We present the case of an immunocompetent adult Filipino female with mycetoma-like botryomycosis, secondary to coagulase-negative *Staphylococcus simulans*.

CASE PRESENTATION

A 46-year-old Filipino female who previously worked in a wet market presented with a 13-year history of suppurative

papules on a gradually enlarging right foot, and associated progressive pain on ambulation. She had no systemic symptoms or co-morbidities, and does not recall history of trauma prior to onset of the cutaneous changes. Physical examination showed brawny edema of the right foot with multiple sinus tracts draining purulent discharge on the dorsal and lateral aspect (Figure 1).

The clinical diagnosis at presentation was mycetoma. A 6-mm punch biopsy of a draining sinus on the dorsum of the right foot demonstrated compact hyperkeratosis, irregular epidermal hyperplasia, spongiosis, and a dense diffuse dermal infiltrate composed of lymphocytes, histiocytes, neutrophils, eosinophils, and plasma cells (Figure 2).

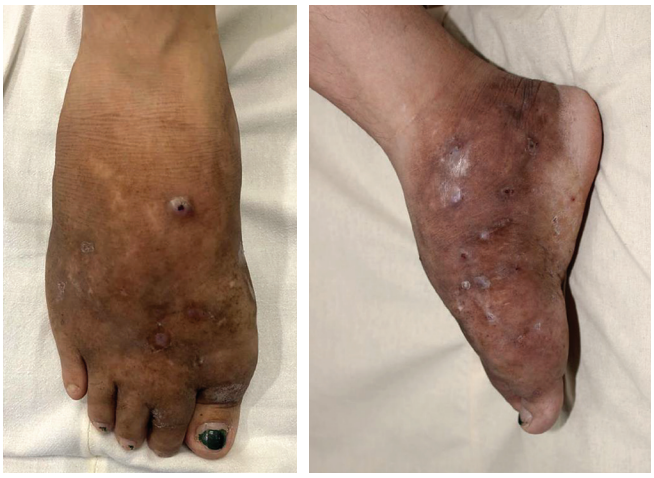

Figure 1. Brawny edema of the right foot with multiple sinus tracts draining purulent discharge on the dorsal and lateral aspect.

These findings supported the presence of a suppurative granulomatous dermatitis, typical of chronic infectious processes. X-ray of the foot revealed extensive multiple, well-defined, punched-out lytic lesions scattered throughout the foot osseous structures, some with sclerotic and overhanging margins giving a rat-bitten appearance. Magnetic resonance imaging showed a heterogeneously-enhancing soft tissue mass involving the right foot and ankle with subcutaneous fat stranding and further evidence of bone destruction. The dot-in-circle sign corresponding to grains (dots) and granuloma (circle) present in mycetoma was not observed. Further work-up was done to determine the etiologic agent. Staining of the biopsy specimen with Grocott methenamine silver did not highlight any fungal elements. Potassium hydroxide mount of the purulent discharge did not show grains or hyphal elements on direct microscopy. Bacterial, mycobacterial, and fungal tissue cultures were also performed, with noted growth of co-trimoxazole-susceptible *Staphylococcus simulans*. Given the presence of a purulent, chronic subcutaneous infection secondary to a *Staphylococcal* infection, the patient was managed as a case of botryomycosis and treated with co-trimoxazole 800 mg/160 mg/tab 1 tab twice a day. After 10 months of treatment, there was noted significant decrease in the right foot circumference along with scarring and resolution of pain on ambulation (Figure 3).

Repeat biopsy showed no evidence of ongoing infection, and repeat tissue GS/CS showed no growth. The timeline of onset of symptoms and corresponding management can be seen in Figure 4.

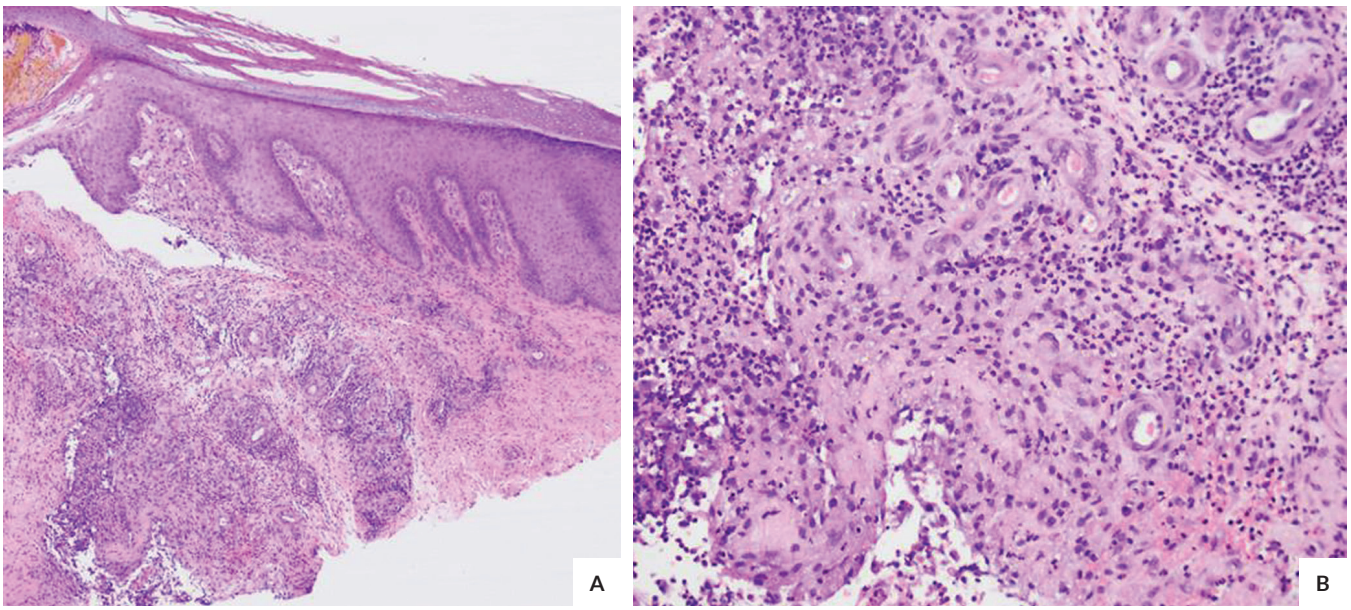

Figure 2. Biopsy showed irregular epidermal hyperplasia and a dense diffuse infiltrate composed of lymphocytes, histiocytes, neutrophils, eosinophils, and plasma cells in the dermis.

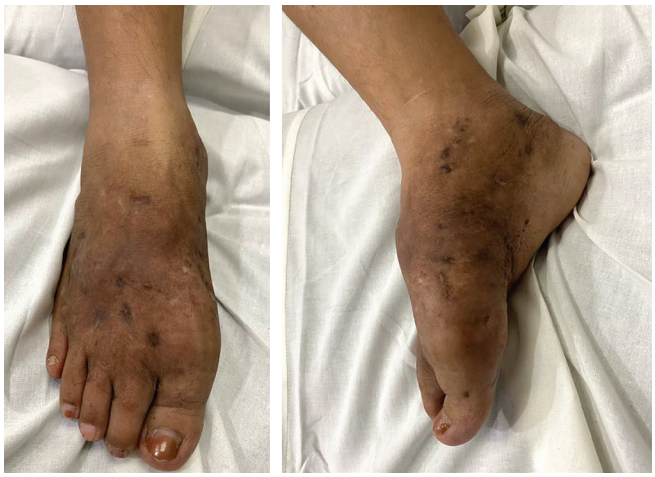

Figure 3. Right foot of patient after completing 10 months of co-trimoxazole. There is a significant decrease in the size of the right foot, resolution of draining sinuses, and residual scarring.

DISCUSSION

Approximately 200 cases of botryomycosis worldwide have been reported in the literature.[1] An estimated 40% of cases are attributed to the organism *Staphyloccocus aureus* and 20% to *Pseudomonas aeruginosa*.[3] Coagulase-negative staphylococci (CoNS) have also been cited as causative organisms. However, *Staphylococcus simulans*, a coagulase-negative staphylococci and the etiologic agent in our patient, has not yet been reported in association with the development of cutaneous botryomycosis.

Staphylococcus simulans is an animal pathogen affecting cattle, goats, horses, and sheep.[4] Human infection with *S. simulans* is infrequent but has been implicated in cases of osteomyelitis, prosthetic joint infections, native valve endocarditis, and urinary tract infections, supporting the observation that it is may be more virulent relative to other CoNS.[5-7] In terms of skin and soft tissue infections, there have been two reports of *S. simulans* causing vesicobullous and pustular lesions in humans.[4,8] For both cases, the patients' occupations entailed regular handling of animals, implying that frequent and repeated contact with animals as an important risk factor. Although our patient could not recall a history of local trauma, she had recurrent exposure to fresh meat when she worked as a wet market vendor.

The varied clinical manifestations of infection with *S. simulans* suggest that this organism should not be easily disregarded as a sample contaminant. Available data explaining the pathogenicity of *S. simulans* is limited. Virulence factors previously identified in infectious animal isolates include methicillin-resistance gene mecA, tissue necrosis cytotoxin Panton-Valentine leukocidin (pvl), and staphylococcal enterotoxins.[4] Notably, pvl production is associated with the development of cutaneous abscesses, furuncles, and skin necrosis.[9]

Antecedent trauma is an important risk factor for developing botryomycosis as this facilitates the entry of

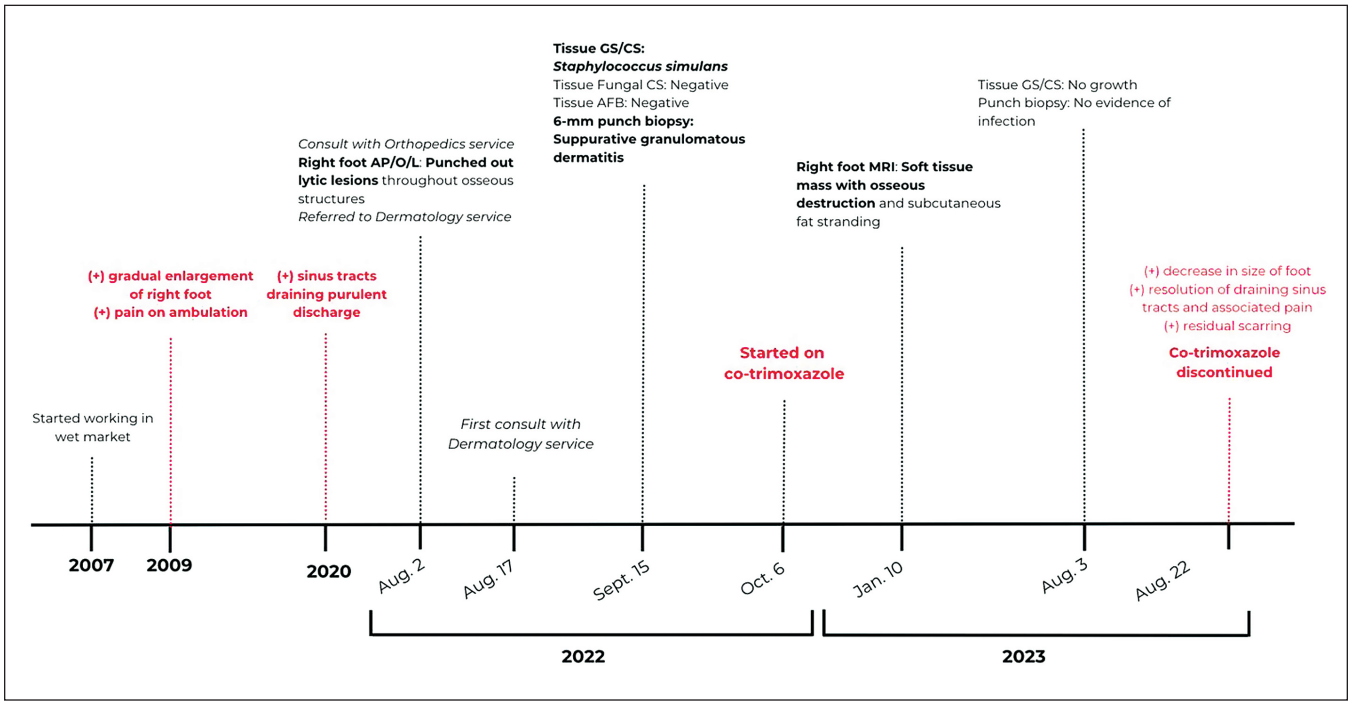

Figure 4. Timeline of symptoms, radiographic and laboratory studies, and treatment.

causative organisms into the skin, leading to local infection. The trauma may occur months to years before the diagnosis of botryomycosis, and includes surgical procedures, accidents, manual labor, as well as microtrauma that may arise from walking on bare feet.[2] Co-morbidities such as diabetes mellitus, liver disease, alcoholism, lupus, cystic fibrosis, malnutrition, and HIV/AIDs also predispose a patient to developing botryomycosis.[1,2]

For this patient, our initial assessment was mycetoma due to the presence of an enlarged and deformed right foot with draining sinus tracts, characteristic of a Madura foot. Several cases of mycetoma have been reported in the Philippines, with an annual incidence of 0.10 cases / 100,000 people-year noted in 2016.[10] On the other hand, cutaneous botryomycosis has not yet been reported locally based on our literature review. Botryomycosis can present as abscesses, nodules, and sinuses with grains and purulent discharge, making it an important disease entity to consider in all patients with a chronic, purulent, subcutaneous swelling that exhibits osseous involvement.[3] In addition to mycetoma, other differentials we considered for this patient include actinomycosis, cutaneous tuberculosis, sporotrichosis, and Charcot arthropathy. However, the results of the microbiologic cultures along with the absence of diabetes mellitus in the patient made these conditions less likely.

The diagnosis of botryomycosis can be confirmed through culturing of bacteria from tissue in patients with clinical features of botryomycosis, demonstration of characteristic histopathology findings, and identification of non-filamentous bacteria within granules of pus from draining sinuses.[1] The Splendore-Hoeppli phenomenon, which presents as clusters of microorganisms surrounded by refractile eosinophilic material, is the most consistently reported histopathologic feature of botryomycosis.[2] However, this finding is not pathognomonic of botryomycosis as it can also be found in other chronic bacterial and fungal infections. In the case of our patient, although the Splendore-Hoeppli phenomenon was not observed, the presence of multiple papules and draining sinuses on the right foot, a tissue culture positive for coagulase-negative staphylococci, and histopathologic changes suggestive of a chronic infectious process, supported the diagnosis of cutaneous botryomycosis. Cutaneous botryomycosis has also been previously diagnosed in a patient whose histopathology did not exhibit the Splendore-Hoeppli phenomenon.[11]

The mainstay of treatment for cutaneous botryomycosis is a course of systemic antibiotics. Most reported cases achieved resolution of infection with oral antibiotics. The choice of therapy should be guided by culture and sensitivity results, whereas the duration is variable and typically extended until lesions have completely resolved. Surgical debridement may be considered for patients who are unresponsive to antimicrobial treatment, for those with extensive lesions, and for patients in an immunocompromised state.[2] Medical treatment and surgical debridement for cases of cutaneous botryomycosis must be instituted promptly to prevent substantial bone involvement, which may necessitate amputation. Guided by our susceptibility data, we treated our patient with co-trimoxazole with noted clinical resolution after 10 months, as supported by a decrease in the size of the right foot, resolution of draining sinuses and pain on ambulation, and residual scarring. Repeat tissue GS/CS showed no growth, while repeat skin biopsy showed no evidence of ongoing infection, thus supporting microbiologic and histopathologic resolution.

CONCLUSION

This is the first reported case of botryomycosis in the Philippines. This is also the first report citing *Staphyloccocus simulans* as the causative agent of botryomycosis. Cutaneous botryomycosis is an important differential in patients clinically presenting as mycetoma, and animal pathogens may need to be considered as etiologic agents in at-risk patients with chronic invasive subcutaneous infections.

Statement of Authorship

Both authors certified fulfillment of ICMJE authorship criteria.

Author Disclosure

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