Case Studies

Cervicofacial Botryomycosis: Is Atopic Dermatitis a Predisposing Factor?

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Key Words

Atopic dermatitis · Atopic eczema · Botryomycosis · Granuloma · Immunocompromised patient · Immunodeficiency · Pyoderma · *Staphylococcus aureus*

Abstract

Background: Botryomycosis is a rare infectious disease which usually affects the skin. The low virulence of the bacteria tending to form grains and the immune status of the host are important factors in the development of the disease. **Methods:** We report a case of cervicofacial botryomycosis and review the current literature. **Results:** A 47-year-old male with a long history of moderate-to-severe atopic dermatitis presented with painful and suppurative nodules of the head and neck. A skin biopsy revealed granules consisting of Gram-positive bacterial colonies in a blossom-like assembly in the center and an eosinophilic rim in the periphery, which are pathognomonic features of botryomycosis. The lesions responded well to systemic antibiotics; however, they rapidly relapsed upon cessation of the treatment. **Conclusions:** We highlight the well-defined histologic features and recall an almost forgotten disease. We review common predisposing conditions and present evidence that atopic dermatitis might be an additional predisposing factor.

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Fig. 1. Clinical presentation. **a** Active lesion on the right cheek as well as postinflammatory hyperpigmentation on the left cheek and on the forehead. **b** Painful large nodule draining pus on pressure. **c** Ulcerating and crusted nodule on the scalp.

Introduction

Botryomycosis is a chronic suppurative bacterial infection that can affect either the skin or viscera. It is defined by the presence of grains consisting of bacterial colonies in a pathognomonic flower-like assembly with a peripheral deposition of intensely eosinophilic material and surrounded by neutrophil-rich and granulomatous inflammation. Causative bacteria most commonly include *Staphylococcus aureus*, streptococci and Gram-negative bacilli. To our knowledge, the case we report here is the first case of botryomycosis that is explicitly associated with atopic dermatitis.

Case Report

A 47-year-old male presented with itchy and painful nodules of the head and neck (fig. 1). The lesions had developed slowly over a period of 6 months and had gradually increased in number and size.

The patient had a 15-year-long history of diabetes mellitus II treated with insulin aspart as well as a history of allergic rhinitis and atopic dermatitis with recent flares. His filaggrin status was not known. Skin examination revealed multiple erythematous nodules on the scalp and the face that were painful on pressure. The lesions varied in size, with the biggest nodule measuring up to 2 cm (fig. 1b). A few scaly eczematous patches were detected on his arms and trunk. His skin was notably dry.

A skin biopsy taken from one of the nodules showed blossom-like basophilic bacterial aggregations with a homogeneous eosinophilic rim surrounded by a dense mixed infiltrate with areas of abscess and granuloma (fig. 2a, b). Modified Gram stain (Brenn-Brown) revealed Gram-positive cocci in the center of the grains (fig. 2c). Microbiologic swabs from one of the lesions identified *Staphylococcus aureus* sensitive to methicillin. PCR on the same material was negative for mycobacteria of the tuberculosis complex. Throat, nasal and perianal swabs revealed physiologic flora. Mycological cultures yielded no growth. Blood values were largely within normal limits and showed no evidence for a severe immune dysfunction. Total serum levels of IgE and IgG were normal with only minor changes in the IgG3 and IgG4 subclass fractions, which were most likely due to a pronounced atopic predisposition and to chronic inflammation.

Altogether, the clinical presentation and the diagnostic workup including a skin biopsy and microbiologic examinations confirmed the diagnosis of botryomycosis due to infection with *S. aureus*.

We initiated treatment with systemic rifampicin, flucloxacillin and fusidic acid, supported by topical disinfectant agents. No surgical intervention was performed.

Fig. 2. Histopathologic findings diagnostic of botryomycosis. **a** Scan showing grains and inflammation within the dermis of an active nodule. **b** HE stain revealed a dense inflammatory neutrophilic infiltrate surrounding dense grains, consisting of a strongly basophilic blossom-like assembly of bacteria in an eosinophilic capsule (**inset**). **c** Brenn-Brown stain identified Gram-positive bacteria which were identified in cultures as *S. aureus*.

The first follow-up 2 weeks later indicated a good response. However, the lesions relapsed on the scalp 4 weeks later. The further course of the disease was tenacious with rapid relapses and flares upon cessation of the treatment.

Discussion

The etiology of botryomycosis is not uniform. In most patients, *S. aureus* can be identified as the causative agent. The bacteria isolated from affected skin lesions usually exhibit low-to-intermediate virulence maintaining a chronic suppurative and granulomatous inflammation. The majority of isolated strains are sensitive to methicillin; however, the rate of methicillin-resistant *S. aureus* strains is not known and poorly investigated.

The clinical manifestations of botryomycosis are unspecific and diverse. Patients most commonly present with subcutaneous nodules, small skin abscesses or confluent fistulas. The lesions most frequently appear on the head and neck. Characteristically, they develop slowly over several weeks and months. Atypical onset often occurs in HIV-positive patients. Symptoms can fluctuate but usually get worse as the disease progresses. Patients ultimately seek medical attention due to a painful flare of the chronic infection.

Botryomycosis is diagnosed by means of microbiologic analysis and histologic examination of a skin biopsy. The histopathologic appearance is well defined and pathognomonic. The main criterion is the presence of granules or grains surrounded by a neutrophil-rich and granulomatous inflammatory infiltrate within the dermis (fig. 2a, b). They have a zonal composition with clusters of basophilic non-filamentous bacteria in the center and an amorphous eosinophilic rim in the periphery commonly referred to as ‘Splendore-Hoeppli phenomenon’. To date, it is not entirely clear what the rim is made of. It might reflect depositions and debris of the host’s inflammatory response such as antigen-antibody complexes [1]. It is likely to prevent bacteria from invading the adjacent tissue and to contribute to the characteristic assembly in lobules resembling a bunch of grapes.

Differential Diagnosis

The differential diagnosis comprises certain mycotic infections such as sporotrichosis or mycetoma. Sporotrichosis results from direct fungal inoculation; the clinical presentation with ulcers and painful nodules can resemble botryomycosis. However, they are often accom-

panied by a painful lymphadenopathy. Eumycetoma is common in warm and humid areas like the tropics but rarely seen in Europe. It is characterized by tumefaction and abscess formation, most commonly on the legs and feet. PAS and Grocott-Gomori staining can identify fungal elements like thick filamentous and septate hyphae.

Specific bacterial infections must be distinguished from botryomycosis including infection with mycobacteria. Furthermore, cervicofacial actinomycosis can become manifest in a similar clinical and histologic presentation.

In hyperimmunoglobulin E syndrome, the cellular immune response and chemotaxis of neutrophils is attenuated resulting in the formation of ‘cold’ abscesses of the skin. It has an early onset within the first few months to years of life and is characterized by dermatitis, recurrent sinopulmonary infections and elevated serum levels of IgE.

Predisposing Conditions

With very few exceptions, cutaneous botryomycosis never develops in healthy individuals. Most cases reported up to now were associated with conditions that attenuate the host’s immune response, most commonly with HIV infection and AIDS. On the one hand, the clinical presentation can be classic in terms of a chronic pyoderma with draining sinuses and abscesses [2]. On the other hand, manifestation can be atypical with pruritic papules or lichenification [3]. The differential diagnosis in such cases is difficult and comprises conditions like nodular prurigo or lichen simplex. The first step in the diagnosis of botryomycosis in HIV-positive patients is considering it, particularly if skin lesions do not respond to conventional therapeutic agents and if the CD4+ cell count is low. Our patient was reportedly HIV negative, and laboratory values did not point at a major immune deficiency.

Some authors emphasize the importance of preceding skin trauma in the pathogenesis of botryomycosis. This notion has been supported by the fact that it often affects hands and feet which are the most subjected to mechanical and traumatic stress. Animal bites, venous punctures and major surgery are reported risk factors. One HIV-positive patient developed botryomycosis on the anterior abdominal wall. Skin lesions were assembled along an old scar from a laparotomy he had undergone several years before suggesting that both an impaired T-cell response and structural skin damage were relevant in the development of botryomycosis [4].

The association of botryomycosis with diabetes mellitus is less common than with chronic HIV infection. However, it can have a severe clinical course with extensive cutaneous and visceral involvement [5].

Our patient had a long history of moderate-to-severe atopic dermatitis with numerous and recurrent flares. Dry skin, strong pruritus and lichenification in the flexural areas of the knees and elbows were noted at initial presentation. A review of the current literature revealed that cutaneous botryomycosis has never been reported in atopic dermatitis up to now. The contributory role of humoral immunity in botryomycosis is not well established and poorly understood. Recently, it has been associated with eosinophilic cellulitis, angioedema and blood eosinophilia [6]. In children, botryomycosis can rarely occur in association with hyperimmunoglobulin E syndrome. Even though it is unclear if there is a causal relationship between skin lesions and elevated IgE, serum levels of eosinophils, IgG and IgE should be part of the diagnostic laboratory workup in botryomycosis.

A predominant TH2 response can also be found in patients with atopic dermatitis. High levels of IgE are commonly seen in severe extrinsic atopic eczema as compared to mild and moderate disease [7]. In atopic dermatitis, the skin barrier is impaired due to structural and functional alterations. Colonization with *S. aureus* is increased due to the reduced production of antimicrobial peptides and a decreased TH1 response. Thus, it is comprehensible that botryomycosis can emerge more easily in atopic dermatitis even though it remains unclear if there is a causal relationship between both diseases.

Conclusions

The association of botryomycosis with atopic dermatitis is novel. The reported case shows that cutaneous botryomycosis is a chronic infection of the skin with a high tendency to relapse. The clinical presentation can be unspecific and atypic, whereas the histopathologic features are well defined. Botryomycosis has a broad differential diagnosis and is probably underdiagnosed nowadays. Due to predisposing factors, effective treatment is difficult. It is important to recognize the clinical and histologic features of botryomycosis at an early stage and to distinguish it from other pyodermic conditions because it requires a prolonged and intensive systemic treatment.

Disclosure Statement

The authors declare no conflicts of interest.

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