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Case report

The conundrum of granular bacteriosis in the submandibular region—A case report

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ABSTRACT

Botryomycosis has emerged as a multifaceted entity caused by both the aerobes as well as the anaerobes, however, the exact nature of this entity is not understood in entirety as there are varying reports pertaining to its association with other conditions, clinical presentations and the host's immune status. In the present report we describe a case of granular bacteriosis in a 34 year old male patient with an unclear clinical presentation. The use of the term "granular bacteriosis" when there is misconstrued clinical and microbiologic presentation is the highlight of this paper and the isolated causative factor in the present case is *Propionibacterium acnes* (*P. acnes*).

1. Introduction

Botryomycosis, as described by Winslow (1959), is a granulomatous lesion characterized by chronic course and suppurative foci [1]. It is an inexplicable reaction to a bacterial infection that is more often confused with mycoses. It was first reported by Bollinger in 1870 and subsequently termed "botryomycosis" by Rivolta in 1884 [2]. "Botrys" in Greek means a bunch of grapes, a term which was used due its close resemblance to the granular presentation and termed mycosis because it was perceived to be of fungal origin. Although the aforementioned lesion was reportedly found in horses, the first report of a human case was published by Opie in 1913 [3]. Since then, the disease has been described under diverse terminologies such as staphylococcic actinophytosis, granular bacteriosis, bacterial pseudomycosis, bacterial ball, and actinobacillosis. Others have even considered the terms like botryomycoma and granuloma pyogenicum suggesting its mysterious presentation [1,2].

Essentially botryomycosis could affect any part of the body and head and neck region is no exception, although the number of reported cases is surprisingly low [2]. Over a period of time botryomycosis has emerged as a multifaceted entity caused by both the aerobes as well as the anaerobes [4]. The exact nature of this baffling entity is not understood in entirety as there are varying reports pertaining to its association with various conditions, clinical presentations and the host's immune status. The increase in the recurrence rate of this entity necessitates aggressive treatment plan and a long term follow up [4].

In the present report we describe a case of granular bacteriosis in a 34 year old male patient with an unclear clinical presentation. A comprehensive work up of the differential diagnosis, microbiology-pathologic correlation, and rational treatment approach along with periodic follow up is highlighted. The use of the term "granular bacteriosis" when there is misconstrued clinical and microbiologic presentation is the central theme of this paper. The isolated causative factor, *Propionibacterium acnes* (*P. acnes*) is the focal point of the report.

2. Case report

A 34 year old male patient reported to the clinics with the complaint of recurrent boils in the right submandibular region and left para mental region. History revealed that he was previously treated for the fractured maxilla and mandible following a road traffic accident. Bone union was attempted in the right body of the mandible, left parasymphyseal and the zygomaticomaxillary region. Few years later, the patient presented with multiple sinuses in the right sub-mandibular region with metal plate breaking away, which was surgically removed and the bone decorticated. The patient had a recurrence of the swelling with pus discharge in the same region within a year. The exudate from the draining sinus was sent for microbiological examination and biopsy performed for histopathologic evaluation. A diagnosis of osteomyelitis was made as the culture from pus showed heavy growth of *S. aureus* which was found to be resistant to amoxicillin, cefazolin as well as cefadroxil. However, *S. aureus* was shown to be susceptible to

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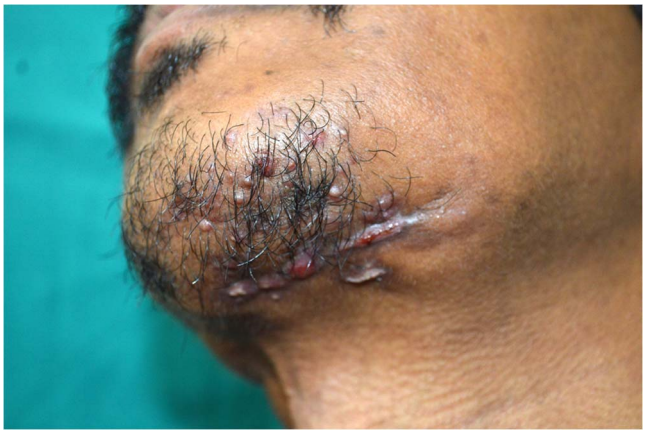

Fig. 1. Reddened skin over the chin and left submandibular region with multiple draining nodules and pustule.

amoxicillin-clavulanic acid combination. A complete regimen was continued following the decortication of the right mandibular body region. Presently, a year later, the patient reported for second recurrence with reddened skin over the chin and right submandibular region with many draining pustules (Fig. 1). The pustules had increased in number gradually over six months and drained spontaneously with no evidence of healing. The regional lymph nodes were not enlarged or palpable. Patient had compromised oral hygiene status. Past medical history was non-contributory and there was no evidence of weight loss or fever. Pus and exudate were sent for culture and susceptibility testing and biopsy was performed for histopathologic confirmation.

Considering the chronicity of the lesion, the conditions included in the differential diagnosis were actinomycosis, botryomycosis, scrofuloderma and mycological infection. The symptoms were treated empirically and the patient was admitted for a complete work up. The routine haematological and serology yielded values, which were within normal limits. The screening for tuberculosis (TB), human immunodeficiency virus (HIV) and hepatitis B was negative.

Microscopic examination revealed areas of central abscess formation within which colonies of microorganisms were evident. Colonies were granular at the centre and surrounded by eosinophilic zone (Splendore Hopley Phenomenon) (Fig. 2A), infiltrated by PMNs. The intervening stroma was fibrous with many proliferating endothelial cells and budding capillaries. The Gram staining of the tissue sections showed the presence of gram positive cocci arranged as clusters and appearing granular (Fig. 2B). The Grocott's methenamine silver stain (GMS) (Fig. 2C) as well as Periodic Acid Schiff (PAS) stain (Fig. 2D) did not show any indication for the presence of fungal hyphae. Microbiologic examination of the exudate cultured first in Robertson's cooked meat (RCM) media and then isolated on anaerobic media showed circular raised colonies of reddish brown color which were suggestive of *Propionibacterium acnes*. Aerobic cultures showed the heavy growth of *Staphylococcus aureus.* The colonies were subjected to biochemical assessment for confirmation and then antimicrobial susceptibility tests. The confluence of histopathological and microbiological findings along with the clinical presentation culminated in the diagnosis of granular bacteriosis.

The antibiotic regimen was switched to amoxicillin/clavulanic acid, 625 mg BID and metronidazole (400 mg BID) as the antimicrobial susceptibility tests showed susceptibility to these drugs. Patient was discharged after a week when his condition had reasonably improved and was followed up on monthly basis. During the second follow-up, persistence of infection was noted in the same area. The pus was again sent for microbiologic examination and biopsied again. Colonies of *P. acnes* and black colored fungal filaments were noticed giving an impression of phaeohyphomycosis. The tissue sections however did not show the morphologic characteristics of hyphae or yeast like cells compelling us to retain the diagnosis of granular bacteriosis with a phaeohyphomycosis superinfection. The therapeutic management of the condition included the addition of voriconazole to cefpodoxime/metronidazole course. Following this, the condition showed significant improvement and the patient was discharged after 3 days of stay in the hospital. He was put on itraconazole (2 tablets of 100 mg BID for 15 days), doxycycline (100 mg tablet OD for 15 days) and metronidazole (400 mg BID for 5 days). Patient could resume his routine lifestyle effectively and found disease free in 5 months of follow-up.

3. Discussion

The present case underlines the dilemma faced by a clinician, a pathologist, and microbiologist while interpreting an explicit case veiled with complex clinical presentation of a chronic granulomatous disease. A multiple pus discharging sinuses in the cervicofacial region, more often than not forces a presumptive diagnosis of actinomycosis. Histopathologically, the demonstration of actinomycete filaments in tissue sections remains a gold standard as it is very difficult to isolate and grow actinomyces anaerobically and clinically, sulphur granules are not pathognomonic of actinomycosis [5]. Absence of filaments and presence of colonies with granular centre and eosinophilic periphery confirms the diagnosis of botryomycosis [6].

Botryomycosis of the head and neck region are rare [7]. The first case of botryomycosis in the oral cavity was reported in 1967 involving the tongue [4]. The present case occurring in the submandibular region was intriguing as it had features which was mimicking actinomycosis and microbiologic testing yielded confounding results. The diagnosis of botryomycosis is not commonly reported in the cervicofacial region despite an abundant oral flora and chronicity associated with many dental infections [4]. The behaviour of the disease is still a subject of debate and its correlation with the host's immune status is undetermined [2].

The granulomatous diseases were originally grouped into eumycetoma; schizomycetoma including actinomycetoma and botryomycosis; and mixed mycetoma [8]. A modification to this grouping is the one proposed by Bonifaz and Carrasco, where mycetoma, actinomycosis and botryomycosis have been segregated as separate entities [2]. Ever since it was first described, botryomycosis has been divided into the visceral and the cutaneous forms [1]. The disseminated visceral type is rare and has poor prognosis. The localized cutaneous form is common, has a better prognosis despite its involvement extending into the underlying muscle and bone [6].

Practically, botryomycosis may present in all the age groups with a slight predilection for men [2]. The clinical presentation of botryomycosis is similar to that of any chronic suppurative, granulomatous condition [1]. Most of the cases present with nodules, sinuses, fistulae, abscesses and ulcers with seropurulent secretions in which granules, if present, could be observed. A number of systemic factors may influence and be associated with the development of botryomycosis although in rare instances it may embroil healthy individuals too [4].

The usual predisposing factors include skin injuries, postoperative complications, diabetes mellitus, liver disorders, cystic fibrosis, osteomyelitis, alcoholism. Malnutrition, glomerulonephritis, bronchial asthma, follicular mucinosis, hyperglobulinemia E and acquired immunodeficiency syndrome (AIDS) are also found to be associated, though less commonly [2,9,10]. In our case, patient was treated following a road traffic accident and developed post-operative complications in the form of osteomyelitis. Because of the slow and innocuous clinical course, patients may most often not recount the events leading to the disease process. A comprehensive history is mandatory in all cases suspected of botryomycosis.

A clear predominance of *Staphylococcus aureus* and *Pseudomonas aeruginosa* is observed as responsible microorganisms [1,2]. However, most of the isolated strains are of low virulence and are only