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Case Report

Microbiology Section

Rare Case Report of Dual Pathogen Causing Chronic Subcutaneous Infection: *Alternaria alternata* and *Staphylococcus aureus* in an Immunocompetent Patient

LAVANYA JEYAMANI[1], SHANMUGASUNDARAM VENKATACHALAM[2], PRABHURAJAN RAJAN[3], VIVEKANANDAN RAMALINGAM[4], PREETHI SHALINI GANDI[5]

ABSTRACT

Chronic pyo-granulomatous infection of subcutaneous tissues with recurrence and exacerbations are predominantly of bacterial origin in Southern India. Most of the infections may not present with the classic triad to be labeled as mycetoma. Frequently, granular discharge is absent or not elicited. More often the infection is monomicrobial. However, rare polymicrobial infections are posing challenges in the treatment of the same. The genus *Alternaria* belongs to phaeoid fungi infecting immunocompromised hosts. They are associated with cutaneous and subcutaneous infections (70-80%) predominantly. We recount a rare case of chronic subcutaneous mixed infection by *Alternaria alternata* and methicillin sensitive *Staphylococcus aureus* in a healthy, immunocompetent, non-diabetic woman.

Keywords: Botryomycosis, Phaeohyphomycosis, Soft tissue infections

CASE REPORT

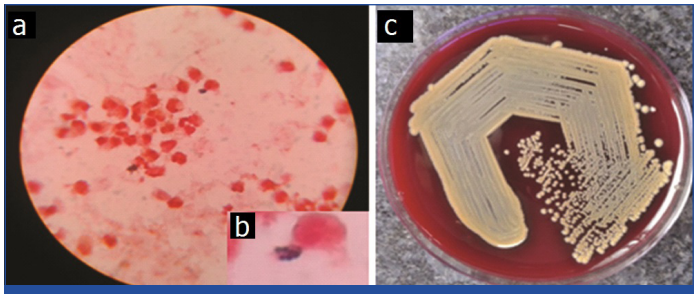
A 30-year-old female, agricultural worker, presented to Dermatology in May 2017, with ulceroproliferative lesions in the sole of right foot. She developed a nodular lesion of 0.5 cm diameter, a month ago. It had progressively enlarged in size to 2×3×2cm. Black discolouration of the skin over the lesion seen. The lesion started ulcerating on 15th day discharging black granules. The patient had presented to Dermatology OPD with a weeping lesion. Firm nodular swelling measuring 5×7 cm was seen in the sole region of arch of foot. Edges of the swelling were not appreciable. There were three discharging sinuses in the lesion. Purulent discharge was oozing out. There were multiple black granule-like materials studded on the non-ulcerated surface of the swelling (trans-epidermal elimination). The swelling was tender on palpation unlike her previous episodes [Table/Fig-1a].

[Table/Fig-1]: a) Image of the foot lesion; b) Radiographic image of the affected foot.

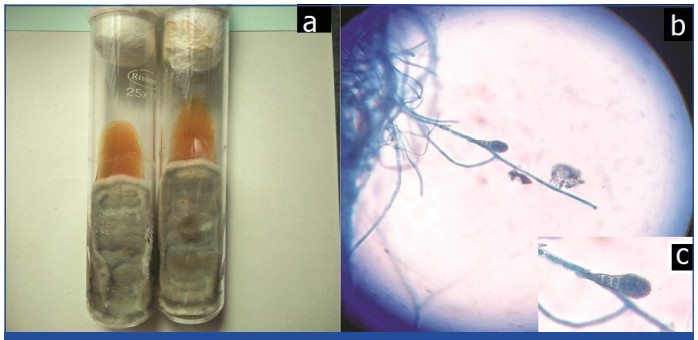
The patient had a past history of accidental injury with a wooden stick piercing the sole near the arch of the foot, 10 years back, during her field work. The wound was attended and treated with native medicines. Subsequently after three months, she started to develop a small painless nodular lesion in the injured area. The nodule enlarged in size and turned to be painful ulcerative lesion. She was treated with allopathic medicines and recovered completely. Details and records of the treatment were not available. Since then she developed similar lesions on and off at the same site. She had multiple exacerbations in the past 10 years.

The patient was non diabetic, vitals were stable. She had no fever. She had a poor hygiene practice. Patient had a history of walking bare foot in the fields and nursing the wound with unclean materials. Her laboratory parameters revealed dimorphic anaemia with Haemoglobin 6.7 gm/dL and WBC count of 5,500 cells/cumm. Her globulin levels were slightly elevated (3.90 gm/dL).

Radiography of the affected foot shows soft tissue swelling and periosteal thickening [Table/Fig-1b]. Bones beneath the lesion was normal. Purulent discharge from the wound and the granules from the sinus tract were sent to diagnostic microbiology lab for gram stain, bacterial culture, KOH mount and fungal culture. Gram stain showed Gram positive cocci in clusters with numerous pus cells [Table/Fig-2a,b]. Discharge was inoculated in 5% sheep blood agar, chocolate agar and Mac Conkey agar for aerobic incubation at 37°C for one week. Blood and chocolate agar showed golden yellow pigmented, small, convex colonies on 2nd day of incubation [Table/Fig-2c]. The organism was identified as Methicillin sensitive *Staphylococcus aureus* by gram stain, catalase and coagulase positivity and susceptibility in cefoxitin screen test by Kirby Bauer disc diffusion test. The granular material from the discharging sinus was collected aseptically in sterile gauze. It revealed no significant finding in gram stain/KOH mount/Modified Zeihl Neelson stain. Patient was treated with amoxicillin clavulanic acid combination for seven days. The inflammation and pain subsided completely. The sinus had stopped oozing and was replaced with a rapid growing black verrucous mass of 1×1.5 cm rising above the skin level. Surface of the growth was irregular. Several small satellite lesions appeared around it in subsequent days. KOH mount of the biopsy from the fungating mass showed septate, phaeoid hyphal elements. Fungal culture of the discharge obtained on 1st OPD visit and subsequent culture of the tissue biopsy from the verrucous lesion grew mould with a blackish



[Table/Fig-2]: a) Gram stain showing numerous pus cells and Gram positive cocci in cluster (magnification 100X); b) Magnified image of Gram positive cocci; c) Beta haemolytic, golden yellow pigmented colonies of *Staphylococcus aureus* in Blood agar.



[Table/Fig-3]: a) Sabouraud dextrose agar showing the growth of fungus *Alternaria*; b) Lactophenol cotton blue wet mount of the growth showing macroconidia of *Alternaria alternata* (magnification 40X); c) Magnified image of the conidia.

cottony obverse and a black reverse on Sabouraud dextrose agar after five days of incubation at 37°C [Table/Fig-3a]. Lacto Phenol Cotton Blue (LPCB) mount and slide culture identified the mould as *Alternaria alternata* [Table/Fig-3b,c]. Histopathological examination showed a mixed lymphoplasmacytic and neutrophilic reaction in the epidermal region. No evidence of sclerotic body or fungal hyphae was seen. Occasionally, brown pigmented large yeast like structures measuring 5-7 µm was seen in the epidermal regions.

Differential diagnosis was Botryomycosis complicated with secondary phaeoid fungal infection or Phaeohyphomycosis with secondary bacterial infection.

The patient was started on tablet amoxicillin clavulanic acid combination 625 mg thrice daily and oral Itraconazole 200 mg/day for three months. As there was no significant improvement, antibiotic was changed to tablet Dapsone 100 mg once daily was prescribed for six months. Patient refused surgical intervention and amphotericin B due to financial constraint. She had shown slowly progressing improvement over one year. Verrucous lesion had resolved and sinus had closed in a month of initiating therapy. Trans-epidermal eliminations had decreased in few months.

DISCUSSION

Skin and Soft Tissue Infections (SSTIs) can be acute or chronic. Prevalence of acute pyo-granulomatous SSTI has increased over years. Causative organisms include filamentous bacteria like *Nocardia* and *Actinomyces* and facultative anaerobes like *Staphylococcus aureus, Escherichia coli*, fungal pathogens like *Madurella, Streptomyces,* Phaeoid fungi, Entomophthorales [1]. Rare case reports of ocular infections, osteomyelitis, etc., have been reported in recent years [2,3]. Most common site affected is limbs especially lower limb which is more prone to trauma [4]. There is a sustained prevalence of chronic pyo-granulomatous infection in immunocompetent patients [5]. Patients acquire infections through direct inoculation of the pathogens either during or following a trauma. However their prevalence among immuno-compromised patients has increased over years [6,7]. More often cutaneous and subcutaneous fungal infection in these patients is a part of systemic infection.

Two common groups of pathogen causing chronic pyo-granulomatous infection of skin and soft tissues are facultative anaerobic bacteria and hyphomycosis causing fungi. Most common bacteria causing the chronic pyo-granulomatous infection of skin and soft tissues are *Staphylococcus aureus* followed by *Pseudomonas aeruginosa, Streptococcus, Escherichia coli,* etc., [1,7]. SSTI associated with tumefaction and discharging sinus is called botryomycosis. Infections are usually monomicrobial. Rare instances of more than one group of bacteria causing infection have been reported in literature [8]. Treatment involves targeted antibiotic therapy for two weeks or more depending on the clinical prognosis.

SSTI by fungi will be slow-progressing and indolent in nature. With advancement in medicine, fungal infections are becoming more common due to increasing use of antibiotics, immunosuppressant and increased incidence of immunodeficient diseases. Phaeohyphomycosis is an opportunistic infection caused by dematiaceous moulds. Humans acquire the infection by accidental inoculation of the fungi. Lesions start as nodule and grow into an indolent mass [9]. The lesion ulcerates or produces a verrucous mass with time. Histopathological picture reveals mixed granulomatous and pyogenic infiltrates in both botryomycosis and phaeohyphomycosis. Pseudoepitheliomatous hyperplasia is a characteristic feature of phaeoid fungal infection. The infected epithelium multiplies abnormally and eliminates the fungus which is seen as black dots in the skin surface [4,9]. Infection is diagnosed by classic clinical presentation and culture for both fungus and bacteria. Presence of typical brown hyphal elements in histopathological examination may not be seen in rare instances [9]. In this case, only brown pigmented yeast like cells was seen occasionally. Phaeohyphomycosis is known to have poor prognosis. Combination therapy of local excision followed by intravenous amphotericin B and oral flucytosine/azoles is ideal. Saturated Solution of Potassium Iodide (SSKI) and azole combinations have proved to be successful in certain cases [10].

CONCLUSION

In this report, we present a case of mixed bacterial and fungal infection leading to chronic subcutaneous infection. Two well identified pathogens-*Staphylococcus aureus* and phaeoid fungi *Alternaria alternata* has caused the infection. Patient responded to treatment with a combination of amoxicillin-clavulanic acid and Itraconazole. Early identification of the causative agents of SSTI is mandatory for a better prognosis. Sole investigation for bacterial infection might have delayed the significant diagnosis in this case scenario. Hence, it is advisable to look for both fungal and bacterial pathogens in SSTIs.

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PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Microbiology, Karpagam Faculty of Medical Science and Research, Coimbatore, Tamil Nadu, India.
2. Associate Professor, Department of Dermatology and Venereology, Karpagam Faculty of Medical Science and Research, Coimbatore, Tamil Nadu, India.
3. Tutor, Department of Microbiology, Karpagam Faculty of Medical Science and Research, Coimbatore, Tamil Nadu, India.
4. Tutor, Department of Microbiology, Karpagam Faculty of Medical Science and Research, Coimbatore, Tamil Nadu, India.
5. Tutor, Department of Microbiology, Karpagam Faculty of Medical Science and Research, Coimbatore, Tamil Nadu, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Lavanya Jeyamani,
197/13, Asiad Colony, 7th Avenue, Annanagar West, Chennai-600101, Tamil Nadu, India.
E-mail: jlavanya152@gmail.com

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