A Rare Case Report of Subcutaneous Mycoses by *Rhytidhysteron Rufulum*

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**ABSTRACT**

Phaeohyphomycosis is a term to describe cutaneous and systemic or disseminated mycoses caused by a variety of dematiaceous fungi. *Rhytidhysteron rufulum* is a poorly known, common, pantropical phaeoid fungal species, and are rare human pathogens. Here, we describe a clinical case report of subcutaneous phaeohyphomycosis; to the best of our knowledge, this is the fourth report of infection with the *Rhytidhysteron rufulum*. A 54-year-old male presented to medicine outpatient department with complaints of respiratory distress. The patient was diagnosed as a case of chronic bronchitis with acute exacerbation. On examination, a well-defined soft subcutaneous swelling was detected on anterior aspect of right leg. The molecular identification revealed its homology with *Rhytidhysteron rufulum*. The phaeohyphomycotic infections are increasingly reported globally. This case highlights the need of awareness and high degree of suspicion for fungal aetiology, so that an early and adequate treatment can be given in such cases.

**Keywords:** Phaeohyphomycosis, *Rhytidhysteron*, subcutaneous

**INTRODUCTION**

Dematiaceous fungi cause a wide range of human diseases including phaeohyphomycosis, chromoblastomycosis, and eumycotic mycetoma [1,2]. Phaeohyphomycosis is a term to describe cutaneous and systemic or disseminated mycoses, caused by a variety of dematiaceous fungi [3]. Human diseases caused by phaeohyphomycotic agents are increasingly reported with a wide range of clinical presentation. *Rhytidhysteron rufulum* is a poorly known, common, pantropical phaeoid fungal species, capable of utilizing different substrata and occupying diverse habitats [4]. Very few reports of mycoses caused by *Rhytidhysteron* spp. have been described in literature. To our knowledge, only three cases of subcutaneous phaeohyphomycoses due to *Rhytidhysteron rufulum* are reported in the literature [3,5,6]. We report fourth case of subcutaneous mycoses caused by *Rhytidhysteron rufulum* in an immunocompromised patient.

A 54-year-old male presented to medicine outpatient department with complaints of respiratory distress. He was a chronic smoker, taking about 8-10 bidis per day for last 10 years. The patient was diagnosed as a case of chronic bronchitis with acute exacerbation. The patient also gave history of hospitalisation for similar episodes of respiratory distress. There was no history of tuberculosis, diabetes, and hypertension. He was kept on antibiotics and bronchodilators.

On examination, a well-defined subcutaneous swelling of about 5 cm × 1.5 cm in size, was detected on anterior aspect of right leg. The patient described it as painless and slowly increasing in size for 4-5 years. The swelling was soft, non-mobile and non-tender with normal overlying skin. The patient did not recollect any history of trauma or any similar swelling present elsewhere on the body.
On laboratory investigations, haemoglobin was 10.6 gm/dl, total leucocyte count 13,400, differential leucocyte count-neutrophils 86%, lymphocytes 12%, monocytes 1%, eosinophils 1%, basophils 0%, platelet count 2.7 lakh/cumm. The random blood glucose, liver and renal function tests were within normal range. Serology for Human Immunodeficiency Virus (HIV 1 and 2) and Hepatitis B surface antigen were negative. The sputum examination for acid fast bacilli was negative. X-ray chest showed prominent bronchovesicular markings. X-ray of the right leg showed a soft tissue swelling with no pathological findings.

On FNAC, 3 ml of dirty white pus like material, free from any discrete granules, was aspirated. Smears revealed intact and degenerated inflammatory cells including neutrophils, few lymphocytes, macrophages, and red blood cells in a necrotic background. Few thick, long septate hyphae were also observed (Figure 1). Periodic Acid Schiff (PAS) stained smears showed fungal hyphae which were PAS positive.

The sample was sent to microbiology department for further analysis. Gram stain of the aspirate showed inflammatory cells with gram variable hyphal elements. KOH mount showed long, thick, and septate hyphae. The material was inocculated onto the blood agar, MacConkey agar and Sabaraud dextrose Agar (SDA) with and without cycloheximide and incubated at 37°C. Bacteriological cultures were negative. On SDA, light gray velvety growth with light brown pigmentation on the reverse was observed after 10-11 days. On further incubation for 2-3 weeks, multiple soft cottony phaeoid colonies developed on the obverse side with dark pigmentation on the reverse (Figures 2A and 2B). Lactophenol cotton blue (LCB) mount revealed brown colored, broad, septate, irregularly branched tortuous hyphae (Figures 2C-2F). As we could not identify the isolate on macroscopic and microscopic examination despite repeated efforts, the isolate was then sent to national culture collection for pathogenic fungi (NCCPF), post graduate institute of medical research and education (PGIMER), Chandigarh for molecular analysis.
The molecular identification was performed by amplifying ITS1 and ITS4 regions of 18s rRNA. A homology of the obtained sequence was carried out by using BLAST in the national centre of biotechnology information GenBank database. The clinical isolate was identified as Rhytidhysteron rufulum and the BLAST showed 98% homology and 99% query cover with Genbank ACCESSION no.KP162181.1. The patient was kept on oral antifungal therapy with itraconazole 200 mg daily.

Phaeohyphomycosis is a clinical term to describe the cutaneous and systemic mycoses caused by a variety of dematiaceous fungi [3]. The genus Rhytidhysteron is characterized by hysteriform ascomata that become discoidal at maturity and paraphyses covered by gelatinous layer [4]. On the basis of amino acid and sequence data, the Rhytidhysteron genus, has been transferred from Patellariaceae to the Hysteriaceae [6,7]. R. rufulum and R. hysterinum are the two commonest species encountered [3]. Our isolate was identical to those of R. rufulum deposited in GenBank. Although worldwide in distribution, it is mostly prevalent in tropical and subtropical countries.

Rhytidhysteron spp. are not known human pathogens and rarely implicated in human infections. It is commonly observed in patients with some degree of immunosuppression resulting from diseases like tuberculosis, diabetes, acquired immunodeficiency syndrome (AIDS), hematological malignancies, or other neoplasia or iatrogenic causes e.g. organ transplantation, corticosteroids, or immunosuppressive therapies 8. Mahajan and co-authors have also described a case of subcutaneous phaeohyphomycosis by R. rufulum in a diabetic patient [3]. Although the patient was a known case of chronic bronchitis in our study, there was no history of long term intake of corticosteroids but intermittent prescription of steroids was available.

R. rufulum is a lignicolous species and generally exist as saprophytes on dead and decaying vegetation. The lesion usually results from the traumatic inoculation of the fungus or following wound contamination [6,9]. The patient is a...
farmer by occupation with no definite history of trauma or any evident exposure in the present study. The daily chores in rural areas like walking barefooted, collecting woods for fuel or harvesting in the fields are some occupational exposures to such kind of trauma, which usually go unnoticed.

The clinical manifestation begins with a usually single, slowly enlarging subcutaneous nodule on the extremities in 60% to 85% of cases [3,8]. In the present study, the patient complains of a solitary painless swelling of chronic duration. In a chronic and painless course, phaeohyphomycosis begins with the appearance of small subcutaneous nodule at the penetration point, and then evolves into a mobile cyst filled with pus. However, in immunocompromised subjects, phaeohyphomycosis may become opportunistic, and potentially generates a disseminated or invasive infection that is associated with a very poor prognosis. Similar findings were observed by Chowdhary, et al. in a case of chromoblastomycosis in a renal transplant patient [5].

The pleomorphic nature, of the diverse species of subcutaneous or systemic phaeohyphomycotic agents, can make their identification a challenge. Molecular studies may sometimes be necessary to identify a causative fungus if attempts to grow it in artificial culture media fail. Moreover, the presence of fungal elements in direct microscopic examination of clinical specimens is of immense importance in determining the significance of a fungal isolate. Few recommendations are available about the treatment of phaeohyphomycosis. Surgical excision and antifungal drugs have been used in various combinations with variable degrees of success [3,5,6].

To conclude, phaeohyphomycotic infections are increasingly reported globally. These rare fungal conditions can simulate as a tuberculous lesion leading to delay in initiation of antifungal therapy. Management of the disease becomes more difficult if the patient is immunocompromised. This case highlights that the fungal aetiology should be suspected in cases of subcutaneous swelling even in the immunocompetent patients of rural background. Early diagnosis promotes quick and adequate treatment to reduce morbidity.

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REFERENCES