

# Fungal Carbuncle Due to *Apophysomyces elegans*—A Case Report

Dev Merlin Samuel\*, Narayanasami Bharath, Manoj Prabu, Khalilur Rahman, Arcot Rekha

Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technological Sciences, Chennai, India

Email: \*sammerlin.work@gmail.com

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## Abstract

**Background:** Deep seated cutaneous fungal infection is a rare entity in surgical practice and is very often under diagnosed. Due to the atypical presentation and slow but aggressive progression of the disease, the associated mortality is high. **Aim:** The aim of this article to update clinicians about the peculiar presentation of mucormycosis caused by *Apophysomyces elegans*. **Case Presentation:** A 50 year old gentleman with a painful swelling and fever was admitted into our care. He had history of trivial trauma and no medical comorbid. His initial labs came back relatively unremarkable. He did not respond to an empirical antibacterial regimen and progressively worsened. The region was debrided and found to have granular secretions with sloughed tissue. On opening the dressing post operative, a fungal mould was found. Fungal etiology was suspected and KOH mount confirmed the diagnosis. He was started on empirical IV antifungals, and local therapy while awaiting culture and sensitivity reports. However, he progressively deteriorated and succumbed to the disease eventually. **Conclusion:** Here we describe a deep seated cutaneous fungal infection in an immunocompetent patient and the challenges we faced during the course of his management. Fungal etiology is generally encountered in immunocompromised hosts. Deep seated cutaneous fungal infections with poor response to antifungal therapy and systemic sepsis led to this patients' demise. This being the case, the onus is on the clinicians to diagnose a fungal etiology early and start appropriate anti fungal measures.

## Keywords

Mucormycosis, Deep Seated Cutaneous Fungal Infections, *Apophysomyces elegans*

## 1. Introduction

Deep seated cutaneous infections are a relatively rare entity in surgical practice, with varied ethology and significant morbidity. Mucormycosis, previously known

as Zygomycosis has been found to have significantly worse prognosis as compared to their bacterial counterparts. Multiple organisms are implicated to cause Mucormycosis such as, but not limited to, *Rhizopus spp.*, *Mucor spp.* and *Apophysomyces spp.* Their presentations are atypical, require longer duration to arrive at a clinching diagnosis, require prolonged intensive care and have worse manifestations of sepsis with high mortality. Here, we describe an atypical case of a soft tissue infection of the back, wherein the patient was immunocompetent with a very trivial injury. He was diagnosed with a fungal etiology and was debrided extensively. Here we discuss his presentation, challenges in diagnosis and therapy and the associated mortality.

## 2. Case Presentation

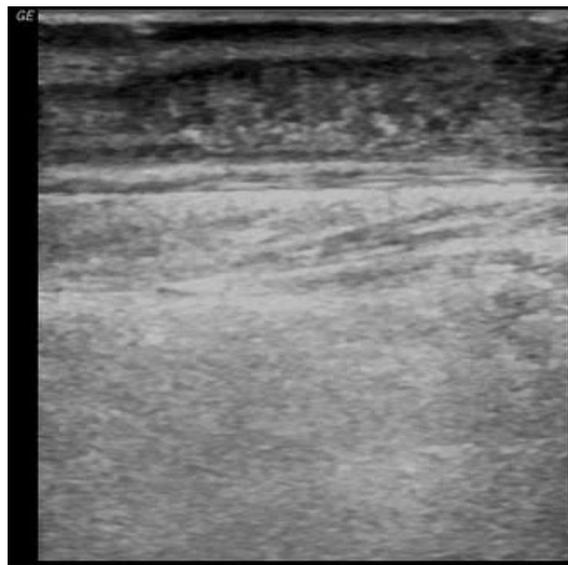
A 50 year old gentleman, a daily wage worker who carries gunny sacks for a living, from Thiruvallur district in Tamil Nadu, presented to us with pain and swelling over the upper back for a period of 10 days. He gave a history of fever for 2 - 3 days and a preceding history of trauma (a thorn prick) about 10 days back, over the affected region, prior to onset of the complaints. He had no known medical comorbid conditions.

At admission, he was febrile but haemodynamically stable. Systemic examination was unremarkable. Local examination of the back showed a 12 × 8 cm region of induration over the interscapular region of the upper back, with minimal fluctuation in the centre, with a discharging sinus (greenish serous fluid). Local warmth and tenderness was present.

He was admitted to our ward with a working diagnosis of cellulitis of the back and routine investigations along with a culture of the fluid. He was started on IV Cefotaxim and IV Metronidazole. His labs showed a raised total count ( $19,900/\text{mm}^3$ ) and neutrophils. He was found to have high random sugars (206 mg/dl), with normal HbA1c (5.9). Ultrasonogram showed soft tissue oedema with no collection (**Figure 1**). Aerobic and anaerobic cultures were found to have no growth. After 3 days of bed rest, regular local care and IV antibiotics, he still had fever spikes, with increasing total leucocyte counts ( $26,000/\text{mm}^3$ ). IV Antibiotics were stepped up to Cefaperazone + Sulfbactem. Locally a central necrotic patch with multiple discharging sinuses, resembling a carbuncle was found on day 3. He was taken up for emergency deroofing of the carbuncle (**Figure 2**).

Intraoperatively, a cruciate incision was placed and deepened. White to straw coloured flakes was found deep in the subcutaneous, up to the muscular plane, with minimal granular fluid exudating. Devitalised necrotic tissue was excised. Tissue was sent for culture and histopathology. Debridement was done. Post operatively his total leucocyte counts continued to increase ( $39,000/\text{mm}^3$ ). On POD1, his dressing was opened to find severely necrosed tissue, with extensive areas of necrotising fasciitis, granular discharge and a mould formation around the edges (**Figure 3**). He was taken up for debridement again. The mould was removed and necrosed tissue was excised aggressively until active bleeding was

noted from all quadrants of the wound and fungal culture was sent. Post operatively patient developed hypotension and required ICU care. A significant drop in haemoglobin was noted, for which transfusion of packed cells was given. Total counts dropped marginally (38,000) but was not significant. A bit of tissue taken from the wound was examined with a KOH mount. Multiple branching hyphae were noted (**Figure 4**). A working diagnosis of a fungal aetiology was reached. Empirical IV antifungals (Amphotericin B) were started and local care was initiated with an experimental application of candid powder on one half of the wound and fluconazole ointment on the other side. After 3 days of regular daily dressings, the side which was applied with the ointment showed considerable improvement as compared to the side with the powder (**Figure 5**). During the course of these days, fresh frozen plasma and packed cells were transfused.



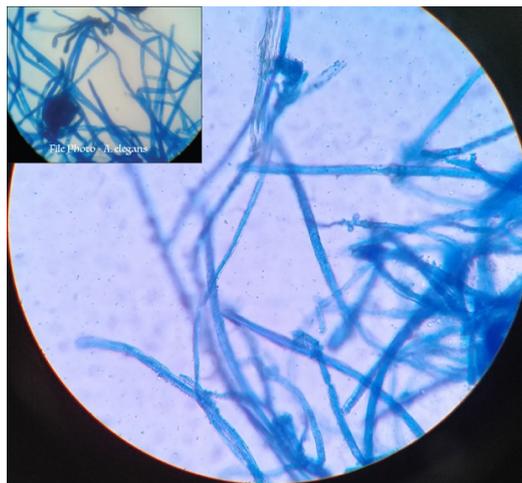
**Figure 1.** Image depicting the ultrasonogram of the back on presentation to the hospital. It showed subcutaneous edema, with no evidence of a collection.



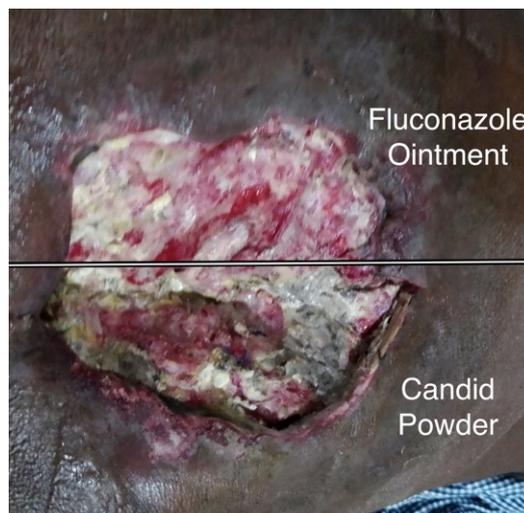
**Figure 2.** Intra operative picture during the first debridement, showing extensive invasion with sloughed tissues upto the muscular plane.



**Figure 3.** Image taken on first post operative day showing extensive necrosis with a fungal mould formation at the edges of the wound.



**Figure 4.** KOH Mount of tissue taken during first debridement showing multiple branching hyphae with separations.



**Figure 5.** Image depicting wound after 3 days of experimental local therapy with candid cream and fluconazole ointment. The side that was dressed with fluconazole ointment showed considerable local control as opposed to side with candid cream.

However, Patients general condition rapidly deteriorated and he died on the 14<sup>th</sup> post operative day.

The fungal culture sent was later found to have slow growing cottony colonies which was further inoculated in potato dextrose agar and was found to grow *Apophysomyces elegans*.

The patients' relatives present were informed regarding the rarity of the case and their informed consent was obtained to publish his case in a journal.

### 3. Discussion

Cellulitis is often caused by gram positive cocci. Anaerobes are another cause for more severe and aggressive forms of cellulitis. Approximately 50% of such infections are polymicrobial; the remainder is caused by single organisms. Fungal aetiology in cellulitis is as such very rarely seen.

Fungi of relevance in cellulitis include those that cause nosocomial infections in surgical patients as part of polymicrobial infections or fungemia (e.g. *Candida albicans* and related species), rare causes of aggressive soft tissue infections (e.g. *Mucor*, *Rhizopus*, and *Absidia spp.*), and opportunistic pathogens that cause infection in the immunocompromised host (e.g. *Aspergillus fumigatus*, *niger*, *terreus*, and other spp., *Blastomyces dermatitidis*, *Coccidioides immitis*, and *Cryptococcus neoformans*).

Fungal infections may be superficial, cutaneous, subcutaneous or deep (systemic). Superficial and cutaneous infections usually involve the hair, nail and superficial skin layers. They are caused mainly by the *Candida spp.* of fungi. Subcutaneous or deep seated infections are more severe and have a worse course. *Chromoblastomycosis*, *Mycetoma* and *Sporotrichosis* are among the most common.

Mucormycosis (previously called zygomycosis) is a serious but rare fungal infection caused by a group of moulds called *Mucormycetes*. Fungi that most commonly cause mucormycosis are: *Rhizopus species*, *Mucor species*, *Cunninghamella bertholletiae*, *Apophysomyces species*, and *Lichtheimia* (formerly *Absidia*) species [1]. Mucormycosis can affect nearly any part of the body, but it most commonly affects the sinuses or the lungs in people who have weakened immune systems. The common forms are Rhino cerebral, Pulmonary, Cutaneous, Gastrointestinal and Disseminated [1]. Cutaneous (skin) mucormycosis can look like blisters or ulcers, and the infected area may turn black. Other symptoms include pain, warmth, excessive redness, or swelling around a wound [2]. Mucormycosis is rare, but it's more common among people with weakened immune systems such as diabetes, especially with diabetic ketoacidosis, cancer, organ transplant, stem cell transplant, neutropenia, long-term corticosteroid use, skin trauma (due to surgery, burns, or other skin injuries). Treatment with IV antifungals is the mainstay of therapy, with Amphotericin B, posaconazole, itraconazole or isavuconazole being the first line drugs. Hyperbaric Oxygen Therapy [3] showed promise in treatment of cutaneous mucormycosis post debridement.

The overall prognosis depends on several factors, including the rapidity of diagnosis and treatment, the site of infection, and the patient's underlying conditions and degree of immunosuppression. The overall mortality rate is approximately 50% [1], although early identification and treatment can lead to better outcomes.

Fungi typically are identified by use of special stains (e.g. potassium hydroxide (KOH), India ink, methenamine silver, or Giemsa). Initial identification is assisted by observation of the form of branching and septation in stained specimens or in culture. Final identification is based on growth characteristics in special media, similar to bacteria, as well as on the capacity for growth at a different temperature (25°C vs. 37°C), which takes around 2 weeks. No sporulation has been noted on slide cultures even after 7 days of incubation on SDA, corn meal dextrose agar, or potato dextrose agar. Stimulation of sporulation has been attempted by the method of Ellis and Ajello [2]. Abundant sporulation has been noted after 5 days on 1% water agar by this procedure [4]. The use of Soil extract media to enhance sporulation of *A. elegans* was attempted. The growth of *A. elegans* in this media was observed much earlier as compared to other methods [5]. However this method has been only documented once in literature and requires further study.

*Apophysomyces elegans* [6] is a filamentous fungi that is found in soil and decaying vegetables. It's a thermotolerant fungus that grows at temperatures of 26°C and 37°C. It goes rapidly at 42°C. It produces cottony colonies. It is a rare cause for mucormycosis, which is often fatal. It is usually acquired via traumatic implantations associated with still or decaying vegetables matter. Unlike other zygomycosis, affected host is usually immunocompetent. *A. elegans* infections present most commonly as necrotising fasciitis, osteomyelitis, systemic infections and secondary renal or bladder infections.

Kindo AJ *et al.* have described a case of left sided orbital cellulitis secondary, wherein the patient inspite of aggressive debridement and treatment with amphotericin B succumbed after 3 weeks [7]. Andresen D *et al.* have reported a post tsunami survivor who developed cutaneous mucormycosis and succumbed to the disease with multi organ failure and muscle and fat necrosis [8]. Wolkow N *et al.* have described a case of chronic rhino orbito cerebral mucormycosis due to *A. elegans*, who underwent multiple courses of antifungal therapy (primarily posaconazole) over a year and survived after a slow intermittent course [9]. Chakrabarti A *et al.* have published a series of 75 cases of Zygomycosis wherein 19% of cases were caused by *A. elegans*. Overall mortality of 45% was noted in their study [10].

Mucormycosis is treated with IV antifungal agents, mainly Amphotericin B, Isavuconazole, Posaconazole. Early initiation of antifungals is essential in enhancing the survival of patients. Amphotericin B is most commonly initiated, with a loading dose of 0.25 - 0.5 mg/kg over 2 - 6 hours followed by maintenance dose of 0.25 - 1 mg/kg qDay or upto 1.5 mg/kg qOD. It is highly nephrotoxic, and creatinine clearance must be calculated prior to administration. If CrCl < 10 mL/min, 0.5 - 0.7 mg/kg q24 - 48 hr is given. Patient may require haemodialy-

sis, in which cases, 0.5 - 1 mg/kg q24 hr after dialysis session may be given. Recently, resistance to Amphotericin B has been noted [11]. In these patients Posaconazole has been shown effective. It is given as 300 mg IV twice on day 1 and followed by 300 mg IV daily. IV administration can be changed to oral (300 mg BD on day 1 followed by 300 mg daily) if eGFR < 50 ml/min in patients with moderate to severe renal impairment. Posaconazole, Itraconazole have been shown to be most active against *A. elegans* [12]. Liposomal Amphotericin B can be used to minimize nephrotoxicity. Caspofungin, is an echinocandin, used in antifungal therapy. Its role in mucormycosis has not been specifically documented, but has been used in treatment of aspergillosis and candidiasis. Other azoles such as fluconazole, voriconazole are ineffective against *Mucorales species*.

In this particular case, the patient presented to us with a trivial trauma to the back and cellulitis. He was an immunocompetent patient with no known comorbid illnesses. He did not respond to empirical antibiotics and the subsequently added higher generation antibiotics. On debridement granular exudate was noted which gave rise to the suspicion of a fungal aetiology. However, it was the presence of a fungal mould that confirmed our suspicions. The diagnosis was confirmed by KOH mount and empirical antifungals were started. Fungal cultures were sent. Experimental local therapy with fluconazole ointment and candid powder was initiated. The side which was dressed with fluconazole showed considerably better granulation tissue. The wound bled severely during debridements and dressing changes and this proved to be a challenge. He required repeated transfusions and prolonged ICU care. The fungal culture required long incubation periods and were not available until the patients eventual demise.

#### 4. Conclusion

*Apophysomyces elegans* affects immunocompetent hosts and causes severe morbidity and mortality. Hence high degree of suspicion is required to identify deep seated fungal infections and initiate appropriate management at the earliest.

#### Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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