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A Rare case of Aggressive Cutaneous Zygomycosis Caused by Apophysomyces Variabilis

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ABSTRACT

Necrotizing fasciitis is a life-threatening soft tissue infection that can be caused by various bacterial and fungal pathogens. Among the fungal etiologies, mucormycosis typically associated with several species such as Mucor, Rhizopus, and Lichtheimia. However, the infection is caused by Apophysomyces spp., particularly Apophysomyces variabilis that are rare but increasingly reported in tropical regions, including India. Here, we report a case of a 59-year-old diabetic female who developed necrotizing fasciitis on her face following minor trauma. Initially, she was managed with antibiotics and surgical debridement. However, subsequent identification of Apophysomyces variabilis necessitated an adjustment in her treatment regimen to include Posaconazole. As a result of this adjustment, along with ongoing surgical debridement and antifungal therapy, the patient achieved successful wound healing and subsequently underwent skin grafting. In this report, we highlights the diagnostic challenges associated with Apophysomyces infections and emphasizes the critical importance of early recognition and targeted therapy to enhance patient outcomes.

***Keywords*:** *Apophysomyces variabilis, Mucormycosis, Necrotizing fasciitis, Antifungal therapy, Skin grafting*

INTRODUCTION

Necrotizing fasciitis is a rapidly progressive and serious soft tissue infection characterized by widespread necrosis of the fascia and surrounding tissues [1]. It often arises following minor trauma, surgical procedures, infections, and can be caused by a diverse range of bacterial and fungal pathogens. While bacterial etiologies, particularly those involving *Streptococcus* and *Staphylococcus* species, are more commonly recognized, fungal infections, including mucormycosis, are increasingly noted, especially in immunocompromised individuals.

Mucormycosis is primarily associated with species such as *Mucor, Rhizopus,* and *Lichtheimia*; however, rarer genera like *Cunninghamella, Syncephalastrum, Apophysomyces*, and *Saksenaea* are also reported, previously [2]. Among the species, *Apophysomyces* is a soil-dwelling fungus predominantly found in tropical and subtropical regions [3]. Infections caused by *Apophysomyces* spp., particularly *Apophysomyces variabilis*, have become more prominent in tropical counties, including India [4]. Although these infections are rare, they pose significant diagnostic and therapeutic challenges due to their aggressive nature and the difficulty of early identification.

In this case report, we describe the clinical presentation, management, and outcomes of a 59-year-old diabetic female who developed necrotizing fasciitis caused by Apophysomyces variabilis following minor facial trauma. This case highlights the necessity for heightened awareness of fungal infections in the differential diagnosis of necrotizing fasciitis and emphasizes the critical importance of prompt recognition and targeted treatment to improve patient outcomes.

METHODOLOGY

A 59-year-old female with diabetics presented after a slip and fall incident resulting in an abrasion on the left side of her face. Initially, she used a native treatment involving lime application, which subsequently led to an abscess formation. She sought medical care at a nearby hospital, where an incision and drainage of the abscess was performed along with excision of necrotic tissue.

Following this initial treatment, the patient was referred to our hospital with complaints of pain for 20 days, swelling for 15 days, purulent discharge for 12 days, and low-grade fever for 10 days, characterized by intermittent episodes. She reported no symptoms of dizziness, loss of consciousness, vomiting, or bleeding from the ear, nose, or throat.

Upon examination, she had a Glasgow Coma Scale (GCS) score of 15/15 and was alert and oriented. Her vital signs were constantly stable. Local examination of the wound revealed a single ulcer measuring 3.5x5 cm on the left zygomaticotemporal region of her face, about 1 cm posterior to lateral canthus of her left eye (Figure 1). The ulcer exhibited a circular shape with well-defined margins, undermined edges, and a slough-covered floor. Purulent discharge was present, and signs of inflammation were evident in the surrounding skin.

Palpation confirmed these findings, revealing local warmth, tenderness, and induration extending around the ulcer. Palpable lymph nodes measuring 0.5 x 1 cm were noted at levels I and II. The diagnosis of necrotizing fasciitis of the face was established based on these clinical findings.

Routine blood investigations were largely normal, except for elevated blood sugar levels of 253 mg/dL and an HbA1c of 8.47%. A wound swab was sent for bacterial culture. The patient was started on oral hypoglycemic medications, broad-spectrum antibiotics, and other supportive treatments. On day 2, surgical debridement was performed under anesthesia (Figure 2). A flap was raised through an incision in the pre-auricular area. Necrotic tissue was identified in the superficial musculoaponeurotic system (SMAS) layer, involving the zygomatic, temporal, and cheek regions. This tissue was thoroughly debrided and sent for bacterial culture, fungal culture, and fungal polymerase chain reaction (PCR) via amplification of the internal transcribed spacer.

After achieving hemostasis and placing a corrugated drain at the mandibular angle, the flap was sutured into position. On day 3, white cottony slough reappeared (Figure 3), prompting a second surgical debridement (Figure 4). While awaiting fungal culture results, fungal staining returned negative, but bacterial culture identified Pseudomonas aeruginosa. Consequently, the patient was started on meropenem on day 4. Given the suspicion of a fungal infection despite negative fungal culture results, broad-spectrum antifungal therapy with voriconazole was initiated after consulting with an infectious diseases specialist.

Histopathological examination of skin sections revealed extensive necrosis, thrombosed blood vessels, and acute inflammatory exudate, with no granulomas, fungal elements, or bacterial colonies observed. Daily bedside debridement continued until day 7 (Figure 5). Fungal culture and PCR results were negative for growth. Due to progressive necrosis, magnetic resonance imaging (MRI) of the head and neck was performed, which showed inflammation in the subcutaneous tissue of the left temporal and zygomatic regions, as well as the left cheek, ruling out deeper tissue involvement. Left cervical lymphadenopathy was noted but deemed insignificant.

On day 8, a third surgical debridement was performed (Figure 6), and tissue samples were sent again for fungal staining and culture. Daily bedside debridement and dressing changes continued as we awaited results (Figure

7). By the end of the second week, the fungal cultures exhibited some growth, which was subcultured. The subcultures displayed white cottony growth, and microscopy revealed aseptate hyphae with funnel-shaped sporangiophores (Figure 8). The growth was sent for PCR, and the organism was identified as *Apophysomyces variabilis* based on the presence of funnel-shaped apophysis, sporangiophore, pigmented subapical thickening, foot cell, and pear-shaped multispored sporangium in the lactophenol cotton blue mount (Figure 9).

Following consultation with the infectious diseases consultant, the patient was started on posaconazole (600 mg twice daily for the first day, followed by 300 mg once daily for six months). Daily bedside cleaning and dressings continued. After a week (day 28) of appropriate wound care and antifungal therapy, the wound bed was prepared for coverage (Figure 10). The patient subsequently underwent split-thickness skin grafting of the face, with excellent graft take observed by postoperative day 5 (Figure 11), and she was discharged from the hospital.

Figures

Figure 1: Ulcer containing slough on the floor.

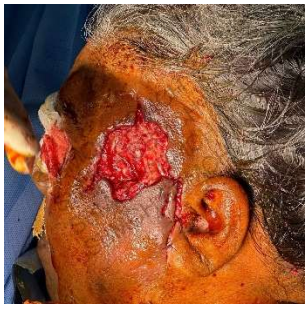

Figure 2: Day 2- First Debridement intra operative picture

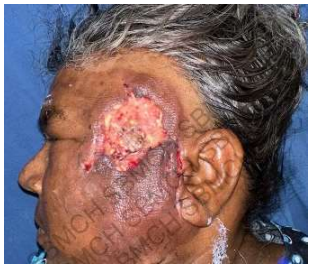

Figure 3: Day 3- Slough reappears on the wound.

Figure 4: Day 5- clinical picture after second debridement.

Figure 5: Day 7- The infection still persists with slough.

Figure 6: Day 8- Post operative Day one of the 3rd debridement

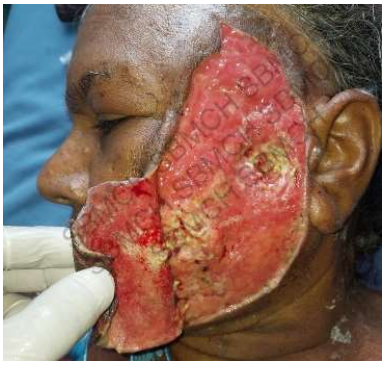

Figure 7: Day 18- The picture shows persistent slough.

Figure 8: *Apophysomyces variabilis* colonies on SDA.

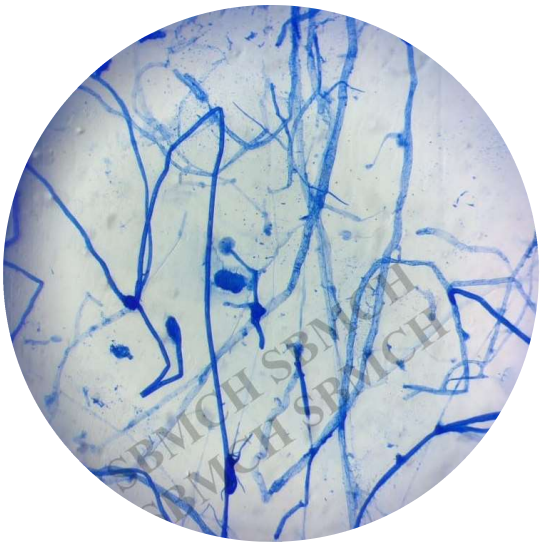

Figure 9: 40X in lactophenol cotton blue mount (LPCB) - *Apophysomyces variabilis*

Figure 10: Day 22, 25 & 28 respectively - the wound bed is free of infection and ready for grafting

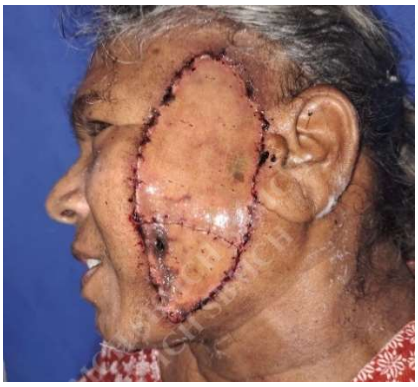

Figure 11: Day 34 - first look graft uptake was 100%

Figure 12: After 3 months results

RESULTS

The skin graft achieved 100% take, with an excellent color match to the surrounding skin. There was no functional loss concerning oral competence, mouth opening, or eyelid movements. The cosmetic outcome was also satisfactory. The patient was advised to continue posaconazole for six months and was monitored regularly in the outpatient setting for any signs of infection recurrence. One year postoperatively, the graft remained well-integrated, and there was no recurrence of infection (Figure 12).

DISCUSSION

Apophysomyces is a rare yet significant cause of mucormycosis. The first isolation of *Apophysomyces elegans* was reported by Misra et al. in 1979 from soil in a mango orchard in North India. Since then, the genus has evolved to include five species: *A. variabilis, A. elegans, A. trapeziformis, A. mexicanus,* and *A. ossiformis,* distinguished by their morphology, genetics, and biochemical characteristics.

While infections caused by *Apophysomyces* are uncommon, recent years have seen an uptick in cases, particularly in tropical and subtropical regions, including India. Other countries reporting an increase in cases include Sri Lanka, Thailand, South America, and Australia. Among the various clinical manifestations of *Apophysomyces* infections, skin and soft tissue infections account for approximately 52.7%, with pulmonary and renal involvement at 10.8%, and rhino-orbito-cerebral infections at 25.7%. Skin and soft tissue involvement is the most prevalent presentation, typically characterized by ulceration, central necrosis, and surrounding induration with erythema. The most common mode of infection is contamination from soil through breaches in the skin, often due to trivial trauma, injection sites, surgical procedures, or burns. Disseminated infections, while rare, can lead to angioinvasion, vascular thrombosis, septicemia, and central nervous system damage, with mortality rates as high as 80% in such cases.

Infection with *Apophysomyces variabilis* presents unique diagnostic challenges. The organism's fragile hyphae can be easily damaged during biopsy and handling, complicating microscopic examination, particularly with KOH mounts techniques that further compromise hyphal integrity. Additionally, this fungus is notoriously difficult to isolate in cultures due to its slow growth and fragile hyphae. Standard fungal media such as Sabouraud's dextrose agar (SDA) may not support sporulation; instead, *Apophysomyces* species require specialized media like Czapek agar and thrive at higher temperatures (40-42°C) with prolonged incubation periods exceeding seven days.

To enhance detection, a subculture of colonies from SDA onto special media using the Scotch Tape technique often yields better results, revealing *Apophysomyces* as white cottony growth. The entire identification process is time-consuming, which can lead to delays in initiating specific antifungal therapy. Routine broad-spectrum antifungals tend to have minimal efficacy against this organism, making posaconazole the drug of choice for *Apophysomyces variabilis* infections, effectively controlling both localized and disseminated disease. A combined approach of surgical intervention and antifungal therapy has been shown to yield the best outcomes in disease management and facilitates timely reconstruction.

CONCLUSION

One emerging and concerning cause of primary cutaneous necrotizing infections is *Apophysomyces variabilis*. Patients with necrotizing fasciitis, particularly those with diabetes and a history of trauma, should be thoroughly evaluated for potential fungal etiologies. Atypical fungal infections must always be considered, and appropriate diagnostic tests should be conducted promptly, especially in tropical countries like India.

This case underscores the critical importance of early identification of atypical fungal infections to facilitate timely antifungal treatment and prevent local and systemic spread. There is a pressing need for further research and increased awareness regarding *Apophysomyces variabilis*, including its epidemiology, pathophysiology, clinical significance, and antifungal therapy options.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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