CASE REPORT

Rhinofacial Conidiobolomycosis Mimicking Facial Cellulitis: A Diagnostic Challenge in an Immunocompromised Man

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ABSTRACT

Conidiobolomycosis is a fungal infection caused by *Conidiobolus spp.* Common symptoms include epistaxis, nasal discharge, nasal obstruction, sinus tenderness, and persistent extensive facial swelling leading to facial mutilation. Our case describes an indolent presentation of conidiobolomycosis in an immunocompromised young man, resulting in delayed diagnosis and treatment. A 29-year-old Malay gentleman, a chef, who was hearing disabled and on anti-tuberculosis treatment, presented with a five-month history of unwellness, poor oral intake, and painless left nasal cavity swelling. Despite classic symptoms of conidiobolomycosis being absent, biopsy and PCR confirmed *Conidiobolus megalotocus*. After antifungal treatment initiation, his condition significantly improved, with resolution of facial swelling, after two months. This case highlights the importance of considering conidiobolomycosis in immunocompromised patients even with atypical presentations.
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INTRODUCTION

Conidiobolomycosis, also known as rhinofacial entomophthoromycosis, is a rare fungal infection predominantly found in tropical regions such as Southeast Asia including Malaysia. The infection is more common in immunocompetent patients, usually chronic, and indolent. It spreads slowly from the nasal submucosa and paranasal sinuses to the nasal skin, glabella, cheek, upper lip, and pharynx. The infection typically commences with uncomplicated nasal discharges, epistaxis, and unilateral nasal congestion, which may subsequently advance to facial oedema and deformity if left untreated. Children rarely contract the infection, and men are more likely to contract it globally (1).

Early diagnosis of conidiobolomycosis relies on clinical suspicion, histopathological examination, and isolation of the fungal agent. However, due to its rarity, the disease is easily misdiagnosed (1). Conidiobolus infections can mimic other more frequent illnesses which may delay accurate diagnosis and treatment. Furthermore, the scarcity of information on optimal treatment strategies emphasizes the value of sharing clinical experiences. Effective communication with laboratory personnel is crucial to help in guiding the correct diagnosis as there is a specific stain for fungal detection.

This case report will present a detailed clinical case of Conidiobolus infection, outlining the patient's clinical presentation, diagnostic process, therapeutic measures, and patient outcome.

CASE REPORT

A 29-year-old Malay gentleman, a chef, presented with a five-month history of feeling unwell and poor oral intake for the past one-week. He has underlying hearing disability and was known to have smear-positive pulmonary tuberculosis on day 43 anti-tuberculosis treatment. On initial examination noted there was painless swelling of the left nasal cavity extending onto the bilateral maxilla with loss of nasolabial folds which was noticed in the last five months. However, he

appeared alert and not tachypnoeic.

A rigid nose endoscopy could not be performed due to an oedematous left nasal wall and thick nasal discharge. Initially, based on a CT scan finding, he was diagnosed with facial cellulitis, while his nasal biopsy showed epidermal hyperplasia without granulomas. Oral fluconazole 200mg twice daily (BD) and his ongoing anti-tuberculosis treatment were initiated. Unfortunately, the patient discontinued treatment against medical advice after day 50 of anti-tuberculosis and four days of oral fluconazole. He subsequently defaulted on follow-up appointments.

He was readmitted four months later due to worsened facial swelling that extended to the lip (Figure 1), which was accompanied by a weight loss. The upper airway narrowing was caused by a worsening soft tissue mass, which was identified by a repeat CT scan of the neck, paranasal sinus, and thorax, as well as cervical lymphadenopathy. A successful open tracheostomy was performed, which included direct laryngoscopy, nasoendoscopy, and biopsy. The patient was immediately administered intravenous amphotericin B 40mg once daily (OD) to address the invasive fungal infection, and the anti-tuberculosis regimen was promptly resumed.

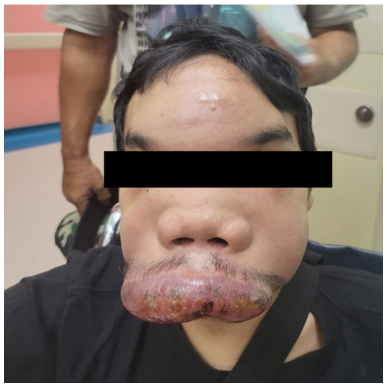

Figure 1: Facial swelling prominently involving the lip and nasal region.

Initial blood investigations on the first presentation showed only mild hyponatremia. However, on the second presentation, he had eosinophilia, elevated CRP, and ESR, likely due to disease progression. Otherwise, there was no anaemia or hypoalbuminemia to suggest chronic disease. His infective and autoimmune screenings were negative.

The second biopsy showed inflamed tissue with focal areas of the Splendore-Hoeppli phenomenon, with underlying stroma densely infiltrated by numerous eosinophils. Grocott methenamine silver (GMS) stain of the tissue shows scattered thick wall fungal bodies and hyphae with occasional septation (Figure 2). Tissue for fungal cultures grew mold colonies after three days incubation on Sabaroud dextrose agar (SDA), Mycosel agar, and brain heart infusion agar (BHIA). Macroscopically, the colony was flat and waxy tan to brown colony with white reverse. Under the microscope, septate hyphae were noted with unbranched sporophores bearing single-celled round spores. Some of the mature spores that were forcefully ejected had tapering projections at the site of former attachment (Figure 3).

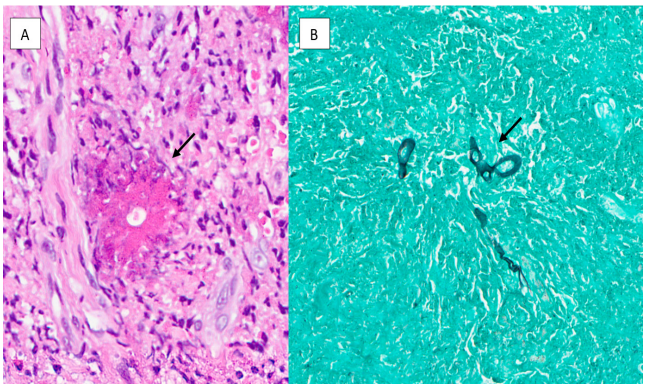

Figure 2: (A) Splendore-Hoeppli phenomenon or formation of intensely eosinophilic material radiating outward with star-like appearance from the tissue biopsy indicated by the black arrow (Haematoxylin and eosin stain, 400Ч magnification), and (B) Thick wall fungal bodies and hyphae with occasional septation as indicated by black arrow (Grocott methenamine silver stain, 400Ч magnification).

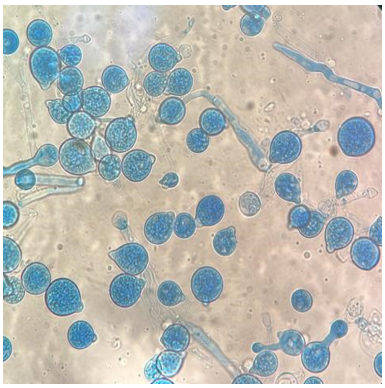

Figure 3: Microscopic appearance of the colony by Lactophenol Cotton Blue (LPCB) (400Ч magnification) showing septate hyphae of unbranched sporophores bearing round spores with some of the spores had tapering projections.

The tissue culture was reported as Conidiobolus sp. which are further confirmed by fungal polymerase chain reaction (PCR). Unfortunately, matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) spectrometry identification of this isolate failed due to inaccessibility of their database. The reference laboratory detected *Conidiobolus megalotocus* after amplifying and sequencing the rDNA internal transcribed spacer 1 (ITS1), ITS4, and large subunit region.

Antifungal susceptibility testing was also conducted on the isolate at the reference laboratory for a variety of antifungal agents, as indicated in Table I. The patient's treatment regimen for conidiobolomycosis included oral Lugol's iodine 2ml OD, fluconazole 200mg BD, and intravenous amphotericin B 40mg OD. He was later

switched to voriconazole after reviewing the antifungal susceptibility result.

Table I: Summary of patient's microbiological investigations

Test	Result	
Blood culture and sensitivity (MycoFlytic)	No growth after 14 days of incubation	
Tissue for fungal culture and sensitivity	*Conidioblus sp.*	
Tissue for fungal PCR	*Conidiobolus megalotocus*	
Antifungal Susceptibility Testing for Mold	Antifungal	MIC (ug/mL)
	Anidulafungin	>16
	Posaconazole	4
	Voriconazole	2
	Itraconazole	1
	Fluconazole	8
	Amphotericin B	>16

After two months of treatment, his facial swelling improved significantly. The treatment plan is for him to continue receiving antifungal medications for up to one year with regular follow-up appointments. During the writing of the case report, he had completed six months of treatment, and his condition steadily improved.

DISCUSSION

Conidiobolomycosis is predominantly found in tropical regions of Africa, South and Central America, and Asia, with a particular prevalence in India. It primarily affects adult males who are professionally involved in outdoor activities (2). However, because of low index of suspicion about the disease among clinicians, it may be missed in the initial differential diagnosis if the patient presented with an atypical presentation like this case until late presentation when the deformities had come into the picture.

For a patient presented with similar symptoms such as the case, some of the differential that needs to be rule out are more common fungal infections such as mucormycosis which tend to be more aggressive and rapid tissue destruction, or bacterial infection like nocardiosis which usually can be cultured in laboratory or parasitic infections like leishmaniasis which are rare in the country due to unavailability of the vector. Other differential like malignancy also needs to be exclude.

Although most conidiobolomycosis cases involve *Conidiobolus coronatus*, our patient's infection was caused by the less common *Conidiobolus megalotocus*. Other species affecting human are *Conidiobolus incongruus*, and *Conidiobolus pachyzygosporus* (1). Conidiobolus infection particularly have high risk in certain occupations such as farmers, veterinarians, gardeners or working in waste management due to the exposure of decaying organics material that might contain high conidiobolus spore. This patient works as a chef and may have indirect contact with the spore during food handling.

While conidiobolomycosis is more frequent in immunocompetent individuals, cases of co-infection with tuberculosis have been reported (2). In our particular instance, the patient was already undergoing anti-tuberculosis treatment. Further studies are needed to investigate any potential link between Conidiobolus infection and tuberculosis.

A definitive diagnosis for the infections requires histopathologic evidence of the etiologic agent and isolation of the agent in culture (1). However, in this case, the initial investigations, including CT scan and the first biopsy, did not reveal the underlying fungal infection. The indolent presentation and initial misdiagnosis of facial cellulitis highlight the challenges in diagnosing atypical conidiobolomycosis. Obtaining a good tissue sample can be difficult, and invasive procedures may lead to patient reluctance, further delaying diagnosis.

The histopathology characteristic of the Splendore-Hoeppli phenomena – which is the formation of intensely eosinophilic material radiating outward with a star-like appearance as shown in Figure 2 – is clearly appreciated. However, this phenomenon is not pathognomonic to conidiobolomycosis, as it may also be demonstrated in sporotrichosis, zygomycosis, candidiasis, aspergillosis, and other bacterial and parasitic conditions (3). However, in this case, it was seen in conjunction with significant peripheral blood eosinophilia, which along with clinical suspicion, ultimately led to the correct diagnosis.

The preferred treatment is a combination of medical therapy (antifungal and potassium iodide) and surgical debridement of the affected paranasal sinus (2). A variety of drugs have been employed as a single agent or in combination with different outcomes (4). As such, there is no standardized treatment duration, although some literature suggests antifungal therapy should continue for at least a month after clinical cure (4).

Antifungal susceptibility can vary depending on the specific *Conidiobolus* species, the strain, and the geographical region where the fungus is isolated. There were no established breakpoints in the Clinical and Laboratory Standard Institute (CLSI) for the antifungal susceptibility test. However, as stated in Table 2, we can observe that anidulafungin and amphotericin B had the highest minimum inhibitory concentration (MIC). The clinician should consider this value even if there was no interpretation because the patient was started on amphotericin B. Literature reports successful outcomes with oral itraconazole alone for four months in some cases (5). For our patient, considering the MIC results, the treatment was switched to voriconazole after initial amphotericin B therapy. His facial swelling significantly

improved after two months of treatment.

While *Conidiobolus coronatus* is the most frequently reported species associated with conidiobolomycosis, this case demonstrates successful treatment of *Conidiobolus megalotocus* infection. Further research is needed to understand the potential association between *Conidiobolus megalotocus* and clinical outcomes.

CONCLUSION

Conidiobolomycosis, especially when presenting atypically, can be challenging to diagnose and requires a high index of suspicion from clinicians. This case report underscores the importance of considering conidiobolomycosis in the differential diagnoses for patients with facial swelling, particularly those who are immunocompromised or reside in endemic areas. Obtaining good quality tissue samples is crucial for accurate diagnosis and early initiation of appropriate antifungal therapy. While established breakpoints for antifungal susceptibility testing may not be available, performing the test can still provide valuable information to guide treatment decisions. Early diagnosis and appropriate therapy are essential to prevent complications and improve patient outcomes.

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