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CASE REPORT

Naganishia albidus Causing Perioral Cutaneous Infection: A Rare Case Easily Misdiagnosed

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Abstract: Cutaneous cryptococcosis is rarely caused by *Naganishia albidus*, especially in immunocompetent individuals. We report a unique case of perioral cutaneous infection in a 37-year-old male with scattered erythematous, pruritic, and scaly lesions lasting over a month. Initial clinical presentation mimicked common dermatological conditions, leading to potential misdiagnosis. Diagnosis was confirmed through fungal culture, fluorescence microscopy, MALDI-TOF mass spectrometry and molecular identification. The patient was successfully treated with oral itraconazole and topical fluconazole cream for six weeks. This case underscores the importance of considering rare fungal infections in atypical presentations to prevent misdiagnosis and delays in treatment.

Keywords: *Naganishia albidus*, perioral cutaneous infection, naganishial infection, antifungal therapy

Introduction

Naganishia albidus (*N. albidus*), a saprophytic yeast widely distributed in the environment, is an uncommon pathogen in human infections.[1] It belongs to the genus Naganishia, which includes notable pathogens such as *N. albidus*, known to cause life-threatening meningitis and systemic infections, particularly in immunocompromised individuals. *N. albidus*, formerly known as *Cryptococcus albidus*, was reclassified based on molecular phylogenetic analyses, reflecting a broader revision of Tremellomycetes taxonomy. However, *N. albidus* rarely causes disease, with most reported cases involving bloodstream infections, meningitis, or peritonitis in patients with compromised immune systems, such as those with HIV/AIDS, malignancies, or on immunosuppressive therapies.[2–5]

Cutaneous naganishiosis is even rarer in immunocompetent individuals. When it occurs, the clinical presentation often mimics common dermatological conditions like eczema, dermatitis, or superficial fungal infections, leading to frequent misdiagnosis or delayed diagnosis.[6] Furthermore, superficial infections localized to the perioral region are particularly unusual, and to date, no cases involving *N. albidus* have been reported in the literature.

Given its rarity, there is limited consensus on the optimal management of N. *albidus* infections, and treatment is often extrapolated from protocols for more common Naganishia species. Delayed or incorrect treatment can result in prolonged morbidity or progression to systemic involvement.

In this report, we describe a rare case of perioral cutaneous Naganishia infection caused by *N. albidus* in a previously healthy, immunocompetent individual. The case highlights the diagnostic challenges posed by its atypical presentation and underscores the importance of considering rare fungal pathogens in refractory or atypical cutaneous lesions. Additionally, we discuss the successful therapeutic approach combining oral itraconazole with topical antifungal therapy, offering valuable insights for clinicians facing similar cases.

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Written informed consent was obtained from the patient for the publication of this case report, including clinical details and accompanying images. The patient was fully informed about the purpose of this report, and confidentiality has been strictly maintained throughout.This case report was approved for publication by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Ethics Approval Number: Quick Review 2019 No. 057).

Case Presentation

General Information

A 37-year-old male construction materials vendor presented to the dermatology outpatient clinic of our hospital, with complaints of recurrent erythematous papules and scaling around the perioral region, accompanied by swelling, pain, and pruritus for over one month. The initial presentation involved three erythematous papules around the mouth, which the patient scratched, leading to progressive proliferation and extension to the perioral area and bilateral nasal wings, with associated swelling, itching, and desquamation (Figure 1).

The patient initially sought treatment at another facility and was diagnosed with "atopic dermatitis". Treatment included ebastine tablets, hydrocortisone butyrate cream, recombinant human epidermal growth factor gel, and rupatadine fumarate tablets for over a month. However, symptoms worsened, prompting him to visit our dermatology clinic. The patient denied any fever, cough, sputum production, or headache during the course of the illness.

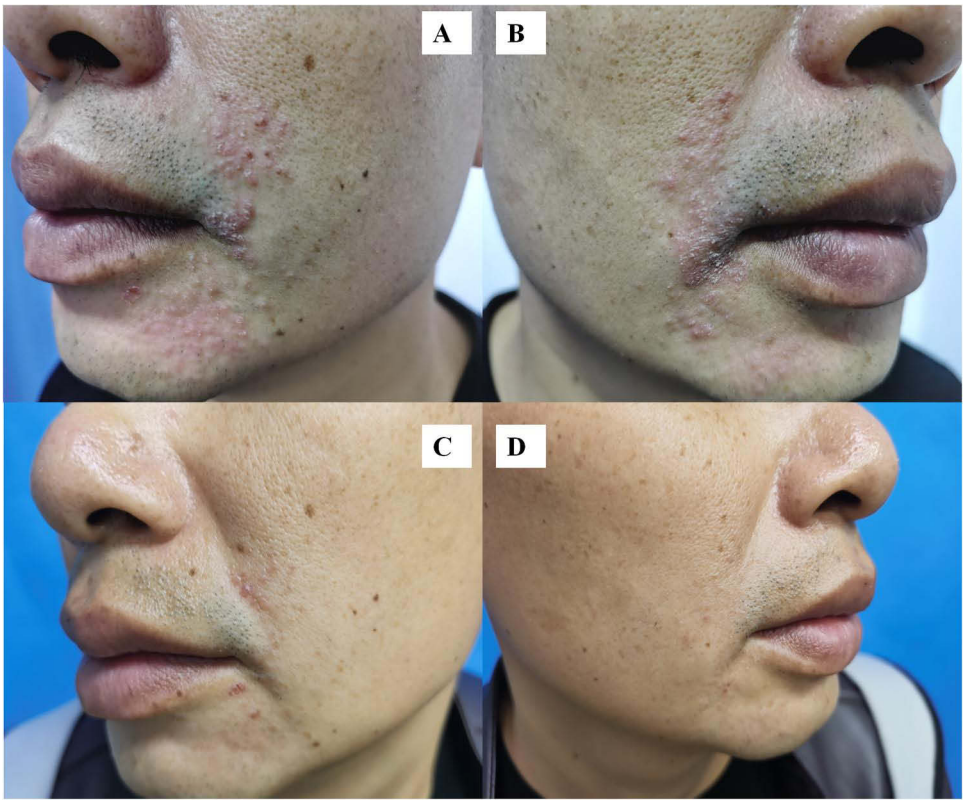

Figure 1 (**A** and **B**) Erythematous papules around the mouth, with associated swelling, itching, and desquamation. (**C** and **D**) The perioral lesions resolved completely, with significant improvement in symptoms.

Medical History

The patient had no prior history of chronic illnesses such as hypertension or diabetes and denied any history of infectious diseases such as hepatitis, tuberculosis, or HIV. He also denied autoimmune conditions such as rheumatoid arthritis or systemic lupus erythematosus. The patient mentioned that his neighbor raised pigeons.

Microbiological Examination

Scrapings from the perioral lesions were subjected to fungal microscopy and culture. Direct fluorescent staining revealed spherical yeast-like fungi emitting blue-green fluorescence (Figure 2A). India ink staining showed round, encapsulated fungal cells with a translucent center, morphologically consistent with Cryptococcus species (Figure 2B). Fungal cultures at 35°C for three days produced white, smooth, dome-shaped yeast colonies (Figure 2C). Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) analysis (ZYBIO-EXSX) identified the isolate as *N. albidus*, with a confidence score of 2.16. The extracted DNA was amplified using ITS1 and ITS4 primers, and BLAST analysis against the NCBI database showed 100% identity with *N. albida* (GenBank accession no. PV660945).

Additionally, a biopsy specimen from the lesion above the left corner of the mouth was obtained. Fungal culture at 35°C for five days yielded similar yeast-like colonies, which were confirmed as *N. albidus* by metagenomic next-generation sequencing.

Histopathological Examination

Histopathology of the biopsy revealed parakeratosis, follicular plugging, and focal epidermal thickening. The dermis showed mixed inflammatory infiltrates surrounding hair follicles, with multinucleated giant cells forming epithelioid granulomas. Special stains were performed: PAS staining was negative, and acid-fast staining was negative. The pathological diagnosis was infectious granulomatous inflammation (Figure 3).

Additional Laboratory Findings

Chest CT was unremarkable. Lymphocyte subset analysis showed CD3+ T lymphocyte count of 1442 cells/μL, CD4+ T lymphocyte count of 914 cells/μL, CD8+ T lymphocyte count of 469 cells/μL, and CD4+/CD8+ ratio of 1.95. Other blood tests were within normal limits, including negative results for HIV antibodies, hepatitis B surface antigen, and serum cryptococcal capsular polysaccharide antigen.

Diagnosis

Considering the patient's clinical presentation, microbiological findings, and histopathological examination, the diagnosis was established as a cutaneous naganishial infection caused by *N. albidus*. The identification of *N. albidus* was supported

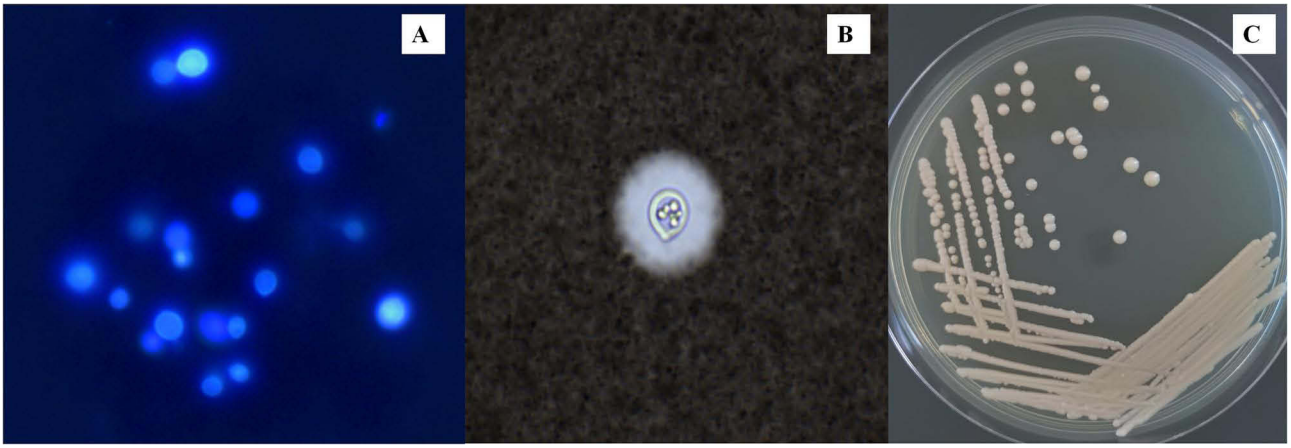

Figure 2 (**A**) Direct fluorescent staining revealed spherical yeast-like fungi emitting blue-green fluorescence (400×); (**B**) India ink staining showed round, encapsulated fungal cells with a translucent center (400×); (**C**) Fungal cultures at 35°C for three days produced white, smooth, dome-shaped yeast colonies.

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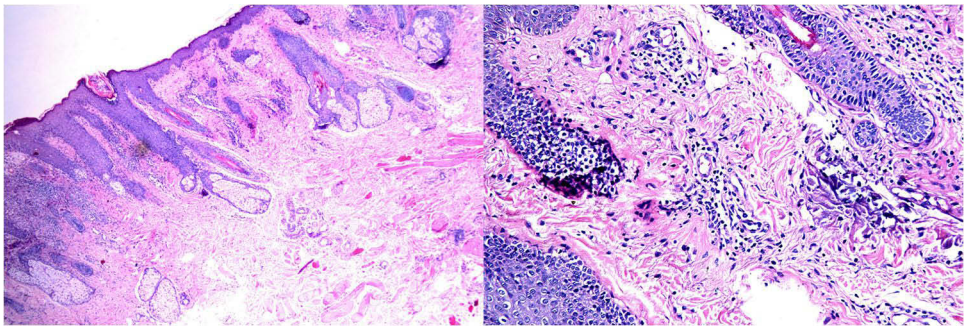

Figure 3 Histopathology of the biopsy revealed parakeratosis, follicular plugging, and focal epidermal thickening. The dermis showed mixed inflammatory infiltrates surrounding hair follicles, with multinucleated giant cells forming epithelioid granulomas.

by direct fluorescent microscopy, culture morphology, MALDI-TOF MS analysis, ITS sequencing, and metagenomic next-generation sequencing. Histopathological findings of granulomatous inflammation further corroborated the diagnosis. Comprehensive laboratory investigations ruled out systemic involvement and underlying immunodeficiency, confirming this as a localized cutaneous infection in an immunocompetent individual.

Treatment and Outcome

The patient was treated with oral itraconazole at a dose of 0.2 g twice daily and topical fluconazole cream applied to the affected areas twice daily. After six weeks of treatment, the perioral lesions resolved completely, with significant improvement in symptoms (Figure 1C and D).

Discussion

N. albidus is a rare cause of human infections, predominantly affecting immunocompromised individuals.[5,7] However, cases involving immunocompetent hosts, particularly with cutaneous manifestations, remain exceptional. The perioral localization of the infection in this case underscores a critical clinical challenge: infections at uncommon sites are prone to being overlooked or misdiagnosed, which could potentially delay appropriate management if not promptly recognized.

The perioral region is an unusual site for fungal infections, often mimicking common dermatological conditions such as Perioral dermatitis, seborrheic dermatitis, or eczema.[8] This overlap in clinical presentation frequently leads to initial misdiagnosis, as seen in our patient, who was treated for atopic dermatitis without improvement. This diagnostic delay not only prolongs patient suffering but also increases the risk of complications or progression to systemic involvement in susceptible individuals. The case highlights the need for heightened clinical suspicion when dealing with refractory or atypical skin lesions, particularly in patients with environmental exposures, such as contact with pigeon droppings, which are known to harbor Naganishia species.[9]

Traditional diagnostic approaches, such as microscopy and techniques like India ink staining, remain fundamental for identifying fungal pathogens and play a crucial role in the initial diagnostic process.[10] However, for rare pathogens, relying solely on these methods may be insufficient.[11,12] In our case, the integration of advanced techniques, including MALDI-TOF mass spectrometry, metagenomic next-generation sequencing (mNGS), and molecular sequencing, provided a comprehensive and definitive identification of *N. albidus*. MALDI-TOF proved effective in distinguishing *N. albidus* from other Naganishia species, while mNGS and ITS sequencing offered precise molecular confirmation.[6] This case highlights the importance of combining traditional and advanced diagnostic tools to enhance accuracy and ensure timely and reliable identification of rare or atypical infections, especially in challenging cases.

The absence of standardized treatment protocols for *N. albidus* infections poses a therapeutic challenge, as most treatment regimens are extrapolated from those established for *C. neoformans*. According to the Infectious Diseases Society of America (IDSA) guidelines, infections caused by *C. neoformans* in immunocompetent individuals, such as isolated pulmonary or skin infections, are often managed with fluconazole (200–400 mg/day) for a minimum of 6–12 weeks. For more severe cases, induction therapy with liposomal amphotericin B combined with flucytosine is

recommended.[13] In contrast, *N. albidus* lacks robust clinical trial data to support specific antifungal regimens. To date, only seven cases have been reported in the literature, among which successful treatments with fluconazole and itraconazole were documented. Including our report, this brings the total to eight.[4] In our case, the perioral infection completely resolved after six weeks of treatment with itraconazole and fluconazole cream.

Our case demonstrated the successful use of a combination of oral itraconazole and topical fluconazole cream therapy, achieving complete lesion resolution within six weeks. This dual approach effectively addressed both systemic and localized fungal burdens, underscoring the potential advantages of integrating systemic and topical therapies for superficial Naganishia infection.

Further comprehensive epidemiological studies, particularly randomized controlled trials, are needed to better characterize the clinical spectrum and risk factors associated with *N. albidus* infections. In particular, randomized controlled trials are essential to establish evidence-based guidelines. These efforts will help refine therapeutic strategies and optimize outcomes for infections involving uncommon sites or immunocompetent hosts.

Conclusion

Perioral cutaneous infection caused by *N. albida* is an exceptionally rare condition that poses significant diagnostic challenges due to its atypical clinical presentation. This case highlights the importance of maintaining a high index of suspicion for uncommon fungal pathogens in refractory or unusual skin lesions. The use of advanced diagnostic modalities, including molecular and proteomic tools, can facilitate accurate identification. Timely diagnosis and appropriate antifungal treatment can lead to excellent clinical outcomes, even in rare and emerging fungal infections.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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