

The Likelihood of Resistant *Tinea Capitis* Caused by *Hortaea Werneckii*: A Case Report

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Abstract: This case study illustrates a 24-year-old Chinese man who presented with tinea capitis associated with a fungal infection. He was administered a therapeutic regimen consisting of terbinafine, ketoconazole cream, and miconazole shampoo for 2 months. However, the symptoms recurred 3 months after the treatment ended. Fungal culture and sequencing confirmed the infection of *Hortaea werneckii*. Drug sensitivity testing showed that the infecting strain of the patient remained sensitive to the five commonly used antifungal drugs in vitro. While most cases infected by *Hortaea werneckii* present with *Tinea nigra*, the possibility of *Hortaea werneckii* infection should be considered in patients with tinea capitis living in coastal cities.

Keywords: fungal infection, immunofluorescent staining, sequencing, treatment

Introduction

Tinea capitis, a common fungal infection affecting the scalp and hair shafts, is a significant dermatological condition, particularly in children. It can be broadly categorized into three clinical varieties: microsporida, trichophytica and favus (caused by *Trichophyton schoenleinii*). In clinical practice, we have encountered a case of tinea capitis caused by a fungal infection of the scalp due to infection with *Hortaea werneckii* (*H. werneckii*).

Tinea nigra is a rare, superficial fungal infection, mainly caused by *H. werneckii*, previously known as *Phaeoannellomyces* or *Exophiala werneckii*.¹ *H. werneckii* belongs to the Ascomycota, Pezizomycotina, Dothideomycetes, Capnodiales, and Teratosphaeriaceae. It is the only species classified in the genus *Hortaea*. This pathogen infiltrates the stratum corneum under microtrauma, the most common manifestation is hyperpigmented plaques on the palms, which appear similarly to melanocytic nevi or melanoma.² The fungus is halophilic and has a worldwide distribution, thriving in high-temperature, low-oxygen, and humid environments, mainly affecting individuals in tropical or subtropical climates. The geographical and climatic environment of Hainan Island is suitable for its growth.²

We report a young male with tinea capitis caused by *H. werneckii*, identified by fungal culture and Internal Transcribed Spacer (ITS) sequencing. The patient was instructed to receive standard antifungal treatment for two months. After a two-month follow-up, his symptoms resolved; after a five-month follow-up, his lesions recurred.

Case Presentation

A 24-year-old man from Haikou, Hainan, a coastal city in southern China, had skin lesions on his scalp after scratching a papule. On physical examination, there was a thumb-sized, ill-defined alopecic area on the top of the head, with raised pustules, two distinct sinus tracts, and mild pain upon pressure. The hair was easily broken upon touch, and there were minor systemic symptoms (Figure 1A). The patient exhibited smooth respiration, with slight congestion observed in the pharynx. Bilateral lung auscultation revealed coarse breath sounds without any adventitious sounds, such as dry or wet rales. No other systemic symptoms were present. The patient had never experienced injuries of this nature before, and there was no history of contact with dogs, cats, or rabbits. Neither family members nor close contacts had similar symptoms. Specimens of broken hair and pus were collected for immunofluorescent staining and microscopic

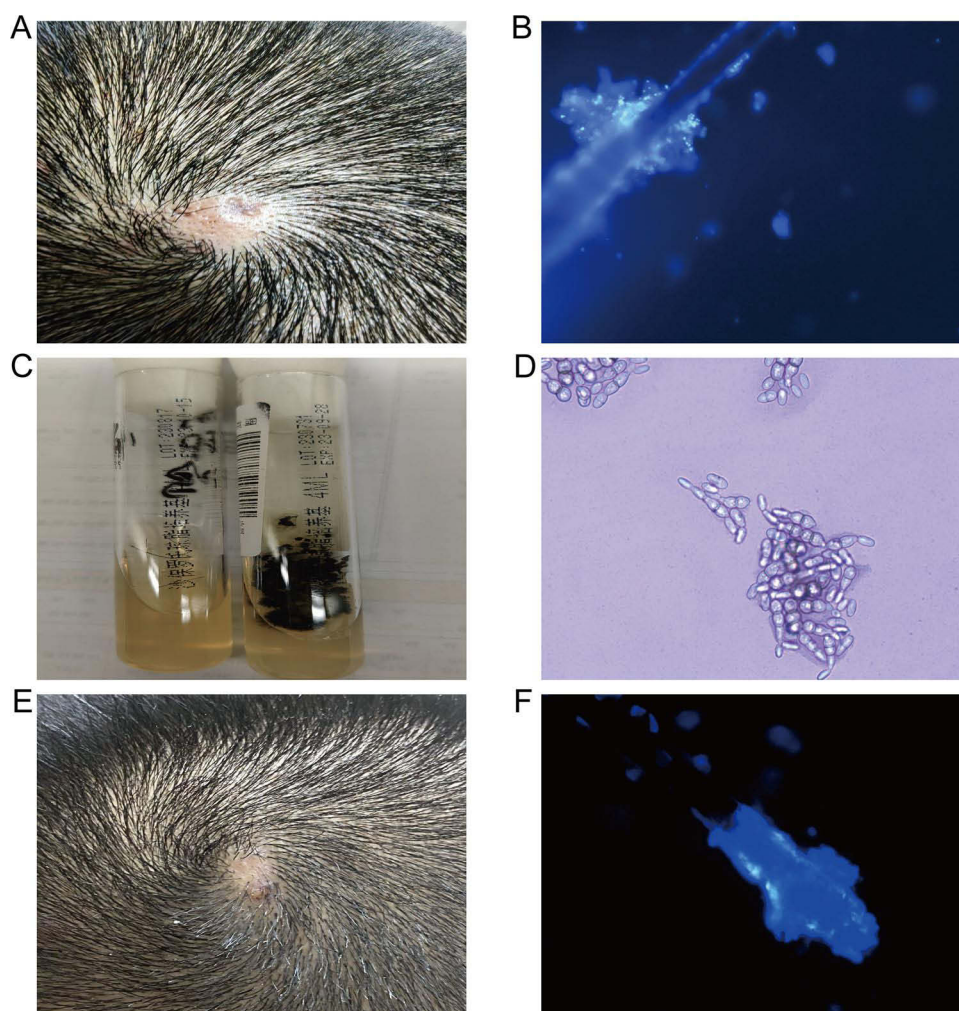


Figure 1 Clinical and mycological symptoms. **(A)** Head before treatment. **(B)** Under microscopic examination with fluorescence, external spores of the broken hair could be seen, without obvious hyphae. **(C)** Sabouraud dextrose agar culture showed smooth, black colonies. On the left side is the hair specimen, and on the right side is the pus specimen. **(D)** Potato dextrose agar culture showed clustered, brown, elliptical conidia with 1–2 cells. **(E)** Head after treatment. The hair loss area had reduced in size. New hair had grown and was not easily pulled out. The abscess had dried up and flattened, and there was no pus being discharged when squeezed. **(F)** Immunofluorescence staining was performed on the scalp scales obtained from the lesion. No spores or hyphae were observed under the microscope.

examination, which showed damaged hair structure but no internal spores or hyphae. Spores were seen in clumps outside the hair, but no obvious hyphae were present (Figure 1B). In addition, broken hair and pus that squeezed from the purulent mouth were inoculated into two tubes of Sabouraud dextrose agar media (SDA), and cultured at 28°C for 7 days. Small colonies were observed at the inoculation site of pus, initially transparent and pale greenish-yellow, gradually turning smooth and black over time. After 14 days of culture, aerial hyphae were seen growing around the colony. No fungal growth was detected in the broken hair culture after 14 days (Figure 1C). Using cultures of Potato dextrose agar media (PDA), conidia were seen in clumps, brown, elliptical, with 1–2 cells in the sporangia under a microscope after 7 days of culture at 28°C (Figure 1D).

The patient was treated with oral terbinafine 0.25 g/d, topical ketoconazole cream twice daily, and miconazole shampoo twice weekly for 2 months, with complete clinical resolution upon discontinuation. However, the symptoms recurred 3 months later. The minimum inhibitory concentrations (MICs) of itraconazole, voriconazole, terbinafine, ketoconazole, and fluconazole were detected by microdilution method according to the CLSI M38-A2 standard. The results showed MICs of 0.1254 mg/L for itraconazole, 0.03134 mg/L for voriconazole, 0.03134 mg/L for terbinafine, 0.03134 mg/L for ketoconazole, and 2 mg/L for fluconazole. The treatment plan was adjusted to topical ketoconazole cream twice daily, miconazole shampoo twice weekly, and halometasone cream once daily for 2 weeks. After this, the

clinical and mycological symptoms resolved completely (Figure 1E and F). Additionally, scalp scales were collected from the lesion site and analyzed by ITS1 and ITS4 sequence analysis after 7 days of culture on PDA at 28°C. The samples were amplified by PCR using fungal universal primers ITS1 and ITS4, and the resulting products were sequenced. The two complementary sequences were spliced using DNAMAN, and then made a blast in NCBI database. Reference sequences with high similarity to known sequences were downloaded from BLAST results, and similarity analysis was performed with rDNA-ITS sequences of existing strains in GenBank database to assist strain identification (Supplementary Material). The sequence was deposited in GenBank database and the accession number is PQ455599. Based on morphological characteristics, molecular biology methods, and ITS sequence analysis, the fungus was identified as *H. werneckii*.

Discussion

H. werneckii is the classic pathogen of *Tinea nigra*, with excellent light resistance. It is the only fungus known to grow in a wide range of salinities.³ Cases of *Tinea nigra* caused by *H. werneckii* have been reported both domestically and internationally, including cases of children with palm involvement in Hainan Island.⁴ In recent years, there have also been reports of infections caused by *H. werneckii* from other sites, such as nails, chest, soles of feet, and fingers,^{5–7} as well as systemic infections such as peritonitis, bloodstream infections, and involvement of the spleen.^{8,9} However, there have been no reports of scalp involvement caused by *H. werneckii*. The patient in this case is a resident of Hainan Island, China, who developed scalp involvement with *H. werneckii* for unknown reasons, which may be related to the coastal living environment surrounding Hainan Island. *H. werneckii* has been proven to be the predominant fungal species in environments with a salinity of over 20% sodium chloride, and it is widely present in saltwater, beach soil, salt microbial mats, submerged wood, fish, coral, and salt marsh plants.^{10,11}

In previous case reports, most patients with *Tinea nigra* had hyperhidrosis or a history of playing in the sand at the seaside.¹² Our case originated from the subtropical coastal zones of Hainan, where the patient was in contact with high salinity. The patient had a history of scratching the scalp before the onset of the disease. We speculate that he might have contacted some fungi present in the coastal environment, such as *H. werneckii*, which led to the residual fungi on his nails. When he scratched the papule on his scalp, the skin lesions were infected by *H. werneckii* from his hands. Alternatively, the papule may have been scratched, causing skin damage, and the patient may have been infected by coming into contact with *H. werneckii* while playing at the seaside. The detection of the fungus in the same location as the papule also supports these speculations.

In this case, the location of the patient's lesions on the scalp makes the problem more complex. *Tinea nigra* typically occurs on the palm and sole surfaces, and considering this uncommon presentation, a biopsy may be needed to confirm the diagnosis. However, scalp biopsies are generally not recommended for the diagnosis of *tinea capitis* because the incision is difficult to heal. Direct microscopic examination of fungal elements after 10% KOH solution smear and fungal culture are the most direct and simple laboratory diagnostic methods for *Tinea nigra*. Fluorescent staining microscopy is a newly emerging microscopic method in recent years, which has a higher positive detection rate than the KOH method. In recent years, molecular biology techniques have been widely used to identify the pathogenic fungi of *Tinea nigra* due to their convenience and high reliability.¹³ Here, we used non-invasive detection methods such as fluorescent microscopy, fungal culture, and molecular biology sequencing to help achieve timely diagnosis.

Usually, shallow fungal infections caused by *H. werneckii* are sensitive to common antifungal drugs such as ketoconazole cream and terbinafine cream, with an average treatment duration of 1–3 weeks.¹⁴ However, for patients with unclear efficacy in treating *H. werneckii* infections, combination therapy guided by *in vitro* drug sensitivity testing should be considered. Previous studies have shown that itraconazole, voriconazole, terbinafine, ketoconazole, and fluconazole have low MIC values against *H. werneckii*.¹⁵ In this case, the patient's clinical symptoms completely resolved after using antifungal drugs for 2 months according to the standard treatment. Interestingly, the symptoms recurred after a 3-month discontinuation of medication. The infecting strain of the patient remained sensitive to the five commonly used antifungal drugs *in vitro*, which is consistent with previous research results. We speculate that the patient may have frequently come into contact with environments where *H. werneckii* survives during the discontinuation of medication, leading to reinfection.

The prevalence of drug-resistant strains in the population is steadily increasing.¹⁶ In this manuscript, we present a case of tinea capitis potentially caused by *H. werneckii* that exhibits drug resistance. The emergence of drug resistance is linked to several factors, including natural selection, genetic mutations, misuse of antifungal medications, suboptimal healthcare conditions, environmental influences, globalization, population movement, and immunosuppressive states. Antifungal-resistant dermatophyte infections may arise from inappropriate use of antifungal drugs and topical corticosteroids or antibacterial agents.¹⁷ Environmental factors, such as temperature and humidity, can impact fungal growth patterns and their response to antifungal treatments, thereby increasing the risk of infection.¹⁸ For environmentally-related resistant fungi, tourists carrying drug-resistant fungi from one region to another may lead to an increase in infection rates among local populations.¹⁹ In this study, the case originated from Hainan Island, a popular tourist destination in the tropics. The island's climate is characterized by high temperatures and humidity, coupled with significant population mobility and prolonged use of ketoconazole and miconazole, which may promote the development of drug resistance in *H. werneckii*.

In this study, we employed techniques such as fluorescent staining microscopy and molecular biological sequencing to accurately identify *Hortaea werneckii*. However, due to the patient's financial constraints, sequencing was not conducted during the initial visit. Instead, the fungal species was identified based on colony morphology in conjunction with clinical experience. Following the initial treatment, we were unable to obtain samples for mycological analysis as the patient did not return to the hospital for follow-up.

Conclusion

In this study, we report for the first time that a case of tinea capitis caused by *Hortaea werneckii*. This finding suggests that the etiology of tinea capitis may be more complex, involving not only common fungal infections but also the influence of *Hortaea werneckii*.

Antifungal medications have proven to be effective in treating such infections, providing clinicians with a viable therapeutic option. For tinea capitis patients residing in coastal cities, clinicians should be vigilant to identify and diagnose *Hortaea werneckii* infections to ensure timely and appropriate treatment.

Abbreviations

H. werneckii, *Hortaea werneckii*; SDA, Sabouraud dextrose agar media; PDA, Potato dextrose agar media; MICs, minimum inhibitory concentrations; ITS, Internal Transcribed Spacer.

Ethics

Written informed consent for publication of the patient's clinical details and/or clinical images was obtained from the patient. The procedures followed were in accordance with the ethical standards of the Ethics committee of the the Fifth People's Hospital of Hainan Province and with the Helsinki Declaration of 1975, as revised in 2013. We have obtained an approval from the Ethics committee of the Fifth People's Hospital of Hainan Province to study the case and publish the case details (IRB no. 2024-007).

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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.

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Disclosure

The authors have no conflict of interest to declare.

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