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A case report of childhood onychomycosis caused by the rare yeast *Kodamaea ohmeri*

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ABSTRACT

Onychomycosis is an uncommon disease in pediatric patients with dermatophytes and *Candida* spp. being the main causative agents. *Kodamaea ohmeri* has recently emerged as a human pathogen, including an onychomycosis causative agent. Here, we report the first case of childhood onychomycosis caused by *K. ohmeri* in Vietnam, presenting clinically as a white superficial onychomycosis. Fungal identification was confirmed by sequencing of the ITS1-2 region. Antifungal susceptibility testing revealed low minimum inhibitory concentrations for all tested agents, except fluconazole and caspofungin. The patient was treated with 2 % ketoconazole cream one month, resulting in complete resolution of the nail damage with no relapse observed after six months.

1. Introduction

Onychomycosis is a common nail disease caused by pathogenic fungi including yeast, dermatophytes, and non-dermatophytes moulds [1]. This disease is often associated with risk factors such as diabetes, tinea pedis, poor circulation, immunosuppression, psoriasis, occlusive synthetic footwear, and obesity [1]. The prevalence is also high in the elderly [1]. Onychomycosis is rarely reported in children, with a rate of 0.14 % compared to 6.4 % in adults [2]. This may be because children are less exposed to fungal pathogens, resulting in fewer cases of onychomycosis. They also tend to have less nail trauma, thinner nail plates, faster nail plate ingrowth, better peripheral blood supply and a lower rate of tinea pedis [2,3]. However, several studies have shown that the prevalence of onychomycosis is increasing in children [2,3]. This condition is more common in immunocompromised children or those with Down syndrome than in other children, with the most common clinical type being distal and lateral subungual onychomycosis.

Among the pathogens causing onychomycosis, yeasts are increasingly considered to be the causative agents of nail disease, with *Candida* being the most common pathogen [4]. In addition, other rare yeasts including *Trichosporon*, non-*neoformans Cryptococcus*, *Geotrichum*, *Rhodotorula*, and *Kodamaea* have been reported to cause onychomycosis in immunocompromised patients [5,6]. *Kodamaea ohmeri* (*K. ohmeri*), formerly known as *Pichia ohmeri*, belongs to the class Ascomycetes and the family Saccharomycetaceae. It is isolated from environmental sources, such as sand, water, sea, and fruit [7], and has recently emerged to cause fungaemia in immunocompromised patients, as well as in endocarditis, peritonitis, urinary tract infections, otomycosis, and onychomycosis [7–10], with mainly isolated from fungaemia patients [7, 11]. It has been reported to cause high mortality in invasive mycosis [9]. Fluconazole and amphotericin B are recommended for invasive *K. ohmeri* infection [12]. Onychomycosis caused by *K.ohmeri* has been rarely reported, mainly in patients with diabetes mellitus. In a 2008 study by Manzano-Gayosso and co-authors, *Trichophyton rubrum* and *K. ohmeri* were isolated from distal and lateral subungual onychomycosis in patients with type 2 diabetes mellitus, accounting for 1.4 % of cases [13]. Gonza'lez-Avila reported the isolation of *K. ohmeri* from the toenails of a 51-year-old female patient with diabetes mellitus in 216 cases of onychomycosis [14]. In addition, Ferreria EO reported that *K. ohmeri* was also isolated from onychomycosis in AIDS patients [5].

The recommended oral antifungals drugs for the treatment of onychomycosis in children are terbinafine, itraconazole, fluconazole and griseofulvin. Topical agents including ciclopirox, amorolfine, tavaborole, and efinaconazole are also used [2]. Less data have been published on the susceptibility of *K. ohmeri* to antifungal agents compared to *Candida* species, as well as the outcome of antifungal therapy in this pathogen. This case report aims to present a rare case of onychomycosis case in a child in which *K. ohmeri* was identified and successfully treated

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with topical 2 % ketoconazole cream.

2. Case presentation

A 5-year-old female patient, accompanied by her mother, presented to the Dermatology outpatient clinic at Hue University of Medicine and Pharmacy Hospital, Hue City, Vietnam. The child had suffered damage to her fingernail over the previous two weeks (day 0). One month earlier, the child had been diagnosed with streptococcal pharyngitis, characterized by sore throat, fever, erysipelas and fatigue, which was confirmed by a positive anti-streptolysin O (ASLO) test. The patient has received antibiotic therapy for treatment. The family history was unremarkable for fungal infections, chronic diseases, or immunocompromising conditions. During the medical examination, the child's general condition was assessed as normal. Dermatological examination reveals the presence of nail abnormalities on the middle finger of the left hand and on both the index and middle fingers of the right hand (Fig. 1A).

The nail scalp samples were collected and examined for fungal infection. Samples treated with 20 % potassium hydroxide revealed the presence of yeast cells with round, oval, and budding shapes (Fig. 2A). The diagnosis was made as white superficial onychomycosis. The nail samples were cultured for two days at 28 °C on Sabouraud dextrose agar (HiMedia, India) with chloramphenicol, resulting in the growth of white creamy colonies (Fig. 2B). Microscopic examination of these colonies revealed yeast cells (Fig. 2C). Subsequent subculture on Brilliance Candida agar (Oxoide, UK) showed dark green colonies, indicating the presence of a non-*Candida albicans* species (Fig. 2D). Further identification using the API 20C system (BioMerieux, France) confirmed the fungal pathogen as *Kodamaea ohmeri* with 99.9 % accuracy.

The internal transcribed spacer (ITS) sequence identification of this isolate was performed according to the protocol published [15]. The sequence was compared with available NCBI references, which show 100 % nucleotide identity with *K. ohmeri* (accession number FJ215865). The sequence in this study was subsequently deposited in GenBank under accession number PQ596196. Phylogenetic trees were reconstructed from the ITS1-ITS4 region of various yeasts using MEGA version 11 (www.megasoftware.net) with the maximum likelihood method and the general time reversible plus gamma distribution model with 1000 boostrap replicates. The resulting phylogenetic tree was annotated and visualised using the online tool iTOL v6 (https://itol.embl.de/) (Fig. 3).

The minimum Inhibitory Concentrations (MICs) of the antifungal agents for this isolate was determined using broth microdilution method

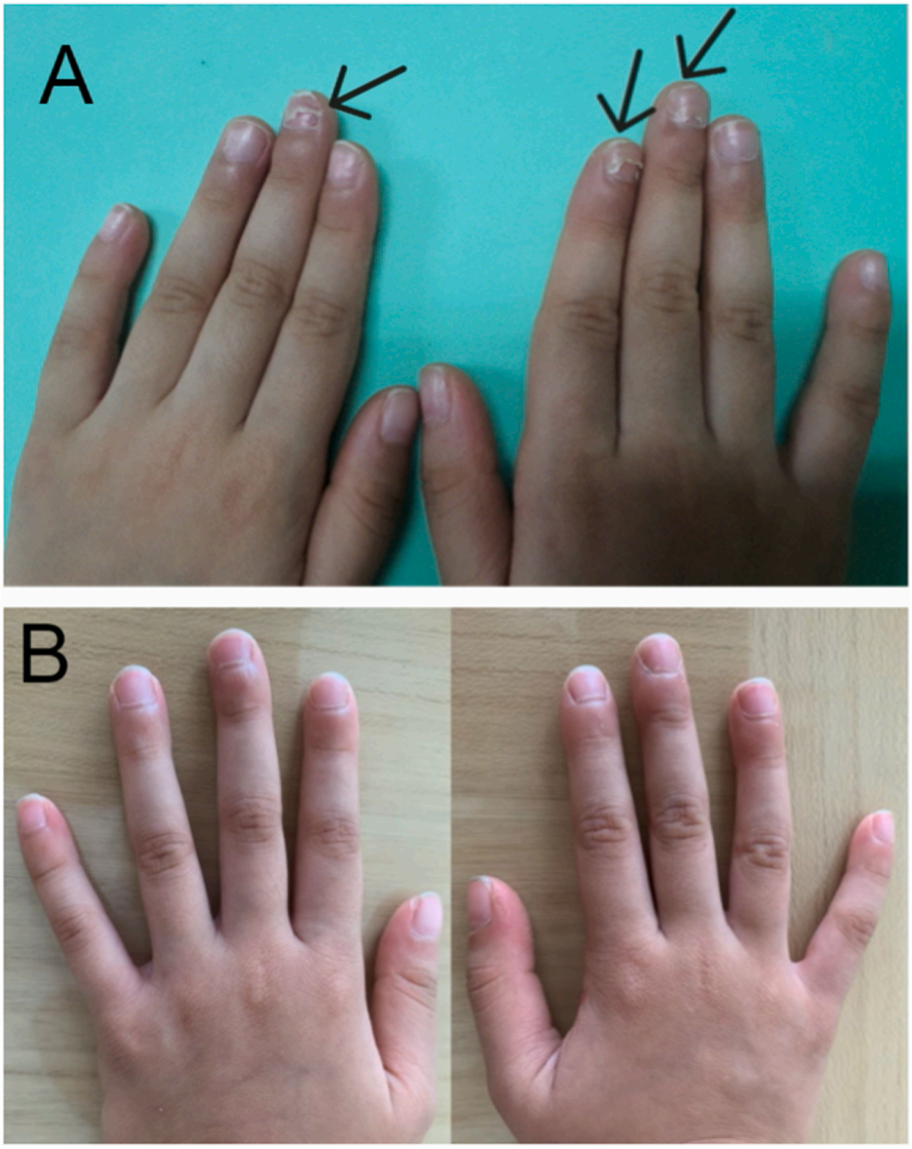

Fig. 1. Clinical images of the patient's fingernails. (A) At the beginning of treatment with nail damage (see arrows), (B) Six months after treatment, demonstrating complete resolution.

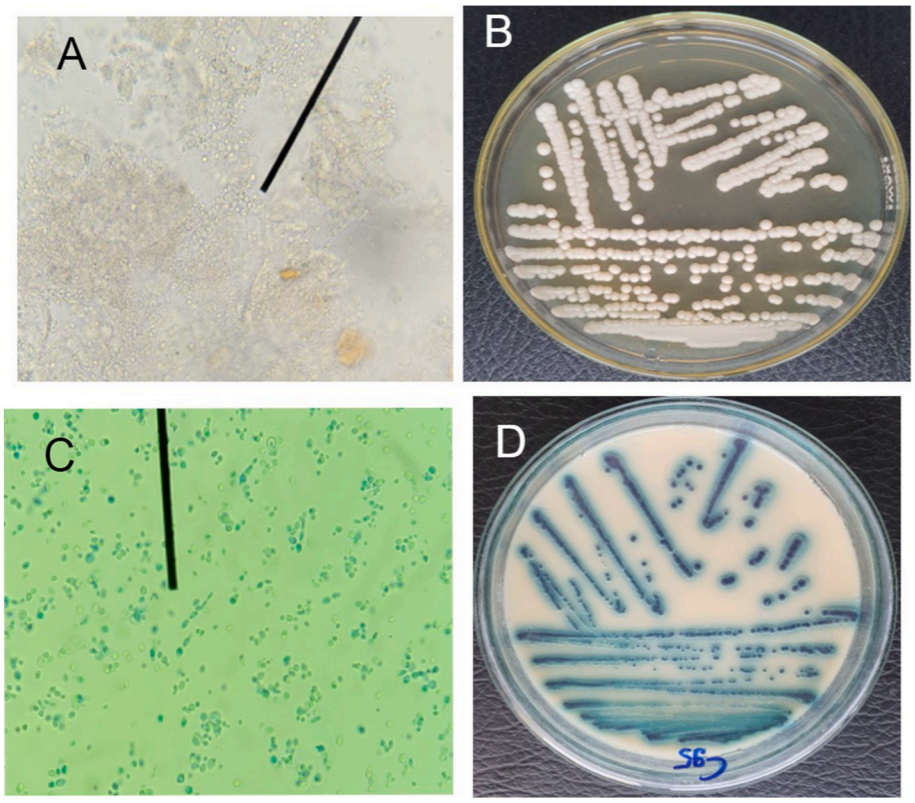

Fig. 2. Microscopic and macroscopic examination of the fungus. (A) Microscopic characteristics of a nail scraping treated with 20 % KOH, (B) Yeast colonies grown on Sabouraud dextrose agar with chloramphenicol after 2 days of culture, (C) Microscopic examination of the yeast culture grown on Sabouraud dextrose agar with chloramphenicol, (D) Yeast colonies on Brilliance Candida agar medium.

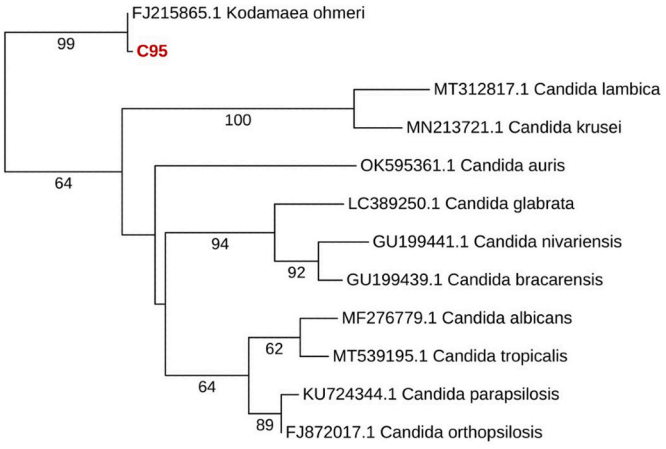

Fig. 3. Phylogenetic tree of yeasts based on the ITS1-ITS4 region (with Interactive Tree of Life: iTOL v6) includes the *Kodamaea ohmeri* sequences obtained in this study (isolate code C95).

and the Thermo Scientific™ Sensititre™ YeastOne™ YO10 AST (SYO) plate according to the manufacturer's instructions. The standard reference strains *C. albicans* ATCC 90028 and *C. glabrata* ATCC 66032 were included in the assay for calibration. MICs were determined after 24 hours of incubation. As there are no clinical breakpoints and epidemiological cut-off values available for *K. ohmeri* as defined by CLSI or EUCAST guidelines, so the MICs values could not be interpreted according to these standards. The MIC values of antifungal agents for this isolate were listed in Table 1 together with MIC values from other studies.

The results of complete blood count and liver and renal function tests were within normal limits for this patient. The child was treated topically with a 2 % ketoconazole cream three times a day for four weeks. This treatment effectively eliminated the nail damage and no relapse was observed during a six months follow-up period (day 194) (Fig. 1B).

3. Discussion

Onychomycosis is a relatively rare disease in children, with dermatophytes being the predominant pathogens, especially *Trichophyton rubrum*, and *Candida* species is less commonly reported than dermatophyte infections [3]. In addition, rare cases of onychomycosis have been associated with a variety of less common fungal species [6]. To our knowledge, this is a first documented case of onychomycosis caused by *K. ohmeri* in Vietnam.

Predisposing factors for tinea unguium in children include tinea pedis, a family history of onychomycosis or tinea pedis, and immunosuppression. In contrast, *Candida* onychomycosis is primarily associated with various forms of immunodeficiency [16]. In this case, the child's nail damage associated with post-streptococcal infection may facilitate the fungal infection. The literature suggests that group A streptococcal infections can disrupt both the innate and adaptive immune response [17], potentially predisposing individuals to opportunistic infections.

In terms of phenotypic identification, the isolate in this case showed yeast-like characteristic, with the color of colony on chromogenic agar resembling that of *C. tropicalis* (Fig. 2D). *K. ohmeri* was often misidentified as *C. albicans* or *C. tropicalis* [8,11]. In addition, various commercially available sugar assimilation tests may misidentify this pathogen as other *Candida* species, such as *C. albicans*, *C. glabrata*, *C. tropicalis*, *C. guilliermondii*, *C. lusitaniae*, *C. famata*, *C. pelliculosa* and *C. rugosa*, or even *Cryptococcus neoformans* [8]. The accurate identification of these fungal species requires the use of DNA sequencing techniques. Recently, matrix-assisted laser desorption/ionization-time-of-flight (MALDI-TOF)

Table 1
Minimum inhibitory concentration of antifungals against *Kodamaea ohmeri* isolated from the present study and the others studies.

Clinical types (No. isolates)	MIC range/Geometric Mean MIC (mg/mL)									References
	AND	MF	CAS	ITR	VOR	POS	FLU	FC	AMB	
Fungaemia (n = 30)			0.12-1/ 0.32	0.06-4/ 0.24	0.03–8/0.09	0.06-4/0.11	0.5–64/ 0.89		0.25-1/ 0.89	[11]
Fungaemia (n = 1)		0.03	0.12	0.25	0.06		8	0.5	1	[24]
Fungaemia (n = 1)	1	1	>16	0.125	0.03	0.06	4	<0.03	0.5	[18]
Mycosis (n = 62)	0.03-2/ 0.192	0.12-1/ 0.473	0.25-2/ 0.691	0.06-1/ 0.399	<0.015–2/ 0.075	<0.015–0.5/ 0.136	1- >256/ 5.115	0.03-1/ 0.087	0.5-1/ 0.598	[8]
Otomycosis (n = 2)							32			[10]
Onychomycosis (n = 1)				<0.125-0.25			<2-4	<0.5	<0.5	[25]
Onychomycosis (n = 1)				<2-4			<16-32	<0.5	<0.5	[14]
Onychomycosis (n = 3)				0.062-0,125			8		0.5–1	[5]
Onychomycosis (n = 1)	1	1	8	0.12	0.12	0.12	16	<0.06	0.5	This study

(AND: anidulanfungin, MF: micafungin, CAS: caspofungin, ITC: itraconazole, VRC: voriconazole, POS: posaconazole, FLU fluconazole, FC: flucytosine, AMB: amphotericin B, MIC: minimal inhibitory concentration).

mass spectrometry after protein extraction has proven to be a fast and accurate method for the identification of yeast pathogens, with a hit rate of 96.8 % for *K. ohmeri* [8].

The optimal treatment of onychomycosis caused by *K. ohmeri* is still unclear. The available literature suggests that systemic antifungal therapy is recommended for invasive infection caused by this fungus, with amphotericin B and echinocandins recommended as options [12]. Susceptibility testing is critical in making treatment decision. In this study, the isolate had a low MIC value for all antifungal agents tested except fluconazole (Table 1). This pattern is consistent with results from previous studies [5,8,10,11,14], except for the high MIC value of caspofungin noted in this study. High caspofungin MIC (>16 μg/ml) was reorted from study of Distasi MA [18]. *K. ohmeri* is a rare pathogen associated with human mycoses and its environment sources, such as sand, water, seawater, and fruits. Therefore, the susceptibility of environmental isolates to antifungal agents warrants attention. In a study from China, a high resistance rate of 12.5 % to fluconazole was found in *K. ohmeri* isolates from the environment [19].

Although oral ketoconazole is no longer recommended for onychomycosis due to its significant side effects, topical ketoconazole remains a safe and effective treatment for superficial mycosis such as dermatophytosis and cutaneous candidiasis [20]. In this case, the patient was treated exclusively with 2 % ketoconazole cream, which effectively eradicated the infection. Previous reports have demonstrated the efficacy of topical 2 % ketoconazole cream in the treatment of onychomycosis, including a case of an 11-year-old girl with *Trichophyton rubrum* and *Trichophyton schoenleinii* infections [21]. A low MIC of ketoconazole against *K. ohmeri* was also reported in previous studies [5,18]. In addition, topical antifungal creams generally have limited penetration through the nail plate [22]. In this case, although the patient was affected by nail damage, it is possible that preexisting paronychia was present prior to the hospital visit. This underlying condition may have favoured the subsequent nail involvement and contributed to patient's positive response to topical treatment. Antifungal therapy of nail diseases usually requires systemic treatment or in combination with topical agents. The efficacy of topical therapy in this case may be due to the thinner nail plate observed in younger individuals, which facilitates better drug absorption [2]. In addition, superficial white onychomycosis is considered to be less invasive to the nail than other forms of onychomycosis. Moreover, prolonged systemic antifungal treatment may be associated with the risk of systemic toxicity, whereas children often show a better response to topical monotherapy compared to adults. Therefore, topical antifungal therapy represents a viable treatment option for paediatric patients and further studies are warranted to identify the most appropriate candidates for this therapy in children [20,23].

In conclusion, this study represents the first documented case of childhood onychomycosis caused by the rare pathogen *K. ohmeri* in Vietnam, manifesting clinically as white superficial onychomycosis. The condition was successfully treated with 2 % ketoconazole cream for one month, achieving complete resolution of the nail infection at six months without recurrence. Further studies should be conducted to investigate the clinical characteristics and antifungal susceptibility profile of this fungal species, thereby improving diagnostic and therapeutic strategies.

CRediT authorship contribution statement

Thi Minh Chau Ngo: Writing – review & editing, Writing – original draft, Methodology, Investigation. **Dong Duong Ton That:** Methodology, Investigation. **Phuong Anh Ton Nu:** Writing – original draft, Methodology. **Le Chi Cao:** Writing – review & editing, Writing – original draft. **My Nguyen Thi Tra:** Investigation. **Thi Quynh Trang Tran:** Investigation.

Ethical form

This case report is part of a study approved by the Ethics Committee of Hue University of Medicine and Pharmacy (H2024/547). Informed consent for publication was obtained from the patient's guardian.

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Conflict of interest

The authors have no conflict of interest.

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