


Onychomycosis Caused by *Kodamaea ohmeri* in a Patient with Human Immunodeficiency Virus (HIV) – A Case Report

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ABSTRACT

Introduction: Onychomycosis is a fungal nail infection usually caused by dermatophytes. *Kodamaea ohmeri* is a rare fungus that has been reported as a pathogen capable of causing onychomycosis and systemic infections. This yeast-like fungus is often misidentified as *Candida sp*. A complete identification is required for accurate results. **Case**: A 40-year-old male with HIV presented with yellow and brittle fingernails for 2 months. KOH examination of nail scrapings was performed, followed by fungal culture. The isolate was identified in parallel using the Integral System Yeast Plus, Vitek-2, MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry), and sequencing, and the result was *Kodamaea ohmeri*. The patient received oral itraconazole and topical ketoconazole. **Discussion**: Onychomycosis in HIV patients is caused by low immunity, high viral load, and low CD4 values. In this case, *K. ohmeri* was successfully identified using Vitek-2, MALDI-TOF, and ITS (Internal Transcribed Spacer) area sequencing, while the Integral System Yeast Plus misidentified the isolate as *Candida tropicalis*. There was clinical improvement in the nail after treatment. **Conclusion**: Onychomycosis in HIV patients can be caused by *Kodamaea ohmeri*. Identification can be done with Vitek-2 and MALDI-TOF.

Keywords: Case report, fungal nail infection, HIV, *Kodamaea ohmeri*, onychomycosis.

ABSTRAK

Pendahuluan: Onikomikosis adalah infeksi jamur pada kuku yang umumnya disebabkan oleh dermatofita. *Kodamaea ohmeri* merupakan jamur langka yang saat ini dilaporkan dapat menyebabkan onikomikosis dan infeksi sistemik. Jamur mirip ragi ini sering salah diidentifikasi sebagai *Candida sp.* Identifikasi yang lengkap diperlukan untuk mendapatkan hasil yang akurat. **Kasus:** Laki-laki berusia 40 tahun dengan HIV berobat dengan keluhan kuku jari kedua tangan berwarna kuning dan rapuh sejak 2 bulan. Dilakukan pemeriksaan KOH dari kerokan kuku dilanjutkan dengan biakan jamur. Isolat diidentifikasi secara paralel menggunakan Integral System Yeast Plus, Vitek-2, MALDI-TOF (Matrix-Assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry), serta sekuensing, dan diperoleh hasil *Kodamaea ohmeri*. Pasien mendapat antijamur *itraconazole* oral dan *ketoconazole* topikal. **Pembahasan:** Onikomikosis pada pasien HIV disebabkan oleh imunitas rendah, *viral load* tinggi, serta nilai CD4 yang rendah. Pada kasus ini, hasil sediaan KOH dan biakan jamur menunjukkan morfologi menyerupai *Candida sp*. Pada kasus ini, *K. ohmeri* berhasil diidentifikasi menggunakan Vitek-2, MALDI-TOF, dan sekuensing area ITS (Internal Transcribed Spacer), sementara Integral System Yeast Plus dalah mengidentifikasi isolat tersebut sebagai *Candida tropicalis*. Secara klinis, tampak perbaikan pada kuku setelah pengobatan. **Simpulan:** *Kodamaea ohmeri* dapat menjadi patogen onikomikosis pada pasien HIV. Identifikasi *K.ohmeri* dapat dikerjakan dengan *Vitek-2* dan MALDI-TOF. **Siti Nadliroh, Mardiastuti, Fithriyah, Cliff Clarence Haliman, Sandra Widaty, Rizka Mutiara, Aditya Indra Pratama, Rizkia Chairani Asri, Robiatul Adawiyah, Ardiana Kusumaningrum. Onikomikosis yang disebabkan oleh *Kodamaea ohmeri* pada Pasien dengan *Human Immunodeficiency Virus* (HIV) – Laporan Kasus**

Kata Kunci: Laporan kasus, infeksi jamur pada kuku, HIV, *Kodamaea ohmeri*, onikomikosis.

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INTRODUCTION

Onychomycosis is a fungal infection of the nails. This infection can be caused by various types of fungi, including dermatophytes, non-dermatophyte fungi, and yeasts. The worldwide prevalence of onychomycosis is estimated at 10%, with dermatophytes being the most common causative organisms.[1] Risk factors for onychomycosis include age, obesity, tinea pedis, peripheral vascular disease (PVD), venous insufficiency, diabetes mellitus, human immunodeficiency virus (HIV), and use of public swimming pools.[2]

Kodamaea ohmeri, a yeast-like fungus, is currently recognized as a pathogen, particularly in immunocompromised individuals.[3,4] This fungus was previously known as *Pichia ohmeri*. *K. ohmeri* can cause human infections, including fungemia, other invasive diseases, and onychomycosis, particularly in patients with diabetes and immunocompromised individuals.[3] To date, there is limited data on onychomycosis caused by *K. ohmeri*.

Kodamaea ohmeri can be isolated from the environment and is generally used in the food fermentation industry.[3] *Kodamaea ohmeri* is often misidentified as *Candida sp.*[3,5] Therefore, it requires precision and caution when identifying it. *K. ohmeri* can be identified by assessing phenotypic characteristics and using sophisticated tools such as Vitek-2 compact, MALDI-TOF, or by sequencing the internal transcribed spacer (ITS) area.[3,6–7] Onychomycosis caused by *K. ohmeri* can be treated with antifungals such as amphotericin B, fluconazole, intraconazole, or with echinocandin antifungals.[8] This case report aims to highlight that *K. ohmeri* can cause infections in immunocompromised patients and to describe more accurate methods for identifying the fungus, enabling patients to receive better treatment.

CASE

A 40-year-old man presented with yellowing of the fingernails for 2 months. Initially, the nails felt dry and appeared white, then gradually turned yellow. Subsequently, the nails became brittle and easily detached. The condition first appeared on the ring finger of the right hand, followed by the middle fingernail of the left hand. The patient frequently used the nails of his ring and middle fingers to scratch when his body felt itchy. There were no complaints of itching or pain in or around the nails, and no pus was ever discharged. The patient had a history of oral thrush the previous year, which resolved with nystatin drops. The patient has a history of two courses of treatment for pulmonary tuberculosis; the most recent was one year ago, during which the patient underwent treatment for 9 months and was declared cured. The patient has been living with HIV for 2 years and regularly takes antiretroviral (ARV) medication. Initially, the patient was on the TLE regimen (a combination of tenofovir, lamivudine, and efavirenz). However, after one year of treatment, the patient's viral load remained high (3.05×10^5 copies/mL) and CD4 count remained low (347 cells/μL); treatment was then switched to Duviral (lamivudine and zidovudine) and dolutegravir (DTG). After two months of use, the patient experienced zidovudine intolerance, followed by TLD (tenofovir + lamivudine + dolutegravir) plus cotrimoxazole 1x960mg for the past 3 months.

Physical examination revealed onycholysis, onychoschizia, and subungual hyperkeratosis on the fourth finger of the right hand and the third finger of the left hand (**Figure 1**). Laboratory samples were collected from both fingers. Nail scrapings were obtained from the infected fingers. Prior to sample collection, the nails and surrounding areas were cleaned with 70% alcohol. The damaged nails were then trimmed using a sterile nail clipper. The underside of the nail plate was scraped with the blunt edge of a sterile scalpel to remove the white, damaged, and degenerated portion. Nail debris and nail clippings were collected for subsequent microbiological testing.

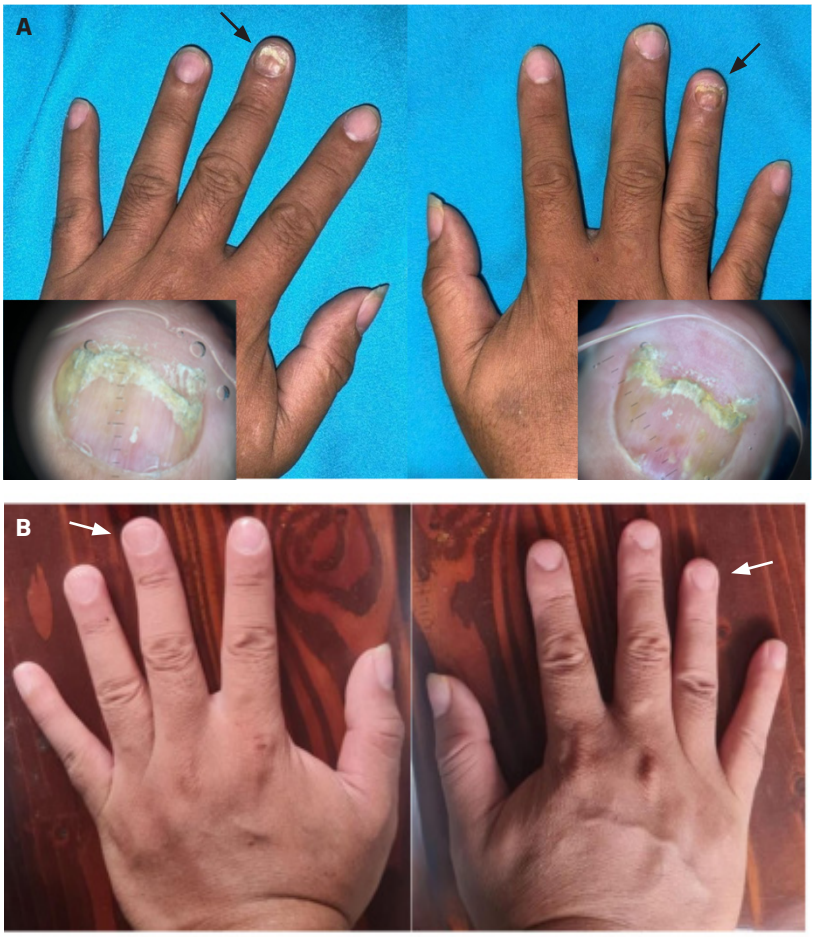

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Figure 1. Clinical overview of the patient's fingernails.

A. Photograph of the fingers of both hands at the start of treatment. Nail damage is visible (arrows) on the third digit of the left hand and the fourth digit of the right hand. B. Photograph of both hands two months after treatment. Complete resolution of both nails is visible (arrows).


Microbiological examinations were performed macroscopically and microscopically. The first specimen was examined microscopically with KOH. The steps were as follows: Place a portion of the nail and nail fragments on a slide containing a few drops of 20% KOH solution, then spread them evenly. Then, cover with a coverslip, press gently to remove air bubbles, and wait 15–30 minutes. The slide was examined under a microscope, starting at low magnification (10x objective lens), with the light adjusted to minimize glare. Once the fungal elements were visible, the magnification was increased to 40x (40x objective lens), and the morphology was observed, revealing the blastospores (**Figure 2A**).

The second examination was a fungal culture. Nail fragments and nails were planted in three places each on two Sabouraud dextrose agar (SDA) + chloramphenicol (K). The three points were marked by circling the back of the nail plate to monitor growth; this was true for the sample and not the contaminants. The two agar plates were incubated at different temperatures: 37°C and 25°C. Growth monitoring was carried out daily. On the second day, yeast growth began on both SDA + K plates. Growth began with small white colonies. Macroscopically, on SDA + K plates, round ivory-white yeast colonies appeared with uneven, opaque, rough, and dry edges (**Figures 2B and 2C**). The colonies were then stained with Gram and 10% KOH. The Gram staining step began with preparing the colonies, after which they were fixed. Then they were counterstained in a solution of crystal violet dye and left for 1 minute, then rinsed with water. Then it was poured with Lugol's iodine for 1 minute and rinsed with water. Decolorize with 95% alcohol for 10–15 seconds, then rinse with water. Then, pour safranin for 20–30 seconds, then rinse with water, and dry. After drying, observe under a microscope at 10 x 10 and 10 x 100 magnification. The results showed pseudohyphae and spores (**Figure 2D**). KOH staining revealed pseudohyphae and spores at 10 x 40 magnification (**Figure 2E**).

The examination continued with subculturing yeast colonies onto two CHROMagar *Candida* plates, each incubated at 25°C and 37°C. After 24 hours of incubation, pink colonies grew; the next day, they turned pink-purple, then blue-green (**Figures 3 and 4**).

The examination continued with fungal identification using the semi-automatic method of the Integral System Yeast Plus, the automatic method of the Vitek 2 Compact system, Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), and the molecular method of sequencing the ITS region. The Integral System Yeast Plus is a yeast identification method based on changes in the pH and color of the well resulting from yeast assimilation of sugar.[9] Vitek 2 compact is an automatic identification system through biochemical analysis using fluorescence-based colorimetric technology.[10,11] The Vitek-2 compact results showed 90% *Kodamaea ohmeri*, indicating that this identification is most likely correct. Next, a confirmation test was performed using MALDI-TOF identification. MALDI-TOF is an identification technique using mass spectrometry to analyze proteins/peptides from microbial isolates for accurate identification. Currently, MALDI-TOF can rapidly and precisely identify bacteria and fungi to the subspecies level.[12,13] The MALDI-TOF identification results of the yeast colony in the case obtained the species *Kodamae ohmeri* with a confidence value of 2.19

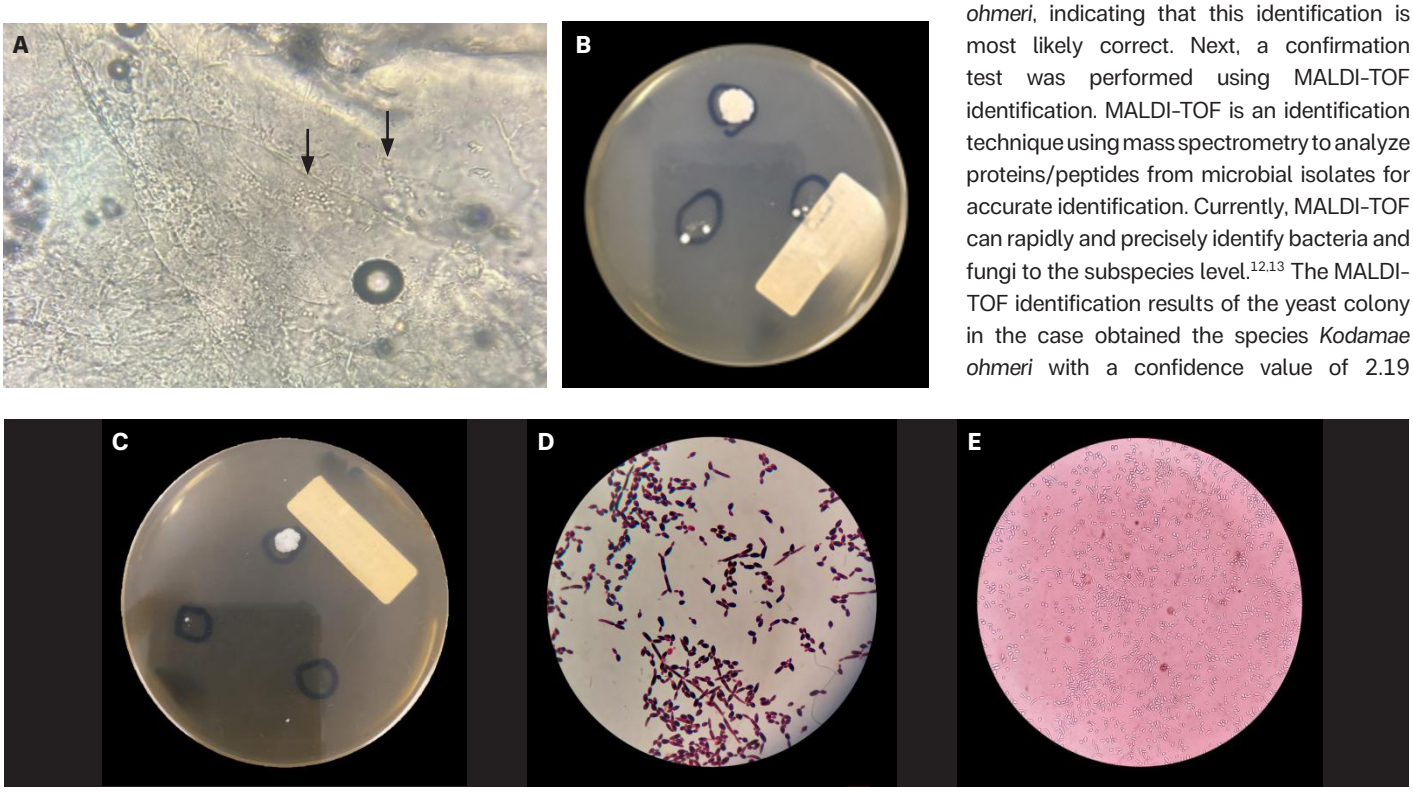

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Figure 2. Macroscopic and microscopic images of fungi on SDA + K after 5 days of incubation.

A. Microscopic characteristics of nail scrapings dipped in 20% KOH. B. Yeast colonies growing on SDA + K after 5 days of incubation at 25°C. C. Yeast colonies growing on SDA + K at 30°C. D. Gram-stained microscopic examination of yeast culture (10 x 100 magnification). E. KOH microscopic examination of yeast culture (10 x 40 magnification).


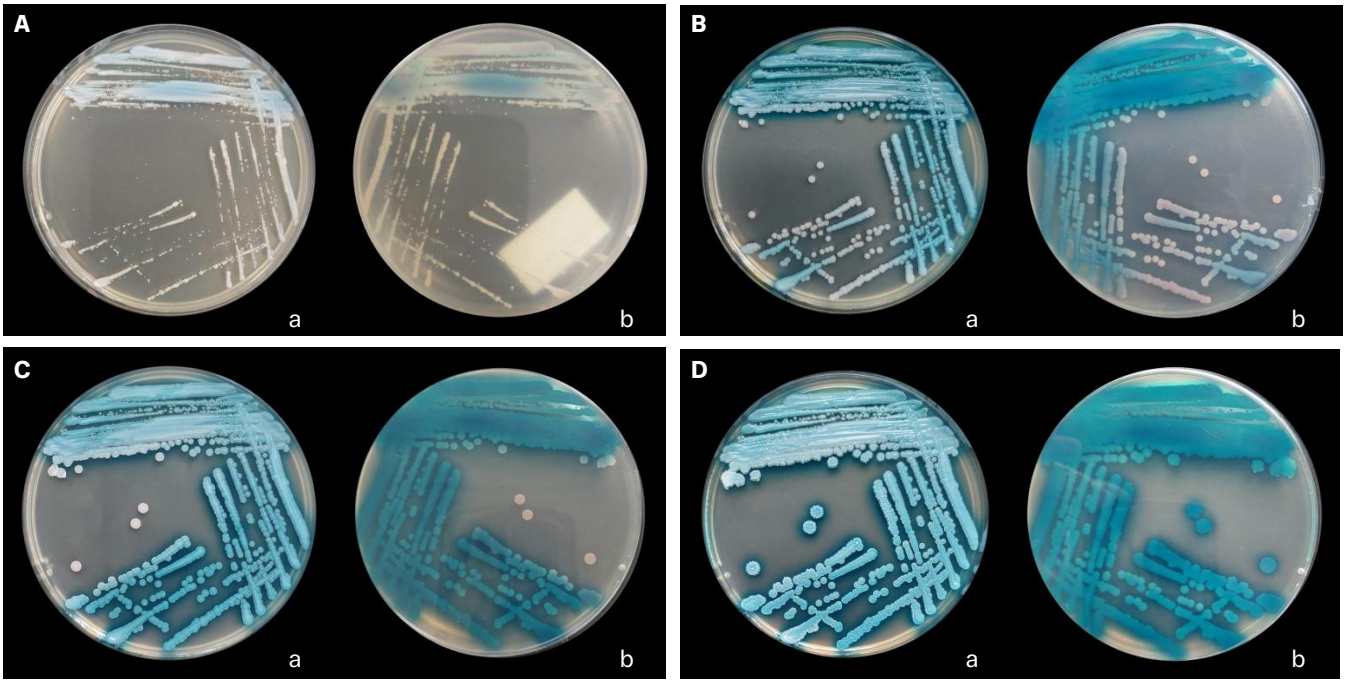

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Figure 3. CHROMagar *Candida* incubation at 25°C.
a. Top view, b. Bottom view.
A. 24-hour incubation; B. 2 x 24-hour incubation; C. 3 x 24-hour incubation; D. 6 x 24-hour incubation.

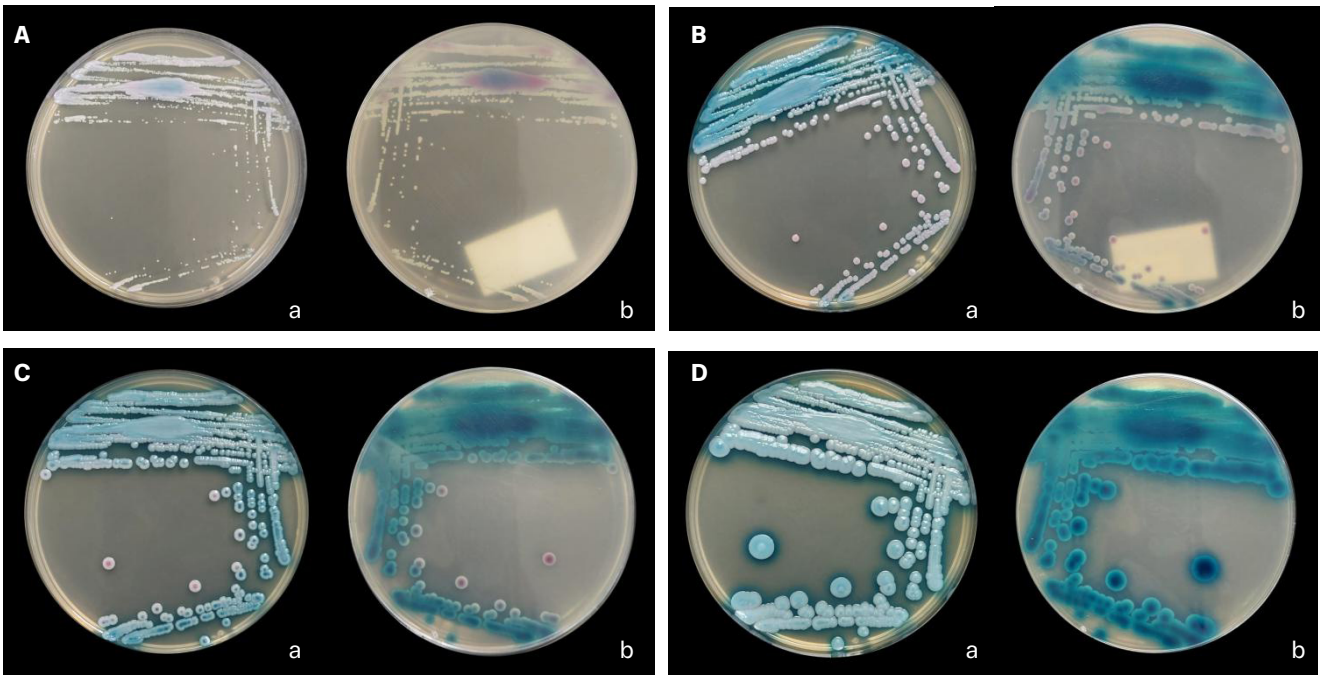

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Figure 4. CHROMagar *Candida* incubation at 37°C.
a. Top view, b. Bottom view.
A. 24-hour incubation; B. 2 x 24-hour incubation; C. 3 x 24-hour incubation; D. 6 x 24-hour incubation.


(**Figure 5A**). Values above 2 indicate highly reliable species-level identification, and the sample mass spectrum matches the reference database. Then, the identification process was continued molecularly by sequencing the ITS (Internal Transcribed Spacer) region. This method is a genomic method for fungal identification that targets the ITS region of fungal ribosomal DNA (rDNA). The ITS region has high variability between fungal species, making it ideal for distinguishing closely related fungi.[14] This process was carried out through amplification of the ITS (Internal transcribed spacer) regions 1 and 4 (UKK LMK FKUI) with i-MAX™2 DNA Polymerase (iNtRON's Maxime™ PCR) beginning with the extraction of yeast genetic material with the QIAamp DNA mini Kit. The PCR reaction proceeded with initial denaturation at 94°C for 4 minutes, followed by denaturation (94°C for 30 seconds), annealing (58°C for 30 seconds), and extension (72°C for 1 minute) for 30 cycles. The final step was extension at 72°C for 10 minutes. After amplification, the PCR product was electrophoresed on a 1% agarose gel, and an amplicon of 411 bp was obtained. The PCR product was then sent to PT. Genetika Science for sequencing analysis. The obtained nucleotide sequence was analyzed against the GenBank database, and the species *K. ohmeri* was identified with 99.76% confidence (**Figure 5B, 5C, and 5D**).

Laboratory examination revealed that the pathogenic fungus in this patient was *Kodamaea ohmeri*. The patient was treated with oral itraconazole 200 mg twice daily, in pulse doses, every week/month. In addition, 30% salicylic acid in ketoconazole cream was applied once daily at night to the infected nails. After 2 months of treatment, the patient's nails returned to normal (**Figure 1B**). The patient agreed to have this case reported by signing a consent form.

DISCUSSION

Onychomycosis is rare in adults, with a prevalence of 8%–10% in the general population and a higher prevalence with age.[15,16] The most common cause is dermatophytes, accounting for approximately 65%.16 HIV is a risk factor for onychomycosis.[15,17] The prevalence of onychomycosis in HIV patients is approximately 10%–40%.[18,19] Risk factors for onychomycosis in HIV patients include low CD4 counts, high viral load, tinea pedis, and the habit of walking barefoot.[20,21] This patient has HIV and has been undergoing treatment for 2 years with a 3-drug regimen change. These changes were made due to a persistently high viral load (3.05 × 10^5 copies/mL), intolerance to AZT, and a low CD4 count (347 cells/µL). The patient has also been receiving antibiotic therapy for the past 3 months. Long-term antibiotic use can be a risk factor for fungal infections, including those of the nails. This may be due to antibiotics disrupting the normal flora of the skin and nails, allowing opportunistic fungi to multiply and cause infection.[22] In addition, a history of previous fungal infections of the tongue may be a sign of a decreased immune system that makes these patients susceptible to other fungal infections, including onychomycosis.

Onychomycosis can occur on the fingers and toes. In this case, onychomycosis occurred on the fingernails of the right middle finger and the left ring finger. The middle finger is frequently affected, likely due to its frequent exposure to trauma, moisture, and irritants during daily activities, which creates

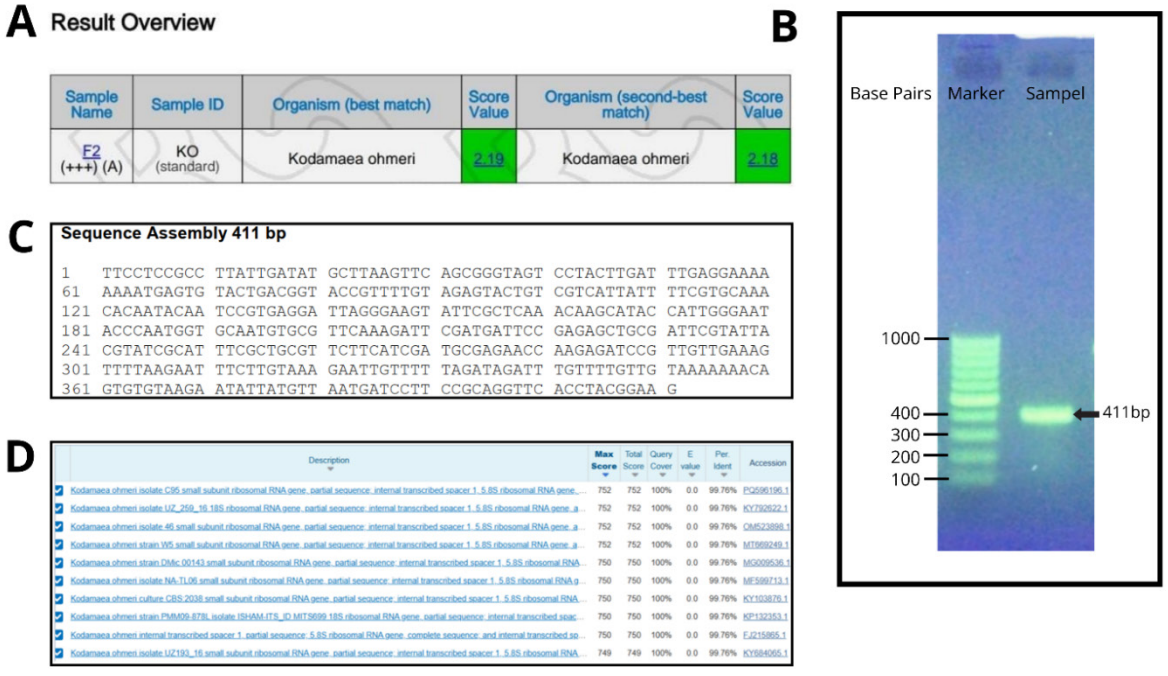

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Figure 5. MALDI TOF and ITS region sequencing results

A. MALDI-TOF results; B. ITS 1 and ITS 4 electrophoresis results; C. Nucleotide sequences from sequencing; D. BLAST results from GenBank.


conditions favorable for fungal infection.[23] In this patient, both fingers are frequently used to scratch the body when itching, possibly due to trauma during scratching. This patient's onychomycosis is classified as distal subungual onychomycosis, the most common form.[24] *Kodamaea ohmeri*, formerly known as *Pichia ohmeri* or *Yamadazyma ohmeri*, is a yeast-like fungus that has recently emerged as a human pathogen, particularly in individuals with compromised immune systems.[3] *K. ohmeri* belongs to the Saccharomycetaceae family.[3] *Kodamaea ohmeri* causes a variety of infections, with a high mortality rate of approximately 30.8%. Several articles note that *K. ohmeri* can cause invasive infections, including fungemia.[3–5,25,26]

In addition, *K. ohmeri* can cause endocarditis, peritonitis, and other infections, including urinary tract infections, pneumonia, and keratitis.[3,27] Currently, there is little literature on onychomycosis caused by *K. ohmeri*. *K. ohmeri* has been reported as a cause of onychomycosis in children and in the toenails of patients with diabetes.[28,29]

Kodamaea ohmeri is often misidentified as *Candida tropicalis, Candida albicans*, or other *Candida sp.*[3,4] *K. ohmeri* can be identified based on phenotypic characteristics, the Vitek-2 compact system, API 20 C, MALDI-TOF, and sequencing of the ITS and D1/D2 rDNA regions.[3,6,25] Phenotypic characteristics can be seen from macroscopic and microscopic morphology. Characteristics of *K. ohmeri* on agar media: forms colonies similar to *Candida*. On CHROMagar *Candida*, a characteristic color change of *K. ohmeri* from pink to blue-green was observed after 72 hours of incubation. This is in accordance with the explanation of other articles that change from pink to blue in 48 hours after incubation[4,26,30] and to blue-green after 72 hours.[31] However, other articles show a greenish color on CHROMagar after 48 hours of incubation.[32] This can lead to misidentification as *Candida sp.*, so further identification examination is needed. On Saboraud dextrose agar (SDA) + K at 37°C and 25°C, *Kodamaea ohmeri* grew after 48 hours of incubation as ivory-white colonies with uneven edges and a slightly rough appearance. This is in accordance with previous findings, *K. ohmeri* can grow in 24–48 hours on SDA and appears as ivory-white/cream colonies, with a slightly rough texture, uneven edges, and wavy[33–35] (**Figure 6A and 6B**). According to other reports, the yeast has an oval shape, pseudohyphae, and blastospores.[31,35] On blood agar, *K. ohmeri* grows as white, round, opaque colonies with irregular edges and can undergo hemolysis during prolonged incubation, in this case after 96 hours (**Figure 6C and 6D**). Previous research on blood agar media showed that *K. ohmeri* colonies grow as round, irregular-edged, rough, dry, and opaque ivory colonies.[33] After four days of incubation, hemolysis occurred in blood agar; this is in accordance with what happened in the Honduran clinical isolate, *K. ohmeri* showed strong hemolysis in blood agar, with an enzymatic activity coefficient (Pz) ≤ 0.69.[32]

Identification of the fungus *Kodamaea ohmeri* was performed semi-automatically using the Integral System Yeast Plus, resulting in *Candida tropicalis*. Meanwhile, identification using the automated Vitek-2 compact system yielded 90% species-specific accuracy for *K. ohmeri*. In one study, the Vitek-2 compact system correctly identified *K. ohmeri* in 82.3% of cases, with 17.7% remaining unidentified/invalid.[6] *Kodamaea ohmeri* can also be identified using API 20C AUX 7.26. The API 20C system is a yeast identification method that observes metabolic changes resulting from fermentation or fungal assimilation in each well of a strip containing a specific substrate. In one study, API 20C AUX successfully identified 90% (9/10) of *Kodamaea ohmeri*.[7] Other identification methods include MALDI-TOF and ITS region sequencing. The identification accuracy using MALDI-TOF reached 98.4%, with

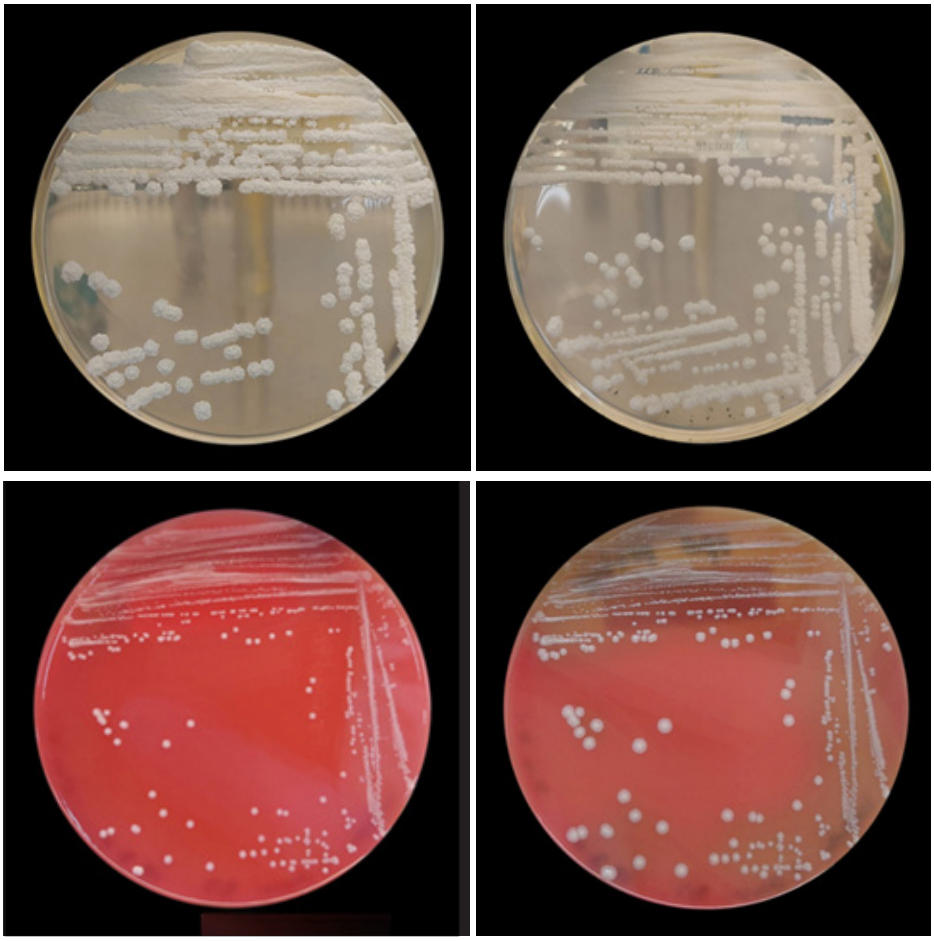

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Figure 6. *K. ohmeri* colony subculture.
A. Yeast colonies growing on SDA + K after 48 hours of incubation at 25°C–30°C; B. Yeast colonies growing on SDA + K after 48 hours of incubation at 37°C; C. Colonies growing on blood agar after 48 hours of incubation at 37°C; D. Colonies growing on blood agar after 96 hours of incubation at 37°C.


only 1 (1.6%) being unidentified.[6] ITS region sequencing can also be used. This sequencing has been recognized as a reference method for characterizing yeast, including *K. ohmeri*.[3,32] Currently, these two methods are the gold standard for *K. ohmeri* identification.[5]

Clinical experience and data on *K. ohmeri* infections are limited. According to the ESCMID and ECMM guidelines, amphotericin B is the treatment of choice for *K. ohmeri* infections. Fluconazole and an echinocandin may also be given in certain circumstances.[5] Previous studies have shown that amphotericin B exhibits low MIC values, and fluconazole susceptibility varies.[3] Some cases of fluconazole-resistant *K. ohmeri* infections can be treated with itraconazole and voriconazole.[26,36] These cases received antifungal therapy with oral itraconazole and ketoconazole cream. Good results were achieved after 2 months of use. In one study, the efficacy was 22.6%.[6]

CONCLUSION

Kodamaea ohmeri is a rare fungus that has now been proven to be a human pathogen. This infection should be considered in the diagnosis, especially in patients with compromised immunity. Identification of *K. ohmeri* based on macroscopic and microscopic phenotypic characteristics, as well as semi-automatic methods, is still insufficient. Caution is needed because it can be misidentified as *Candida sp*. Currently, identification using more sophisticated tools such as the Vitek-2 Compact and/or MALDI-TOF is required.

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DECLARATION ON THE USE OF ARTIFICIAL INTELLIGENCE IN THE MANUSCRIPT

The author declares that AI assistance was utilized during the writing process. The author used AI, specifically Perplexity AI, to assist with the literature/journal search.

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