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The refractory nailbed ulceration caused by *Candida parapsilosis* after nail extraction

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ABSTRACT

An 82-year-old female patient presented to our clinic with refractory nailbed ulceration accompanied by pain in her left fourth toe. Six months prior, she had undergone nail removal surgery to address a persistent paronychia that had not resolved for four months. Crust, necrotic tissue, and secretion on the nailbed were taken for microbiological examination, and *Candida parapsilosis* was discovered in culture. The authors first report one refractory nailbed ulceration caused by *Candida parapsilosis* after nail extraction.

1. Introduction

The incidence of fungal infections is rising alarmingly, posing substantial challenges to healthcare professionals. This escalation is associated with the expanding population of immunocompromised individuals, a trend attributable to the increased use of chemotherapy and immunosuppressive drugs, as well as the prevalence of HIV and other diseases that result in immunosuppression [1]. Fungal infections involve not only systemic infections but also infections with skin and soft tissue involvement [2]. *Candida* spp. are common causes of superficial and life-threatening systemic mycoses, particularly among immunocompromised individuals [3]. It is well known that *Candida albicans* is the most common cause of candidiasis; however, infections due to non-albicans species have emerged over the past years, such as *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis* [4]. The clinical features of the *C. parapsilosis* infection are similar to those of other *Candida* infections, including invasive and superficial infections [5]. Superficial candidiasis are skin and soft tissue (nail) infections classified as cutaneous, mucosal, paronychial and onychial, and chronic mucocutaneous and granulomatous infections [6]. However, *C. parapsilosis* is a rare cause of skin and soft tissue infections, with few cases manifesting as ulceration. Herein, we report a cutaneous candidiasis which manifested as nailbed ulceration caused by *C. parapsilosis* in an immunocompetent adult.

2. Case presentation

An 82-year-old woman was admitted to our clinic (day 0) due to refractory nailbed ulceration with pain in her left fourth toe for six months (- day 180). The patient stated that the nail groove of the left fourth toe developed swelling with pain and purulent secretion ten months ago (- day 300) and was later diagnosed with acute paronychia in a hospital's emergency room. After being treated with antibiotics, the symptoms slightly improved but did not fully recover. A nail removal procedure was administered in another hospital six months ago (- day 180). However, after nail extraction, an unhealed superficial ulcer formed on the nailbed and around the nail, so she visited our clinic. Diabetes or other local and systemic immunosuppressive disorders were excluded. The patient's general condition was good.

Clinical examination revealed erythematous ulceration covered with crust over the left fourth toe (Fig. 1a). The inside of the ulcer contained a purulent extrusion after the crust was removed. The toe was red and swollen, and the skin temperature was slightly higher. The pulse of the dorsal foot artery was regular. In addition, the fifth nail groove was slightly red and swollen. There was no obvious abnormality in the B-ultrasound examination of blood vessels in lower limbs, feet, and toes. We took crust, necrotic tissue, and secretion for direct microscopic examination and culture of bacteria and fungi. The yeast-like colonies grew (Fig. 1b) cultured on potato dextrose agar after two days at 26 °C. *C. parapsilosis* was identified through molecular identification based on

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the ITS sequence (Gene Bank accession no. MN699481). We suggested a biopsy to confirm the diagnosis further. The patient temporarily refused and received the experimental treatment of itraconazole (200mg/day). Although the symptoms improved slightly after one week of treatment, the patient developed edema in both lower limbs, so she stopped taking medicine herself. We successfully took a biopsy when the patient revisited our clinic. Histopathological examination revealed a typical ulcer with epidermal absence, collagen necrosis in the superficial dermis, mixed inflammatory cells infiltrating the middle and lower dermis, and the blood vessel wall blurred with red blood cell overflow in some areas (Fig. 1c). Periodic Acid Schiff staining and Acid-fast staining were conducted but yielded negative results.

Then, the diagnosis of cutaneous candidiasis caused by *C. parapsilosis* infection was made. According to Clinical and Laboratory Standards Institute documents M27-Ed4 [7], broth dilution antifungal susceptibility testing was conducted. *In vitro* antifungal testing revealed that this isolate was susceptible to fluconazole (MIC = 0.5μg/mL). After receiving fluconazole (50 mg/day) for three months, the lesion completely healed, and the inflammation of the fifth toenail groove subsided (Fig. 1d). A six-month follow-up revealed no recurrence.

3. Discussion

C. parapsilosis, the second or third most common non-albicans *Candida* species with a wide range of clinical presentations from colonization to superficial and invasive infections, is an opportunistic human pathogenic yeast [5,8]. However, superficial infections caused by *C. parapsilosis* are comparatively uncommon [9]. Since *C. parapsilosis* is a common colonizer of human skin, it is crucial to identify whether it is the causative fungus of skin and soft tissue infections [5]. Besides positive microscopic examination, fungal culture, and histopathological findings, and effective antifungal therapy supports *C. parapsilosis* infection other than colonization [9].

Skin and soft tissue infections caused by *C. parapsilosis* are relatively rare. Since 2000, nine cases have been found in the Pubmed database [9–16]. Four cases were co-infections of two or three fungi, among which *C. parapsilosis* might be considered a colonizer [10–13]. The other five cases were similar to ours, with *C. parapsilosis* being the only causative fungus [9,14–16]. Ulceration was the common clinical manifestation, including our case (4/6). One of them, who had myelodysplastic syndrome and type 2 diabetes, was found with multiple wart-like nodules on the planta [14]. One patient, with a 12-year history of poorly controlled type 2 diabetes, presented with an infiltrative reddish plaque accompanied by ulceration and purulent secretion on the hand [16]. One case was reported with a prior history of notable trauma; an electrosurgery procedure was performed before the ulcer [15]. Our patient suffered from a refractory nailbed ulcer after trauma, e.g. nail extraction treatment. Thus, the skin and soft tissue infections caused by *C. parapsilosis* might be related to trauma, especially in healthy individuals. The most crucial diagnostic basis was identifying

Fig. 1. (a) Clinical photograph showing erythematous ulceration covered with crust and edema over the left fourth toe. (b) The yeast-like colonies grew cultured on potato dextrose agar after two days at 26 °C. (c) Histopathological examination revealed a typical ulcer with epidermal absence, collagen necrosis in the superficial dermis, mixed inflammatory cells infiltrating the middle and lower dermis, and the blood vessel wall blurred with red blood cell overflow in some areas ((H&E, 40 ×). (d) The ulceration was completely healed after three months of therapy.

C. parapsilosis in tissue culture (6/6). Molecular identification helped further clarify strain species (5/6). Histopathological examination indicated infectious granuloma or hyphae observed by special staining (4/6). All patients received effective antifungal therapy. Itraconazole was the most prescribed medication (4/6), and fluconazole successfully treated the other and our case. *C. parapsilosis* isolates are susceptible to most azoles including fluconazole, itraconazole, voriconazole, posaconazole, and ketoconazole.

Common superficial infections caused by *Candida* species involve not only the skin and soft tissue, but also the nails. Onychomycosis is a common fungal nail infection, and the main cause is related to dermatophytes [17]. The second cause of onychomycosis is related to *Candida* species [18]. The most frequently isolated *Candida* species in onychomycosis is *C. albicans*; the second species reported is *C. parapsilosis*, showing a growing trend in recent years [18]. Different from *C. albicans*, onychomycosis cases caused by *C. parapsilosis* seem to be mainly related to trauma and fungal pollution from soil and animals [19]. Therapeutic drugs used to treat *Candida* onychomycosis include polyenes (amphotericin), triazoles (fluconazole, itraconazole), imidazole (clotrimazole, ketoconazole, miconazole), and morpholines (amorolfine); however, triazoles represent the most used and effective treatment [18]. The drug of choice should not be terbinafine, as *Candida* species are in general not susceptible to it, except *C. parapsilosis* showing low terbinafine MIC [17, 20].

Herein, we first report one refractory nailbed ulceration caused by *C. parapsilosis* after nail extraction. We speculate that *C. parapsilosis* might have played a pathogenic role throughout the disease. The paronychia might have been caused by *C. parapsilosis* but was not identified at the time. Then, the pathogen invaded the wound caused by nail removal and formed a nailbed ulcer that was difficult to heal. Fortunately, *C. parapsilosis* was detected in the crust and necrotic tissue culture in our clinic. Antifungal treatment with fluconazole was effective in treating the inflammation around the fifth toenail, confirming our suspicion that the paronychia of the fourth toe before nail extraction might also have been caused by *C. parapsilosis*. Finally, we emphasize the importance of pathogenic examination in chronic paronychia and the careful choice of traumatic treatment.

CRediT authorship contribution statement

Siyue Kan: Writing – original draft, Visualization, Methodology, Conceptualization. **Lulu Li:** Writing – original draft. **Lulu An:** Validation, Methodology. **Hong Yang:** Visualization. **Lianjuan Yang:** Writing – review & editing, Visualization, Supervision, Methodology, Conceptualization.

Ethical form

The authors have obtained written and signed consent to publish the case report from the patient.

Declaration of competing interest

None.

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References

[1] G. Garber, An overview of fungal infections, Drugs 61 (2001) 1–12, https://doi.org/10.2165/00003495-200161001-00001.
[2] S.D. Gunaydin, S. Arikan-Akdagli, M. Akova, Fungal Infections of the Skin and Soft Tissue, 2020, p. 33.
[3] Y.-L. Chang, S.-J. Yu, J. Heitman, M. Wellington, Y.-L. Chen, New facets of antifungal therapy, Virulence 8 (2017) 222–236, https://doi.org/10.1080/21505594.2016.1257457.
[4] M. Gómez-Gaviria, U. Ramírez-Sotelo, H.M. Mora-Montes, Non-albicans Candida species: immune response, evasion mechanisms, and new plant-derived alternative therapies, JoF 9 (2022) 11, https://doi.org/10.3390/jof9010011.
[5] M. Govrins, C. Lass-Flörl, Candida parapsilosis complex in the clinical setting, Nat. Rev. Microbiol. 22 (2024) 46–59, https://doi.org/10.1038/s41579-023-00961-8.
[6] X. Feng, B. Ling, G. Yang, X. Yu, D. Ren, Z. Yao, Prevalence and distribution profiles of Candida parapsilosis, Candida orthopsilosis and Candida metapsilosis responsible for superficial candidiasis in a Chinese university hospital, Mycopathologia 173 (2012) 229–234, https://doi.org/10.1007/s11046-011-9496-5.
[7] P. Wayne, Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts, fourth ed., Clinical Laboratory Standard Institute, 2017. Document M27-E4.
[8] T. Chakraborty, Z. Tóth, R. Tóth, C. Vágvölgyi, A. Gácser, Iron metabolism, pseudohypha production, and biofilm formation through a multicopper oxidase in the human-pathogenic fungus Candida parapsilosis, mSphere 5 (2020) e00227, https://doi.org/10.1128/mSphere.00227-20, 20.
[9] J. Wu, J. Tan, H. Yang, Z. Gao, L. Yang, Two cases of primary cutaneous candidiasis caused by Candida parapsilosis: a report and literature review, J. Med. Mycol. 31 (2021) 101158, https://doi.org/10.1016/j.mycmed.2021.101158.
[10] L. Xi, X. Li, J. Zhang, C. Lu, T. Xie, R. Yin, Good response in a patient with deep-seated subcutaneous ulcer due to Candida species, Mycopathologia 164 (2007) 77–80, https://doi.org/10.1007/s11046-007-9030-y.
[11] E.R. Geddes, K. Polder, J.E. Cutlan, C.A. Torres-Cabala, S.R. Hymes, Ulcerated plaque under a ruby ring in an immunosuppressed patient, Dermatol. Online J. 16 (2010) 4, https://doi.org/10.5070/D32JB121RB.
[12] M.J. Fellner, Trichotillomania in a young male complicated by tinea capitis associated with Cryptococcus laurentii and Candida parapsilosis, Clin. Cosmet. Invest. Dermatol. 6 (2013) 71–73, https://doi.org/10.2147/CCID.S43047.
[13] Y. Huang, S. Pradhan, L. Li, Y. Ran, Dermoscopy hints the diagnosis of Candidal granuloma coinfected with Candida parapsilosis and Candida guilliermondii, Mycopathologia 188 (2023) 155–157, https://doi.org/10.1007/s11046-022-00691-0.
[14] Y. Honda, Y. Hattori, T. Terashima, T. Manabe, H. Tanabe, Y. Miyachi, Plantar wart-like Candida granuloma in a patient with myelodysplastic syndrome, J. Dermatol. 44 (2017) e298–e299, https://doi.org/10.1111/1346-8138.13953.
[15] A. Pietrzak, K. Janowski, G. Chodorowska, K. Trela, M. Szymanek, D. Krasowska, Candida parapsilosis infection following the electrosurgery procedure, Dermatol. Ther. 24 (2011) 131–133, https://doi.org/10.1111/j.1529-8019.2010.01386.x.
[16] X. Yang, X. Jin, Z. Yang, Y. Wang, A. Wei, X. Yang, Isolated cutaneous granuloma caused by Candida parapsilosis: case report and literature review, Mycopathologia 189 (2024) 20, https://doi.org/10.1007/s11046-023-00812-3.
[17] B.M. Piraccini, A. Alessandrini, Onychomycosis: a review, J. Fungi (Basel, Switzerland) 1 (2015) 30–43, https://doi.org/10.3390/jof1010030.
[18] T.-S. Andrés, B. Alexandro, Candida onychomycosis: an old problem in modern times, Current Fungal Infect. Rep. 14 (2020) 209–216, https://doi.org/10.1007/s12281-020-00394-3.
[19] E.C. Van Asbeck, K.V. Clemons, D.A. Stevens, Candida parapsilosis: a review of its epidemiology, pathogenesis, clinical aspects, typing and antimicrobial susceptibility, Crit. Rev. Microbiol. 35 (2009) 283–309, https://doi.org/10.3109/10408410903213393.
[20] V.T. Figueiredo, D. De Assis Santos, M.A. Resende, J.S. Hamdan, Identification and in vitro antifungal susceptibility testing of 200 clinical isolates of Candida spp. responsible for fingernail infections, Mycopathologia 164 (2007) 27–33, https://doi.org/10.1007/s11046-007-9027-6.