Onychomycosis caused by *Pichia guilliermondii*: A case report and mini-review

Mei-jie Zhang¹, Guan-zhao Liang¹, Huan Mei, Ge Song, Wei-da Liu* 

Department of Mycology, Institute of Dermatology, Chinese Academy of Medical Sciences, Peking Union Medical College, 12th JiangWangMiao Street, Nanjing, Jiangsu, 210029, China

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ABSTRACT

Onychomycosis has been reported to be mainly caused by dermatophytes. Recently, more attention has been paid to yeasts for its increasing morbidity, especially the candida species. Here we reported a fingernail infection caused by *Pichia guilliermondii*, the sexual reproduction period of *Candida guilliermondii*. Itraconazole was used for three courses, and the patient achieved improvement without any significant side-effects. This might be the first onychomycosis case of *Candida guilliermondii*.

1. Introduction

Onychomycosis, accounting for approximately 50% of the nail diseases, is a common chronic fungal infection of the nail plate or nail bed caused by dermatophytes, yeasts, and nondermatophyte molds (NDMs) [1]. With healthy nail appearance becoming more and more important for social reasons, increasing attention is paid to the treatment of onychomycosis [2].

While the incidence of onychomycosis keeps growing up and the worldwide prevalence shows 5.5%, dermatophytes, particularly *Trichophyton rubrum*, are still responsible for the most of fungal nail infection [2]. Among patients with onychomycosis in Dakar, to our surprise, yeasts can be as high as 68.4%–75% of the isolates [3,4]. In spite of *C.albicans*, non-*C.albicans* candida species such as *C.tropicalis*, *C.parapsilosis* and others were also reported sharing 40% of the fingernail onychomycosis.

*C.guilliermondii* is a normal component of human microbes on skin and mucous membranes, conditionally causing infection, especially among immunodeficient people [5]. *C.guilliermondii* onycomyasis is reported for the first time; in addition, the patient is an immunocompetent person.

2. Case

A 50-year-old healthy male farmer showed up in our clinic on day −7, several fingernails of whose left hand turned yellow and thickened in one year without any symptom. He denied any hand trauma or glucocorticoid using. In general, his left thumb, middle finger and little finger appeared as the type of distal and lateral subungual onychomycosis (DLSO) with crumbed nail plate, yellowish, brownish, partially thickened and friable; while the forefinger showed proximal subungual onychomycosis (PSO) with slight indentations (Fig. 1a).

Scales of the nail lesion were collected and then observed directly under the microscopy, presenting plenty of spores (Fig. 2). The result of culture turned out with yeast-like colonies as white and smooth as cheese, illustrating the characteristic morphophysiological features of candida species (Fig. 3). rRNA gene sequence analysis after PCR using the universal primer internal transcribed spacer (ITS1/ITS4) confirmed that it had 99.67% homology with that of *Pichia guilliermondii* (Meyer-ozyma guilliermondii) (GenBank Accession No. MN473285.1).

Considering all of the clinical characters and experimental results, the patient was diagnosed as *C.guilliermondii* onychomycosis. Antifungal therapy was started on day 0 with oral itraconazole in doses of 200mg twice daily and finished on day +7 as the first treatment course. The same dosage of the second course and the third course, respectively, from day +28 to day +35 and day +56 to day +63. At his first follow-up on day +28, the nail lesions improved significantly (Fig. 1b). The patient reported cured in a telephone follow-up on day +6 months, but regretfully, haven't provided with any picture.

This case promoted us to analyze the epidemiology of onychomycosis...
tology in China. We searched the database in CNKI (www.cnki.net/), WANFANG DATA (www.wanfangdata.com.cn/) and VIP (www.cqvip.com/) for analyzing the human cohorts of onychomycosis of the last 20 years (see Table 1). All the data we have collected and analyzed is presented in the supplement with references. Comparisons among the proportions of species have been made within different periods and different provinces (see detail in supplement). The comparison came out with more yeast while less dermatophyte cases happening than before (Fig. 4), especially in Jiangsu Province and Guangdong Province (Fig. 5).

3. Discussion

Although majority of the former studies declared dermatophytes to be the predominant pathogens, different sounds appear in etiology recently. We did a partial analysis of the epidemiology in Iran [6], grouping them into two periods with one from 2000 to 2007 and the other from 2007 to 2015, finding that dermatophytes decreased significantly during years while NDMs increased instead (Fig. 6). Meanwhile, a novel systematic review and meta-analysis in Iran has demonstrated that yeasts are the predominant etiologic agents in 17 studies (70.8%) while dermatophytes in 5 studies (20.9%) [6], similar to the findings in Colombia [7] and Italy [8]. The epidemiology of onychomycosis in China has also shown changes for many years (see the supplements), as the number of yeast cases increased in recent years. Since the epidemiology of onychomycosis has changed and the yeast proportion has increased, more attention should be paid on yeast onychomycosis, especially the most important candida ones.

Pichia guilliermondii is the sexual reproduction period of C. guilliermondii, with another name of Meyerozyma guilliermondii, inducing infections as opportunistic pathogens particularly in immunocompromised patients. Pichia guilliermondii has been rarely reported, one pulmonary nodules [9] and few candidemia [10], and the patients infected are often accompanied by type 2 diabetes and those who receiving total parenteral nutrition. Our report might be the first time to present such a particular onychomycosis case of C. guilliermondii.

In literatures, the recommending oral medications for onychomycosis, especially the most important candida ones.

Fig. 1. General appearance of patient hands (a) exhibiting the thumb, middle finger and little finger of left hand showing DLSO marked with coarse arrows, as well as the forefinger showing PSO marked with thin arrow, (b) exhibiting significant improvements.

Fig. 2. Direct microscopy of C. guilliermondii presenting plenty of spores (40 × ).

Fig. 3. Fungal culture turning out with yeast-like colonies as white and smooth as cheese.
| No | Years       | Province | Age groups          | Most common age group | Diagnosis methods | Confirmed cases | Etiologic agents (%)       | Predominant spp | Notes | Ref |
|----|-------------|----------|---------------------|-----------------------|-------------------|----------------|--------------------------|----------------|-------|-----|
| 1  | 2006/05-2010/12 | Beijing  | 3–75yrs NA         | S + DM + C            | 1229              |               | Yeast 311/591, NDM 92/591 | T.rub, C.Keusei, |       |     |
| 2  | 2007/02-2010/02 | Hunan    | 6–72yrs NA         | S + DM + C            | 305               |               | Dermatophyte 186/591, Aspergillus spp 106/267 | T.rub, C.glabata, |       |     |
| 3  | 2007/04-2008/04 | Shandong | 5–79yrs NA         | S + DM + C            | 613               |               | T.menta, C.albicans 75/481 | NDM 20/481, 11/481 |       |     |
| 4  | 2008/06-2012/11 | Guangdong| 20–39yrs NA       | S + DM + C            | 805               |               | T.rub, C.Keusei, C.parapsilosis 407/805 | C.albicans 13/805 |       |     |
| 5  | 2008/12-2010/10 | Guangdong| 5–89yrs >25yrs NA | S + DM + C            | 637               |               | T.rub, C.albicans, T.violae 119/637 | C.albicans 76/637 |       |     |
| 6  | 2009/07-2010/10 | Beijing  | 6–90yrs NA         | S + DM + C            | 196               |               | Yeast 120/372, NDM 10/206 | T.rub, C.albicans, T.violae 70/206 |       |     |
| 7  | 2010/01-2013/12 | Zhejiang | 12–73yrs 36–50yrs  | S + DM + C            | 901               |               | Yeast 275/468, NDM 52/468 | T.rub, C.menata |       |     |
| 8  | 2010/07-2012/07 | Shandong | 8–83yrs NA         | S + DM + C            | 361               |               | Yeast 212/491, NDM 5/239 | T.rub, C.albicans, T.menata 202/239 |       |     |
| 9  | 2010/08-2011/08 | Guangdong| 6mon-75yrs NA     | S + DM + C            | 657               |               | Yeast 95/231, NDM 12/231 | T.rub, C.albicans, T.menata 124/231 |       |     |
| 10 | 2010/12-2011/12| Jiangsu  | 3–89yrs 20–29yrs   | S + DM + C            | 328               |               | Yeast 162/196, NDM 12/196 | T.rub, C.albicans, T.menata 122/196 |       |     |
| 11 | 2011/01-2011/12| Jiangsu  | 9–80yrs NA         | S + DM + C            | 800               |               | Yeast 664/800, NDM 42/800 | T.rub, C.albicans, T.menata 94/800 |       |     |
| 12 | 2011/02-2011/12| Hebei    | 2–79yrs NA         | S + DM + C            | 106               |               | Yeast 72/111, NDM 5/111 | T.rub, C.albicans, T.menata 34/111 |       |     |
| 13 | 2011/08-2017/06| Guangdong| 20–40yrs NA       | S + DM + C            | 1162              |               | Yeast 1162/1162, NDM 17/1162 | T.rub, C.albicans, T.menata 359/1162 |       |     |
| 14 | 2011/12-2012/05| Jiangsu  | 3–83yrs 21–30yrs   | S + DM + C            | 127               |               | Yeast 10/127, NDM 36/127 | T.rub, C.albicans, T.menata 81/127 |       |     |
| 15 | 2012/02-2016/03| Guangdong| 3–92yrs NA        | S + DM + C            | 421               |               | Yeast 91/278, NDM 11/278 | T.rub, C.albicans, T.menata 176/278 |       |     |
| 16 | 2012/03-2014/03| Tianjin  | 1–95yrs NA        | S + DM + C            | 4100              |               | Yeast 2998/4625, NDM 318/4625 | T.rub, C.albicans, T.menata 1309/4625 |       |     |
| 17 | 2012/10-2013/12| Jiangsu  | 1–85yrs 21–30yrs   | S + DM + C            | 393               |               | Yeast 295/393, NDM 23/393 | T.rub, C.albicans, T.menata 75/393 |       |     |
| 18 | 2017/01-2017/12| Hubei    | 1–81yrs 19–37yrs   | S + DM + C            | 959               |               | Yeast 820/959, NDM 47/959 | T.rub, C.albicans, T.menata 92/959 |       |     |
| 19 | 2017/01-2017/12| Fujian   | 0–12yrs 10–12yrs   | S + DM + C            | 112               |               | Yeast 73/90, NDM 3/90 | T.rub, C.albicans, T.menata 11/90 |       |     |
| 20 | 2017/01-2017/12| Hubei    | 10mon-6yrs 3–6yrs  | S + DM + C            | 49                |               | Yeast 17/49, NDM 2/49 | T.rub, C.albicans, T.menata 30/49 |       |     |
| 21 | 2017/01-2017/12| Shanghai | 6mon-14yrs 5–9yrs  | S + DM + C            | 33                |               | Yeast 21/33, NDM 1/33 | T.rub, C.albicans, T.menata 21/33 |       |     |
| 22 | 2017/04-2013/04| Guangdong| 60–82yrs NA       | S + DM + C + sequencing | 107         |               | Yeast 86/121, NDM 4/121 | T.rub, C.albicans, T.menata 31/121 |       |     |
| 23 | 2013/01-2014/08| Shanxi   | 31–64yrs 55–65yrs  | S + DM + C            | 153               |               | Yeast 77/108, NDM 4/108 | T.rub, C.albicans, T.menata 27/108 |       |     |

| S: sampling; DM: direct microscopy; C: culture; NA: not available; NDM: nondermatophyte molds; T.rub: Trichophyton rubrum; T.menta: Trichophyton mentagrophytes; C.alb: Candida albicans; C.parap: Candida parapsilosis; C.glab: Candida glabrata; T.inter: Candida interdactylis, T.ru: Trichophyton violaceum; M.gypseum: Microsporum gypseum; C.tropic: Candida tropicalis. |
onychomycosis includes terbinafine, itraconazole and fluconazole. The guidelines of onychomycosis in China [11] and Britain [12] share similar tips that terbinafine and itraconazole are the first-line medication compared to fluconazole. Terbinafine is found to have more effects on dermatophytes onychomycosis with the clearance up to 70%, while itraconazole shows more effective in yeasts infection.

According to the guidelines and our clinical experience, itraconazole shows more significant efficiency than terbinafine in the treatment of candida infections. As a result, we chose oral itraconazole therapy for this patient which finally worked. Unfortunately, drug sensitive test hadn’t been adopted to achieve the most appropriate drug and make a further verification here.

Different from the former cases, we found our patient healthy without personal or family history of diabetes or immunosuppressive therapy, indicating the significance in the further study of species epidemiology and the development of a rapid, accurate and convenient diagnosis of fungal infections in clinic. The low-morbidity species of candida onychomycosis leaves unspecific antifungal therapy, though,

Fig. 4. Comparison of epidemiology of onychomycosis between two 5 years showing more yeast cases and less dermatophytes ones in latest studies.

empirical therapy before the result of drug sensitive test comes out is of great importance.

Ethical Form

Please note that this journal requires full disclosure of all sources of funding and potential conflicts of interest. The journal also requires a declaration that the author(s) have obtained written and signed consent to publish the case report from the patient or legal guardian(s).

The statements on funding, conflict of interest and consent need to be submitted via our Ethical Form that can be downloaded from the submission site www.ees.elsevier.com/mmcr. Please note that your manuscript will not be considered for publication until the signed Ethical Form has been received.

Declaration of competing interest

There are none.
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