

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

Mei-jie Zhang<sup>1</sup>, Guan-zhao Liang<sup>1</sup>, 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



### ARTICLE INFO

#### Keywords:

Onychomycosis  
*Pichia guilliermondii*  
Candida  
Itraconazole

### ABSTRACT

Onychomycosis has been reported to be mainly caused by dermatophytes. Recently, more attention has been paid to yeast 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* onychomycosis 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* (*Meyerozyma guilliermondii*) (GenBank Accession No. MN473285.1).

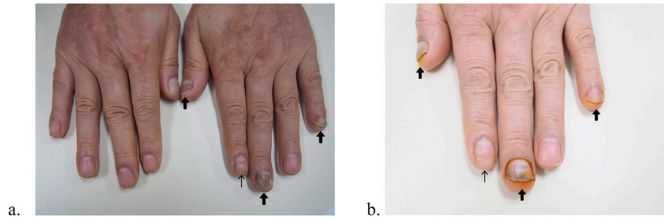
Considering all of the clinical characters and experimental results, the patient was diagnosed as *C.guilliermondii* onychomycosis. Antifungal therapy was started on day 0 with oral itraconazole in doses of 200mg twice daily and finished on day +7 as the first treatment course. The same dosage of the 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 regrettably, haven't provided with any picture.

This case promoted us to analyze the epidemiology of onychomy-

\* Corresponding author.

E-mail address: [liumyco@hotmail.com](mailto:liumyco@hotmail.com) (W.-d. Liu).

<sup>1</sup> Meijie Zhang and Guanzhao Liang contributed equally to this work.



**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.

cosis in China. We searched the database in CNKI([www.cnki.net/](http://www.cnki.net/)), WANFANG DATA ([www.wanfangdata.com.cn/](http://www.wanfangdata.com.cn/)) and VIP([www.cqvip.com/](http://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

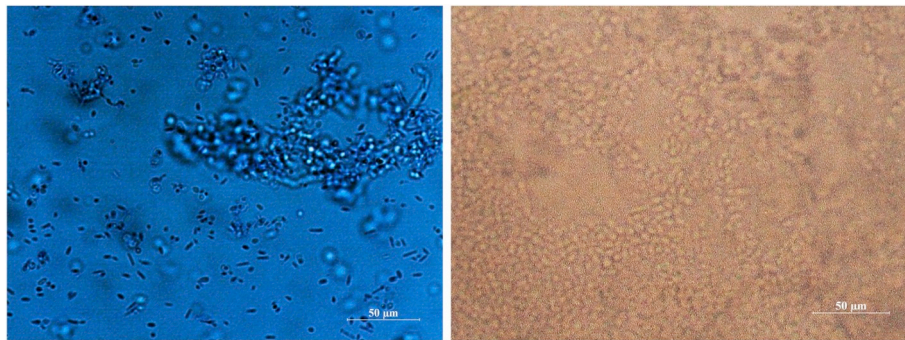


**Fig. 3.** Fungal culture turning out with yeast-like colonies as white and smooth as cheese.

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



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

**Table 1**  
Characteristics of the included studies in China.

| No | Years           | Province  | Age groups | Most common age group | Diagnosis methods       | Confirmed cases | Gender             | Etiologic agents (%) |               |          | Predominant spp                   | Notes | Ref           |
|----|-----------------|-----------|------------|-----------------------|-------------------------|-----------------|--------------------|----------------------|---------------|----------|-----------------------------------|-------|---------------|
|    |                 |           |            |                       |                         |                 |                    | Yeast                | Dermatop-hyte | NDM      |                                   |       |               |
| 1  | 2006/05–2010/12 | Beijing   | 3–75yrs    | NA                    | S + DM + C              | 1229            | F = 803, M = 426   | 188/591              | 311/591       | 92/591   | T.rub, C.krusei, Aspergillus spp  |       |               |
| 2  | 2007/02–2010/02 | Hunan     | 6–72yrs    | NA                    | S + DM + C              | 305             | F = 173, M = 132   | 106/267              | 143/267       | 18/267   | T.rub, C.glabrata, C.albicans     |       | [12]          |
| 3  | 2007/04–2008/04 | Shandong  | 5–79yrs    | NA                    | S + DM + C              | 613             | F = 385, M = 228   | 75/481               | 386/481       | 20/481   | T.rub, T.menta, C.albicans        |       | (13)          |
| 4  | 2008/06–2012/11 | Guangdong | NA         | 20–39yrs              | S + DM + C              | 805             | F = 444, M = 361   | 407/805              | 385/805       | 13/805   | T.rub, T.menta, C.glabrata        |       | (27)          |
| 5  | 2008/12–2010/12 | Beijing   | 5–89yrs    | > 25yrs               | S + DM + C              | 637             | F = 265, M = 372   | 119/637              | 442/637       | 76/637   | T.rub, C.albicans, T.menta        |       | (17)          |
| 6  | 2009/07–2010/10 | Guangdong | 6–96yrs    | NA                    | S + DM + C              | 196             | F = 120, M = 140   | 70/206               | 124/206       | 10/206   | T.rub, C.albicans, T.vio          |       | [9]           |
| 7  | 2010/01–2013/12 | Zhejiang  | 12–73yrs   | 36–50yrs              | S + DM + C              | 901             | F = 516, M = 385   | 141/468              | 275/468       | 52/468   | T.rub, T.menta, C.albicans        |       | (19)          |
| 8  | 2010/07–2012/07 | Shandong  | 8–83yrs    | NA                    | S + DM + C              | 361             | F = 212, M = 149   | 25/239               | 202/239       | 5/239    | T.rub, C.albicans, T.menta        |       | (28)          |
| 9  | 2010/08–2011/08 | Guangdong | 6mon–75yrs | NA                    | S + DM + C              | 657             | F = 271, M = 386   | 124/231              | 95/231        | 12/231   | C.albicans, T.rub, C.parapsilosis |       | (15)          |
| 10 | 2010/12–2011/12 | Jiangsu   | 3–89yrs    | 20–29yrs              | S + DM + C              | 328             | F = 134, M = 194   | 22/196               | 162/196       | 12/196   | T.rub, T.menta, C.albicans        |       | (16)          |
| 11 | 2011/01–2011/12 | Jiangsu   | 9–80yrs    | NA                    | S + DM + C              | 800             | F = 390, M = 410   | 94/800               | 664/800       | 42/800   | T.rub, Candida spp, T.menta       |       | [11]          |
| 12 | 2011/01–2011/12 | Hebei     | 2–79yrs    | NA                    | S + DM + C              | 106             | F = 76, M = 30     | 34/111               | 72/111        | 5/111    | T.rub, T.menta, C.albicans        |       | (14)          |
| 13 | 2011/08–2017/06 | Guangdong | NA         | 20–40yrs              | S + DM + C              | 1162            | F = 712, M = 450   | 359/1162             | 750/1162      | 36/1162  | T.rub, Candida spp, T.inter       |       | (29)          |
| 14 | 2011/11–2012/05 | Jiangsu   | 3–83yrs    | 21–30yrs              | S + DM + C              | 127             | F = 67, M = 60     | 81/127               | 10/127        | 36/127   | T.rub, T.menta, Candida spp       |       | (30)          |
| 15 | 2012/02–2016/03 | Guangdong | 3–92yrs    | NA                    | S + DM + C              | 421             | F = 235, M = 186   | 176/278              | 91/278        | 11/278   | T.rub, C.albicans, C.parapsilosis |       | (18)          |
| 16 | 2012/03–2014/03 | Tianjing  | 1–95yrs    | NA                    | S + DM + C              | 4100            | F = 2265, M = 1835 | 1309/4625            | 2998/4625     | 318/4625 | T.rub, C.albicans, T.menta        |       | (31)          |
| 17 | 2012/10–2013/12 | Jiangsu   | 1–85yrs    | 21–30yrs              | S + DM + C              | 393             | F = 238, M = 155   | 75/393               | 295/393       | 23/393   | NA                                |       | (21)          |
| 18 | 2017/01–2017/12 | Hubei     | 1–81yrs    | 19–37yrs              | S + DM + C              | 959             | F = 587, M = 372   | 92/959               | 820/959       | 47/959   | T.rub, Candida spp, T.menta       |       | (20)          |
| 19 | 2010/01–2014/02 | Fujian    | 0–12yrs    | 10–12yrs              | S + DM + C              | 112             | F = 48, M = 64     | 11/90                | 73/90         | 3/90     | T.rub, T.menta, C.albicans        |       | Children (32) |
| 20 | 2010/06–2015/06 | Hubei     | 10mon–6yrs | 3–6yrs                | S + DM + C              | 49              | F = 22, M = 27     | 30/49                | 17/49         | 2/49     | C.glabrata, T.rub, C.parapsilosis |       | Children (33) |
| 21 | 2011/10–2012/10 | Shanghai  | 6mon–14yrs | 5–9yrs                | S + DM + C              | 33              | F = 12, M = 21     | 10/33                | 21/33         | 1/33     | T.rub, C.albicans, C.parapsilosis |       | Children (34) |
| 22 | 2011/04–2013/04 | Guangdong | 60–82yrs   | NA                    | S + DM + C              | 107             | F = 49, M = 58     | 31/121               | 86/121        | 4/121    | T.rub, T.menta, C.albicans        |       | Elderly (35)  |
| 23 | 2013/01–2014/08 | Shanxi    | 31–84yrs   | 55–65yrs              | S + DM + C + sequencing | 153             | F = 452, M = 673   | 27/108               | 77/108        | 4/108    | T.rub, C.albicans, T.menta        |       | DM (36)       |

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 interductylis; T.rub: Candida; T.schoe: Candida; T.vio: Trichophyton violaceum; M.gypseum: Microsporum gypseum; C.tropic: Candida tropicalis.

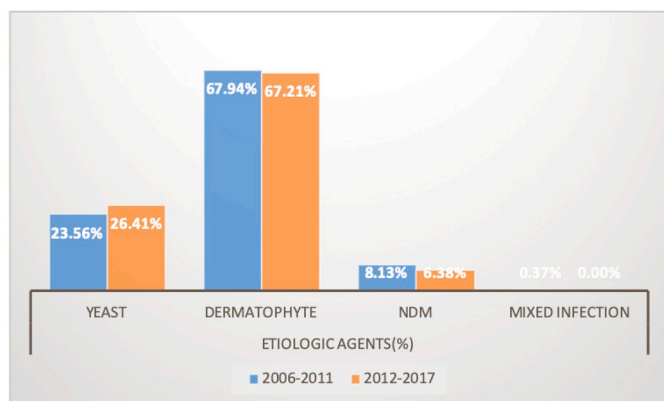


Fig. 4. Comparison of epidemiology of onychomycosis between two 5 years showing more yeast cases and less dermatophytes ones in latest studies.

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,

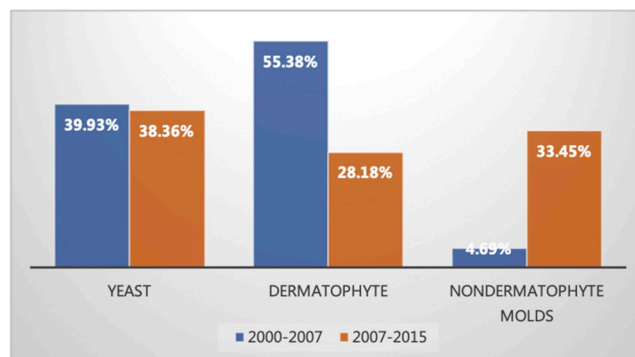


Fig. 6. Comparison of epidemiology of onychomycosis in two different times in Iran showing more NDMs cases and less dermatophytes ones in the latest study.

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](http://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.

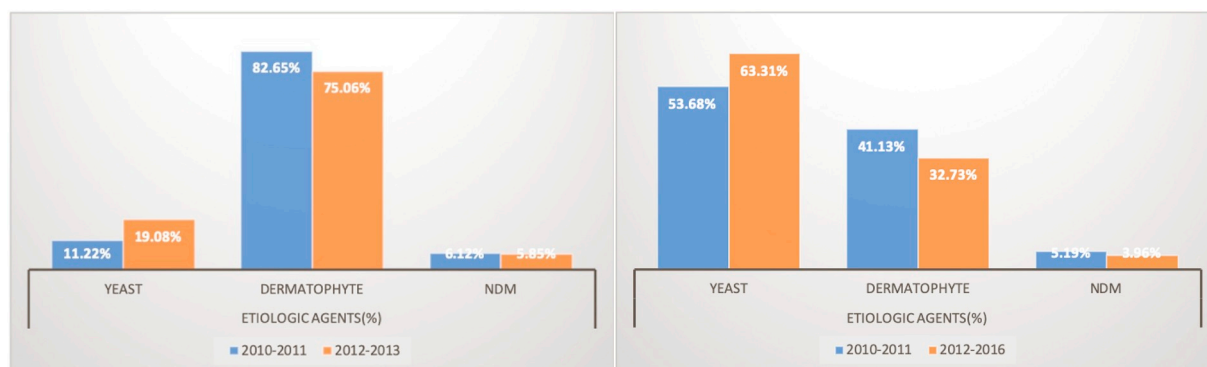


Fig. 5. Comparison of epidemiology of onychomycosis in two different times in (a)Jiangsu and (b)Guangdong showing more yeast cases and less dermatophytes ones in the latest study.

## Acknowledgements

Thank Professor Lv Guixia a lot for her kindly assistance and guidance in our work, especially the detection and differential diagnosis of fungus morphism.

## References

- [1] A.K. Gupta, S.G. Versteeg, N.H. Shear, Onychomycosis in the 21st century: an update on diagnosis, epidemiology, and treatment, *J. Cutan. Med.* 21 (2017) 120347541771636.
- [2] S.R. Lipner, R.K. Scher, Onychomycosis: clinical overview and diagnosis, *J. Am. Acad. Dermatol.* (2018).
- [3] Y.A. Ben, A. Kallel, Z. Azaiz, S. Jemel, N. Bada, A. Chouchen, et al., Onychomycosis: which fungal species are involved? Experience of the laboratory of parasitology-mycology of the Rabta hospital of tunis, *J. Mycol. Med.* (2018) S1156523318300052.
- [4] M.C. Seck, D. Ndiaye, K. Diongue, M. Ndiaye, O. Ndir, Mycological profile of onychomycosis in Dakar (Senegal), *J. Med. Mycol.* 24 (2) (2014).
- [5] A.K. Gupta, D. Daigle, K.A. Foley, The prevalence of culture-confirmed toenail onychomycosis in at-risk patient populations, *J. Eur. Acad. Dermatol. Venereol.* 29 (2014) 1039–1044.
- [6] Z. Rafat, S.J. Harshemi, A.A. Saboor-Yaraghi, B. Pouragha, A. T. aherinya, A. Moosavi, et al., A systematic review and meta-analysis on the epidemiology, casual agents and demographic characteristics of onychomycosis in Iran, *J. Mycol. Med.* 29 (2019) 265–272.
- [7] A. María Inés, G. Luz ángela, C. Luz ángela, Onychomycosis in cali, Colombia, *Mycopathologia* 158 (2004) 181–186.
- [8] R. Clara, G. Claudia, M.D. Elisa, Retrospective study of onychomycosis in Italy: 1985-2000, *Mycoses* 48 (2005) 42–44.
- [9] F. Frenzen, C. Röder, B. Wollschläger, E. Großer, K. Krohe, B. Schmidt, *Pichia guilliermondii* infection - a rare differential diagnosis of pulmonary nodules, *Pneumologie* 70 (2016) 605–607.
- [10] N. Cebeci Güler, Tosun, F. Aydin, The identification of *Meyerozyma guilliermondii* from blood cultures and surveillance samples in a university hospital in Northeast Turkey: a ten-year survey, *J. Med. Mycol.* (2017) S1156523317300677.
- [11] Dermatology, Venereology branch of Chinese Medical Association, Guidelines for diagnosis and treatment of onychomycosis in China(2015), *Chin. J. Mycol.* (2015) 68–75 02.
- [12] M. Ameen, J.T. Lear, V. Madan, M.F. Mohd Mustapa, M. Richardson, British Association of Dermatologists\' guidelines for the management of onychomycosis 2014, *Br. J. Dermatol.* 171 (5) (2014) 937–958.