Lodderomyces elongisporus: a bloodstream pathogen of greater clinical significance

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Abstract

The true clinical significance of Lodderomyces elongisporus remains underestimated as a result of problems associated with its identification by the VITEK 2 yeast identification system. Here we describe a case of L. elongisporus primary progressive fungaemia in a woman with no known risk factors for invasive fungal infections. The isolate was identified by PCR sequencing of the internally transcribed spacer region of ribosomal DNA. Despite treatment with caspofungin, the patient died within 3 days of onset of fungaemia. Our literature review highlights this organism’s emerging role as a bloodstream pathogen. A need for application of molecular methods for its accurate identification is emphasized. © 2018 The Authors. Published by Elsevier Ltd.

Keywords: Ascospores, bloodstream pathogen, emerging significance, lodderomyces elongisporus, molecular identification

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Case summary

A 71-year-old woman with a history of hypertension, ischaemic heart disease and peripheral vascular disease was brought to emergency room in an unconscious state. Head computed tomographic scan revealed a stroke. On day 2, her condition deteriorated rapidly, requiring inotropic support. She developed septic shock, as indicated by elevated levels of inflammatory markers (erythrocyte sedimentation rate, 70 mm/h; C-reactive protein, 78 mg/L). Blood obtained at this time grew a yeast in both aerobic and anaerobic BacT/ALERT culture bottles. Pending identification, caspofungin was administered immediately, but she died on day 3 of her hospital stay.

The yeast isolate (Kw553/18) was identified as C. parapsilosis by the VITEK 2 yeast identification system (bioMérieux, Marcy l’Etoile, France). It produced turquoise blue colonies (Fig. 1) instead of cream-coloured colonies with a pinkish shade, which is characteristic of C. parapsilosis, thus prompting further identification. On acetate ascospore agar after 7 days of incubation at 25°C, the isolate formed long ellipsoidal-shaped ascospores (Fig. 2), suggesting its identity as L. elongisporus.

Introduction

Lodderomyces elongisporus was considered as a sexual state of Candida parapsilosis [1], and its role in human infection was unknown until recently. Sequencing of the ribosomal RNA gene revealed that L. elongisporus represents a distinct species [2]. The aetiologic role of L. elongisporus was subsequently established in human infections [3]. Of ten clinical isolates identified as L. elongisporus, eight originated from Mexico, while one each came from China and Malaysia [4]. These isolates were previously misidentified as C. parapsilosis by the VITEK 2 yeast identification system. L. elongisporus has been isolated from bloodstream and from the catheter tip of a case of suspected fungaemia patient in Kuwait [3–5].

Here we describe a case of primary fungaemia by L. elongisporus that progressed rapidly with fatal outcome despite prompt initiation of treatment with caspofungin.
Antifungal susceptibility was determined by Etest (bio-Mérieux) on RPMI 1640 medium supplemented with 2% glucose, as described previously [9]. MIC values (μg/mL) were as follows: amphotericin B, 0.012; fluconazole, 0.125; voriconazole, 0.004; posaconazole, 0.003; itraconazole, 0.008; flucytosine, 0.064; caspofungin, 0.064; micafungin, 0.003.

Results

The unusual aspect of our case is that there were no apparent risk factors in the patient when fungaemia was diagnosed. However, she had a history of heart disease and had also experienced a stroke. She was not receiving any antibiotics; nor had any central lines been emplaced. She was hospitalized earlier for lower limb ischaemia due to peripheral vascular disease, but she was discharged 2 weeks before the current episode. It is not clear how she developed fungaemia as a result of this unusual yeast in the absence of any known risk factors. However, the possibility of inoculation of the yeast from the skin or translocation from the gastrointestinal tract cannot be ruled out.

Although *L. elongisporus* is a recognized bloodstream pathogen [3], little is known about its virulence attributes or its environmental niche. Like other opportunistic yeast pathogens, this species is also capable of causing diverse clinical conditions, including endocarditis. The species has a global prevalence: it has been isolated from patients in distant geographic regions, including Mexico, Malaysia and China [3], Australia [10], the
plex members, to which generally show reduced susceptibility to echinocandins [15]. The
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Data on antifungal susceptibility of L. elongisporus are scanty, and no susceptibility breakpoints are available. C. parapsilosis complex members to which L. elongisporus is closely related, the current Infectious Disease Society of America guidelines still favour therapeutic use of echinocandins for the treatment of candidaemia caused by C. parapsilosis [17].

Uncommon yeast pathogens are often misidentified as a result of limitations of the currently available commercial yeast identification systems, such as VITEK 2, which identify C. parapsilosis complex but do not distinguish C. parapsilosis, C. orthopsilosis, C. metapsilosis and L. elongisporus [18]. A retrospective characterization of 380 C. parapsilosis complex isolates available in the Mycology Reference Laboratory culture collection and previously speciated by VITEK 2 by a multiplex PCR assay [19] that simultaneously detected C. parapsilosis, C. orthopsilosis, C. metapsilosis and L. elongisporus identified three L. elongisporus isolates. One isolate was obtained from sputum of a cancer patient (isolate Kw2486/06); another isolate (Kw554/08) was recovered from the catheter tip of a patient with fungaemia [5]; and a third isolate (Kw3047/14) was isolated from the bloodstream of a cancer patient. However, clinical details of the two cancer patients were not available.

Recently matrix-assisted laser desorption/ionization time-of-flight mass spectrometry has also been used for the identification of L. elongisporus [20].

**Discussion**

**TABLE 1. Summary of salient findings of published cases of Lodderomyces elongisporus fungaemia**

| Case no. | Study | Country | Age/sex | Comorbidities or risk factors | Identification method |
|---------|-------|---------|---------|------------------------------|-----------------------|
| 1       | Daveon 2012 [10] | Australia | 30/M | Endocarditis, osteomyelitis and brain embolic lesions, intravenous drug user | Blue-green colonies on CHROMagar (BD Diagnostics), ITS region sequence analysis. |
| 2*      | Ahmad 2013 [5] | Kuwait | 63/M | Cardiovascular attack, vascular catheter | Turquoise blue colonies on CHROMagar Candida (Becton Dickinson), Identified as Candida parapsilosis by VITEK 2 yeast identification system (bioMérieux), PCR sequencing of ITS region of rDNA. |
| 3       | Taj-Aldeen 2014 [11] | Qatar | 22/M | Trauma | MALDI-TOF MS, Sequence analysis of ITS region and D1–D2 domains of rDNA. |
| 4       | Hatana 2016 [12] | Japan | 39/M | Thoracoabdominal aortic replacement complicated with aortoesophageal fistula, catheter | Dark green colonies Candida agar medium, Identified as C. parapsilosis by VITEK 2 system (bioMérieux), Sequence analysis of ITS region and D1–D2 domains of rDNA. |
| 5       | Fernández-Ruiz 2017 [13] | Spain | 79/M | COPD, diabetes mellitus, ESRD | Sequencing ITS region of rDNA. |
| 6       | Lee 2018 [14] | Korea | 56/F | Lung cancer, receiving immunosuppressive agents, vascular catheter | Turquoise blue colony on CHROMagar, Candida medium, VITEK 2 YST ID (bioMérieux) and API 20C AUX (bioMérieux) system identified it as C. parapsilosis, MALDI-TOF MS (Bruker Daltonics) analysis indicated likely identification of L. elongisporus (score value = 1.79), Sequence analysis of ITS region of rDNA. |
| 7       | Present case | Kuwait | 71/F | Hypertension, ischaemic heart disease, peripheral vascular disease | Blue colonies in CHROMagar Candida, Identified as C. parapsilosis in VITEK 2 yeast identification system (bioMérieux), PCR sequencing of ITS region of rDNA. |

COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; ITS, internally transcribed spacer; MALDI-TOF MS, matrix-assisted desorption ionization–time of flight mass spectrometry; rDNA, recombinant DNA.

*In case 2, L. elongisporus was isolated from catheter tip culture.

Middle East [5,11], Japan [12], Spain [13] and Korea [14] (Tables 1 and 2).

The salient findings of seven individual case reports of L. elongisporus fungaemia are summarized in Tables 1 and 2. All patients had associated comorbidities and/or risk factors including an intravenous drug user (patient 1). Four (57.5%) of seven patients died even though six patients were treated with antifungal drugs. Because the number of patients is small, it is difficult to assess the impact of antifungal therapy on the outcome. It is also not clear if use of echinocandins (caspofungin in four patients and micafungin in one patient) was an appropriate therapy for L. elongisporus fungaemia because three of five patients died.
TABLE 2. Treatment and outcome of Lodderomyces elongisporus fungaemia

| Case no. | Study                  | Treatment                               | Outcome                        |
|----------|------------------------|-----------------------------------------|--------------------------------|
| 1        | Daveson 2012 [10]      | Caspofungin before cardiac surgery      | Survived                       |
|          |                        | than amphotericin B plus flucytosine followed by voriconazole |                                |
| 2        | Ahmad 2013 [5]         | Fluconazole                             | Survived                       |
| 3        | Taj-Aldeen 2014 [11]   | Caspofungin, fluconazole                | Died                           |
| 4        | Hatanaka 2016 [12]     | Micafungin                               | Survived                       |
| 5        | Fernández-Ruiz 2017 [13]| Caspofungin 3 days                      | Died                           |
| 6        | Lee 2018 [14]          | Not provided                            | Died before removal of indwelling catheter or antifungal treatment |
| 7        | Present case           | Caspofungin (one dose)                  | Died                           |

*In case 2, L. elongisporus was isolated from catheter tip culture.

TABLE 3. Antifungal susceptibility profile of Lodderomyces elongisporus isolates

| Study                  | No. of isolate | Method            | MIC (μg/mL) of: |
|------------------------|----------------|-------------------|-----------------|
|                        |                |                   | AP  S-FC  FL    | IT  KE  VO  POS  ISA  CS  AND  MYC |
| Lockhart 2008 [3]      | 9              | BMD, CLSI         | 0.37–0.75 NA    | 0.12–0.025 NA    | NA | NA | NA | NA | 0.015–0.03 | 0.015–0.12 | 0.015–0.03 |
| Tay 2009 [16]          | I              | Etest             | 0.012 NA 0.125  | 0.047 0.004 0.004 | NA | NA | NA | NA | NA          | NA          | NA          |
| Daveson 2012 [10]      | I              | Etest             | 0.35 0.66 <0.125 | 0.06 <0.008 0.008 | 0.03 | NA | 0.03 | NA | NA          | NA          | NA          |
| Ahmad 2013 [5]         | I              | Etest             | 0.094 0.32 NA   | 0.002 0.023 NA   | 0.094 | NA | NA | NA | NA          | NA          | NA          |
| Taj-Aldeen 2014 [11]   | I              | BMD, CLSI         | 0.5 NA 0.25     | 0.031 <0.016 0.063 | 0.016 0.5 | NA | 0.016 | NA | NA          | NA          | NA          |
| Hatanaka 2016 [12]     | I              | BMD, CLSI         | 0.35 0.5 0.35   | 0.15 NA 0.015 NA | NA | NA | NA | NA | NA          | 0.015        | NA          |
| Fernández-Ruiz 2017 [13]| I              | BMD, CLSI         | 0.031 0.125     | NA | 0.0017 0.007 NA | NA | 0.015        | 0.015        | NA          | NA          | NA          |
| Lee 2018 [14]          | I              | ATB Fungus 3      | 0.25 1.00 1.00  | NA | NA | 0.12 | NA | NA | 0.25        | NA | 0.06        |
| Present case           | I              | Etest             | 0.012 0.064 0.125 | 0.008 0.003 0.004 | 0.003 NA | 0.064        | 0.08 | 0.032    |

S-FC, 5-fluorocytosin; AND, anidulafungin; AP, amphotericin; BMD, broth microdilution; CLSI, Clinical and Laboratory Standards Institute; CS, caspofungin; FL, fluconazole; ISA, isavuconazole; IT, itraconazole; KE, ketoconazole; MYC, micafungin; NA, not available; POS, posaconazole; VO, voriconazole.

Rare yeast species often exhibit reduced susceptibility to one or more commonly used antifungal agents [18]. A number of factors have been attributed to their increased occurrence, such as prolonged survival of seriously ill patients admitted in intensive care units, administration of multiple broad-spectrum antibiotics, dependence on life support systems and extended use of intravascular catheters [21]. It is also possible that these relatively less susceptible yeasts take advantage of the selection pressure created by prophylactic and therapeutic use of antifungal agents, resulting in increased colonization and invasive infection [18,21]. Perhaps a delay in accurate identification and a lack of experience in the management of such rare yeast infections pose diagnostic and therapeutic challenges with consequently higher mortality rates.

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Conflict of interest

None declared.

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