Challenge M243-5

November 2024

Blood: *Candida parapsilosis*

HISTORY

A simulated blood culture sample collected from a 70 year old patient on dialysis was sent to category A laboratories.

Participants were expected to isolate and report *Candida parapsilosis*

CMPT QA/QC/STATISTICS

All simulated blood samples are produced at CMPT according to CMPT internal protocols. The sample contained a pure culture of Candida parapsilosis

The samples are assessed for homogeneity and stability using in-house quality control methods and random selection of samples before and during production, and post sample delivery. The number of random samples selected is 15% of the total production batch.

The challenge sample lot was confirmed to be homogeneous and stable for 14 days. Organism identification was confirmed by a reference laboratory.

All challenge components have in-house assigned values based on the most clinically appropriate result; the most clinically appropriate result is determined by expert committee evaluation. No further statistical analysis is performed on the results beyond that described under "Suitability for grading."

MAIN EDUCATIONAL POINTS from M243-5

It is important to differentiate species of *Candida* isolated from blood cultures for several reasons:

1. Patients with blood stream infection caused by *Candida* species require specific antifungal therapy. The Gram smear in the initial report for a positive blood culture should clearly identify that this is a yeast so that antifungal therapy can be started quickly.

2. Different species of *Candida* have different antifungal resistance profiles. For example, *C. krusei* is intrinsically resistant to fluconazole. *C. parapsilosis* has increased resistance to amphotericin B and itraconazole.

3. *C. parapsilosis* while ubiquitous in the environment, has found niches in some hospitals. Surveillance of positive *C. parapsilosis* isolates from patient infections including blood cultures is helpful for infection prevention and control purposes.

SURVEY RESULTS

Reference laboratories: 12/12 labs reported **Candida parapsilosis**, 1 lab indicated it does not normally process this type of sample

Participants: 34/45 (76%) reporting participant reported *Candida parapsilosis* or *Candida* species and referred. 8 labs reported yeast, refer (Table 1)

Suitability for Grading

A challenge is considered suitable for grading if agreement is reached by 80 percent of selected reference group and at least 50 percent of the participants.

Grading

Maximum grade: 4

Reporting *Candida parapsilosis* or *Candida* species, refer was graded 4

Table 1. Identification results

Reported	Total	Grade
Candida parapsilosis ± complex ± refer	29	4
Candida species, refer ± not albicans	5	4
Yeast/Leuvres, refer ± other than *C. albicans*, ± or *C. krusei* or *C. tropicalis*	8	4
Yeast, not *C. albicans* or *krusei*	1	3
Candida parapsilosis, Moraxella osloensis	1	0
Candida parapsilosis, refer, *Staphylococcus epidermidis*	1	0
no report	1	0
sample not normally processed	5	ungraded
Total	**51**	

Organism identification was correctly performed by at least 80 percent of reference laboratories and greater than 50 percent of all laboratories and was thus, determined to be suitable for grading.

COMMENTS ON RESULTS

This challenge was performed quite well by the large majority of participating laboratories. A couple of notes are worthy to include here:

The term: not albicans: is not strictly correct, although those 5 labs were graded as 4 because they recognized the isolate was not *Candida albicans*. Reporting Just "albicans" has no meaning – it should be identified as not *C. albicans*.

The two laboratories that included bacterial species (*Moraxella* and *Staphylococcus*) were graded as 0, only because they reported the *C. parapsilosis* correctly. This was a pure culture of *C. parapsilosis*, and isolated from a patient on dialysis, not on a person who for example might develop a blood stream infection from injection of dirty water, or drugs.

The single No report result was graded as 0. All blood stream cultures should be reported whether an organism grows or not.

ISOLATION AND IDENTIFICATION

Direct Identification: *Candida* species are gram positive but may stain in a spotty manner, and the morphology is typically oval, elliptical and elongated. Often pseudohyphae (blastoconidia produced in a linear fashion, without separations) are seen.

Culture Identification: Most yeast species grow well on common mycological and bacteriological media at 37°C. Growth is very similar to that of bacteria, although it may take 48 to 72 hours or longer for typical colonies to develop, which are white to off-white in color, creamy, and somewhat larger than bacterial colonies.

Colony morphology of *C. parapsilosis* is indistinguishable from that of *Candida albicans*. Unlike *C. albicans*, which is germ tube positive, *C. parapsilosis* is germ tube negative.

Germ tubes are true hyphae (short hyphae not constricted at the junction), not pseudohyphae, that develop from the yeast cells when incubated in plasma or serum. *C. albicans* (and some strains of *C. dublinienesis*) are germ tube positive, while other species are germ tube negative. Not all strains of *C. albicans* will be germ tube positive and further testing may be required. Corn meal agar is very useful to demonstrate the unique microscopic appearance of different *Candida* species. A discussion of the microscopic morphology of all *Candida* species is beyond the scope of this critique, but the pseudohyphae of *C. parapsilosis* appear short, crooked, or curved on cornmeal agar. [1] Single or small clusters of blastospores can be seen along the pseudohyphae at or near the septae. [2-4]

Chromogenic media have also been developed that can be a useful for the identification of yeast species, although currently not all Candida species can be identified with these media.

Once isolated, a variety of commercially available kits can be used to identify *Candida* species based on biochemical and other phenotypic properties. Unfortunately, some kits (Microscan, Rapid Yeast Plus) may misidentify *C. auris* as potentially several species of *Candida* species and can cause confusion between *Candida parapsilosis* and Candida auris. [9,10]

In a recent comparison study, two MALDI TOF MS systems improved the identification of *Candida parapsilosis* complex over conventional phenotypic methods.[11]

A fluorogenic assay of beta-glucosidase activity may also be useful for rapid differentiation of *C. parapsilosis* from other *Candida* species.

ANTIMICROBIAL SUSCEPTIBILITY

The increased incidence of systemic fungal infections, the broader choice of antifungal agents available for treatment, and the standardization and availability of commercial testing methods has made antifungal susceptibility testing an important addition to diagnostic microbiology testing menus. Broth macrodilution and microdilution reference methods are available for susceptibility testing of yeasts (CLSI document M27 – Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts). [5] A disk diffusion method for testing Candida species against fluconazole and voriconazole has been also developed (CLSI document M44-A –Method for Antifungal Disk Diffusion Susceptibility Testing of Yeasts). [6]

A recent International Standards Organization (ISO) revision: (ISO16256: 2021; Broth micro-dilution reference method for testing the in vitro activity of antimicrobial agents against yeast fungi involved in infectious diseases) is published and provides updated information on testing and quality control ranges of the latest antifungal agents against *Candida* species and *Cryptococcus neoformans*.[12]

The isolation of a yeast from a sterile fluid, the intrinsic resistance of some yeast species to commonly used antifungal agents, and the emerging resistance in other yeast species should be reason for laboratories in large tertiary care facilities to consider offering antifungal susceptibility testing in-house or, if not possible, to send the isolate to a reference laboratory that can provide rapid turn-around of results.

C. parapsilosis is susceptible to fluconazole, voriconazole and echinocandins such as caspofungin. Nearly 15—20% of *C. parapsilosis* strains may be resistant to amphotericin B and Itraconazole (national Canadian data).

Combination therapy with fluconazole and amphotericin B may be associated with antagonism.[7] Strains isolated from sterile sites should have susceptibility testing performed.

CLINICAL RELEVANCE

Candida species are ubiquitous, and *C. parapsilosis* is a common component of normal human flora of skin, mucosal surfaces, and the gastrointestinal tract. It is also frequently isolated from soil, plants, and water. [7]

The incidence of *Candida parapsilosis* has dramatically increased during the last decade. Reports in the literature indicate that *C. parapsilosis* is often the second most commonly isolated Candida species from blood cultures. *C. parapsilosis* even outranks *Candida albicans* in some European, Asian, and South American hospitals. [3]

Immunocompromised individuals, such as AIDS patients and surgical patients, particularly those having surgery of the gastrointestinal tract, are at high risk for blood stream infections with *C. parapsilosis*.[3] Morbidity and mortality are greater in these patients, and early identification of yeast species in these patients is important for therapeutic control. In a number of surveillance programs (e.g SENTRY), it has been observed that *C. parapsilosis* appeared to be more common in certain geographical areas in the United States (author – personal communication). The reasons are not well understood, but is important for infection prevention and control purposes to monitor laboratory data for rates of such pathogens in the hospital.

C. parapsilosis is notorious for its capacity to grow in total parenteral nutrition and to form biofilms on catheters and other implanted devices, for its nosocomial spread by hand carriage and for its persistence in the hospital environment. [8] There is a well-documented association between *C. parapsilosis* infection and the presence of an intravascular device. [4,7,8] These sources in the compromised patient are often a prelude to serious episodes of sepsis. Catheter removal is an essential part of therapy in such cases.

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